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CLINICAL PEARLS UPDATE#39

Immune Tolerance

October 1, 2004

Dear Colleague,

Immune tolerance refers to our defense and repair (immune) systems ability to identify and recycle (neutralize) anything foreign to the body that gains entrance. Loss of immune tolerance is associated with the induction of autoimmune, immune dysfunction, and chronic inflammatory conditions. Loss of tolerance is associated with B and T lymphocyte activations and inductions. Knowing an individual's reactive immune burden of delayed hypersensitivities / delayed allergies opens new clinical and therapeutic possibilities. Functional lymphocyte response assays are the clinical 'gold standard' for measuring delayed hypersensitivity reactions. With LRA by ELISA/ACT® tests and plans, an even larger number of items can be tested in a shorter time and with greater precision. This improves outcomes and, with your inspiration and encouragement to comply along with our nutrition and program counseling staff, as an extension of your office, can achieve consistently outstanding results. We are grateful for the opportunity to serve. The studies by Zinkernagel (Nobelist in Medicine) and Steinman (Nobel candidate) are supportive of our research combining comprehensive, *ex vivo* functional delayed allergy detection by lymphocyte response with specific Alkaline Way diet, targeted supplementation, and healing actions to reset the body to healthy tolerance, homeostasis, energetic resilience and sustained remission.

We encourage you to share this valuable clinical update newsletter with your colleagues and staff so they can learn more about how our comprehensive approach can be applied to their practice with beneficial results. Please also let us know if any of your colleagues or staff would like to be added to our email distribution list. We are grateful for the opportunities to be of service to you and your patients.

Sincerely,

Russ Jaffe, MD, Ph.D., CCN, NACB
Lab Director

Zinkernagel RM. On immunity against infections and vaccines: Credo 2004. *Scand J Immunol* 2004 Jul-Aug;60(1-2):9-13.

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Resistance of vertebrate hosts against infections comprises important natural or innate resistance combined with adaptive immune responses of T and B cells. Viruses, bacteria or classical parasites all probe the limit of immune responses and of immunity. They, therefore, offer an excellent opportunity to assess the biology, physiology and molecular aspects of immune responses and help in characterizing the three basic parameters of immunology-- specificity, tolerance and memory. **Various experiments are summarized that indicate that the rules of antiviral, antitumour, antiorgan graft and of autoimmune responses are basically the same.** The practical specificity repertoire of T and B cells is probably in the order of 10^4 - 10^5 specificities expressed by T cells or by neutralizing antibodies. Tolerance is best defined by rules of reactivity to eliminate infections while avoiding destruction of normal cells by complete elimination of T cells that are specific for antigens persisting within the blood and lymphatic (lymphohaemopoietic) system. Induction of a T-cell response is the result of antigens newly entering lymph nodes or spleen, initially in a local fashion and exhibiting an optimal distribution kinetics within the lymphohaemopoietic system. Antigen staying outside lymphatic tissues are immunologically ignored (e.g. are non-events). **Thus immune reactivity is regulated by antigen dose, time and relative distribution kinetics.** Memory is the fact that a host is resistant against disease caused by reinfection with the same agent. Memory correlates best with antigen-dependent maintenance of elevated antibody titres in serum and mucosal secretions, or with an antigen-driven activation of T cells, such that they are protective immediately against peripheral reinfections in solid tissues. **While antibodies transferred from mother to offspring are a prerequisite for the survival of otherwise unprotected immuno-incompetent offsprings, activated memory T cells cannot be transmitted.** Thus, attenuation of infections in newborns and babies by maternal antibodies is the physiological correlate of man-made vaccines. **T cells not only play an essential role in maintaining T-help-dependent memory antibody titres, but also in controlling the many infections that persist in a host at rather low levels (such as cell mediated (e.g. tuberculosis), B cell / humoral (e.g. measles) and T cell / lymphocyte subset (e.g. HIV).**

Steinman L. Immune therapy for autoimmune diseases. *Science* 2004 Jul 9;305(5681):212-6.

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Our increasing understanding of the pathophysiology of autoimmune disease has revealed a number of checkpoints that can be targeted with immune therapy, including key mediators of lymphocyte adhesion and migration, destructive cytokines involved in tissue damage, and the complex of molecules critical in the presentation of self-

antigen and the activation of autoaggressive T lymphocytes. In many organ-specific autoimmune diseases, the **identity of the molecules attacked by T cells and autoantibodies is known and attempts are under way to tolerize the immune system with a high level of specificity to these targets.**