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CLINICAL PEARLS UPDATE#30

Silent thyroiditis

June 18, 2004

Dear Colleague,

What we have come to call chronic inflammation and autoimmunity may be a blocked effort of the body to repair itself. The following articles help us understand more deeply autoimmune activities in **silent thyroiditis**. **LRA by ELISA/ACT® tests and plans** identify the reactive causes of autoimmune induction for each individual. This allows personalized plans to **reduce the reactive burden by substitution while a repair / energizing alkaline way diet, supplementation plan, and healing actions can be concurrently engaged**. These can now be considered **first line comprehensive care** and a suitable platform on which to build any immune rebuilding, resetting clinical program for silent thyroiditis.

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

Janssen OE, Mehlmauer N, Hahn S, Offner AH, Gartner R. High prevalence of autoimmune thyroiditis in patients with polycystic ovary syndrome. *Eur J Endocrinol* 2004;150(3):363-369.

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OBJECTIVE: To investigate the prevalence of autoimmune thyroiditis (AIT) in patients with polycystic ovary syndrome (PCOS). **DESIGN:** Over a period of 30 months, 175 patients with PCOS were recruited to a prospective multicenter study to evaluate thyroid function and morphology; 168 age-matched women without PCOS were studied as a control group. **METHODS:** PCOS was defined as a- or oligomenorrhea, hyperandrogenism and exclusion of other disturbances of estrogen or androgen synthesis. All laboratory parameters were determined with automated immunoassays. Thyroid morphology was assessed by ultrasound. **RESULTS:** PCOS patients were characterized by an increased LH/FSH ratio, low progesterone, elevated testosterone and a high prevalence of hirsutism (PCOS 83%, control 3%; mean hirsutism score 12+/-5 and 3+/-2 respectively), but no differences in estrogen levels were found. Thyroid function and thyroid-specific antibody tests revealed elevated thyroperoxidase (TPO) or thyroglobulin (TG) antibodies in 14 of 168 controls (8.3%), and in 47 of 175 patients with PCOS (26.9%; P<0.001). On thyroid ultrasound, 42.3% of PCOS patients, but only 6.5% of the controls (P<0.001) had a hypoechoic tissue typical of AIT; while thyroid hormone levels were normal in all subjects, PCOS patients had a higher mean TSH level (P<0.001) and a higher incidence of TSH levels above the upper limit of normal (PCOS 10.9%, controls 1.8%; P<0.001). **CONCLUSION:** This prospective study demonstrates a threefold higher prevalence of AIT in patients with PCOS, correlated in part with an increased estrogen-to-progesterone ratio and characterized by early manifestation of the disease.

Okosieme OE, Parkes AB, Premawardhana LD, Evans C, Lazarus JH. Thyroglobulin: current aspects of its role in autoimmune thyroid disease and thyroid cancer. *Minerva Med* 2003;94(5):319-330.

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Thyroglobulin (Tg) is a large glycoprotein (molecular weight: 660000) with 2 polypeptide chains of approximately 2768 amino acids each. It functions both as a prohormone and storage hormone for thyroid hormones. The complete Tg gene sequence has been determined for human, rat and bovine species. Tg is one of the thyroid autoantigens recognised in patients with autoimmune thyroid disease (AITD). Antibodies to Tg (TgAb) are present in the serum of patients with AITD and are also sometimes present in healthy euthyroid subjects. Though at least 40 antigenic epitopes on human Tg have been identified, only 2 or 3 of these bind TgAb. Epitope mapping studies suggest that TgAb in AITD patients express a restricted binding pattern while TgAb in the serum of healthy individuals do not show such specific binding. There is evidence to suggest that iodination of Tg may alter these epitope binding patterns. TgAb IgG on the other hand, do not appear to be subclass restricted. Several Tg

fragments capable of inducing a T-cell response have been described. Tg is routinely used in the postoperative monitoring of patients with differentiated thyroid cancer. Its use has been limited by problems with assay methods, which include poor inter-laboratory standardization, poor inter-assay variation, low functional sensitivity of the assays, hook effects, and interference from TgAb present in patients serum. The use of rh-TSH in stimulating Tg prior to testing has improved the sensitivity of Tg values in the suppressed state.

Nielsen CH, Hegedus L, Leslie RG. Autoantibodies in autoimmune thyroid disease promote immune complex formation with self antigens and increase B cell and CD4+ T cell proliferation in response to self antigens. *Eur J Immunol* 2004;34(1):263-272.

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B cells are centrally involved as antigen-presenting cells in certain autoimmune diseases. To establish whether autoantibodies form immune complexes (IC) with self-antigen, sera from patients with Hashimoto's thyroiditis (HT), Graves' disease (GD) and healthy controls were incubated with human thyroglobulin (Tg) before adding normal peripheral blood mononuclear cells. The deposition of immunoglobulins and C3 fragments on B cells was then assessed. Inclusion of Tg in serum from HT patients promoted B cell capture of IgG and C3 fragments. Furthermore, the binding of Tg to B cells in preparations of normal blood cells was higher in HT serum than in serum from controls and correlated positively with the serum anti-Tg activity, as did the B and CD4+ T cell proliferation.

Disruption of the three-dimensional structure of Tg by boiling reduced the proliferative responses. The data indicate that anti-Tg antibodies associated with AITD facilitate the formation of complement-activating Tg/anti-Tg complexes, binding of IC to B cells, and the subsequent proliferation of B and T cell subsets. This represents a novel mechanism for the maintenance of autoimmune processes in AITD and links autoreactive T cell responses with the presence of autoantibodies.