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LRA by ELISA/ACT[®]

CLINICAL PEARLS UPDATE#17

Thyroiditis

January 19, 2004

Dear Colleague:

Thyroiditis is the most commonly undiagnosed illness in America (according to Prof. Noel Rose). It is a common concomitant of other chronic illnesses. Thyroiditis starts with a repair deficit in the blood-thyroid barrier. When persistent, this can lead to anti-thyroid antibodies produced locally in the gland and exported into the blood stream. The reports below show that when the cause of the thyroiditis is removed (by surgery), the anti-thyroid antibodies slowly disappear. We favor a more conservative approach: Repair the blood-thyroid barrier and the same disappearance marks the sustained remission that follows. This is what the **LRA by ELISA/ACT[®] tests and plans are designed to do for the full continuum of thyroidities now recognized to autoimmune in origin.**

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

Chiovato L, Latrofa F, Braverman LE, Pacini F, Capezzone M, Masserini L, Grasso L, Pinchera A. **Disappearance of humoral thyroid autoimmunity after complete removal of thyroid antigens.** *Ann Intern Med* 2003;139(5 Pt 1):346-351.

BACKGROUND: The development of antibodies to thyroid peroxidase, thyroglobulin, and thyroid-stimulating hormone (TSH) receptor is a main feature of autoimmune thyroid diseases. **OBJECTIVE:** To investigate whether complete removal of thyroid antigens results in the abatement of humoral thyroid autoimmunity. **DESIGN:** Retrospective chart review study of patients treated and monitored with a standard prospective protocol. **SETTING:** University hospital in Pisa, Italy, between 1976 and 1994. **PATIENTS:** 182 patients with differentiated thyroid carcinoma and serum antibodies to thyroid peroxidase, thyroglobulin, or TSH receptor due to coexistent clinical Hashimoto thyroiditis, Graves disease, or focal autoimmune thyroiditis. **INTERVENTION:** Total thyroidectomy and radioiodine treatment to ablate residual or metastatic thyroid tissue. Regular follow-up with iodine-131 whole-body scanning and serum thyroglobulin measurement. Mean follow-up (\pm SD) was 10.1 \pm 4.1 years (range, 4 to 20 years). **MEASUREMENTS:** Serum antibodies to thyroid peroxidase, thyroglobulin, and TSH receptor. **RESULTS:** Thyroid peroxidase, thyroglobulin, and TSH-receptor antibodies progressively disappeared after the initial treatment. The median disappearance time was 6.3 years for thyroid peroxidase antibodies and 3.0 years for thyroglobulin antibodies. There was a statistically significant correlation between the disappearance of thyroid tissue and that of thyroid antibodies. The coexistence of Hashimoto thyroiditis or Graves disease with thyroid cancer did not modify the pattern of disappearance of thyroid antibody compared with patients with focal autoimmune thyroiditis. **CONCLUSIONS:** Complete ablation of thyroid tissue with its antigenic components results in the disappearance of antibodies to all major thyroid antigens, thus supporting the concept that continued antibody production depends on the persistence of autoantigen in the (thyroid) body.

Weetman AP. **Autoimmune thyroid disease: propagation and progression.** *Eur J Endocrinol* 2003 Jan;148(1):1-9.

Autoimmune thyroid disease is the archetype for organ-specific autoimmune disorders. Progress in treating these disorders lies in improvements of our understanding of the predisposing factors responsible, the mechanisms responsible for progression of disease, and the interaction between thyroid antigens and the immune system at the level of the T cell and antibody. In common with other autoimmune diseases, genetic, environmental and endogenous factors are required in an appropriate combination to initiate thyroid autoimmunity. At present the only genetic factors which have been confirmed lie in the HLA complex and CTLA-4 or a closely linked gene. Identifying other predisposing genes will require large-scale family studies, or further insights into likely candidate genes. A number of environmental factors are known to predispose to autoimmune thyroid disease, including smoking, stress and iodine intake, while immunomodulatory treatments are revealing new pathways for disease emergence. The thyroid cell itself appears to play a major role in disease progression, interacting with the immune system through expression of a number of immunologically active molecules including HLA class I and II, adhesion molecules, cytokines, CD40 and complement regulatory proteins. New techniques, in particular phage display libraries, are providing the methods with which to identify autoantibody diversity in autoimmune thyroid disease and to provide tools for mapping autoantigenic epitopes. Application of these techniques is likely to lead to an understanding of how



TSH receptor antibodies interact with the receptor to cause Graves' disease and also to the identification of novel orbital autoantigens in thyroid-associated ophthalmopathy.

Collins J, Gough S. **Autoimmunity in thyroid disease.** *Eur J Nucl Med Mol Imaging* 2002;29 Suppl 2:S417-24.

The autoimmune thyroid diseases, Graves' disease and autoimmune hypothyroidism, represent the two ends of a disease spectrum where an immune response is directed against the thyroid gland. In Graves' disease, antibodies directed against the thyrotropin receptor (TSH-R) lead to the development of glandular overactivity, while in autoimmune hypothyroidism, cell-mediated and humoral thyroid injury leads to destruction of thyroid tissue and thyroid hormone deficiency. The mechanisms by which these diseases develop are unknown, although it is likely that both diseases occur in genetically susceptible individuals exposed to a permissive environment. A number of environmental factors have been postulated to be involved in the development of autoimmune thyroid disease. There is, however, no direct evidence to support clear causality. Susceptibility loci within immune response genes have been identified although a significant component of the genetic predisposition to disease remains unknown. This review will focus on some of the studies designed to identify genes that confer susceptibility to the autoimmune disease process within the thyroid gland.

