

## **AUTOIMMUNE THYROID DISEASE – INTERACTION WITH ENVIRONMENTAL TRIGGERS**

There is an agreement that etiology of autoimmune thyroid diseases (AITD), equal to other autoimmune diseases, is multifactorial: both several genetic and environmental factors act together and produce the clinical phenotype of these disorders.

Genetic factors have significant role in the pathogenesis of AITD. About 80% of the susceptibility to develop Graves' disease (GD) is attributable to genes. On the other hand the concordance rate for AITD among identical twins is below 1.0 and environmental factors therefore must play an important role. The purpose of this report is to offer a review of some of the environmental triggers namely stress, bacterial infection, tobacco and alcohol, irradiation, trace elements, drugs, chemicals and fetal microchimerism capable to bring about AITD in up to that time genetically predisposed individuals.

There are many epidemiologic and clinical reports that demonstrate an association between stress and GD, but a direct influence of stress on the onset and course of GD remains to be clarified. However, most of the recent case-control studies have supported stress as a factor that affects the onset of GD but there are very few reports on the relationship between stress and Hashimoto's thyroiditis. The onset of Hashimoto's thyroiditis (HT) is generally subtle, so the effect of stress on HT might be overlooked.

There are several hypotheses to explain the association between autoimmune diseases and bacterial infections. The first implies molecular mimicry. Another is the release of sequestered antigens by local infection. A link with AITD may be suggested by the observation that GD patients have higher levels of anti-hsp72 antibodies than controls. Whether bacterial infections play a role in AITD has not been studied, with one exception: *Yersinia enterocolitica*, an intestinal pathogen which is the cause of an enterocolitis and infection of the mesenteric lymph nodes. Two studies reported a higher prevalence of *Y. enterocolitica* antibodies in GD patients (50 and 66% respectively) than in controls (28 and 8% respectively).

Smoking decreases the thyroid's ability to uptake iodine and secrete hormones, and limits the hormones' action. Heavy smokers are more prone to have goiter. Smoking is the most important risk factor for the occurrence of Graves' ophthalmopathy and is likely to be far more important than any genetic contribution to this complication. The association between thyroid disease with alcohol intake has only been investigated in few studies.

There is sufficient data to validate thyroid disease – radiation connection. Since the Chernobyl accident several studies have been published that appear to link radiation exposure to an increased risk of AITD.

Several trace elements are essential for normal thyroid function. Before all are iodine, iron, selenium and zinc. Iron deficiency impairs thyroid hormones synthesis by reducing activity of heme-dependant thyroid peroxidase. Excessive iodine intake can cause hypothyroidism and/or goiter, but if autonomously functioning nodules or a subclinical form of Graves' disease are present, it can also induce hyperthyroidism. Both phenomena guide to presentation of thyroidal antigens to the immune system leading to an autoimmune reaction. Normal thyroid gland is rich in selenium which is main part of selenocystein-containing proteins such as glutathione peroxidase, deiodinase and thioredoxine reductase. Sufficient selenium nutrition supports efficient thyroid hormone synthesis and metabolism and protects the thyroid gland from damage caused by excessive iodine exposure.

Thyroid function can be suppressed by antidiabetic and sulfa drugs, barbiturates, prednisone, estrogen, some cough medicines, lithium, salicylates and thousands of chemical food additives in

processed food. Some data show that populations drinking fluoridated water have lower levels of thyroid hormones. The exact mechanism remains unclear. Hyperthyroidism and hypothyroidism are frequent consequences and side effects during Amiodarone therapy. Whether Amiodarone can provoke autoimmunity is uncertain but thyroid disfunctions occur more frequently in females with high titres of thyroid antibodies.

Several recent studies have investigated a potential role of fetal microchimerism or naturally acquired fetal cells in autoimmune diseases, including systemic sclerosis, thyroiditis, primary biliary cirrhosis, Sjögren syndrome, systemic lupus erythematosus, dermatomyositis, and neonatal lupus syndrome. While lending support to the concept that microchimerism may contribute to some autoimmune diseases, studies have also shown that naturally acquired fetal and maternal microchimerism are common in healthy individuals.

Because of significant relevance to public health elimination of some or all environmental triggers of autoimmune thyroid disease is a principal objective of medical workers in the field

**Ruben Han**, MD, PhD, professor of Nuclear Medicine, University of Belgrade, School of Medicine e-mail: [han@tehnicom.net](mailto:han@tehnicom.net)