**Topic:** HASHIMOTO’S DISEASE IN SOUTHERN ITALY

**Title:** Changed presentation of Hashimoto's thyroiditis in North-Eastern Sicily & Calabria (Southern Italy) based on a 31-year experience.

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**Reference:** Thyroid 18: 429-441, 2008

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**SUMMARY**

**Objective:** To quantify the yearly prevalence of Hashimoto's thyroiditis (HT) at the Division of Endocrinology in the University Hospital of Messina (Sicily, Italy) and evaluate changes in its clinical presentation over the period 1975-2005.

**Design & Patients:** The authors have reviewed retrospectively the clinical records of patients admitted to their hospital (January 1975 through December 2005). This facility attracts patients from North-Eastern Sicily and most of Calabria. HT was diagnosed based on various combinations of clinical, laboratory, and instrumental findings. The study group consisted of 4,064 HT patients diagnosed during these 31 years.

**Main Outcome:** The following indices were evaluated on a yearly basis: number of new HT diagnoses; age at presentation; male-to-female ratio; functional status; goitrous or nongoitrous variants with or without nodule(s); above-normal titers or levels of serum thyroid autoantibodies (thyroglobulin antibodies and thyroperoxidase antibodies). Several indices have changed over those 31 years. Particularly, HT has become 10 times more common than it was until the early 1990s and males are relatively more represented. Patients are relatively younger, with a nongoitrous thyroid; the rate of subclinical hypothyroidism (SCH) exceeds largely the rate of overt hypothyroidism (HO). Serum thyroid autoantibodies have become less frequently positive, and when positive, they are present at a lower concentration.

**Conclusion:** Only environmental changes, as opposed to genetic changes, can account for such alterations in the presentation of HT in this geographical area.

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**COMMENT**

Autoimmune thyroid diseases (AITD) from a group of distinct diseases, representing the most frequent endocrine & immunologic disorders in humans. Among the spectrum of AIT diseases, Hashimoto’s disease (HT) is the most representative in terms of prevalence/incidence in the general population. HT is diagnosed in its classical goitrous form as well as that associated with normal thyroid size or glandular hypotrophy, already described by Paul Bastenie and his colleagues in Belgium in the 1950s. There is mounting evidence in several parts of the world that the incidence of HT may be rising (for instance, studies from the Mayo Clinic in Minnesota & the “JUICE” studies [Jutland-Iceland] carried out by our Danish colleagues) and this is believed to be related to changing environmental factors. Present study by our Italian colleagues in Sicily is particularly interesting, as the investigators have the merit of having evaluated retrospectively their accumulated experience, over a period of three decades, in diagnosing HT in one hospital setting. The main results were to show that the presentation of HT has changed starting in the mid-1990s, coinciding with the period when the yearly frequency of HT started to
increase. For instance, the number of new HT patients observed in 2005 (N=484) was 14-fold greater than the average number of cases diagnosed annually between 1975 & 1990 (N=35). Another interesting finding was the progressive downward trends in age at diagnosis (48 → 40 yrs) and F/M ratio (9:1 → 7:1). When comparing relative frequencies of subclinical (SCH) versus overt hypothyroidism (OH), the overall SCH frequency increased (13% → 35%) while that of OH decreased (33% → 9%) between periods 1975-1990 versus 1991-2005. Until 1990, the goitrous or nodular form of HT was the most prevalent, while ranking only 3rd in the list of frequencies after 2001.

What do these striking epidemiological changes mean? They appear not to be random changes, but related to the environment. The authors evoke first the role of the environment on autoimmune diseases in general, as they compare the increase observed for AITD to similar increases seen for diabetes type I, multiple sclerosis & Addison’s disease. They discuss the possible role of viral infections to trigger autoimmune responses in predisposed individuals, and that of endocrine disruptors ‘thyroid-entrapped pollutants’ (heavy metals, industrial chemicals, petrochemical pollutants, etc.).

A second factor could be changes in iodine supplementation (silent or voluntary) in the population. However, it should be noted that such changes occurred in opposite directions when comparing Iceland & the USA (where the iodine intake was high – too high – and decreased more recently) to areas such as Sicily & Jutland (where the iodine intake was low – too low – and increased more recently).

This commentator is surprised (to say the least) that the authors of this fascinating study did not comment about the major change that occurred during these 3 decades, that is the way we conduct medical check-ups in the thyroid field. Namely, the sensitivity of our assays to measure Tg-Ab & TPO-Ab has been markedly improved when compared to microsomal antibodies and hemagglutination tests in use (when I was a young doctor). Also, the routine use of ultrasonography has brought a new tool, equivalent to a “stethoscope” for endocrinologists. Finally, many subjects who consult their physician for annual check-ups have serum TSH & free T4 measured, as well as patients admitted to hospitals for non endocrine causes. The specific role of each of these – and potentially other not yet identified – environmental factors remains to be established.

(Daniel Glinoer, M.D.; Ph.D.)

See Figure