**Topic**: AUTOIMMUNE HYPOPHYSITIS & THYROID DISEASE

**Title**: Prevalence and functional significance of antipituitary antibodies in patients with autoimmune and non-autoimmune thyroid diseases.


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**SUMMARY**

**Background**: Circulating antipituitary antibodies (APA) are markers of autoimmune hypophysitis, which may impair pituitary function. The prevalence of APA in autoimmune thyroid disorders (AITD) is uncertain.

**Objectives**: The aims of this study were: a) to evaluate the prevalence of APA in a large series of patients with AITD and non-AITD, and b) to investigate the functional significance of APA by assessing pituitary function in APA-positive patients.

**Design and Setting**: Health survey on consecutive AITD and non-AITD patients at a tertiary referral center, the Department of endocrinology in Pisa.

**Patients**: Subjects, including 1,290 consecutive patients with thyroid disorders (961 AITD & 329 non-AITD) and 135 controls, were enrolled in the study.

**Methods**: APA (indirect immunofluorescence), free T4, free T3, TSH, and organ-specific autoantibodies were assayed in all patients. Functional pituitary evaluation was performed in most APA-positive patients.

**Results**: APA frequency was higher in AITD than non-AITD patients (11.4% versus 0.9%; P < 0.0001). All control subjects had negative APA tests. APA were more frequently found in Hashimoto’s thyroiditis (13%) than in Graves’ disease (7.1%). Of 110 APA-positive AITD patients, 20 (18.2%) were known to have autoimmune polyglandular syndrome, whereas 90 (81.8%) had apparently isolated AITD. APA positivity increased the percentage of autoimmune polyglandular syndrome in this series from 10.4 to 13.5%. Of 110 APA-positive patients, 102 were submitted to dynamic testing for functional pituitary assessment: 36 patients (35.2%) had mild or severe GH deficiency (GHD). No additional anterior pituitary hormone deficiencies were found; one patient had central diabetes insipidus. Pituitary abnormalities at MRI were found in most APA-positive patients with GHD.

**Conclusions**: APAs are frequently present in patients with AITD. Patients should be tested for APA because positive tests are associated with GHD.

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**COMMENT**
Autoimmune thyroid disorders (AITD) often present isolated, but may also be associated with other autoimmune disturbances in autoimmune polyglandular syndromes (APS). In the large experience of this group, AITD was known to be associated with other autoimmune disorders in 10.4% of their patients, namely atrophic gastritis, Addison’s disease, chronic hypoparathyroidism, diabetes mellitus, coeliac disease, vitiligo, premature ovarian failure, and Sjogren’s syndrome. In the context of APS (see Table below), AITD was associated with the APS type 1 in 3 patients, type 2 in 28 patients, and the type 3 in 99 patients. Concerning the assessment of pituitary function, the most interesting result was the finding of growth hormone deficiency (GHD) in 36/102 AITD-positive patients (35.2%) who tested positive for APA. During the past years (1988-2005), six studies have looked at the prevalence of APA in patients with AITD. The results of these studies showed a wide variability of APA positivity, ranging between 9% and 56%. This variability may be ascribed to possible biases in the selection of the patients, or differences in the methods used to determine APA. Whether APA represents an autoimmune marker of pituitary deficiency remains a matter of debate. In present study, low APA titers were associated with normal pituitary function, whereas patients with high APA titers had GHD. Furthermore, among the patients identified to have GHD, one half had severe GHD. The authors concluded that APA is frequently found in patients with AITD and they recommend its detection. The detection of APA positive patients allowed them to establish a higher prevalence of APS in AITD patients with apparently no other autoimmune feature than the thyroid. GHD was common in high-titer APA-positive patients, warranting a periodical evaluation of pituitary function in such patients.

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**TABLE (taken from Betterle et al. in Endocrine Reviews 23(3): 327-364, 2002)**
The table shows the general classification of the Autoimmune Polyglandular Syndromes

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<thead>
<tr>
<th>Table 5. Classification of the APS according to Neufeld and Blizzard (71)</th>
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* AD: Addison’s disease