INTRODUCTION

The clinical significance of antibodies reacting with thyroid antigens in apparently healthy individuals is uncertain (1). Some authors claim those antibodies provide evidence of chronic thyroiditis (2), a point of view supported by the presence of lymphocytic infiltration in thyroid glands from autopsied antibody-positive subjects without overt thyroid disease (3, 4). However, other investigations have not found thyroid antibodies in patients with biopsy-proven thyroiditis (3, 5).

A previous article by members of our group reported on the significance of antithyroid microsomal antibodies in the diagnosis of thyroid autoallergic disease (6). However, there have been no studies in Venezuela on the prevalence of thyroid antibodies among the general population, and this prevalence has an extremely important bearing on how to interpret detection of such antibodies in people with symptoms suggesting thyroid disease. Accordingly, the study reported here was designed to establish the prevalence, as well as the clinical and physiopathologic implications, of thyroid-specific antibodies in apparently healthy individuals residing in Caracas.

MATERIALS AND METHODS

The study sample included 145 healthy volunteers (111 females and 34 males) recruited at their places of work. These individuals were textile factory workers, medical students, and laboratory personnel. Their age and sex distributions are presented in Table 1.

All the subjects were questioned about any possible personal or family history of thyroid or other endocrine diseases. Specific inquiry was made...
TABLE 1. Age and sex distributions of the study group.

<table>
<thead>
<tr>
<th>Age (in years)</th>
<th>Females</th>
<th>Males</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>15-24</td>
<td>27</td>
<td>7</td>
<td>34</td>
</tr>
<tr>
<td>25-34</td>
<td>33</td>
<td>16</td>
<td>49</td>
</tr>
<tr>
<td>35-44</td>
<td>43</td>
<td>10</td>
<td>53</td>
</tr>
<tr>
<td>≥ 45</td>
<td>8</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>111</td>
<td>34</td>
<td>145</td>
</tr>
</tbody>
</table>

Average age ± 1 standard deviation

<table>
<thead>
<tr>
<th></th>
<th>Females</th>
<th>Males</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>32.8 ± 8.4</td>
<td>30.2 ± 6.5</td>
<td>31.5 ± 9.1</td>
</tr>
</tbody>
</table>

regarding the following symptoms: asthenia, cold or heat intolerance, diarrhea, constipation, bradypychia or tachypychia, dry or sweating skin, dysphonia, insomnia, sleepiness, hair loss, brittle nails, menstrual disturbances, decreased sexual appetite, depression, anxiety, obesity, weight loss, anorexia, tremor, muscle strength loss, palpitations, chest pain, and exophthalmos.

The physical examination of the subjects included measurement of their weight, height, pulse rate, blood pressure, thyroid size and consistency, and osteomuscular reflexes. We considered that the size of a normal thyroid gland (designated 1n) was that of a gland weighing approximately 20 g.

Sera were obtained from blood specimens after clotting the blood at room temperature, and were stored at −70°C.

Serum antithyroglobulin and antimicrosomal thyroid antibodies were measured by means of the passive hemagglutination test (Fujirebio Inc., Tokyo, Japan) kindly donated by Dr. N. Amino of Osaka, Japan. A titer of 1:20 or more was considered positive for both antimicrosomal and antithyroglobulin antibodies. Thyroid-stimulating hormone (TSH) and free thyroxine (T4) in the study sera were measured by radioimmunoassay (Amersham International PLC, England). Thyroid function data were analyzed by Student’s t test.

**RESULTS**

**Goiter**

Abnormally large thyroids (≥1.5n) were found in 35 individuals (24.1% of the study group). These included 28 women (25.2% of the female study subjects) and seven men (20.5% of the male study subjects).

**Antithyroid antibodies**

The incidence of antithyroid antibodies is shown in Table 2. The positive titers observed ranged from 1:100 to 1:26,214,400 for antimicrosomal antibodies and from 1:400 to 1:6,400 for antithyroglobulin antibodies. It can be seen that antimicrosomal antibodies were found in 16 subjects (11%), there being a higher prevalence in females (13.5%) than in males (2.9%).

Subjects with goiter had a slightly higher frequency of antimicroso-
TABLE 2. Antithyroid antibodies found in the study population of apparently healthy individuals, by sex.

<table>
<thead>
<tr>
<th>Study population</th>
<th>No. of persons</th>
<th>Positive for antimicrosomal antibodies</th>
<th>Positive for antithyroglobulin antibodies</th>
<th>Positive for antimicrosomal and antithyroglobulin antibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>34</td>
<td>1 (2.9)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Females</td>
<td>111</td>
<td>15 (13.5)</td>
<td>4 (3.6)</td>
<td>2 (1.8)</td>
</tr>
<tr>
<td>Total</td>
<td>145</td>
<td>16 (11.0)</td>
<td>4 (2.8)</td>
<td>2 (1.4)</td>
</tr>
</tbody>
</table>

Antithyroglobulin antibodies were found in four of the study subjects (2.7%). All four were females, and three of the four had goiter. Only two study subjects had both antimicrosomal and antithyroglobulin antibodies; both of these were female subjects with goiter (see Tables 2 and 3).

Table 3 gives a brief list of clinical characteristics associated with thyroid disease that were found among some of the 16 subjects with antimicrosomal antibodies. Three (18.7%) had a family history of thyroid disease; two (12.5%) had a personal history of thyroid disease; seven (43.7%) had symptoms suggestive of thyroid disease; and five (31.2%) had goiter.

Thyroid Function

In order to determine whether possible functional disturbances existed among the subjects with thyroid autoallergy, the free T4 and TSH in their sera were measured.

Table 5 presents the results of these hormonal determinations. It can be seen that the average level of free T4...
TABLE 4. Clinical characteristics associated with thyroid disease that were found among the 16 study subjects with antimicrosomal antibodies. Fifteen of these 16 subjects were females, and the average age of the 16 was 35.7 years with a standard deviation of ±7.2 years.

<table>
<thead>
<tr>
<th>Clinical finding</th>
<th>No. (%)</th>
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<tbody>
<tr>
<td>Family history of thyroid disease</td>
<td>3/16 (18.7%)</td>
</tr>
<tr>
<td>Personal history of thyroid disease</td>
<td>2/16 (12.5%)</td>
</tr>
<tr>
<td>Symptoms suggestive of thyroid diseasea</td>
<td>7/16 (43.7%)</td>
</tr>
<tr>
<td>Goiter (thyroid size ≥ 1.5 cm)</td>
<td>5/16 (31.2%)</td>
</tr>
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</table>

a Both had simple goiter. We considered them "apparently healthy" because the goiter had turned up as an incidental finding during a previous routine medical examination given to apparently healthy people.

b The most frequently observed of these symptoms were asthenia, constipation, dry skin, hair loss, menstrual disturbances, and weight increases.

was normal in sera from the whole population sample (1.6 ± 0.4 ng/dl), and also in sera from the subjects with antimicrosomal antibodies (1.5 ± 0.2 ng/dl). Indeed, only one of the 16 subjects with antimicrosomal antibodies showed an abnormally high serum level of free T4 (2.1 ng/dl).

The level of TSH in serum was determined only for individuals with antimicrosomal antibodies. The average TSH value was within normal limits (1.9 ± 1.0 microunits per milliliter) and none of the 16 subjects was found to have an abnormally high serum level of this hormone.

Overall, the thyroid function of individuals with thyroid antibodies appeared normal.

DISCUSSION

It is generally accepted that thyroid autoantibodies are associated with autoallergic thyroid disease. Some 95% of the patients with goitrous Hashimoto's thyroiditis have antimicrosomal antibodies, and 70% have antithyroglobulin antibodies (7, 8). High titers of both antibodies are also found in patients with Graves' disease.

Because of their complement-fixing properties, greater pathogenetic

TABLE 5. Free T4 and TSH found in the sera of all study subjects and those with antimicrosomal antibodies. The values shown are average values ± one standard deviation.

<table>
<thead>
<tr>
<th>Hormone</th>
<th>All 145 study subjects</th>
<th>16 subjects with antimicrosomal antibodies</th>
<th>p value (Student’s t test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Free T4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Normal = 0.9–2.0 ng/dl)</td>
<td>1.6 ± 0.4 ng/dl</td>
<td>1.5 ± 0.2 ng/dl</td>
<td>Not significant</td>
</tr>
<tr>
<td>TSH (Normal = 0.5–3.0 μU/ml)a</td>
<td>Not done</td>
<td>1.9 ± 1.0 μU/ml</td>
<td>–</td>
</tr>
</tbody>
</table>

a μU/ml = microunits per milliliter.
significance has been ascribed to antimicrosomal antibodies, a view further supported by the presence of microsomal antigen at the thyroid cell membrane (9).

The incidence of thyroid autoantibodies among the general population varies in ways that could depend on geographic, ethnic, genetic, or other factors. For example, Volpé has observed that up to 16% of elderly women have thyroid autoantibodies whose presence correlates with occult thyroid disease, and that most individuals with antimicrosomal antibodies do not have overt Hashimoto’s disease (7). Also, Hawkins and coworkers have reported that up to 16% or more of the elderly have thyroid autoantibodies (10).

These same authors (10) have found a 6.7% prevalence of antimicrosomal antibodies among healthy people (9.8% in females and 2.8% in males), while in the present study we found a prevalence of 11% in the whole sample (13.5% in females and 2.9% in males). Our results are similar to those reported by Amino et al. (11).

Other population differences have been reported by Mittra et al., who found a higher incidence of microsomal and thyroglobulin antibodies in healthy British women than in healthy Japanese women (12).

In our study, we found the overall prevalence of antithyroglobulin antibodies to be 2.7%, which is higher than the percentage reported by Ericsson et al. for Swedish people (1) but lower than the prevalence reported in Australia by Hawkins’ group (10). On the other hand, the prevalence we found of antithyroglobulin antibodies in women (3.6%) was lower than the prevalences reported elsewhere in Australian (9.8%), British (9.9%), and Japanese (5.2%) women (12).

Variable antithyroglobulin antibody frequencies have also been reported in other populations. For example, Dingle et al. found a prevalence of 16% among females and 4% among males in Northeast England (13); Couchman et al. found prevalences ranging from 2% to 15% in New Zealand women, depending on their age (14). Gordin has reported prevalences of 8% to 11% for Finnish people (15), and Tunbridge has reported finding a 2% prevalence in England (16). Some of the variations appear to arise from methodologic differences and also from the cutoff values used as criteria for positivity. Among other things, it has been suggested that the enzyme-linked immunosorbent assay (ELISA) and radioimmunoassay are more sensitive than hemagglutination, immunofluorescence, or complement fixation (1, 8, 12). Unfortunately, we have not been able to find information in the literature dealing with antithyroid antibodies in Latin American populations.

An intriguing question is the relative importance of antimicrosomal and antithyroglobulin antibodies in the diagnosis of autoallergic thyroid disease. In this respect, we found that our normal population had a higher prevalence of antimicrosomal antibodies (11%) than of antithyroglobulin antibodies (2.7%), a finding different from that reported by Irvine, who found 15% of his study population to have antimicrosomal antibodies and 17% to have antithyroglobulin antibodies (17).
Like other authors, we found thyroid antibodies more frequently in women than in men. This is not an unexpected observation, since it is well known that antibody responses are stronger in the female sex and that autoantibodies and autoallergic diseases occur more often among women.

The high prevalence of goiter among our study subjects (a prevalence of 24%) clearly deserves notice. However, no correlation was found between thyroid autoantibodies and goiter, since only 14% of those with goiter were found to have antimicrosomal antibodies. We postulate that other unidentified causes, distinct from autoallergic thyroid disease, must be responsible for the high prevalence of enlarged thyroid glands found in our study subjects.

Regarding thyroid function, we found that levels of free T4 and TSH were normal in the sera of antibody-positive subjects. These results do not agree with those of Hawkins et al., who observed increased serum TSH in 72% of a group of subjects with persistent antimeirosomal antibodies (10). However, the apparent discrepancy should be interpreted cautiously, since some authors have suggested that serum levels of T3, T4, and TSH may be variable in Hashimoto's thyroiditis—depending on the degree of lymphocytic infiltration versus the degree of follicular hyperplasia of the gland (18)—and that an increase of serum TSH in response to an intravenous bolus of thyrotropin-releasing hormone would be a better indication of subclinical thyroid dysfunction (19, 20).

It appears that follow-up of antibody-positive individuals could help to define the clinical significance of thyroid autoantibodies in healthy people. In this regard, Volpe has stated that about 10% of such people will develop overt disease within 10 years (7).

Our results support the concept that autoallergic phenomena occur in the absence of clinical or physiologic disturbances. Interestingly, Ruf et al. (21) have recently found identical fine specificities for antithyroglobulin antibodies in subjects with normal and pathologic conditions. On the basis of their results, they theorize that autoantibodies are produced in normal subjects but are kept at low levels by regulatory processes that fail with respect to selected epitopes in autoimmune diseases (21).

**CONCLUSIONS**

- A high incidence of goiter (24.1%) was observed among a group of 145 apparently healthy study subjects.
- Antithyroid microsomal antibodies were found in 11% of the study subjects, and antithyroglobulin antibodies were found in 2.7%.
- No correlation was found between increased thyroid size and the presence of thyroid autoantibodies.
- Levels of free T4 and TSH in the sera of subjects with antithyroid antibodies were within normal limits.
- These results suggest the existence of thyroid autoallergy without clinical disease.

**ACKNOWLEDGMENTS**

We wish to thank Dr. Nobuyuki Amino for his expert advice and the Olimpico Textile Company for its kind cooperation.
SUMMARY

To help assess the frequency of thyroid autoantibodies in the general population of Caracas, a sample population of 145 healthy individuals was studied. A high incidence of goiter (24%) was found. Antimicrosomal antibodies were found in 11% of the study subjects (13.5% of the women, 2.9% of the men), whereas antithyroglobulin antibodies were found in 2.7% (3.6% of the women and none of the men).

No correlation was observed between the presence of antithyroid antibodies and the presence of goiter. Healthy subjects with antithyroid antibodies in their sera appeared to have normal thyroid function, as indicated by serum levels of free T4 and TSH. We conclude that thyroid autoallergy is common in our healthy population and does not necessarily imply a morbid state.

REFERENCES


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**New Video Program Available on Natural Disasters**

PAHO's Emergency Preparedness and Disaster Relief Coordination Program has produced a new 25-minute video program entitled "Myths and Realities of Natural Disasters." It addresses the most commonly held myths regarding the health outcomes of disasters in an effort to guide the utilization of scarce resources. For reasons ranging from lack of prior planning to demands made by a fearful population, wasteful recovery measures are sometimes taken in the aftermath of a disaster. The donor community that so generously offers help may be an unwitting accomplice in counterproductive activities because of lack of information about real needs.

The video program is available in English and Spanish, in Beta, VHS, or 3/4" U-Matic format, and in NTSC, PAL, or SECAM broadcasting standards. For further information on ordering, write to: Editor, Disaster Preparedness in the Americas, 525 Twenty-third Street, N.W., Washington, D.C. 20037, U.S.A.