Thyroid Function and Autoimmunity in Sarcoidosis: A Case-Control Study
Ioannis Ilias, Georgios Panoutsopoulos1, Christos Batsakis1, Dimitra Nikolakakou2, Nikiforos Filippou2, Ioulia Christakopoulou1
Departments of Medicine, 1Nuclear Medicine, and 2The 9th Department of Pulmonary Medicine, Sotiria Hospital, Athens, Greece

Aim. To evaluate thyroid function and the presence of antithyroid autoantibodies in patients with sarcoidosis, compared to patients with chronic obstructive pulmonary disease (controls).

Methods. Sera were obtained from 26 patients (19 women and 7 men) with active sarcoidosis, age and sex matched to 26 patients with diagnosed chronic obstructive pulmonary disease. Baseline thyrotropin, total triiodothyronine and thyroxine, antithyroglobulin autoantibodies, and antithyroid peroxidase autoantibodies were analyzed.

Results. Only antithyroglobulin autoantibodies were significantly elevated in sarcoidosis patients (p=0.041, Wilcoxon two-sample test).

Conclusion. Basic thyroid function parameters, with the exception of antithyroglobulin autoantibodies, were within the normal limits in patients with sarcoidosis. Their presence should be interpreted as another characteristic of a generalized immune dysfunction in sarcoidosis. Screening of thyroid disease in patients with sarcoidosis does not seem necessary.

Key words: autoantibodies, thyroid peroxidase; pulmonary disease, chronic obstructive; sarcoidosis, pulmonary; thyroglobulin

Sarcoidosis is a disease of unknown, possibly autoimmune etiology (1,2), characterized by the presence of noncaseating granulomas. The disease may, although rarely, affect the hypothalamic–pituitary–thyroid axis because of pituitary granulomas (3-5), altering the secretion of thyrotropin. In a few cases, sarcoidosis has been codiagnosed with goiter and/or thyroiditis (6).

Screening for autoimmune thyroid disease with sensitive thyrotropin assays and autoantibodies directed against antigens, such as thyroglobulin and microsomal thyreoperoxidase found in normal thyroid colloid, has been advocated in the patients with autoimmune diseases (7). The aim of the present study was to evaluate the thyroid function and presence of antithyroid autoantibodies in patients with sarcoidosis compared to patients with chronic obstructive pulmonary disease.

Patients and Methods
Sera from 26 patients (19 women and 7 men; mean age: 57±3 years, range: 31-78 years) with active sarcoidosis were obtained. Twenty one patients had newly diagnosed sarcoidosis, either by scalene fat pad biopsy, bronchoscopically executed bronchial biopsy or the highly specific simultaneous appearance on radiogallium scintigraphy of the “panda” and “lambda” patterns (8), whereas the remaining 5 patients presented with a reactivated disease. Only one female patient had reached the stage of pulmonary fibrosis.

The patients were sex- and age- matched (within five years) to 26 patients with chronic obstructive pulmonary disease. They were in good clinical condition upon their discharge from our hospital after brief hospitalization for respiratory infections. Both the patients and control subjects did not suffer from thyroid disease prior to the study and were free from goiter. None of the subjects was under any regimen of medications altering thyroid status.

The following measurements were performed: baseline thyrotropin (TSH) by IRMA (Gammacoat hTSH, INCSTAR Corporation, Stillwater, Mich, USA), total triiodothyronine (T3) and thyroxine (T4) by RIA (Amerlex T3 and T4, Ortho-Clinical Diagnostics, Amersham, UK), antithyroglobulin autoantibodies by IRMA (AB-HTGK-3, Sorin Biomedica Diagnostics, Saluggia, Italy), and antithyreoperoxidase (microsomal) autoantibodies by RIA (AB-TPO, Sorin Biomedica Diagnostics).

In view of the skewed distribution of the obtained values, statistical analysis was performed using non-parametric, distribution-free methods (Wilcoxon matched pairs signed ranks test).

Results
Results are shown in Tables 1 and 2. Basal TSH levels were below normal limits in two patients with sarcoidosis and in one control subject. A patient with sarcoidosis and two controls had an abnormally low total T3. Total T4 levels were within normal limits in all the examined sera.
Antithyroglobulin autoantibodies were slightly elevated in patients with sarcoidosis (in three patients over the 100 U/mL – upper limit of normalcy for 95% of healthy subjects) and differed significantly (p=0.041) from controls, whereas antithyreoperoxidase autoantibodies titers were within normal limits for all subjects and did not significantly differ between the two study groups. The patient suffering from pulmonary fibrosis due to sarcoidosis had normal findings for TSH, thyroid hormones, and autoantibodies.

### Discussion

Sarcoidosis is known to alter endocrine function due to pituitary infiltration. Reports on the percentage of concomitant existence of thyroiditis in patients with sarcoidosis vary from 1.3% (9,10) to 6% (11). A recent report indicated T3 and T4 depression along with TSH and thyroxine-binding globulin elevation in sarcoidosis (12). The disease presents a potential for autoantibody production against tissue antigens (13–15). In the present study, the evaluation of thyroid function was limited to standard tests for routine diagnostics, which accounts for the absence of resin uptake, free hormone or thyroid hormone–binding proteins. Basal TSH levels were assayed with a sensitive method, which is considered sufficient for screening (16). No hyper- or hypofunction of the pituitary–thyroid axis was observed, possibly because patients with sarcoidosis were studied rather early in the course of their initial or reactivated disease and no compromising involvement of the pituitary had taken place. Some patients with sarcoidosis had elevated serum autoantibodies levels against thyroglobulin, one of the major thyroid colloid antigens. However, in contrast to antithyreoperoxidase autoantibodies, the presence of high levels of antithyroglobulin autoantibodies is not specific for thyroiditis. Moreover, autoantibodies, including these against thyroid antigens, can be found in the serum of older “normal” individuals (17) and in various non-thyroidal diseases, such as gastric cancer, connective tissue diseases, B12 deficiency, and diabetes mellitus (18). Thus the pathophysiologic significance of antithyroglobulin autoantibodies in the serum of patients with sarcoidosis has yet to be elucidated and, at the present time, it should be interpreted as another non-specific characteristic of a generalized immune dysfunction of the disease.

In conclusion, no major clinical influence of sarcoidosis on thyroid function and autoimmunity was found and screening for thyroid disease in such patients does not seem imperative.

### References


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Correspondence to: Ioannis Ilias
Dept of Medicine (Building 300 GYN)
Sotiria Hospital
152, Mesogion Avenue
Athens GR-11527, Greece
ilias@compulink.gr

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