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# Clinical THYROIDOLOGY

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## ETIOLOGY IS THE MAJOR FACTOR INFLUENCING THE PROGRESSION OF SUBCLINICAL HYPERTHYROIDISM

Schouten BJ, Brownlie BE, Frampton CM, Turner JG. **Subclinical thyrotoxicosis in an outpatient population—predictors of outcome.** Clin Endocrinol (Oxf) 2011;74:257-61.

### SUMMARY

#### BACKGROUND

Subclinical hyperthyroidism (SCH) is readily detected with sensitive serum thyrotropin (TSH) assays. The rate of progression to overt hyperthyroidism is still uncertain and has not been related clearly to various etiologic factors. The authors performed a retrospective study of their patients at Christchurch Hospital in New Zealand to determine the rate of progression to overt hyperthyroidism and the risk factors for its development.

#### METHODS

During a 6-year period, 96 patients were identified with autonomous SCH. Patients on drugs known to influence thyroid function or other disorders that might lower TSH were excluded. Measurements included serum TSH, total thyroxine (T<sub>4</sub>), free T<sub>4</sub> index based on thyroxine-binding globulin, total triiodothyronine, and antithyroid antibodies. The lower limit of serum TSH was 0.25 mU/L. Ninety-four patients had pertechnetate thyroid scintiscans. Follow-up ranged from 3 to 9.4 years (mean, 3.8).

#### RESULTS

Based on the scintiscan and clinical evaluation, 12 patients had subclinical Graves' disease, 70 had multinodular goiter and 14 had an autonomous nodule. Mean serum TSH was 0.03 mU/L in those with subclinical Graves, 0.08 in those with multinodular goiter, and 0.07 in those with an autonomous nodule. Progression to overt hyperthyroidism occurred in 8% of the total group at 1 year, 16% at 2 years, 21% at 3 years, and 26% at 5 years. During a 5-year follow-up, the progression to overt hyperthyroidism was 9% for the group with subclinical Graves' disease, 21% for those with multinodular goiter, and 61% for those with autonomous nodules. Statistical analysis was performed to assess the relative importance of age, sex, family history of thyrotoxicosis, symptoms at presentation (tremor, weight loss, or heat intolerance), thyroid nodule(s) on clinical examination, entry TSH level, antithyroid antibody status, and scintiscan category on subsequent development of overt disease. Only the underlying thyroid pathology determined by scintigraphy was an independent predictor of outcome (P = 0.003).

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### CONCLUSIONS

Progression of SCH to overt hyperthyroidism occurred at a rate of 5 to 8% per year with disease etiology,

as determined by thyroid scintigraphy, significantly influencing the risk of progression.

### COMMENTARY ●●●●●●●●●●●●●●●●

This is the largest series examining the influence of etiology on the progression of SCH to overt hyperthyroidism. It should be noted that of the 14 patients with autonomous nodules, it took only 2 years for overt hyperthyroidism to develop in the 8 in whom it occurred. Although it is difficult to generalize from such a small group, this was clearly a faster progression to overt disease than occurred with the multinodular group. However, among the 70 patients with multinodular goiter, 11 had thyroidectomy for obstructive symptoms. My experience in patients with multinodular goiter is that most with mild lowering of serum TSH do not progress for many years. I agree

with the authors' recommendation that close follow-up is an important aspect of care.

Although the authors did not find that initial serum TSH influenced progression, the mean serum TSH was <0.1 mU/L in each group. Only the group with multinodular goiter had the upper TSH value of 0.15 mU/L. This is significant because the patients who are likely to progress and bear closer follow-up are those with serum TSH <0.1 mU/L, as shown in the recent large survey in Scotland (1), summarized in the January 2011 issue of *Clinical Thyroidology*.

— **Jerome M. Hershman, MD**

### Reference

1. Vaidveloo T, Donnan PT, Cochrane L, Leese GP. The Thyroid Epidemiology, Audit, and Research Study (TEARS): the natural history of endogenous subclinical hyperthyroidism. *J Clin Endocrinol Metab* 2011;96:E1-E8.