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# Thyroid Stimulating Hormone (TSH) in the Evaluation of Subclinical Hypothyroidism

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## CASE PRESENTATION

A 62-year-old woman presented with a 6-month history of hair thinning, itchy scalp, and cold sensitivity. She reported no fatigue, depression, memory problems, dry skin, or constipation. She had hyperlipidemia for which she took fish oil and red yeast rice extract. Heart rate was 80 beats per minute and BMI was 31 kg/m$^2$. Physical examination demonstrated a thyroid gland of normal size and consistency, without palpable nodules. Deep tendon reflexes were normal. Her laboratory values are reported in Table 1.

## HOW DO YOU INTERPRET THESE TEST RESULTS?

**A.** The patient has overt hypothyroidism.

**B.** The patient has subclinical hyperthyroidism and does not need a repeat TSH level.

**C.** The patient has subclinical hypothyroidism and does not need a repeat TSH level.

**D.** The patient has subclinical hypothyroidism and should have a repeat TSH in 1–3 months.

### Answer

**D** The patient has subclinical hypothyroidism and should have a repeat TSH in 1–3 months.

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The authors have completed and submitted the JCMJE Form for Disclosure of Potential Conflicts of Interest.

## TEST CHARACTERISTICS

Serum TSH is the initial screening test for primary thyroid dysfunction. TSH is a glycoprotein hormone produced by the pituitary gland. It stimulates the thyroid gland to secrete thyroid hormones, which regulate tissue metabolism. TSH assays are named historically by “generation”; third generation assays are widely used and have a detection limit of 0.01 mIU/L, as compared to first (1 mIU/L) and second generation assays (0.1–0.2 mIU/L).[1] The 2016 Medicare midpoint reimbursement for TSH is $30.93.[2]

Serum TSH is reliable in the outpatient setting and is more sensitive and specific than free thyroxine (free T4) for diagnosing thyroid dysfunction. A free T4 level can be added if serum TSH is abnormal. In suspected secondary hypothyroidism, TSH is inadequate for diagnosis, and both serum TSH and free T4 should be measured. Serum TSH is not reliable in diagnosing thyroid dysfunction in hospitalized patients with severe non-thyroidal illness. TSH remains the preferred test during pregnancy and in situations affecting thyroid hormone binding proteins.

A serum TSH above the upper reference limit with a normal free T4 level indicates subclinical hypothyroidism, which has a prevalence of 4.3–8.5%.[3] Mild TSH fluctuations may occur in patients without thyroid disease, with subsequent normalization. The diagnosis of subclinical hypothyroidism is only applicable when thyroid function has been stable for one month, the hypothalamic-pituitary-thyroid axis is normal, and there is no recent or ongoing severe illness.[4]

## APPLICATION OF TEST RESULT TO THIS PATIENT

Upon presentation, the patient had mild TSH elevation (between the assay upper limit and 10 mIU/L), hair thinning, cold sensitivity, and elevated LDL and total cholesterol. Her symptoms are not specific to hypothyroidism and their relationship to her thyroid status is unclear. The TSH elevation indicates subclinical hypothyroidism, which is present in 15% of adults aged ≥65.[3] Mild TSH elevations may not reflect thyroid dysfunction and may be a normal manifestation of aging.[3] There is controversy over the appropriateness of diagnostic testing and treatment in this setting.[5]

## WHAT ARE THE ALTERNATIVE DIAGNOSTIC TESTING APPROACHES?

There are no alternative diagnostic testing approaches for subclinical hypothyroidism. However, one single serum TSH result may not be a reliable indicator due to transient fluctuations.[9] Thus, observation with a repeat serum TSH in 1–3 months without treatment is acceptable. Prior to TSH, non-specific tests were employed to diagnose hypothyroidism, including basal metabolic rate, sleeping heart rate, and Achilles reflex time. The presence of thyroid peroxidase antibody (TPOAb) suggests underlying autoimmune thyroid disease and slightly improves prediction of progression to overt hypothyroidism (4.3%/year with vs. 2.6%/year without elevated TPOAb titers).[6]

## PATIENT OUTCOME

A free T4 was not obtained during the initial evaluation. The patient was started on 25 micrograms of levothyroxine by her primary care physician. Her itchy scalp improved and her bowel movements became more regular, without changes in other symptoms. Her TSH was 2.75 mIU/L three months after initiation of levothyroxine. Her lipid profile remained unchanged with a total cholesterol 250, triglycerides 53, HDL 90, LDL 149.

Upon endocrinology consultation, a TPOAb test was obtained and was normal (<20 IU/ml). Levothyroxine was discontinued. Placebo-controlled trials of levothyroxine therapy in patients with subclinical hypothyroidism do not demonstrate improved symptoms.[7,8] Even though subclinical hypothyroidism is associated with an adverse lipid profile, studies investigating the effect of levothyroxine therapy on lipids have shown mixed results, with a small benefit of uncertain clinical significance.[7,8] Lifestyle modifications and lipid-lowering therapy are reasonable options for her hyperlipidemia.

The patient continues to be observed without levothyroxine therapy without recurrence of symptoms. This patient's spontaneous resolution of subclinical hypothyroidism is common, occurring in 46% of individuals with TSH concentrations of 4.5–7.0 mIU/L when retested 2 years later.[9] TSH concentrations four months later, then annually, were 5.14 mIU/L, 3.05 mIU/L, 3.78 mIU/L, 2.75 mIU/L, and 4.14 mIU/L.

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**CLINICAL BOTTOM LINE**

- Subclinical hypothyroidism is defined as an elevated serum TSH with normal free thyroid hormones. However, one single serum TSH result may not be a reliable indicator of subclinical hypothyroidism and repeat testing should be sought in 1–3 months.
- Treatment of subclinical hypothyroidism with TSH values < 7 mIU/L is usually deferred due to high rates of spontaneous reversion to euthyroidism.
- Randomized trials are needed to determine the long-term risks and benefits from treatment of subclinical hypothyroidism.

**Table 1**

Initial Laboratory Values

| Laboratory Test | Patient's Values | Reference Range |
|---|---|---|
| Thyroid stimulating hormone (TSH), third generation, mIU/L | 4.88 | 0.40–4.50 |
| Lipid Panel | | |
| Total cholesterol, mg/dL | 257 | 125–200 |
| Triglycerides, mg/dL | 59 | <150 |
| High-density lipoprotein (HDL), mg/dL | 90 | ≥46 |
| Low-density lipoprotein (LDL-C), mg/dL | 155 | <130 |