Subclinical hypothyroidism: Merely monitor or time to treat?

Principal Source: Roberts LM, Pattison H, Roalfe A, et al. Is subclinical thyroid dysfunction in the elderly associated with depression or cognitive dysfunction? Ann Intern Med. 2006;145:573-581.

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Thyroid dysfunction enters the differential diagnosis for most mood, anxiety, thought, and cognitive disorders. Because more than one-half of the estimated 27 million Americans with hyperthyroidism or hypothyroidism are undiagnosed,[1] the American Thyroid Association recommends universal screening for thyroid dysfunction after age 35, with a recheck every 5 years. Although some clinicians feel this recommendation is excessive, strategic screening with a thyroid-stimulating hormone (TSH) test is important for patients with psychiatric illnesses.

If a patient's TSH is abnormal, repeating the test while measuring the free thyroxine (T4) and in most cases the antithyroid peroxidase antibody (anti-TPO) has good clinical value. Anti-TPO antibodies are a useful biomarker for autoimmune thyroid disease, such as Hashimoto's thyroiditis or Graves' disease. If laboratory findings suggest the hypothyroid spectrum, a fasting lipid profile may help determine risk of adverse cardiovascular outcomes.

Therapy

Symptoms of hypothyroidism—indicated by an elevated TSH (usually >20 mU/L) and low T4—overlap with psychiatric illness (***Table***) but are easy to treat. Psychiatrists who are accustomed to calculating weight-based dosing of medications such as lithium and valproic acid may have little difficulty initiating levothyroxine replacement (typically 1.6 mcg/kg/day) for patients with overt hypothyroidism. Treating hyperthyroidism (low TSH and high T4) can be more complex and generally is left to an internist or endocrinologist. But how should you treat subclinical thyroid dysfunction?

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Treat or wait?

Subclinical hypothyroidism (SH)—in which T4 is normal—usually is a laboratory diagnosis defined in a spectrum:

- TSH of 4.5 to 10 mU/L is mild SH (80% of cases)
- TSH of 10 to 20 mU/L is more severe SH.

Table

Hypothyroidism symptoms that indicate treatment

With psychiatric overlap
Fatigue
Hypersomnolence
Cognitive impairment (forgetfulness)
Difficulty concentrating/learning
Weight gain/fluid retention
Somatic symptoms
Dry, itchy skin
Brittle nails and hair
Constipation
Myalgias
Heavy and/or irregular menses
Increased miscarriage risk
Cold sensitivity

continued

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SH is a well-established risk factor for depression. One study found a nearly 3-fold higher lifetime prevalence of depression in young and middle-aged women with SH.[2] To the practicing psychiatrist, these results may sound like a mandate to treat all patients with SH—particularly those with depression. Consider, however, that in a prospective observational study the TSH of >37% of patients with SH returned to normal with observation alone.[3] In fact, <27% of patients with SH went on to develop overt hypothyroidism during the study period, on average within 31.7 months.

A second study that would argue against treating patients with mild SH noted decreased cardiovascular and noncardiovascular mortality among elderly patients with elevated TSH,[4] implying that SH may be protective compared with the euthyroid state, at least among octogenarians.

Still, do mood, anxiety, or cognitive symptoms in SH patients merit earlier, more aggressive treatment? This question was addressed by a recent cross-sectional study that demonstrated no correlation between mood and SH.[5] Although statistically significant associations were seen among anxiety, cognition, and elevated TSH, the magnitude of the associations lacked clinical relevance. This study was designed to further assess an earlier inconclusive review.[6]

Ultimately, treating SH—although easy to do—may have little impact on your patient's overall mood and cognition until TSH is ≥10 mU/L.

Clinical Point

Treating subclinical hypothyroidism may have little impact on overall mood and cognition until TSH is ≥10 mU/L

Practice Points

- Subclinical thyroid dysfunction is largely a **laboratory diagnosis** that merits observation but not necessarily treatment.
- **Watchful waiting** is preferable in patients age ≥65 with mild subclinical hypothyroidism (TSH <10 mU/L) unless they have prominent mood, cognitive, or medical conditions—such as congestive heart failure or hyperlipidemia—that could benefit from early thyroid replacement.
- In adults age <65, consider **TSH 4.5 to 10 mU/L as a threshold** for initiating thyroid replacement, particularly if anti-TPO antibodies are present (although prevailing recommendations still favor the watchful waiting approach).[6]

Drug Brand Names

Levothyroxine • Levoxyl, Synthroid
Lithium • various
Valproic acid • Depakene

Disclosure

Dr. Raj is a consultant to Alpharma and a speaker for AstraZeneca.

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