

American Thyroid Association Guidelines for Detection of Thyroid Dysfunction

Paul W. Ladenson, MD; Peter A. Singer, MD; Kenneth B. Ain, MD; Nandalal Bagchi, MD, PhD; S. Thomas Bigos, MD; Elliot G. Levy, MD; Steven A. Smith, MD; Gilbert H. Daniels, MD

Objective To define the optimal approach to identify patients with thyroid dysfunction.

Participants The 8-member Standards of Care Committee of the American Thyroid Association prepared a draft, which was reviewed by the association's 780 members, 50 of whom responded with suggested revisions.

Evidence Relevant published studies were identified through and the association membership's personal resources.

Consensus Process Consensus was reached at group meetings. The first draft was prepared by a single author (P.W.L.) after group discussion. Suggested revisions were incorporated after consideration by the committee.

Conclusions The American Thyroid Association recommends that adults be screened for thyroid dysfunction by measurement of the serum thyrotropin concentration, beginning at age 35 years and every 5 years thereafter. The indication for screening is particularly compelling in women, but it can also be justified in men as a relatively cost-effective measure in the context of the periodic health examination. Individuals with symptoms and signs potentially attributable to thyroid dysfunction and those with risk factors for its development may require more frequent serum thyrotropin testing.

Arch Intern Med. 2000;160:1573-1575

THYROID dysfunction is common in adults¹⁻⁵ and frequently has significant clinical consequences. Hypothyroidism and hyperthyroidism can be accurately diagnosed with laboratory tests^{6,7} and are readily treatable. (Although *hyperthyroidism* can be narrowly construed as those causes of thyrotoxicosis that result from glandular hyperactivity, the term here refers to all conditions causing thyroid hormone excess, including certain forms of thyroiditis and exogenous thyroid hormone administration.)

Clinical manifestations of thyroid dysfunction vary considerably among patients in their character and severity. Associated symptoms and signs are often nonspecific and progress slowly. Consequently, the accuracy of clinical diagnosis is limited. Physicians must consider and exclude thyroid dysfunction much more often than they will establish a diagnosis. If only patients presenting with clearly suggestive symptoms and signs are evaluated, many affected individuals will remain undiagnosed. For these persons, appropriate treatment for thyroid dysfunction or conservative monitoring to anticipate its potential future consequences can only be implemented when routine laboratory screening identifies them (see the "Screening for Thyroid Dysfunction" section below).

CASE FINDING FOR THYROID DYSFUNCTION

A number of symptoms and signs are well-established manifestations of thyroid dysfunction. Additional findings in patients' personal and family histories indicate increased risk of developing thyroid dysfunction. Risk factors identifiable in personal history include (1) previous thyroid dysfunction; (2) goiter; (3) surgery or radiotherapy affecting the thyroid gland; (4) diabetes mellitus; (5) vitiligo; (6) pernicious anemia; (7) leukotrichia (prematurely gray hair); and (8) medications and other compounds, such as lithium carbonate and iodine-containing compounds (eg, amiodarone hydrochloride, radiocontrast agents, expectorants containing potassium iodide, and kelp). Risk factors identifiable in the family history include (1) thyroid disease, (2) pernicious anemia, (3) diabetes mellitus, and (4) primary adrenal insufficiency.

Abnormal results in certain commonly obtained laboratory tests also suggest hypothyroidism or hyperthyroidism. Findings of these tests for hypothyroidism may include (1) hypercholesterolemia, (2) hyponatremia, (3) anemia, (4) creatine phosphokinase and lactate dehydrogenase elevations, and (5) hyperprolactinemia; and for hyperthyroidism, (1) hypercalcemia, (2) alkaline phosphatase elevation, and (3) hepatocellular enzyme elevation. Any of these clinical and laboratory findings justify thyroid function testing, particularly if they are sustained for 2 weeks or more, occur in combination, have not been present previously during documented euthyroidism, or occur in individuals with increased risk of thyroid disease.

SCREENING FOR THYROID DYSFUNCTION

Thyroid dysfunction meets many criteria for a condition justifying population screening:

1. The prevalences of various forms of thyroid dysfunction are substantial.
2. Overt hypothyroidism and hyperthyroidism have well-established clinical consequences. Even mild hypothyroidism can progress to overt hypothyroidism,^{1, 8} particularly in patients with antithyroid antibodies or previous thyroid irradiation. (*Mild hypothyroidism* refers to patients in whom there is elevation of the serum thyrotropin [thyroid-stimulating hormone (TSH)] concentration in association with a normal serum free thyroxine [(FT₄)] concentration. This state is also termed *subclinical hypothyroidism*, *compensated hypothyroidism*, *decreased thyroid reserve*, and *prehypothyroidism*.) Mild hypothyroidism can also be associated with reversible hypercholesterolemia,⁹⁻¹² particularly when the serum TSH concentration is greater than 10 mIU/L, and, in some patients, with reversible symptoms^{13, 14} and cognitive dysfunction.^{15, 16} Mild (subclinical) hyperthyroidism has been associated with a higher incidence of atrial fibrillation in older persons¹⁷; reduced bone mineral density,^{18, 19} particularly in postmenopausal women; and symptoms (eg, palpitations) in some patients.²⁰
3. The serum TSH assay is an accurate, widely available, safe, and relatively inexpensive diagnostic test for all common forms of hypothyroidism and hyperthyroidism.²¹
4. There are effective therapies for both hypothyroidism and hyperthyroidism for patients in whom treatment is indicated.

Screening of all newborn children for hypothyroidism is already a widely accepted and legislatively mandated practice. In addition, serum TSH measurement in adults every 5 years has been shown by decision analysis to have equivalent or more favorable cost-effectiveness in comparison with other widely accepted disease detection strategies,²² for example, for hypertension, breast cancer, and hypercholesterolemia. The cost-effectiveness of screening is more favorable in women and older persons and is strongly influenced by the cost of TSH measurement. Consequently, it is recommended that all adults have their serum TSH concentration measured beginning at age 35 years and every 5 years thereafter, the interval at which a periodic health examination has been advocated by the US Preventive Services Task Force.²³ More frequent screening may be appropriate in individuals at higher risk of developing thyroid dysfunction.

LABORATORY TESTING STRATEGIES

Serum TSH measurement is the single most reliable test to diagnose all common forms of hypothyroidism and hyperthyroidism, particularly in the ambulatory setting. An elevated serum TSH concentration is present in both overt and mild hypothyroidism. In the latter, the serum FT₄ concentration is, by definition, normal. While serum TSH measurement confirms or excludes the diagnosis in all patients with primary hypothyroidism, it will not reliably identify patients with central (secondary) hypothyroidism, in whom serum TSH concentrations may be low, normal, or mildly elevated. When there is suspicion of pituitary or hypothalamic disease, the serum FT₄ concentration should be measured in addition to the serum TSH concentration.

Virtually all types of hyperthyroidism encountered in clinical practice are accompanied by suppressed serum TSH concentrations, typically less than 0.1 mIU/L. These include Graves disease, toxic adenoma

and nodular goiter, subacute and lymphocytic (silent, postpartum) thyroiditis, iodine-induced hyperthyroidism, and exogenous thyroid hormone excess. Serum FT₄ measurement and serum triiodothyronine (T₃) assay in patients with a normal serum FT₄ level are indicated to further assess patients with a serum TSH level less than 0.1 mIU/L.

To diagnose hyperthyroidism accurately, TSH assay sensitivity, the lowest reliably measured TSH concentration, must be 0.02 mIU/L or less. Some less sensitive TSH assays cannot reliably distinguish patients with hyperthyroidism from those with euthyroidism. When such less sensitive TSH assays are the only ones available, a serum FT₄ assay or estimate and a total or free T₃ (FT₃) assay should be employed in addition to measurement of the serum TSH concentration. There are 2 rare types of TSH-mediated hyperthyroidism, TSH-secreting pituitary adenomas and selective pituitary resistance to thyroid hormone, that will be overlooked by serum TSH measurement alone; serum FT₄ and FT₃ concentrations should also be measured when these conditions are suspected. Finally, it is important to recognize that isolated abnormalities of the serum TSH concentration do not always connote sustained thyroid dysfunction and may be caused by other conditions and medications.

The causes of isolated TSH elevation include (1) mild (subclinical) hypothyroidism, (2) recovery from hypothyroxinemia of nonthyroid illnesses, and (3) medications such as lithium carbonate and amiodarone. (Inhibition of thyroid hormone production by these drugs may cause both transient reversible elevation of the serum TSH level and true hypothyroidism.) The causes of isolated TSH suppression include (1) mild (subclinical) hyperthyroidism, (2) recovery from overt hyperthyroidism, (3) nonthyroidal illnesses (which can cause a low serum FT₄ concentration), (4) pregnancy during the first trimester, and (5) medications, such as dopamine and glucocorticoids.

CONCLUDING RECOMMENDATIONS

The American Thyroid Association recommends that adults be screened for thyroid dysfunction by measurement of the serum TSH concentration, beginning at age 35 years and every 5 years thereafter. The indication for screening is particularly compelling in women, but it may also be justified in men as a relatively cost-effective measure in the context of the periodic health examination. Individuals with clinical manifestations potentially attributable to thyroid dysfunction and those with risk factors for its development may require more frequent serum TSH testing.

Author/Article Information

From The John Hopkins University School of Medicine, Baltimore, Md (Dr Ladenson); University of Southern California, Los Angeles (Dr Singer); University of Kentucky, Lexington (Dr Ain); Maine Medical Center, Bangor (Dr Bigos); University of Miami, Miami, Fla (Dr Levy); Mayo Clinic, Rochester, Minn (Dr Smith); and Massachusetts General Hospital and Harvard Medical School, Boston, Mass (Dr Daniels). The American Thyroid Association is located in Falls Church, VA (Web address: <http://www.thyroid.org>).

Corresponding author: Paul W. Ladenson, Division of Endocrinology and Metabolism, The Johns Hopkins University School of Medicine, 1830 E Monument St, Suite 333, Baltimore, MD 21287-0003 (e-mail: ladenson@jhmi.edu).

REFERENCES

1. Vanderpump MPJ, Tunbridge WMG. The epidemiology of thyroid diseases. In: Braverman LE, Utiger RD, eds. *Werner and Ingbar's The Thyroid: A Fundamental and Clinical Text*. 7th ed. Philadelphia, Pa: Lippincott-Raven; 1996.

- [2.](#) Tunbridge WM, Evered DC, Hall R, et al.
The spectrum of thyroid disease in a community: the Whickham Survey.
Clin Endocrinol (Oxf). 1977;7:481-493.
- [3.](#) Vanderpump MP, Tunbridge WM, French JM, et al.
The incidence of thyroid disorders in the community: a twenty-year follow-up of the Whickham Survey.
Clin Endocrinol (Oxf). 1995;43:55-68.
- [4.](#) Sawin CT, Castelli WP, Hershman JM, McNamara P, Bacharach P.
The aging thyroid: thyroid deficiency in the Framingham Study.
Arch Intern Med. 1985;145:1386-1388.
- [5.](#) Bagchi N, Brown TR, Parish RF.
Thyroid dysfunction in adults over age 55 years: a study in an urban US community.
Arch Intern Med. 1990;150:785-787.
- [6.](#) Singer PA, Cooper DS, Levy EG, et al.
Treatment guidelines for patients with hyperthyroidism and hypothyroidism.
JAMA. 1995;273:808-812.
- [7.](#) Klee GG, Hay ID.
Biochemical testing of thyroid function.
Endocrinol Metab Clin North Am. 1997;26:763-775.
- [8.](#) Rosenthal MJ, Hunt WC, Garry PJ, Goodwin JS.
Thyroid failure in the elderly: microsomal antibodies as discriminant for therapy.
JAMA. 1987;258:209-213.
- [9.](#) Tanis BC, Westendorp GJ, Smelt HM.
Effect of thyroid substitution on hypercholesterolaemia in patients with subclinical hypothyroidism: a reanalysis of intervention studies.
Clin Endocrinol (Oxf). 1996;44:643-649.
- [10.](#) Arem R, Patsch W.
Lipoprotein and apolipoprotein levels in subclinical hypothyroidism: effect of levothyroxine therapy.
Arch Intern Med. 1990;150:2097-2100.
- [11.](#) Staub JJ, Althaus BU, Engler H, et al.
Spectrum of subclinical and overt hypothyroidism: effect on thyrotropin, prolactin, and thyroid reserve, and metabolic impact on peripheral target tissues.
Am J Med. 1992;92:631-642.
- [12.](#) Franklyn JA, Daykin J, Betteridge J, et al.
Thyroxine replacement therapy and circulating lipid concentrations.
Clin Endocrinol (Oxf). 1993;38:453-459.
- [13.](#) Cooper DS, Halpern R, Wood LC, Levin AA, Ridgway EC.
L-Thyroxine therapy in subclinical hypothyroidism: a double-blind, placebo-controlled trial.
Ann Intern Med. 1984;101:18-24.
- [14.](#) Nystrom E, Caidahl K, Fager G, Wikkelso C, Lundberg PA, Lindstedt G.
A double-blind crossover 12-month study of L-thyroxine treatment of women with "subclinical" hypothyroidism.
Clin Endocrinol (Oxf). 1988;29:63-76.

- [15.](#) Jaeschke R, Guyatt G, Gerstein H, et al.
Does treatment with L-thyroxine influence health status in middle-aged and older adults with subclinical hypothyroidism?
J Gen Intern Med. 1996;11:744-749.
- [16.](#) Baldini IM, Vita A, Mauri MC, et al.
Psychopathological and cognitive features in subclinical hypothyroidism.
Prog Neuropsychopharmacol Biol Psychiatry. 1997;21:925-935.
- [17.](#) Sawin CT, Geller A, Wolf PA, et al.
Low serum thyrotropin concentrations as a risk factor for atrial fibrillation in older persons.
N Engl J Med. 1994;331:1249-1252.
- [18.](#) Uzzan B, Campos J, Cucherat M, Nony P, Boissel JP, Perret GY.
Effects on bone mass of long term treatment with thyroid hormones: a meta-analysis.
J Clin Endocrinol Metab. 1996;81:4278-4289.
- [19.](#) Faber J, Galloe AM.
Changes in bone mass during prolonged subclinical hyperthyroidism due to L-thyroxine treatment: a meta-analysis. *Eur J Endocrinol.* 1994;130:350-356.
- [20.](#) Biondi B, Fazio S, Carella C, et al.
Control of adrenergic overactivity by beta-blockade improves the quality of life in patients receiving long term suppressive therapy with levothyroxine.
J Clin Endocrinol Metab. 1994;78:1028-1033.
- [21.](#) Spencer CA, Takeuchi M, Kazarosyan M.
Current status and performance goals for serum thyrotropin (TSH) assays.
Clin Chem. 1996;42:140-145.
- [22.](#) Danese MD, Powe NR, Sawin CT, Ladenson PW.
Screening for mild thyroid failure at the periodic health examination: a decision and cost-effectiveness analysis. *JAMA.* 1996;276:285-292.
- [23.](#) Guide to Clinical Preventive Services: Report of the U.S. Preventive Services Task Force. 2nd ed. Baltimore, Md: Williams & Wilkins; 1995.