

Hypothyroidism: Diagnosis and Treatment

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Clinical hypothyroidism affects one in 300 people in the United States, with a higher prevalence among female and older patients. Symptoms range from minimal to life-threatening (myxedema coma); more common symptoms include cold intolerance, fatigue, weight gain, dry skin, constipation, and voice changes. The signs and symptoms that suggest thyroid dysfunction are nonspecific and non-diagnostic, especially early in disease presentation; therefore, a diagnosis is based on blood levels of thyroid-stimulating hormone and free thyroxine. There is no evidence that population screening is beneficial. Symptom relief and normalized thyroid-stimulating hormone levels are achieved with levothyroxine replacement therapy, started at 1.5 to 1.8 mcg per kg per day. Adding triiodothyronine is not recommended, even in patients with persistent symptoms and normal levels of thyroid-stimulating hormone. Patients older than 60 years or with known or suspected ischemic heart disease should start at a lower dosage of levothyroxine (12.5 to 50 mcg per day). Women with hypothyroidism who become pregnant should increase their weekly dosage by 30% up to nine doses per week (i.e., take one extra dose twice per week), followed by monthly evaluation and management. Patients with persistent symptoms after adequate levothyroxine dosing should be reassessed for other causes or the need for referral. Early recognition of myxedema coma and appropriate treatment is essential. Most patients with subclinical hypothyroidism do not benefit from treatment unless the thyroid-stimulating hormone level is greater than 10 mIU per L or the thyroid peroxidase antibody is elevated. (*Am Fam Physician*. 2021;103(10):605-613. Copyright © 2021 American Academy of Family Physicians.)

Hypothyroidism occurs when there is inadequate thyroid hormone production by the thyroid gland or insufficient stimulation by the hypothalamus or pituitary gland. Causes may include primary gland failure or can be iatrogenic, transient, or central (*Table 1*).¹⁻⁴ Central causes, such as low levels of thyroid-stimulating hormone (TSH) and free thyroxine (FT₄), are rare.

Clinical hypothyroidism occurs in 0.3% of the U.S. general population, with a higher prevalence in people older than 65 years.⁵⁻⁷ It is seven times more common in females than in males (40 out of 10,000 vs. six out of 10,000).⁸ Other risk factors include autoimmune disease (e.g., type 1 diabetes mellitus, celiac disease, autoimmune gastric atrophy, multiple autoimmune endocrinopathies), Down syndrome, and Turner syndrome.² Cigarette smoking

and moderate alcohol intake decrease the risk of thyroid cancer and hypothyroidism.^{2,9} Untreated hypothyroidism can contribute to numerous physiologic and metabolic derangements.

Signs and symptoms are nonspecific and can vary in individual presentations (*Tables 2 and 3*).^{3,10} Diagnosis is based on blood levels of decreased FT₄, with a corresponding elevated thyrotropin (i.e., TSH) level in primary causes (thyroid source); the TSH level may be normal to low in secondary (pituitary source) or tertiary (hypothalamic source) causes.⁵ Subclinical hypothyroidism describes the state of normal FT₄ levels when the TSH level is elevated. This article focuses on primary hypothyroidism in adults.

Pathophysiology

A sensitive negative feedback loop regulates the thyroid hormone. The hypothalamus produces thyrotropin-releasing hormone that controls anterior pituitary gland secretion of TSH, regulating the secretion of thyroid hormone (triiodothyronine [T₃] and thyroxine [T₄]) by the thyroid gland.^{11,12} Thyroid hormone affects the metabolism and function of many cells and organs. This central role is reflected by the

CME This clinical content conforms to AAFP criteria for CME. See CME Quiz on page 587.

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Patient information: A handout on this topic is available at <https://familydoctor.org/condition/hypothyroidism/>.

Recommendations from the Choosing Wisely Campaign

Recommendation	Sponsoring organization
Do not screen asymptomatic pregnant patients for subclinical hypothyroidism.	Society for Maternal-Fetal Medicine
Do not order multiple tests for the initial evaluation of a patient with suspected thyroid disease. Order thyroid-stimulating hormone level and, if abnormal, follow up with additional evaluation or treatment depending on the findings.	American Society for Clinical Pathology
Do not routinely order thyroid ultrasonography in patients with abnormal thyroid function tests if there is no palpable abnormality of the thyroid gland.	Endocrine Society/ American Association of Clinical Endocrinologists
Do not obtain a total or free triiodothyronine level when assessing levothyroxine dose in patients with hypothyroidism.	Endocrine Society/ American Association of Clinical Endocrinologists

Source: For more information on the Choosing Wisely Campaign, see <https://www.choosingwisely.org>. For supporting citations and to search Choosing Wisely recommendations relevant to primary care, see <https://www.aafp.org/afp/recommendations/search.htm>.

TABLE 1

Causes of Hypothyroidism

Central (hypothalamic or pituitary)

Inappropriately normal or low levels of thyroid-stimulating hormone despite low thyroid hormone

Medications (amiodarone, immune checkpoint inhibitors, interleukin-2, interferon-alfa, lithium, tyrosine kinase inhibitors)*

Pituitary tumor or disorder

Iatrogenic

Hyperthyroid treatment (radioactive iodine or antithyroid medications)*

Radiation therapy to treat head and neck cancers*

Thyroid surgery*

Primary gland failure

Autoimmune thyroiditis (Hashimoto thyroiditis)†

Congenital abnormalities

Infiltrative diseases

Severe iodine deficiency or relative excess‡

Transient

Postpartum thyroiditis

Pregnancy

Silent thyroiditis

Subacute thyroiditis

Thyroiditis associated with thyroid-stimulating hormone receptor–blocking antibodies

*—More common.

†—Most common.

‡—Rare in the United States because of iodized table salt. Iodine is a trace mineral necessary to produce thyroid hormones, but it is the most common cause of hypothyroidism in many parts of the world.

Information from references 1-4.

signs and symptoms of thyroid dysregulation. Thyroid hormone also regulates thyroid metabolism by providing negative feedback to the hypothalamus and pituitary gland. The hypothalamus adjusts the release of thyrotropin-releasing hormone based on circulating levels of thyroid hormone. Together, these hormones regulate the secretion of TSH

EVALUATING FOR SUSPECTED HYPOTHYROIDISM

When signs and symptoms raise the index of suspicion, the clinician should obtain a serum TSH level (*Figure 1*^{2,5-7,15-17}). If the TSH level is within the normal reference range, other etiologies for the signs and symptoms that prompted testing should be sought (*Table 4*^{1,2}). If a pituitary

from the anterior lobe of the pituitary gland. This functioning feedback loop keeps the blood level of the thyroid hormone normal.

Screening

The U.S. Preventive Services Task Force concludes that there is insufficient evidence to assess the balance of benefits and harms of screening for thyroid dysfunction in nonpregnant, asymptomatic adults.¹³ Consider targeted screening at initial diagnosis or medication initiation in patients with Down syndrome, Turner syndrome, subtotal thyroidectomy, type 1 diabetes, autoimmune adrenal insufficiency (Addison disease), radioiodine treatment, radiation therapy of the neck, and use of medications such as amiodarone, lithium, interferons, and rifampin.^{2,3} Other medications that may prompt screening include tyrosine kinase inhibitors, phenobarbital, interleukin-2, and immune checkpoint inhibitors.^{3,14}

Diagnosis

TSH elevation indicates hypothyroidism. Low-end normal TSH is 0.4 mIU per L.^{2,5-7} The upper-end normal range is from 4.0 to 4.5 mIU per L.^{2,5-7} FT₄ level is used to distinguish clinical (low FT₄) from subclinical (normal FT₄) hypothyroidism. Routinely evaluating total T₃, total T₄, or FT₃ levels is not indicated.² Testing for the thyroid peroxidase (TPO) antibody does not help diagnose hypothyroidism; however, a positive test result suggests an autoimmune etiology.² Thyroid ultrasonography is used to evaluate palpable thyroid nodules and is not part of routine evaluation.⁴

cause is suspected, an FT₄ level is obtained. If the FT₄ level is normal, further thyroid or pituitary evaluation is unnecessary. If the FT₄ level is low, the clinician should review medications the patient is taking, evaluate the pituitary gland, or consider euthyroid sick syndrome (i.e., a normal TSH level with abnormal thyroid hormone levels and function tests that can occur in patients with severe nonthyroid systemic disease despite actual normal thyroid function).

If the TSH level is low (less than 0.4 mIU per L), hyperthyroidism is possible.¹⁸ If the TSH level is high (greater than 4.5 mIU per L), a serum FT₄ level should be obtained. A low FT₄ level indicates clinical hypothyroidism, specifically autoimmune hypothyroidism (i.e., Hashimoto thyroiditis) if the TPO antibody test result is elevated). *Table 1* lists other causes.¹⁻⁴ An elevated FT₄ level may suggest a TSH-secreting tumor, and referral to endocrinology is warranted. An FT₄ level within the reference range indicates subclinical hypothyroidism. Rare other causes include adrenal insufficiency, drugs, post-nonthyroidal illness, or thyroid hormone resistance syndrome.² Thyroid hormone resistance syndrome, which occurs in one out of 40,000 live births, results from mutations of the thyroid hormone that cause decreased tissue responsiveness to thyroid hormone, leading to an elevated FT₄ level and a normal or elevated TSH level.¹⁹

Treatment

Clinical hypothyroidism should be treated with levothyroxine to normalize the TSH level and relieve signs and symptoms (*Figure 2*^{2,3,5,7,10,20-25}). Evidence does not support the use of T₃, alone or in combination with levothyroxine.^{5,26} Iodine supplementation, including kelp or other iodine-rich foods, should not be used in iodine-sufficient geographic locations.⁵

Levothyroxine should be taken once per day, 30 to 60 minutes before eating, and four hours before or after drugs that may impede absorption (*Table 5*²⁰). *Table 6* addresses initial dosing of levothyroxine.^{2,3,5,20,21} In patients who are not pregnant, TSH should be monitored every six to eight weeks until within normal range, then every six to 12 months, barring a change in clinical status.²⁰ Some drugs and conditions (*Table 7*^{2,20}) can affect levothyroxine metabolism and effects,

TABLE 2

Clinical Findings (Signs) of Hypothyroidism

Bradycardia	Laboratory abnormalities	Lateral eyebrow thinning
Coarse facies	Anemia (normocytic)	Low-voltage electrocardiography
Cognitive impairment	Elevated C-reactive protein	Macroglossia
Delayed relaxation phase of deep tendon reflexes	Hyperprolactinemia	Pericardial effusion
Diastolic hypertension	Hyponatremia	Periorbital edema
Edema	Increased creatine kinase	Pleural effusion
Goiter	Increased low-density lipoprotein	
Hoarseness	Increased triglycerides	
Hypothermia	Proteinuria	

Information from references 1, 3, and 10.

TABLE 3

Symptoms of Hypothyroidism

Arthralgias	Infertility
Cognitive impairment	Lethargy*
Cold intolerance*	Memory impairment
Constipation*	Menorrhagia
Depression	Muscle cramps
Difficulty focusing/concentrating	Myalgia
Dry skin*	Voice changes*
Edema	Weakness
Fatigue*	Weight gain*
Hair changes (i.e., dryness, thinning, or loss)	

*—More common.

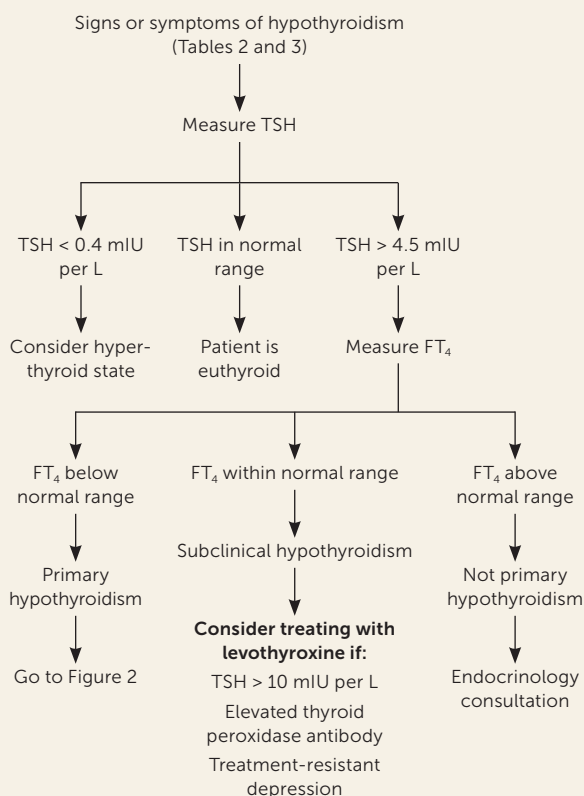
Information from references 1, 3, and 10.

and drug-drug and drug-food interactions (*Table 8*²⁰) can affect levels of levothyroxine or the concomitant drug. A lower symptom threshold should be used to monitor the TSH level in patients at risk of these interactions and when medications or dosing changes are initiated.²⁰

LABORATORY ASSESSMENT AFTER INITIAL DOSING

Once the TSH level is normalized, it should be rechecked in one year or earlier if symptoms change. Extending the frequency beyond one year is reasonable in patients with a normal TSH level, stable symptoms, and daily dosing of levothyroxine of less than 75 mcg per day.²⁷

FIGURE 1



FT₄ = free thyroxine; TSH = thyroid-stimulating hormone.

Algorithm for the diagnosis of hypothyroidism.

Information from references 2, 5-7, and 15-17.

TABLE 4

Differential Diagnoses When Thyroid-Stimulating Hormone Level Is Normal but Symptoms Persist

Anemia (vitamin B ₁₂ or iron deficiency)	Chronic kidney disease
Autoimmune (rare)	Liver disease
Adrenal insufficiency	Menopause
Atrophic gastritis with pernicious anemia	Mental health (i.e., depression, anxiety, or somatoform disorders)
Diabetes mellitus type 1	Obstructive sleep apnea
Rheumatoid arthritis	Viral infections (e.g., mononucleosis, Lyme disease, HIV)

Adapted with permission from Gaitonde DY, Rowley KD, Sweeney LB. Hypothyroidism: an update. *Am Fam Physician.* 2012;86(3):249, with additional information from reference 2.

If the TSH level is abnormal, the clinician should assess patient adherence, evaluate drug-drug interactions, and adjust the levothyroxine dosage every six to eight weeks until the TSH level normalizes (Figure 2^{2,3,5,7,10,20-25}). When TSH is low (over-replacement), the daily dosage should be decreased by 12.5 to 25 mcg. When TSH is high (under-replacement), the daily dosage is increased by 12.5 to 25 mcg per day. If the TSH level or symptoms are not improving after two to three cycles of adjustments, referral to endocrinology may be considered after reassessment of the differential diagnosis, patient adherence, and drug-drug or drug-food interactions.

Special Populations

PATIENTS OLDER THAN 60 YEARS AND PATIENTS WITH ISCHEMIC HEART DISEASE

In older adults, hypothyroidism may have a subtle or more nonspecific presentation. Few older patients with confirmed hypothyroidism have overt symptoms to suggest disease.²⁸ Serum TSH levels can increase with age, and mild elevations do not necessarily reflect subclinical hypothyroidism.²⁹ A randomized placebo-controlled trial of 737 patients older than 65 years with subclinical hypothyroidism demonstrated no significant improvement in quality of life with levothyroxine treatment.⁷ A separate study found no association between subclinical hypothyroidism and ischemic heart disease, heart failure, or cardiovascular death.³⁰ Thyroid hormone has known inotropic effects on cardiac tissue and can increase myocardial oxygen demand. For older patients or those with coronary artery disease, levothyroxine therapy should be started at 25 to 50 mcg per day, with titration of 25 mcg every three to four weeks until a target dosage is achieved to decrease the potential for adverse effects from thyroid excess (e.g., atrial fibrillation, dysrhythmia, angina, osteoporosis). Starting as low as 12.5 mcg per day in patients at higher risk (e.g., advanced age, heart disease) should be considered.^{2,3,5,21}

PREGNANT PATIENTS

Pregnancy is associated with increased levothyroxine requirements as early as the fourth week of gestation.²² TSH levels decrease in early pregnancy because of weak stimulation of TSH receptors by human chorionic gonadotropin in the first trimester, then return to normal throughout pregnancy. Once pregnancy is confirmed, patients with existing hypothyroidism should start taking an extra dose of levothyroxine two days per week for a total of nine doses per week.²² This significantly decreases the risk of maternal

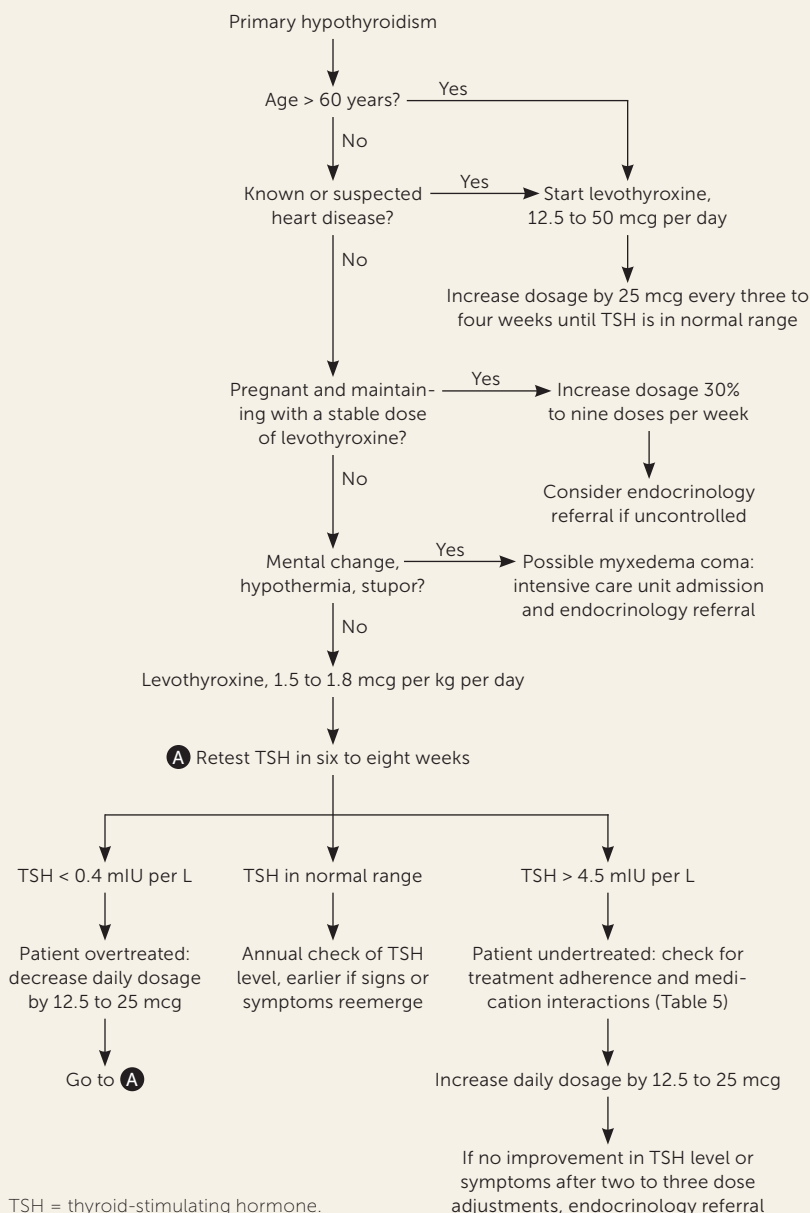
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hypothyroidism during the first trimester.²² Further treatment is guided by measuring TSH levels at the first prenatal visit, then every four weeks with titration of levothyroxine according to the pregnancy-specific TSH reference range.^{22,23} The lower and upper limits of normal TSH drift

downward during pregnancy, which, with geographic and ethnic variation,²¹ supports consideration to include endocrinology referral in managing pregnant patients with hypothyroidism.

Clinical hypothyroidism complicates two to 10 per 1,000 pregnancies; Hashimoto thyroiditis is the most common cause. Untreated hypothyroidism can result in spontaneous abortion, preeclampsia, preterm birth, abruptio placentae, and fetal death.²⁶ TSH should be evaluated in pregnant patients with symptoms of hypothyroidism, a goiter, a history of thyroid disease, TPO antibody positivity, or autoimmune disease.²⁶ Patients with a TSH level greater than 2.5 mIU per L who are TPO antibody-positive have a higher risk of pregnancy-related complications, including preterm birth and pregnancy loss.²³ Universal screening for hypothyroidism in pregnancy is not recommended because the identification and treatment of subclinical hypothyroidism during pregnancy do not improve outcomes.^{23,26} A randomized trial of 21,846 women found no difference in neurocognitive development of children from women screened and treated for subclinical hypothyroidism.³¹

FIGURE 2



Algorithm for the treatment of primary hypothyroidism in adults.

Information from references 2, 3, 5, 7, 10, and 20-25.

PATIENTS WITH PERSISTENT SYMPTOMS

Patients on high dosages of levothyroxine (greater than 200 mcg per day) with persistently elevated TSH levels may be nonadherent or have absorption issues attributed to meal timing or other medications^{1,5,20} (Tables 5 and 8²⁰). Some patients may experience persistent symptoms despite adequate dosing of levothyroxine to a normal TSH level; therefore, other etiologies should be considered and evaluated accordingly (Table 4^{1,2}).

Some patients with a normal TSH level and symptom resolution may become symptomatic again with or without a change in TSH. When symptoms reappear without a change in TSH level, the physician should

TABLE 5

Medications That Can Decrease Levothyroxine Absorption

Bile acid sequestrants (e.g., colestevlam [Welchol], cholestyramine [Questran], colestipol)
 Calcium carbonate
 Ferrous sulfate
 Intragastric pH elevation via hypochlorhydria
 Antacids (e.g., aluminum, magnesium)
 Proton pump inhibitors
 Simethicone
 Sucralfate (Carafate)
 Ion exchange resins (e.g., sodium polystyrene sulfonate, sevelamer [Renvela])
 Orlistat (Xenical)

Note: When these medications are required, they should be ingested four hours before or after levothyroxine.

Information from reference 20.

TABLE 6

Initial Dosing of Levothyroxine in Adults with Primary Hypothyroidism

Patient group	Dosing
Age younger than 60 years	Start with 1.5 to 1.8 mcg per kg per day
Age 60 years or older; known or suspected heart disease	Start with 12.5 to 50 mcg per day
Pregnant on previously stable dose	Increase to nine doses per week; endocrine referral

Information from references 2, 3, 5, 20, and 21.

TABLE 7

Reasons a Stable Thyroid-Stimulating Hormone Level May Become Abnormal

Change in adherence (e.g., missing doses)
 Change in timing of medication relative to eating
 Malabsorption
 Autoimmune atrophic gastritis
 Celiac disease
 Diabetic gastropathy
Helicobacter pylori gastritis
 Medication, new initiation
 Androgens
 Estrogens
 Heroin/methadone
 Medications that decrease absorption of levothyroxine (Table 5)
 Medications that may alter hepatic metabolism of levothyroxine (phenobarbital, rifampin)
 Medications that may decrease levothyroxine conversion to triiodothyronine (amiodarone, high-dose beta-adrenergic agonists, glucocorticoids)
 Medications that may reduce serum protein binding of levothyroxine (carbamazepine [Tegretol] or phenytoin [Dilantin])
 Selective serotonin reuptake inhibitors or tricyclic antidepressants
 Tamoxifen
 Pregnancy

Information from references 2 and 20.

MYXEDEMA COMA

Rarely, severe hypothyroidism can cause myxedema coma, a medical emergency most commonly found in older patients with primary hypothyroidism, with a 25% to 60% mortality rate.²⁴ Early recognition with appropriate treatment is essential. Clinical features include hypothermia and mental status changes (e.g., lethargy, confusion, psychosis), hypotension, bradycardia, hypoventilation, and diffuse nonpitting edema. Abnormal laboratory findings include hypoglycemia, hyponatremia, high TSH, very low FT₄, and low cortisol if associated adrenal insufficiency exists. When myxedema coma is suspected, treatment can be initiated while waiting for confirmation of laboratory test results. Myxedema coma is one of the reasons for referral to endocrinology (Table 9^{1,3-5}).

Few clinical trials exist to guide treatment, although experts recommend levothyroxine, T₃, or both.²⁵ Levothyroxine should be given as a slow intravenous bolus of 200 to 400 mcg initially, followed by 50 to 100 mcg (about 1.6 mcg per kg) orally per day. Reduce dosing by 75% if it is being administered intravenously. For combination treatment, T₃ is given at the same time as levothyroxine and dosed at 5 to 20 mcg, then 2.5 to 10 mcg every eight hours until clinical

consider nonthyroid etiologies. When there is an accompanying change in the TSH level, especially in a patient who has stayed on a stable dosage for some time, other reasons should be explored before adjusting the levothyroxine dosage.

Adding T₃ to levothyroxine does not additionally alleviate symptoms of hypothyroidism. A meta-analysis of 11 randomized trials (n = 1,216) found no difference in symptoms or quality of life in patients treated with levothyroxine monotherapy vs. levothyroxine plus combination therapy.³² The American Association of Clinical Endocrinologists does not recommend desiccated thyroid hormone and finds insufficient evidence to recommend combination levothyroxine/T₃ therapy over levothyroxine monotherapy.⁵ The American Thyroid Association does not recommend genetic testing for polymorphisms to guide treatment; however, a small subset of patients with specific type 2 deiodinase polymorphism may benefit from combination therapy.²¹

TABLE 8

Potential Drug-Drug and Drug-Food Levothyroxine Interactions

Diabetes mellitus medications	May increase dosing of diabetes medications needed to achieve glycemic control
Digitalis	May decrease serum digitalis levels
Foods	Patients who regularly consume walnuts, dietary fiber, soybean flour, cottonseed meal, or grapefruit juice may need higher doses of levothyroxine
Ketamine	Concurrent use may result in significant hypertension and tachycardia
Oral anticoagulants	May increase effects
Selective serotonin reuptake inhibitors	May increase therapeutic and toxic effects
Sympathomimetics	Concurrent use may increase risk of a cardiac event in patients with coronary artery disease
Tricyclic antidepressants	May increase therapeutic and toxic effects
Tyrosine kinase inhibitors	Concurrent use may result in hypothyroidism

Information from reference 20.

improvement. Lower dosages are appropriate in older adults and patients with a history of cardiovascular disease. Stress-dose glucocorticoids (e.g., 100 mg of hydrocortisone intravenously every eight hours) should be administered until adrenal insufficiency is ruled out. Serum FT₄ and T₃ should be monitored every one to two days, with samples drawn at least one hour after dosing T₃. The TSH level should drop by 50% per week on adequate treatment. After clinical improvement, the patient may transition to oral levothyroxine monotherapy.^{21,25}

SUBCLINICAL HYPOTHYROIDISM

Subclinical hypothyroidism is a biochemical finding of an elevated TSH level with a normal FT₄ level. This finding should initiate a TPO antibody test and an additional TSH test in six to 12 months. Subclinical hypothyroidism is present in 3.7% of the U.S. population.⁶ Signs and symptoms of hypothyroidism may or may not be present. After 12 or more months, TSH often spontaneously normalizes.⁷ More than 50% of patients older than 55 years with TSH levels of 5.0 to 9.9 mIU per L will normalize, whereas only 13% and 5% of patients normalize if the TSH level is greater than 10 mIU per L or greater than 15 mIU per L, respectively.³³

Patients with elevated TPO antibody titers are at an increased risk of progression to clinical hypothyroidism.³⁴ Annual progression from subclinical to clinical hypothyroidism is 5.6% for a TSH level greater than 6 mIU per L.³⁴

Subclinical hypothyroidism is common in patients 65 years and older. Despite observed associations with depression, cognitive impairment, hyperlipidemia, and coronary artery disease, there is no evidence that treatment of subclinical hypothyroidism improves outcomes. A study of 737 patients who were 65 years and older with subclinical hypothyroidism found no improvement in quality of life or clinical outcomes with levothyroxine titrated to achieve a normal TSH level compared with patients who received placebo with sham titration.⁷ In patients 65 years and older with subclinical hypothyroidism and TSH levels less than 10 mIU per L, treatment with levothyroxine can increase mortality.³⁵

The benefit of treating subclinical hypothyroidism in many populations is uncertain. One randomized controlled trial found that treating middle-aged adults (mean age of 57 years) with levothyroxine compared with a control medication decreased tiredness.³⁶ However, a systematic review and meta-analysis of 21 randomized controlled trials of 2,192 adults found that the treatment was not associated with improved quality of life or thyroid-related symptoms.³⁷ A Cochrane systematic review was inconclusive about the value of treating subclinical hypothyroidism in women who are infertile.³⁸ Although subclinical hypothyroidism in pregnancy is associated with adverse outcomes such as miscarriage, preterm delivery,

TABLE 9

Reasons to Consider Referral to Endocrinology for Hypothyroidism

- Age 18 years or younger
- Elusive euthyroid state
- Myxedema coma, suspected
- Pregnancy
- Simultaneous presence of another endocrinopathy
- Structural change in thyroid gland (e.g., goiter, nodule)
- Symptoms do not improve or worsen after treatment with levothyroxine
- Unstable ischemic heart disease

Information from references 1 and 3-5.

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	Evidence rating	Comments
Screening for thyroid dysfunction in nonpregnant, asymptomatic adults has uncertain risks and benefits. ¹³	C	No studies have directly compared the benefits and harms of screening vs. no screening
Patients with hypothyroidism should not be treated with triiodothyronine, alone or in combination with levothyroxine. ^{5,26}	A	Evidence-based guidelines generated from consistent, prospective, randomized trials
Patients with hypothyroidism should not be treated with iodine supplementation unless they are from an area with known iodine insufficiency. ⁵	B	Patient-oriented evidence from nonprospective studies and consensus evaluation of those data
In newly diagnosed patients with hypothyroidism who are older than 60 years or with known or suspected ischemic heart disease, levothyroxine therapy should be initiated at 12.5 to 50 mcg per day. ^{2,3,5,21}	C	Consensus, expert opinion
In women with controlled hypothyroidism who become pregnant, the levothyroxine dosage should be increased by 30%, from seven to nine doses per week, with the thyroid-stimulating hormone level checked every four weeks. ^{22,23}	A	Consistent high-quality randomized trials
Nonpregnant patients with subclinical hypothyroidism should not be treated with thyroid hormone therapy unless the thyroid-stimulating hormone level is greater than 10 mIU per L or the thyroid peroxidase antibody is elevated. ^{16,17,34}	A	Consistent, prospective, randomized data and meta-analysis

A = consistent, good-quality patient-oriented evidence; **B** = inconsistent or limited-quality patient-oriented evidence; **C** = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to <https://www.aafp.org/afpsort>.

low birth weight, and lower IQ in offspring, clinical trial results have been mixed. One trial found a decreased risk of preterm birth in patients with subclinical hypothyroidism and TPO antibodies.³⁹ Two trials demonstrated that levothyroxine did not improve adverse pregnancy outcomes or the IQ of offspring of pregnant patients with subclinical hypothyroidism.^{31,40} A systematic review and meta-analysis found an excess risk of depression in patients with subclinical hypothyroidism but no improvement with the use of levothyroxine.⁴¹ Thyroid hormone therapy may benefit patients with treatment-resistant depression and TSH levels greater than 2.5 mIU per L.¹⁵

Most adults older than 30 years with elevated TSH but normal FT₄ levels do not benefit from thyroid hormone therapy, and 60% normalize within five years.^{37,42} Patients who have a TSH level greater than 10 mIU per L are at higher risk of fracture, ischemic heart disease, and heart failure compared with patients who have a TSH level of 2.0 to 2.5 mIU per L.¹⁶ In nonpregnant patients with subclinical hypothyroidism, levothyroxine therapy should be considered when the TSH level is greater than 10 mIU per L or the TPO antibody level is elevated.^{16,17,34} The benefits of treating women with subclinical hypothyroidism who are pregnant or attempting to conceive are unclear.¹⁷

This article updates previous articles on this topic by Hueston,⁴³ and Gaitonde, et al.¹

Data Sources: A search of Dynamed, Essential Evidence Plus, and PubMed was conducted using the key terms hypothyroidism, pregnancy, diagnosis, treatment, and subclinical hypo-

thyroidism. The search included randomized controlled trials, meta-analyses, and guidelines. Search dates: October and November 2019.

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