

# **ALGORITHMS**

## **FOR DIAGNOSIS & MANAGEMENT OF THYROID DISORDERS**

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# INTRODUCTION

Thyroid disorders occur in a significant proportion of the general population and increasingly are being diagnosed and managed by primary care physicians. Appropriate management of thyroid disorders is based on an accurate diagnosis based on clinical presentation, patient history, physical examination for anatomic changes in the thyroid gland and signs of hypothyroidism or hyperthyroidism, and accurate interpretations of appropriate laboratory tests.

Diagnosis of thyroid dysfunction can be difficult for various reasons. Although some thyroid disorders have clinical manifestations that are distinctive (eg, ophthalmopathy associated with Graves disease), many clinical features of hypothyroidism or hyperthyroidism are subtle, nonspecific, and may be difficult to recognize. Patients with subclinical hypothyroidism (mild thyroid failure) or subclinical hyperthyroidism may be asymptomatic. In addition, as the natural history of a thyroid disorder evolves, there are changes in symptoms associated with the underlying thyroid dysfunction. Over the last decade, improvements have been made in laboratory tests to assess thyroid function. Nonetheless, the large number and variety of available tests and their interpretation in various clinical circumstances can be confusing.

Once thyroid dysfunction is diagnosed, its treatment and management must be individualized based on many factors, including the etiology of the dysfunction, the attributes of the patient, the benefits and risks of treatment, and the available medication from managed care formularies.

The following diagnosis and management algorithms were developed to provide an overview of critical aspects of the initial evaluation and management of patients with thyroid disorders. These algorithms are concise, practical guides that can be used by primary care physicians and other specialists for the evaluation and management of patients with certain thyroid diseases. These algorithms are not intended to represent in-depth standards of treatment and do not obviate the need for consultation with an endocrinologist. In fact, consultation with an endocrinologist is recommended at specific points in the algorithms. An endocrinologist should always be consulted when thyroid disorders are suspected in children because of important differences in the management of pediatric patients.

# PRIMARY HYPOTHYROIDISM DIAGNOSIS

## Overview

Adult primary hypothyroidism is caused most frequently by chronic autoimmune thyroiditis (Hashimoto thyroiditis) and is present in 5-10% of the adult US population. Women older than 40 years of age and elderly individuals of both sexes are affected most frequently, although it does occur in individuals of all ages.<sup>1-5</sup> Other causes of hypothyroidism include thyroidectomy, radioactive iodine (<sup>131</sup>I) therapy, antithyroid agents, head or neck irradiation, certain medications, or congenital defects. Although many patients with primary hypothyroidism present with typical signs and symptoms suggestive of the condition (see Signs and Symptoms), patients with subclinical hypothyroidism (mild thyroid failure) may be asymptomatic or have nonspecific signs and symptoms (eg, depression, cognitive dysfunction, weight gain, fatigue, alterations in lipid metabolism, or abnormalities in cardiac, gastrointestinal, or reproductive function).<sup>1,3,5</sup>

## Testing

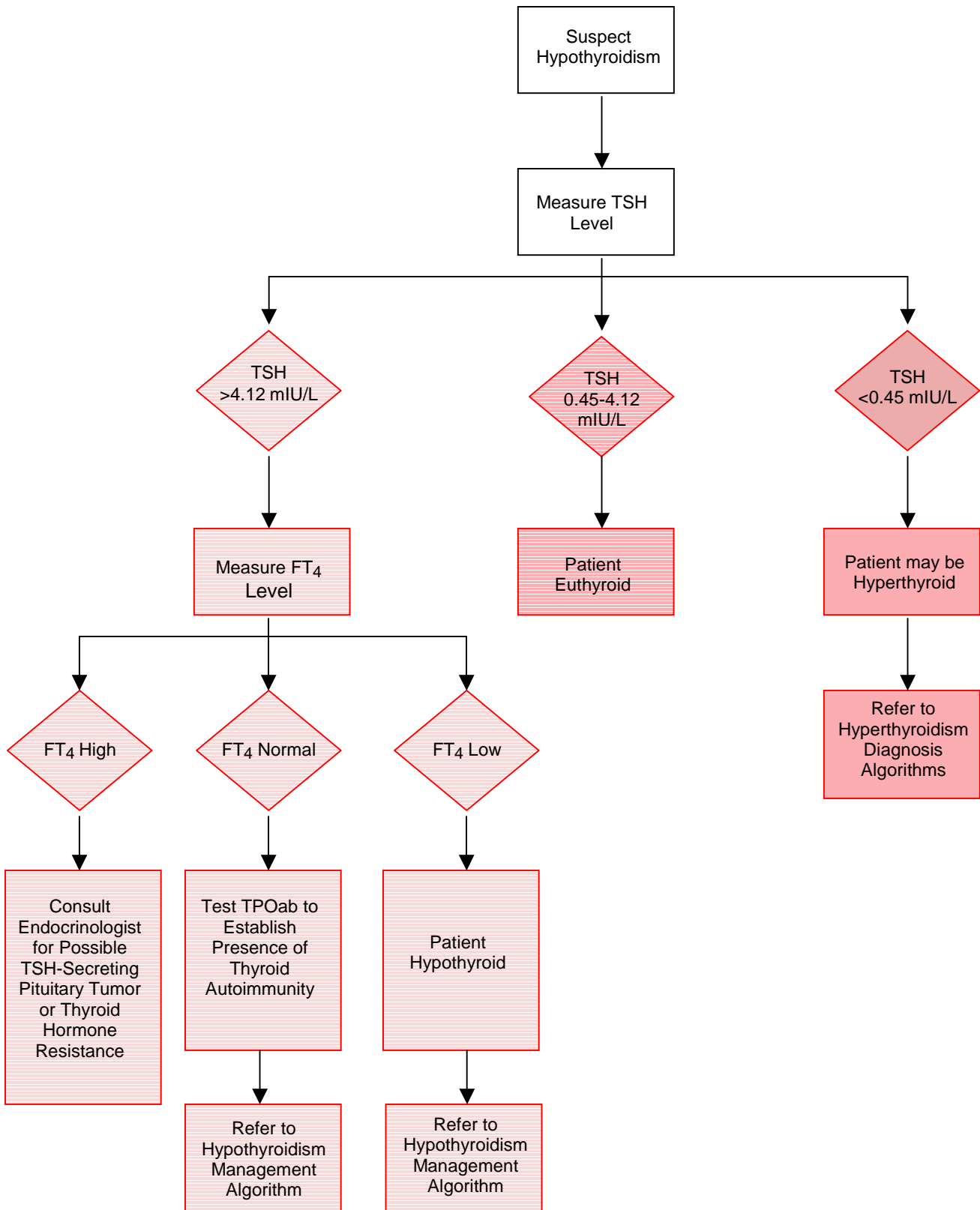
Because many signs and symptoms of hypothyroidism are nonspecific and patients with subclinical hypothyroidism (mild thyroid failure) may be asymptomatic, office-based testing of suspected patients by primary care physicians is important to ensure an early and accurate diagnosis.<sup>1-3,6</sup> A comprehensive medical diagnosis confirmed by thyroid function tests prior to treatment is important to avoid the inappropriate use of thyroid hormone replacement therapy in patients who are not clinically hypothyroid.<sup>1</sup>

The American Thyroid Association recommends that adults be checked for thyroid dysfunction by measurement of the serum thyrotropin (thyroid stimulating hormone, TSH) concentration beginning at 35 years of age and every 5 years thereafter.<sup>7</sup> More frequent testing may be appropriate for individuals at higher risk of developing thyroid dysfunction. The indication for TSH testing is particularly compelling in women, but it can also be justified in men over 60 years of age as a relatively cost-effective measure in the context of a periodic health examination.<sup>6</sup> TSH testing may be particularly useful in elderly patients, since thyroid disease symptoms may mimic characteristics associated with aging (eg, memory loss, fatigue, depression, and alopecia).<sup>1-3,6</sup>

## Test Interpretation

An increased TSH level (>4.12 mIU/L) suggests a diagnosis of primary hypothyroidism; this diagnosis is confirmed if the patient has a low free thyroxine (FT<sub>4</sub>) level.<sup>2-5,8</sup> Because TSH is a more sensitive test than FT<sub>4</sub>, patients with subclinical hypothyroidism (mild thyroid failure) will have a normal FT<sub>4</sub> with an elevated TSH level.<sup>2-4</sup> In the presence of an increased TSH with a normal FT<sub>4</sub>, a thyroid peroxidase antibody (TPOab) test is useful for establishing thyroid autoimmunity as the cause of subclinical hypothyroidism (mild thyroid failure). A normal TSH level (0.45 mIU/L to 4.12 mIU/L)\* generally excludes the diagnosis of primary hypothyroidism, although there may be circumstances when patients with chronic autoimmune thyroiditis have normal TSH levels.<sup>3,5,7,8</sup> A normal TSH level in a patient with low FT<sub>4</sub> suggests secondary hypothyroidism or a hypothalamic-pituitary disorder.<sup>1,4,5</sup> If the FT<sub>4</sub> is high in an individual with a normal or elevated TSH level, an endocrinologist should be consulted for evaluation of possible TSH-secreting pituitary tumor or thyroid hormone resistance.<sup>5</sup> Diagnosis of hypothyroidism in severely ill patients is complex, and the fact that most thyroid function tests (including the TSH test) often give misleading results in patients with other acute medical conditions should be considered; these patients probably should be evaluated by an endocrinologist.<sup>1-4</sup>

# PRIMARY HYPOTHYROIDISM DIAGNOSIS ALGORITHM



## Signs and Symptoms

- History of autoimmune disease
- History of Graves disease treatment, thyroid disease, or thyroid surgery
- Family history of thyroid disease
- History of head/neck irradiation
- Elevated cholesterol
- Elevated creatine phosphokinase (CPK)
- Hyponatremia (serum sodium <130 mEq/L)
- Depression/dementia
- Lithium treatment
- Cardiomegaly
- Pericardial effusion
- Bradycardia
- Low voltage on ECG
- Cold intolerance
- Fatigue
- Infertility
- Irregular menses
- Weight gain
- Vitiligo
- Alopecia
- Coarse or thinning hair
- Hoarse voice

## Consult Endocrinologist if:

- Pre-operative patient; ICU/CCU patient
- Age <15 years
- Cardiac compromised
- Stupor; coma
- Known tracheal compression
- Serum sodium <130 mEq/L
- Pregnancy
- Postpartum thyroiditis
- Symptoms suggest secondary or tertiary hypothyroidism (galactorrhea, infertility, headache, etc)

\*Normal TSH reference ranges have been reported in epidemiological studies<sup>8</sup> and recommended in various national association guidelines and position statements,<sup>7,9,11</sup> though the establishment of a single reference range continues to be controversial. Serum TSH levels of the reference population in the NHANES III study fell within 0.45 and 4.12 mIU/L, the normal TSH range that is cited in these algorithms.<sup>8</sup> The National Academy of Clinical Biochemistry has proposed a normal TSH range of 0.4 to 4.0 mIU/L,<sup>9</sup> whereas others have proposed a narrower TSH range of 0.3 to 3.0 mIU/L.<sup>3</sup> In addition, each laboratory may use different TSH reference ranges; physicians should be aware of and act within the normal TSH values used by their laboratories.

## References

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# PRIMARY HYPOTHYROIDISM MANAGEMENT

## Overview

Thyroid hormone replacement therapy with levothyroxine sodium is the treatment of choice for the routine management of primary hypothyroidism.<sup>1-4</sup> Although replacement therapy in patients with sub-clinical hypothyroidism (mild thyroid failure) can be controversial, most patients benefit from such therapy.<sup>1-6</sup> There is mounting evidence to suggest that patients with a persistent elevation of serum thyrotropin (thyroid stimulating hormone, TSH) may be exposed to greater risk if left untreated.<sup>6</sup> The goal of replacement therapy is to restore the patient to a euthyroid state, as evidenced by normalization of serum TSH levels.<sup>1,4</sup>

## Dosage and Dosage Adjustment

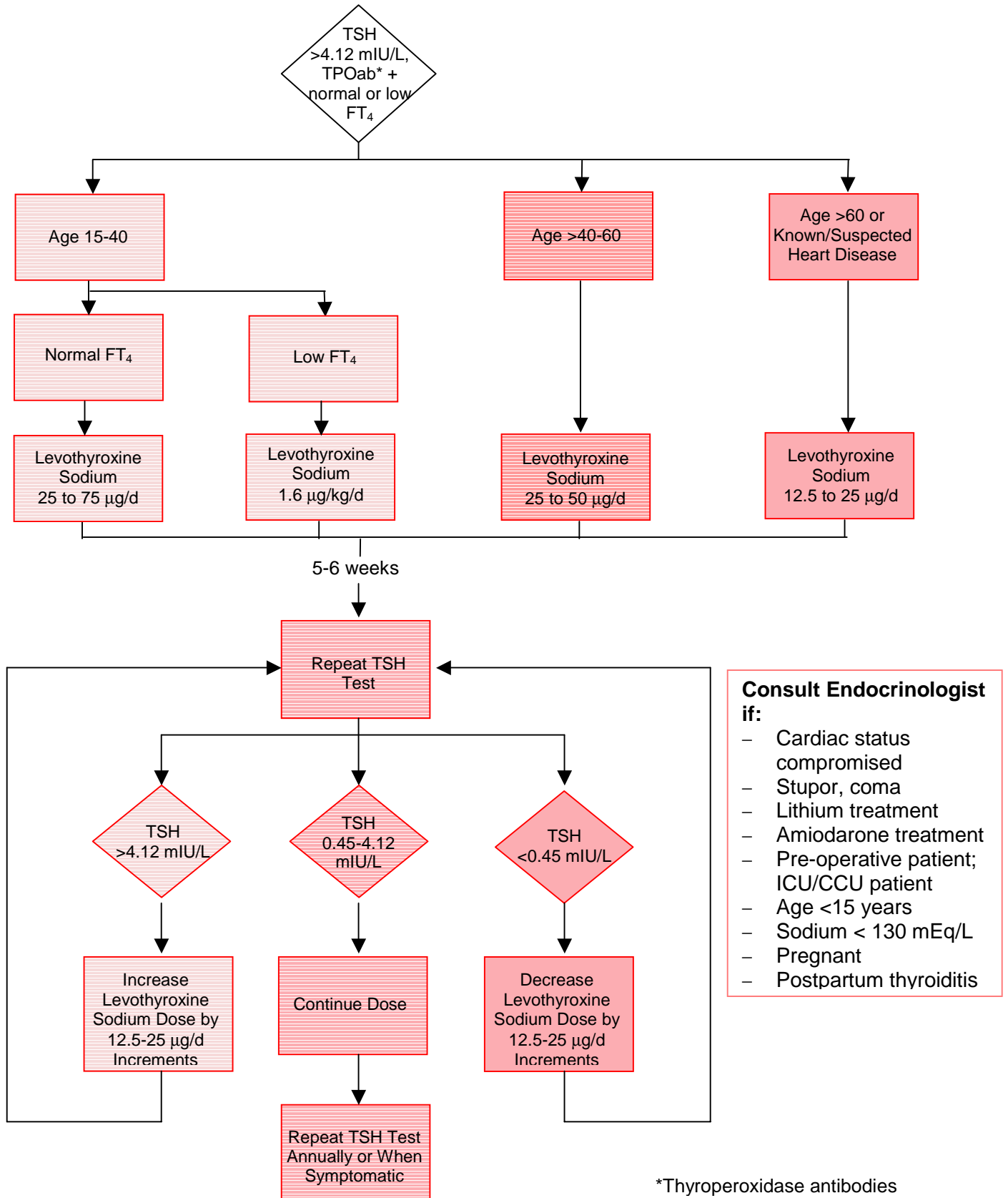
TSH is the test of choice for monitoring long-term thyroid hormone replacement therapy because it is sensitive to small alterations in levothyroxine sodium dosage and generally correlates well with thyroid hormone responsiveness.<sup>4,7-10</sup> A serum TSH level between 0.5 mIU/L and 2.0 mIU/L is considered to be the optimal therapeutic target for levothyroxine sodium therapy.<sup>7</sup> Initial and maintenance doses of levothyroxine sodium must be individualized based on the etiology, severity, and duration of hypothyroidism, as well as the age and clinical condition of the patient.<sup>1,4,11</sup> The fact that dosing requirements may be affected by malabsorptive states or drug interactions should be considered.<sup>1,2,4</sup> Levothyroxine sodium therapy should be initiated in younger healthy adults at the full replacement dose of 1.6 µg/kg/d.<sup>1,2,7</sup> Titration should occur every 6 to 8 weeks until the TSH level reaches 0.5 mIU/L to 2.0 mIU/L.<sup>7</sup> Older adults or those with known or suspected heart disease require a lower initial dosage (12.5 µg/d to 25 µg/d) and close monitoring to avoid overdosage.<sup>1-3</sup> Dosage in older adults should be titrated carefully in increments of 12.5 µg to 25 µg every 3 to 4 weeks until TSH normalizes to 0.5 mIU/L to 2.0 mIU/L.<sup>7</sup> This usually takes several weeks, and the higher the pretreatment TSH level, the longer it will take.<sup>1,4,7</sup> After the TSH level has normalized, maintenance dosage is continued and the TSH test repeated annually or whenever the patient becomes symptomatic.<sup>1,2,4,7</sup> A euthyroid state is usually achieved in adults who require full replacement with a maintenance dosage of levothyroxine sodium that averages 1.6 µg/kg/d.<sup>1,2,4,7</sup>

If TSH remains elevated after initiation of levothyroxine sodium therapy, either the dose is inadequate or there are problems with patient compliance or drug interactions.<sup>2</sup> If noncompliance is excluded, the dose should be increased gradually in increments of 12.5 µg to 25 µg.<sup>2</sup> Dosage reduction generally is indicated if the TSH level decreases below 0.45 mIU/L.<sup>2</sup> Overdosage of levothyroxine sodium should be avoided, since overdosage may cause decreased bone density, accelerated bone turnover, and other adverse effects including alterations in liver enzymes, tachycardia, and other cardiac changes.<sup>2,3</sup> Replacement therapy usually must be continued for life, although a few patients with chronic autoimmune thyroiditis (Hashimoto thyroiditis) spontaneously recover.<sup>2,3</sup>

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# PRIMARY HYPOTHYROIDISM MANAGEMENT ALGORITHM



# HYPERTHYROIDISM INITIAL DIAGNOSIS

## Overview

Thyrotoxicosis results from excess thyroid hormone and is present in a variety of conditions, including hyperthyroidism due to toxic diffuse goiter (Graves disease), toxic multinodular goiter, toxic adenoma, and thyroiditis (painful and subacute, or silent).<sup>1-5</sup> Thyrotoxicosis may also be associated with excessive pituitary TSH production, a trophoblastic tumor, or excessive ingestion of iodine or thyroid hormone.<sup>1,2,4</sup> A wide range of signs and symptoms is associated with hyperthyroidism (see Signs and Symptoms); manifestations and severity depend on the extent of thyroid hormone excess, age of the patient, and duration of the condition.<sup>2,4,5</sup>

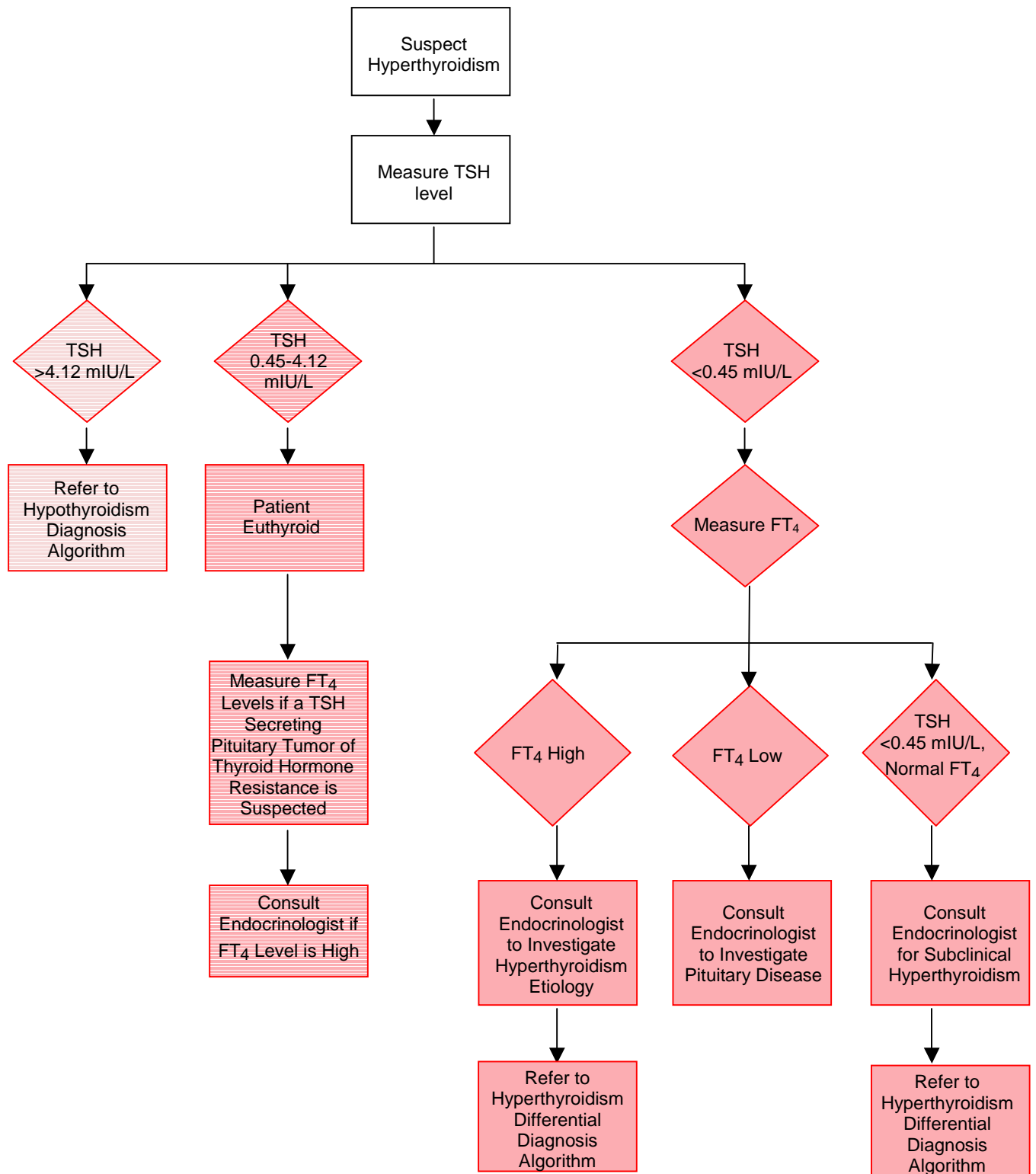
## Initial Evaluation and Testing

Initial evaluation of suspected hyperthyroidism includes a comprehensive medical history and physical examination (to identify goiter, tremors, nodules, exophthalmos, or other signs) and appropriate laboratory tests.<sup>1,3-5</sup> The serum thyrotropin (thyroid stimulating hormone, TSH) level and free thyroxine (FT<sub>4</sub>) estimate are the tests most frequently used for the initial evaluation of possible hyperthyroidism.<sup>1,3-6</sup>

## Test Interpretation

A TSH level of 0.45 mIU/L to 4.12 mIU/L generally indicates that the patient is euthyroid, although some patients with familial thyroid hormone resistance or a TSH-secreting pituitary tumor may have normal TSH levels with an increased FT<sub>4</sub>.<sup>1,3,6-9</sup> A decreased TSH level (<0.45 mIU/L) and an increased FT<sub>4</sub> generally confirm a diagnosis of hyperthyroidism.<sup>1-6,8,9</sup> Individuals with TSH levels <0.1 mIU/L generally have symptoms of hyperthyroidism; those with levels of 0.1 mIU/L to 0.4 mIU/L have intermediate degrees of suppression of the normal hypothalamic-pituitary axis and may be asymptomatic.<sup>4,8</sup> Current studies suggest that TSH values <0.45 mIU/L may represent thyroid hormone excess and in elderly patients may be associated with an increased risk of atrial fibrillation, cardiovascular mortality, and osteoporosis.<sup>8,9</sup> A decreased TSH level with normal FT<sub>4</sub> suggests that the patient may have subclinical hyperthyroidism or hyperthyroidism resulting from triiodothyronine (T<sub>3</sub>) toxicosis, an autonomous thyroid nodule, or effects of certain medications (eg, glucocorticoids or dopamine).<sup>3-6</sup> If results of initial testing indicate hyperthyroidism, further testing using a combination of tests is needed to establish the etiology<sup>1,6</sup>; this usually should be done in consultation with an endocrinologist.<sup>5</sup> Elderly patients may have markedly abnormal tests with few, if any, symptoms of hyperthyroidism and may not even have enlarged thyroid glands.<sup>1</sup> Diagnosis of hyperthyroidism in severely ill patients is complex, and the fact that most thyroid function tests (including TSH) give misleading results in patients with acute medical conditions should be considered; these patients probably should be evaluated by an endocrinologist.<sup>5,10</sup>

# HYPERTHYROIDISM INITIAL DIAGNOSIS ALGORITHM



## Signs and Symptoms

- History of autoimmune disease
- History of previous Graves disease treatment, thyroid disease, or thyroid surgery
- Family history of thyroid disease
- Goiter
- Exophthalmos
- Pretibial myxedema
- Excessive iodine exposure (contrast dyes, medications)
- Unexplained weight loss
- Atrial fibrillation/palpitations
- Depression/dementia
- Vitiligo
- Alopecia
- Coarse or thinning hair
- Heat intolerance
- Sweating
- Hyperdefecation
- Tremor

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# HYPERTHYROIDISM DIFFERENTIAL DIAGNOSIS

## Overview

After an initial diagnosis of hyperthyroidism has been made based on medical history, physical findings, and results of serum thyrotropin (thyroid stimulating hormone, TSH) and free thyroxine (FT<sub>4</sub>) measurements, further testing is necessary to determine the etiology of the condition so that it can be managed appropriately.<sup>1</sup> There are various thyroid function tests that can be used for the differential diagnosis of conditions associated with hyperthyroidism, including triiodothyronine (T<sub>3</sub>) radioimmunoassays, radioactive iodine uptake (<sup>123</sup>I uptake) tests, and thyroid scans.<sup>1,2</sup> It is not feasible or necessary to use all available procedures in every case.<sup>2,3</sup>

## Tests and Test Interpretation

The most probable causes of hyperthyroidism in a patient with decreased serum TSH levels and increased FT<sub>4</sub> are toxic diffuse goiter (Graves disease), toxic multinodular goiter, toxic adenoma, or thyrotoxicosis due to some form of thyroiditis (painful and subacute, or silent).<sup>2,4</sup> Results of <sup>123</sup>I uptake tests in conjunction with physical findings usually can differentiate these.<sup>2,4,5</sup> Although a diagnosis of Graves disease is evident if diffuse goiter and ophthalmopathy are present in patients with hyperthyroidism, a diagnosis of Graves disease in patients without these clinical manifestations can be confirmed by high <sup>123</sup>I uptake.<sup>1,2,5,6</sup> A diagnosis of toxic nodular goiter or toxic adenoma is suspected in the absence of ophthalmopathy or diffuse goiter, especially in elderly patients; normal or only slightly increased <sup>123</sup>I uptake may be seen.<sup>1,2,4-6</sup> A thyroid scan can be used to distinguish toxic nodular goiter and toxic adenoma from Graves disease and to assess the functional status of thyroid nodules.<sup>1,6</sup> A decreased TSH level (<0.45 mIU/L) in conjunction with a low <sup>123</sup>I uptake generally indicates some form of thyroiditis (painful and subacute, or silent); it may also indicate excessive iodine ingestion or factitious T<sub>4</sub>-induced thyrotoxicosis.<sup>1,2,4-6</sup>

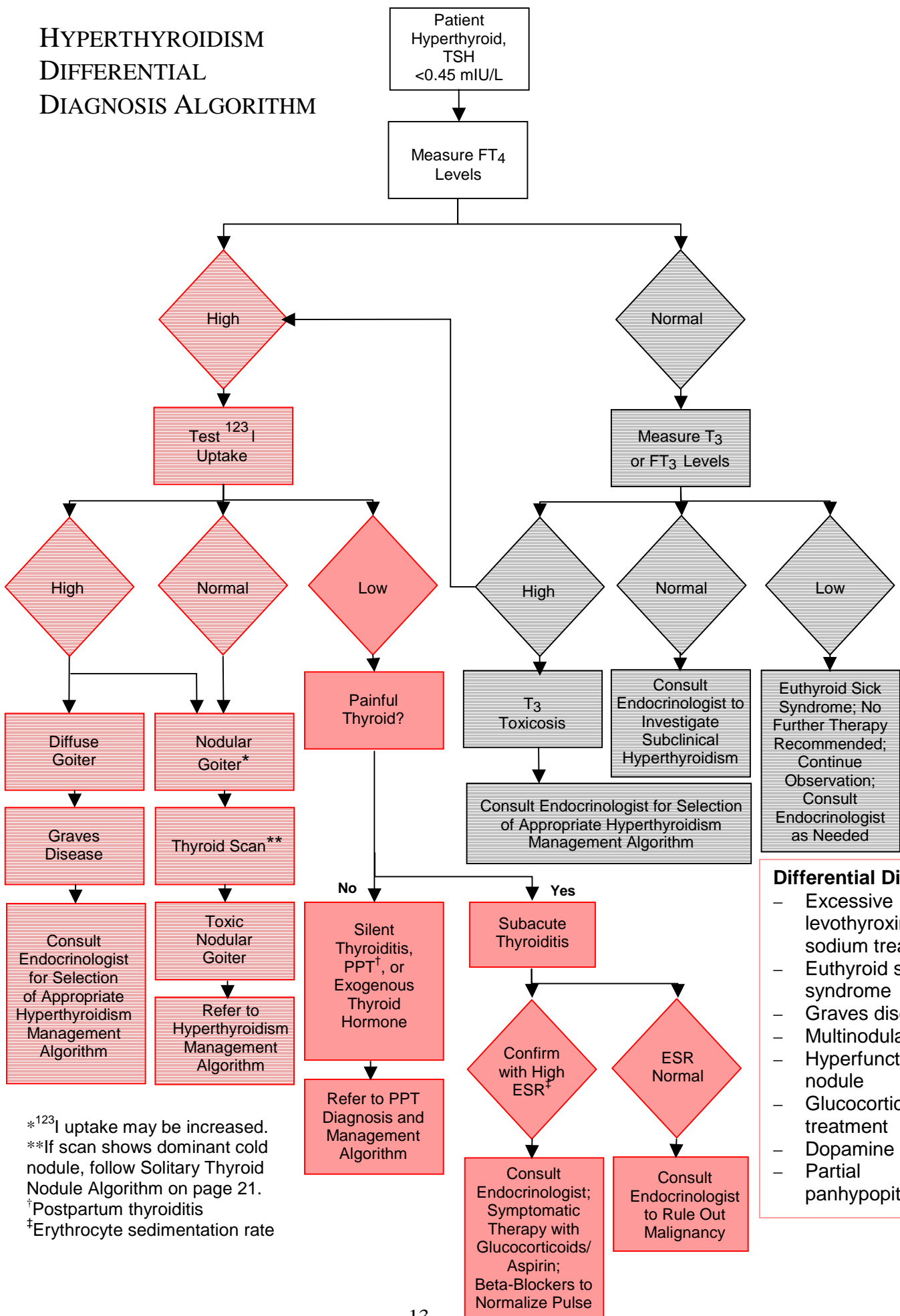
If the FT<sub>4</sub> is normal in a patient with a decreased TSH, a total T<sub>3</sub> (TT<sub>3</sub>) or free T<sub>3</sub> (FT<sub>3</sub>) test may be indicated.<sup>6</sup> A high TT<sub>3</sub> or FT<sub>3</sub> indicates that the patient may have T<sub>3</sub> toxicosis.<sup>2</sup> Patients with subclinical hyperthyroidism may have a normal FT<sub>3</sub>, normal FT<sub>4</sub>, and decreased TSH levels.<sup>1,5</sup> A low FT<sub>3</sub> indicates that the patient may have euthyroid sick syndrome.

If the FT<sub>4</sub> is low in a patient with decreased TSH levels, a brain MRI should be considered to investigate hypothalamic-pituitary disease.

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# HYPERTHYROIDISM DIFFERENTIAL DIAGNOSIS ALGORITHM



\*<sup>123</sup>I uptake may be increased.  
 \*\*If scan shows dominant cold nodule, follow Solitary Thyroid Nodule Algorithm on page 21.  
 †Postpartum thyroiditis  
 ‡Erythrocyte sedimentation rate

- Differential Diagnosis**
- Excessive levothyroxine sodium treatment
  - Euthyroid sick syndrome
  - Graves disease
  - Multinodular goiter
  - Hyperfunctioning nodule
  - Glucocorticoid treatment
  - Dopamine treatment
  - Partial panhypopituitarism

# HYPERTHYROIDISM MANAGEMENT A: $^{131}\text{I}$ THERAPY

## Overview

Radioactive iodine ( $^{131}\text{I}$ ) therapy generally is considered the treatment of choice for Graves disease, especially for patients with recurrent hyperthyroidism after antithyroid drug therapy.<sup>1-5</sup> Radioactive iodine therapy is also used in the management of toxic multinodular goiter and toxic adenoma.<sup>1-4</sup> Because thyroiditis (painful, subacute, or silent) is characterized by a low radioactive iodine uptake and is self-limited, patients with this form of hyperthyroidism should not be treated with antithyroid drugs or  $^{131}\text{I}$  therapy.<sup>1,3</sup> These patients may require symptomatic therapy (eg, beta blockade). An endocrinologist generally should be consulted concerning the management of patients with hyperthyroidism.<sup>1,5</sup>

## Radioactive Iodine Therapy

The goal of  $^{131}\text{I}$  therapy is to destroy enough thyroid tissue to cure hyperthyroidism.<sup>2,3</sup> Radioactive iodine therapy destroys thyroid cells, followed by fibrosis and atrophy, which leads to thyroid failure.<sup>2,4</sup>

For patients 40 years of age or younger with a first episode of hyperthyroidism, some clinicians prefer a trial of an antithyroid drug prior to  $^{131}\text{I}$  therapy (see Hyperthyroidism Management B: Antithyroid Drugs Algorithm).<sup>3</sup> In addition, elderly patients and patients with cardiac disease may require 4 to 8 weeks of antithyroid drugs prior to  $^{131}\text{I}$  therapy to immediately control the hyperthyroidism and to reduce the risk of exacerbation of hyperthyroidism.<sup>1,3,5</sup>

The optimum dosage of  $^{131}\text{I}$  is controversial.<sup>2-4</sup> A high ablative dose more quickly resolves hyperthyroidism, minimizing morbidity associated with the condition.<sup>5</sup> This is used frequently in patients with severe hyperthyroidism, large goiters, and relatively low  $^{123}\text{I}$  uptake.<sup>2,4</sup> Although smaller doses may be used in an attempt to prevent posttreatment hypothyroidism, it is unclear whether this approach effectively decreases the risk and it may increase the failure rate of cure with the first dose.<sup>4,5</sup>

Thyroid function begins to normalize and goiter size decreases in most patients within 6 to 8 weeks following  $^{131}\text{I}$  therapy.<sup>2</sup> A single dose is effective in the majority of patients; a small percentage may require a second or third  $^{131}\text{I}$  dose 6 to 12 months after the initial dose.<sup>2</sup> The principal complication of  $^{131}\text{I}$  therapy is hypothyroidism, which occurs in the majority of patients within 6 to 36 months following therapy.<sup>1,2,4,5</sup>

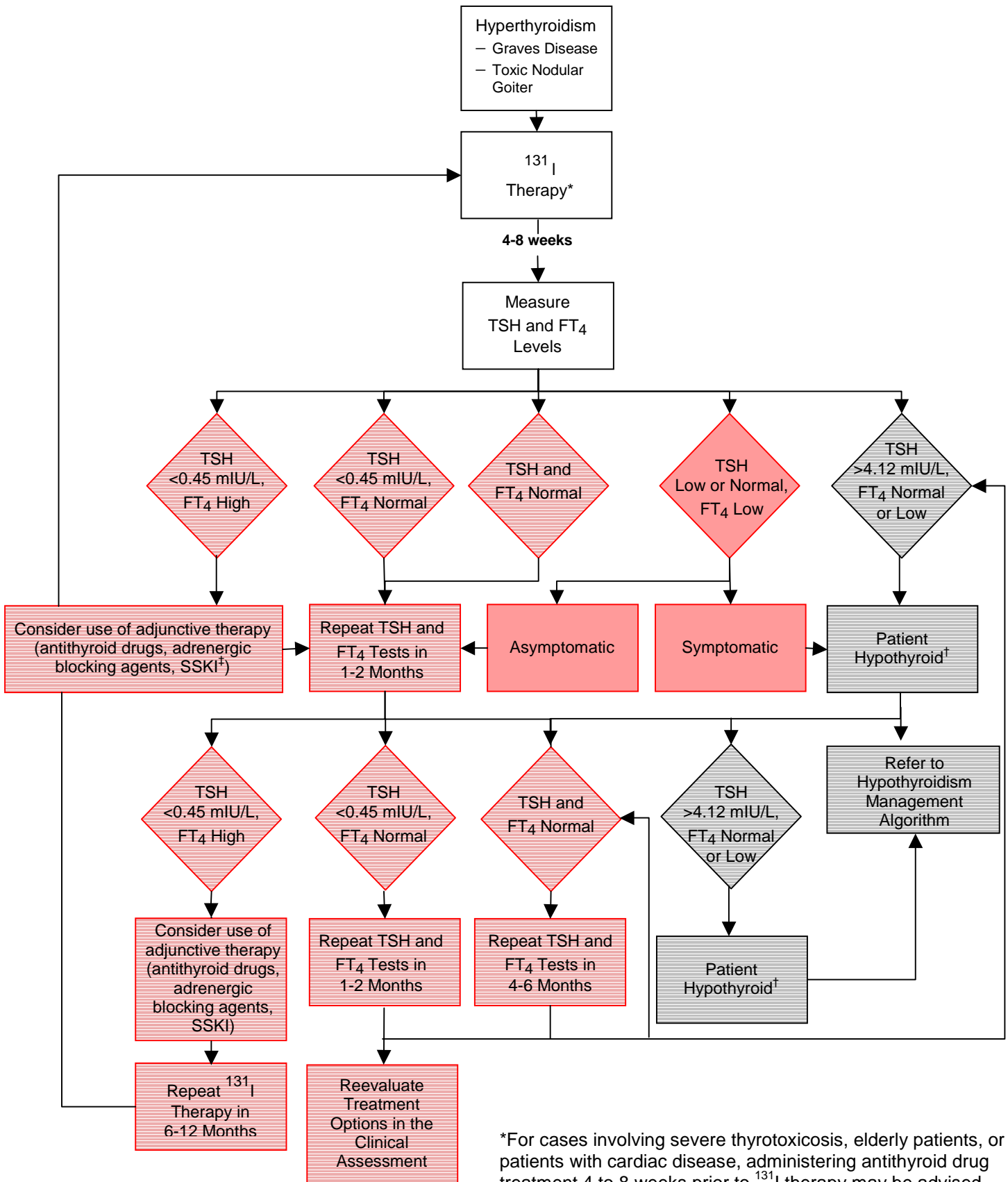
## Follow-Up

Because of the potential for hypothyroidism following  $^{131}\text{I}$  therapy, long-term follow-up is necessary.<sup>4</sup> Patients should be evaluated 4 to 8 weeks after administration of  $^{131}\text{I}$  therapy by monitoring serum thyrotropin (thyroid stimulating hormone, TSH) levels and free thyroxine ( $\text{FT}_4$ ) levels.<sup>1</sup> If thyroid gland failure is indicated by an increased TSH level ( $>4.12$  mIU/L), levothyroxine sodium ( $\text{LT}_4$ ) replacement therapy should be initiated.<sup>1,6</sup> However, early hypothyroidism is only transient in some cases and periodic monitoring of TSH and  $\text{FT}_4$  is recommended in the first post-treatment year to confirm the need for life-long  $\text{LT}_4$  therapy.

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# HYPERTHYROIDISM MANAGEMENT A: <sup>131</sup>I THERAPY ALGORITHM



\*For cases involving severe thyrotoxicosis, elderly patients, or patients with cardiac disease, administering antithyroid drug treatment 4 to 8 weeks prior to <sup>131</sup>I therapy may be advised.  
<sup>†</sup>The most common scenario for any patient prescribed <sup>131</sup>I therapy is hypothyroidism.  
<sup>‡</sup>Saturated solution of potassium iodide

# HYPERTHYROIDISM MANAGEMENT B: ANTITHYROID DRUGS

## Overview

Antithyroid drugs are used in the management of Graves disease, primarily in patients with mild first episodes, children and younger adults, and pregnant women.<sup>1,2</sup> Antithyroid drugs also are used prior to radioactive iodine (<sup>131</sup>I) therapy in the treatment of Graves disease in elderly patients and patients with cardiac disease to immediately control the hyperthyroidism and to reduce the risk of exacerbation of hyperthyroidism.<sup>1,4</sup> Although antithyroid drugs have been used in the management of other forms of hyperthyroidism, including toxic multinodular goiter and toxic adenoma, these uses are generally temporary and they are not the treatment of choice.<sup>1,3,4</sup> Antithyroid drugs are not indicated for the management of thyroiditis.<sup>1,3,4</sup>

## Antithyroid Drug Therapy

Propylthiouracil and methimazole are the antithyroid drugs generally used for management of hyperthyroidism.<sup>1,5</sup> In patients who will subsequently undergo <sup>131</sup>I therapy, methimazole may be preferred because propylthiouracil is associated with a greater propensity for reduced efficacy of ablation. Propylthiouracil may be preferred in severe or life-threatening hyperthyroidism (thyroid storm) because it inhibits the conversion of thyroxine (T<sub>4</sub>) to triiodothyronine (T<sub>3</sub>) and, therefore, may decrease serum T<sub>3</sub> levels more rapidly than methimazole.<sup>3,5</sup>

Antithyroid drugs interfere with thyroid hormone synthesis and some data suggest that they may also have immunologic effects that alter the underlying cause of Graves hyperthyroidism.<sup>1,3-5</sup> A gradual decrease in thyroid hormone levels leads to a euthyroid state. Permanent remissions of hyperthyroidism following withdrawal of antithyroid drugs may occur, although most patients (50% to 80%) have recurrence of the hyperthyroidism.<sup>2,3</sup>

## Follow-Up

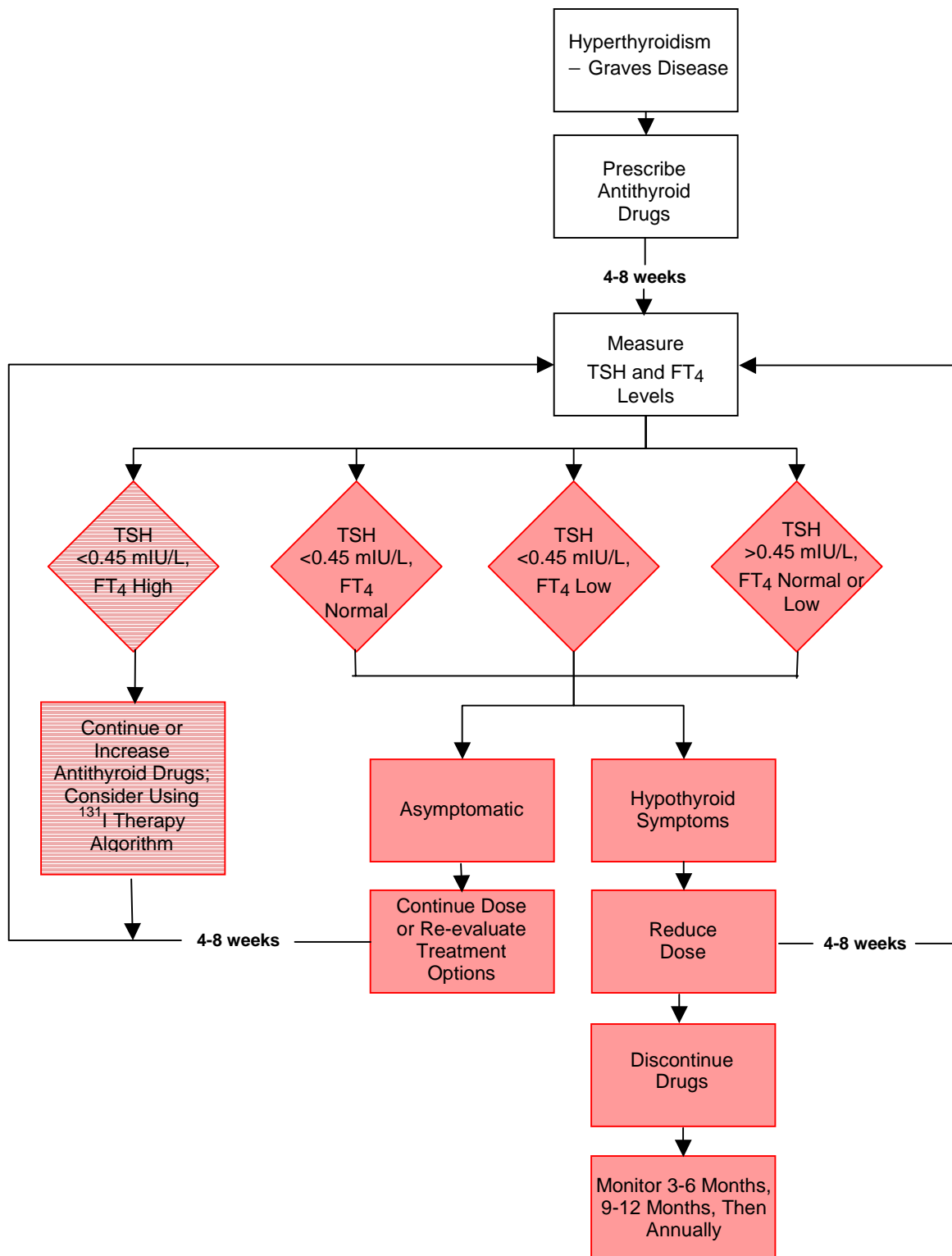
Patients should be monitored and thyroid function evaluated at intervals of 4 to 8 weeks following initiation of antithyroid agent therapy.<sup>1,3,4</sup> Dosage should be adjusted until a maintenance dosage is established that maintains a euthyroid state<sup>1,4</sup>; thyroid function should be evaluated every 3 months thereafter.<sup>1,4</sup> Use of serum thyrotropin (thyroid stimulating hormone, TSH) levels alone to evaluate thyroid function may be misleading; both TSH and free thyroxine (FT<sub>4</sub>) levels should be monitored.<sup>1,4,5</sup>

Optimum duration of antithyroid drug therapy is unclear. Although a few patients may enter remission after only 4-6 months, 1 to 2 years generally is required to decrease the risk of relapse, and longer durations of therapy may be appropriate.<sup>1,3-5</sup> If therapy is discontinued, thyroid function should be monitored every 3 to 6 months, 9 to 12 months, and then annually.<sup>4</sup> Relapse is most likely to occur within the first 3 to 9 months after therapy is discontinued but may occur at any time.<sup>4,5</sup> Because the possibility of delayed relapse or hypothyroidism exists, lifelong follow-up is recommended for all patients.<sup>3</sup>

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# HYPERTHYROIDISM MANAGEMENT B: ANTITHYROID DRUGS ALGORITHM



# GOITER WORKUP

## Overview

Goiter, which is an enlargement of the thyroid gland, may be diffuse or nodular, and may or may not be associated with hypothyroidism or hyperthyroidism.<sup>1-3</sup> Diffuse goiter may result from iodine deficiency, exposure to environmental or pharmacologic goitrogens, or autoimmune processes such as Graves disease or autoimmune thyroiditis (Hashimoto thyroiditis).<sup>1,2,4</sup> Patients with goitrous autoimmune thyroid disorders usually have measurable titers of thyroid autoantibodies and may be euthyroid or hypothyroid.<sup>1,2</sup> Nontoxic goiter is often a precursor to toxic multinodular goiter; the toxic form generally is associated with signs and symptoms of hyperthyroidism.

## Management

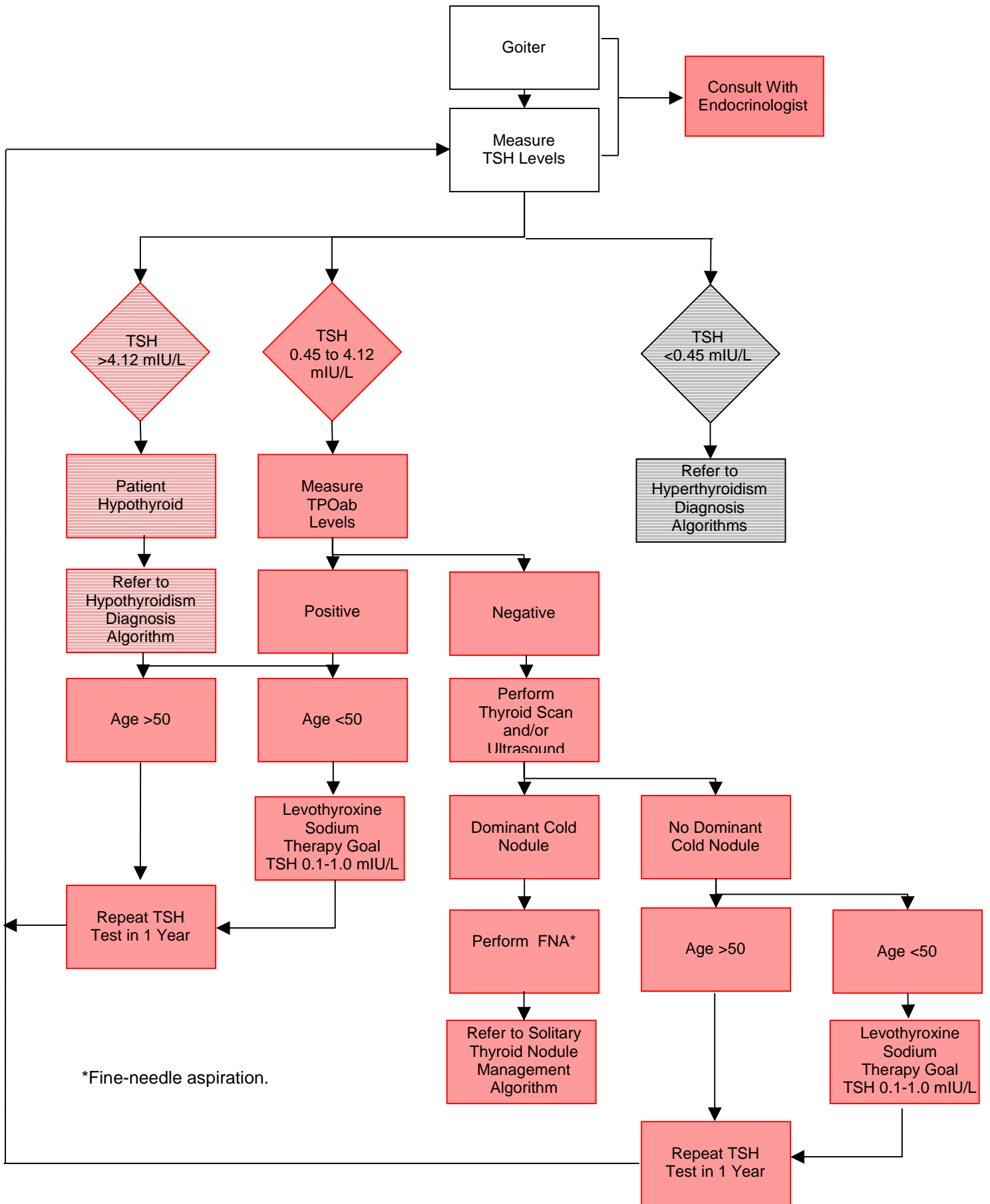
Initial evaluation of goiter includes: a comprehensive physical examination; measurement of serum thyrotropin (thyroid stimulating hormone, TSH) and free thyroxine (FT<sub>4</sub>) levels to determine whether the patient is hypothyroid, euthyroid, or hyperthyroid; testing for thyroid autoantibodies to diagnose autoimmune disorders; and a thyroid scan if nodules are present.<sup>1,3</sup> Diffuse goiter in euthyroid and hypothyroid patients younger than 50 years of age with thyroperoxidase antibodies (TPOab, previously called “antimicrosomal” antibodies) can be treated with levothyroxine sodium.<sup>1-5</sup> The rationale for such therapy is that TSH may act as a cofactor that promotes growth of the thyroid, and effective reduction of TSH levels by levothyroxine sodium may induce regression of nontoxic goiter in some patients.<sup>2-5</sup> The goal of therapy is to maintain TSH levels in the low-normal range (0.1 mIU/L to 1.0 mIU/L).<sup>1</sup> Levothyroxine sodium therapy is not used for the treatment of diffuse goiter in patients with baseline TSH levels <1.0 mIU/L or in patients older than 50 years of age, since efficacy has not been proven and risks of overdosage are more serious. Thyroid stimulating hormone levels should be monitored in patients who do not receive levothyroxine sodium, since increasing levels may indicate progression of the disease to hypothyroidism.<sup>3</sup>

Patients with nodular goiter should have a thyroid scan and/or ultrasound. If nodules greater than 1.0 cm are discovered, the physician should consider performing ultrasound-guided fine-needle aspiration (FNA).<sup>6</sup> Patients younger than 50 years of age with no dominant cold nodule may receive levothyroxine sodium therapy. Nodular goiter responds to levothyroxine sodium therapy less frequently and to a lesser extent than diffuse goiter.<sup>4</sup> If goiter size decreases or remains stable during therapy, levothyroxine sodium therapy generally is continued with periodic monitoring of TSH levels<sup>2</sup>; optimum duration of therapy is not known. In many patients, the thyroid returns to its original size within a few months if therapy is discontinued.<sup>2-4</sup> Prolonged administration of levothyroxine sodium therapy in patients who do not respond to such treatment is not justified.<sup>4</sup>

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# GOITER WORKUP ALGORITHM



# SOLITARY THYROID NODULE

## Overview

Clinically apparent solitary thyroid nodules occur in up to 4% to 7% of the general population and are more common in women than in men.<sup>1</sup> A history of head or neck irradiation is a major risk factor for the development of thyroid nodules and thyroid cancer.<sup>1-3</sup>

## Classification and Management

Thyroid nodules generally are classified as benign (colloid or follicular adenomas), suspicious, or malignant.<sup>1,2</sup> The principal diagnostic tool used is fine-needle aspiration (FNA) for cytology.<sup>1-4</sup> If FNA results indicate that the nodule is malignant or suspicious for malignancy, surgical excision is indicated; the extent of surgery varies depending on factors such as nodule size, location, and the presence of lymph nodes.<sup>1-4</sup>

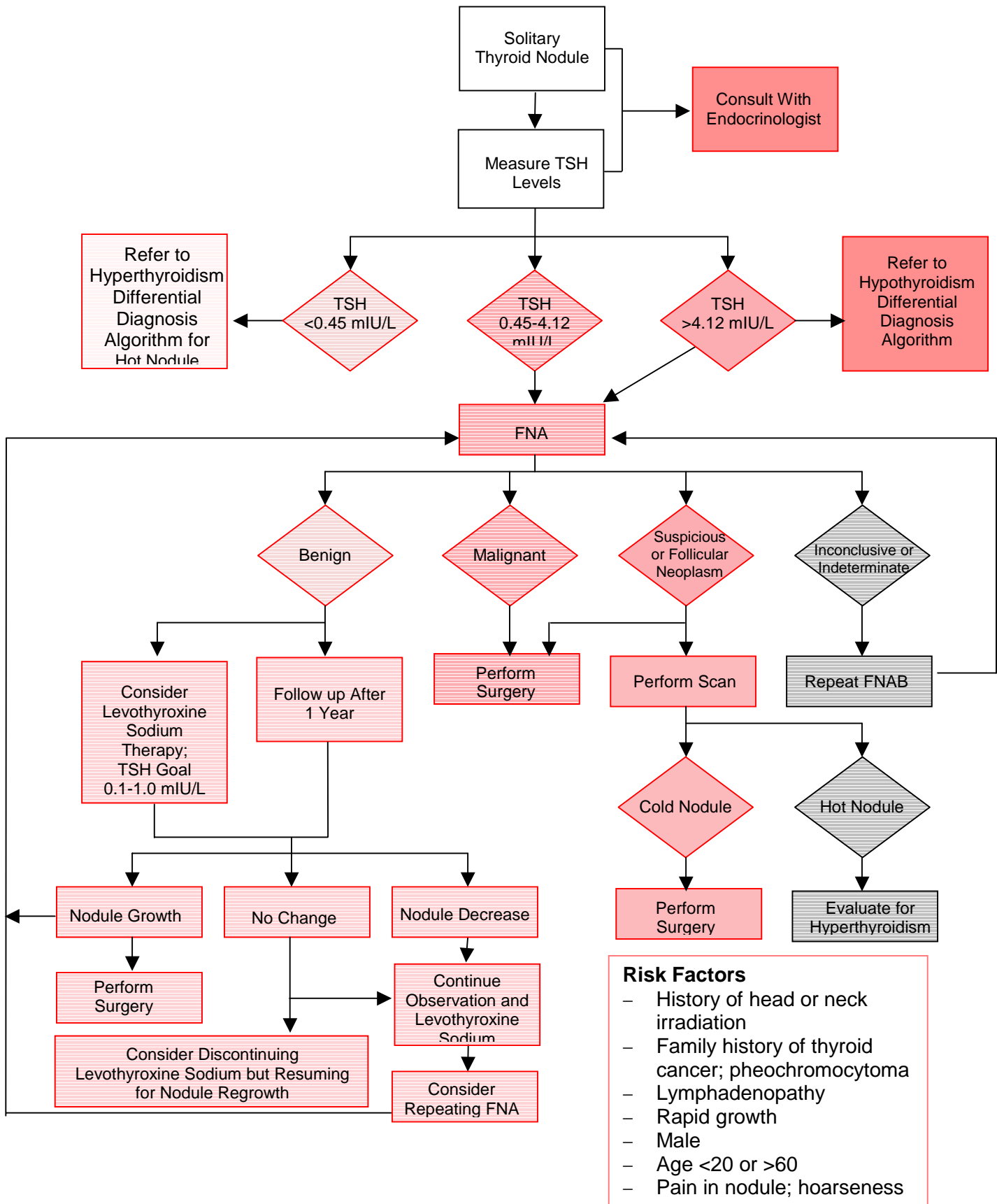
Solitary thyroid nodules identified as benign by FNA generally are managed without surgery unless nodule size or patient concerns indicate excision.<sup>1-4</sup> Levothyroxine sodium (LT<sub>4</sub>) may be used for suppressive therapy of benign nodules, however, the efficacy of LT<sub>4</sub> suppressive therapy is controversial.<sup>4</sup> Because thyrotropin (thyroid stimulating hormone, TSH) may be a contributing factor to nodule formation, suppressive therapy may decrease TSH secretion, reduce nodule size, and prevent further nodule growth.<sup>1-4</sup> Randomized, controlled studies have suggested that only 25% of benign nodules will decrease in size by 50% in response to LT<sub>4</sub> therapy, and it is unclear which patients are most likely to respond.<sup>5,6</sup> If effective, a reduction in nodule size usually is evident during the first 6 to 12 months of therapy.<sup>7</sup> The dosage of levothyroxine sodium used for suppressive therapy ranges from 50 µg to 200 µg daily.<sup>7</sup> The TSH test is used to determine levothyroxine sodium dosage, and the goal is to maintain the TSH in the low-normal range (0.1 mIU/L to 1.0 mIU/L).<sup>1-4,7</sup>

Optimum management of solitary thyroid nodules classified as suspicious by FNA is unclear.<sup>4</sup> Some clinicians recommend surgery for all suspicious solitary thyroid nodules, while a few recommend a trial of levothyroxine sodium suppressive therapy prior to surgery. If results of FNA suggest follicular neoplasm, a thyroid scan can be used to classify the nodule as hyperfunctioning (“hot”) or hypofunctioning (“cold”) depending on its ability to incorporate radioactive isotope.<sup>1-4</sup> Although these scans are not diagnostic, hypofunctioning “cold” nodules have a higher probability of being malignant and are usually managed with surgery.<sup>1-4</sup>

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# SOLITARY THYROID NODULE ALGORITHM



# POSTPARTUM THYROIDITIS DIAGNOSIS AND MANAGEMENT

## Overview

Postpartum thyroiditis (PPT) is a form of transient thyroiditis characterized by the development of hyperthyroidism or hypothyroidism in postpartum women who were euthyroid during pregnancy.<sup>1-6</sup> Postpartum thyroiditis reportedly occurs in 5% to 8% of women, and in up to 25% of women with type 1 diabetes mellitus.<sup>1,2,6</sup> Women with diabetes mellitus or a familial history of autoimmune thyroid disease appear to be at increased risk for PPT (see Risk Factors).<sup>1,3,6</sup>

Patients with PPT may be symptomatic or asymptomatic.<sup>1,3-6</sup> If symptoms develop, they generally are evident within 6 months of delivery; however, they can occur as early as 1 month or as late as 1 year after delivery.<sup>1,3,6</sup> Postpartum thyroiditis is considered to be an autoimmune disorder, and thyroid autoantibodies, including thyroperoxidase antibodies (TPOab), are elevated in a high percentage of patients with PPT.<sup>1,3,6</sup> It may be of benefit to measure these antibodies in all pregnant women in order to identify patients at risk for PPT.\*

## Testing and Test Interpretation

Diagnosis of PPT involves serum thyrotropin (thyroid stimulating hormone, TSH) testing and measurement of TPOab levels; free thyroxine (FT<sub>4</sub>) levels are used as an adjunctive test to confirm that the patient is either hypothyroid or hyperthyroid.<sup>4,6</sup> An endocrinologist generally should be consulted if results of TSH and FT<sub>4</sub> testing indicate hyperthyroidism, subclinical hyperthyroidism, hypothyroidism, or subclinical hypothyroidism (mild thyroid failure) in a postpartum patient.

## Management

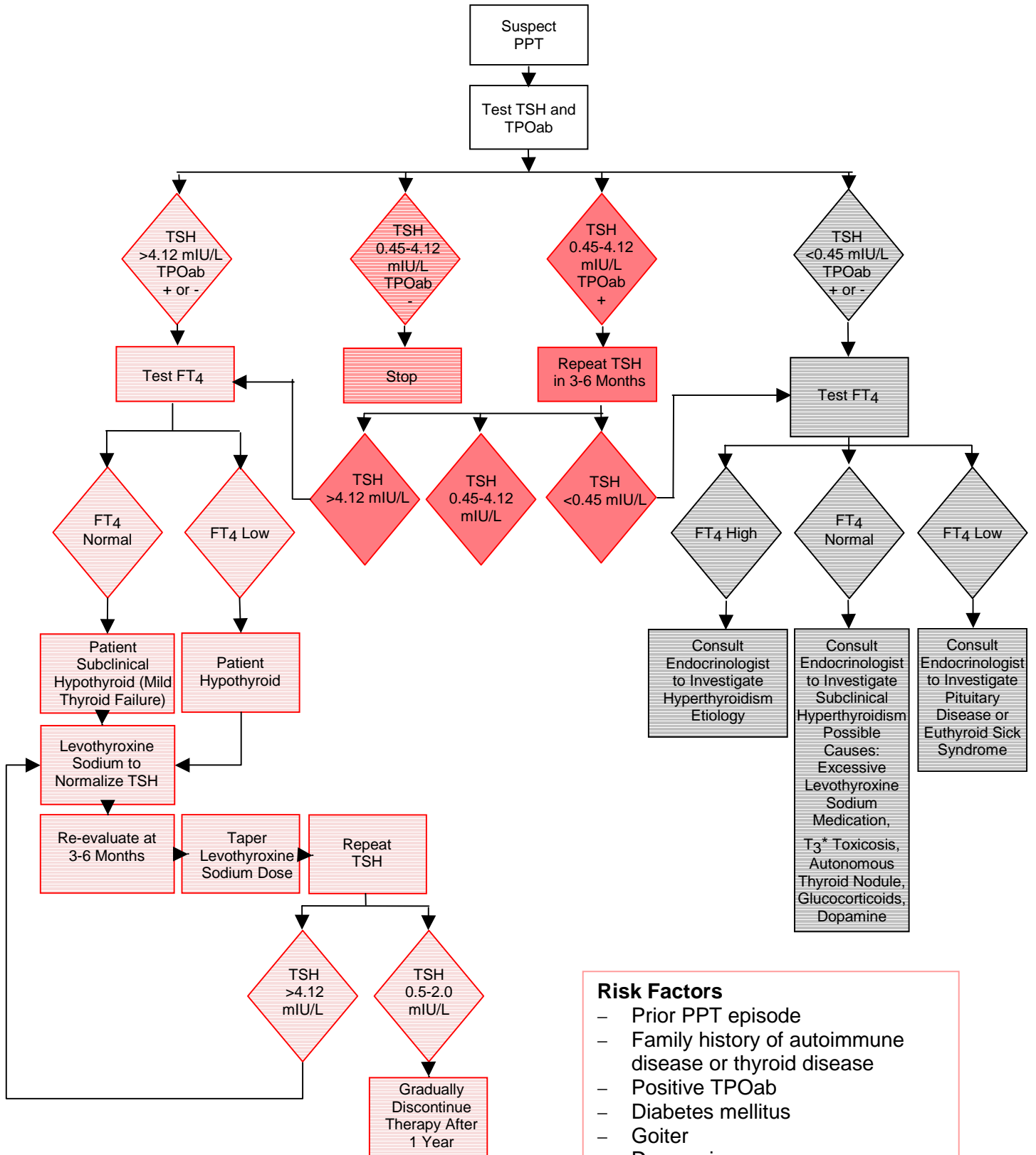
Levothyroxine sodium is used as replacement therapy for the management of PPT in patients who have clinical or subclinical hypothyroidism (mild thyroid failure); the dosage is adjusted based on TSH levels.<sup>5,6</sup> A serum TSH level between 0.5 mIU/L and 2.0 mIU/L is generally considered the optimal therapeutic target for levothyroxine sodium therapy.<sup>7</sup> After several months of therapy, dosage of levothyroxine sodium should be decreased and TSH levels tested to determine whether the patient has returned to a euthyroid state.<sup>6</sup> Most women with PPT return to the euthyroid state within 1 year of delivery, although up to 25% develop permanent primary hypothyroidism.<sup>4-6</sup> Women who develop PPT following pregnancy are at risk for recurrence following subsequent pregnancies.<sup>4</sup>

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\* Ten percent of women will have positive anti-TPO antibodies with normal TSH levels. Fifty percent or more of women with positive anti-TPO antibodies will develop PPT.

# POSTPARTUM THYROIDITIS DIAGNOSIS AND MANAGEMENT ALGORITHM



\*Triiodothyronine

## Risk Factors

- Prior PPT episode
- Family history of autoimmune disease or thyroid disease
- Positive TPOab
- Diabetes mellitus
- Goiter
- Depression
- Signs and symptoms of thyroid disease