

## Thyroid Disease

### Purpose

To identify and promote the most important contributors to improved clinical outcomes for thyroid disease.

### Key Recommendations

- Consider patients for evaluation for hypothyroidism and hyperthyroidism every 5 years as part of a physical or health maintenance visit.
- Order TSH for patients with signs, symptoms, or other indications of hypothyroidism. Order Free T4 for those with pituitary disease, brain injury or in the first trimester of pregnancy.
- Order TSH for suspected hyperthyroidism and confirm elevated FT4 and/or FT3.
- Become familiar with the key points about thyroid nodules.

### High Risk Populations/Disparities

- Women of Jewish descent are nearly two times more likely than other women to have thyroid disease caused by an overactive immune system.<sup>1</sup>
- Among patients with thyroid cancer, blacks have lower survival rates at five years than do whites. A study of a large cancer database found that blacks are 2.3 times more likely to get the most aggressive form of thyroid cancer (anaplastic). Also, thyroid tumors more often are larger and found at a later stage in blacks.<sup>1</sup>
- In the National Health and Nutrition Examination Survey (NHANES), among individuals with no thyroid disease, hypothyroidism and hyperthyroidism was significantly higher in females than males.<sup>2</sup>
- BMI is positively associated with thyroid cancer risk in both men and women. The risk of thyroid cancer was 1.89 and 1.39 times higher in obese subjects (**BMI**≥30) than in normal weight subjects in males and females respectively.

# Thyroid Disease

## **Identification of Thyroid Disease**

Patients should be considered for evaluation for hyperthyroidism and hypothyroidism every 5 years as part of a physical or health maintenance visit.

### **Case Finding:**

- Order TSH for patients with signs, symptoms, or other indications of hypo- or hyperthyroidism.
- Other indications, patients:
  - with autoimmune diseases (e.g. Type 1 diabetes mellitus, B12 deficiency, pernicious anemia, Addison’s disease, and collagen-vascular diseases)
  - with previous thyroid injury (exposure to radiation, excess iodine)
  - with previous thyroid surgery or thyroid function abnormality
- when patient is undergoing treatment with interferon for hepatitis C perform baseline testing before treatment and every 3 months during treatment
- when patient is undergoing treatment with amiodarone or lithium perform baseline testing before treatment and every 3 months during treatment

### **Testing:**

- TSH is the best choice except in rare cases
- TSH + FT4 for patients with secondary diagnosis of thyroid disease and other CNS diseases, including brain injury

**Refer to endocrinologist if results of tests confusing**

## **Identification of Thyroid Disease for Pregnant Women and Those Planning Pregnancy:**

- At initial interview, ask questions to identify potential thyroid problems and test as appropriate. Factors to be considered in case finding:
- Those with autoimmune diseases often associated with thyroid disease, such as type 1 diabetes and pernicious anemia
- Patients with a prior history of thyroid disease or thyroid surgery, an abnormal thyroid exam, or taking drugs known to affect the thyroid
- Patients with a family history of thyroid illness or history of miscarriage
- When testing needed, trimester-specific cut-off values of TSH and T4 should be used for diagnosis of hyper- or hypothyroidism during pregnancy instead of the usual values for non-pregnant individuals.
- This is necessary since in the first trimester HCG mimics TSH and leads to suppressed TSH even when patient euthyroid
- Second/third trimester perform TSH except when thyroid disease is secondary diagnosis (cause is hypothalamic or pituitary)

## **Treatment of Pregnant Women with Thyroid Disease**

- Pregnant women who have hypothyroidism and those on thyroxine, test on regular basis (see above) during pregnancy, treat appropriately
- Thyroid nodules can and should be evaluated, follow up as necessary with obstetrician/gynecologist, surgeon & endocrinologist working together
- Imaging (ultrasound) may be ordered, as indicated, **radioisotope studies should not be done**

## **Hyperthyroidism with pregnancy**

## **Key Points about Hypothyroidism**

- Signs and symptoms of hypothyroidism: decrease in metabolic rate, tiredness, lethargy, sensitivity to cold, menstrual disturbances, goiter, hyperlipidemia
- **For most patients, TSH is the test of choice** for screening and monitoring of hypothyroidism
- Numerous drugs/diseases can alter T4 & T3 levels
- TSH is *not* the test of choice for those with pituitary disease, brain injury or in first trimester of pregnancy
- What is normal TSH (within the reference range) depends largely on individual

## **Key Points about Hyperthyroidism**

- TSH the best diagnostic test for hyperthyroidism
- Asymptomatic patients over age 50 with suppressed TSH (less than 0.1) at risk for atrial fibrillation
- Confirmation of elevated FT4 and/or FT3 required after screening with a TSH
- Workup should include iodine uptake and scan to define etiology of hyperthyroidism
- Review treatment options with patient and family

## **Key Points about Thyroid Nodule (TN) Evaluation**

- Rule of FIVE: 5% of your overall patient population will have palpable TNs, 5% of all palpable TNs are malignant
- Rule of ACTIVITY: Most nodules that are hyperactive are benign (extremely rare exceptions)

### **Refer to Endocrinologist**

- RISK FACTORS for malignancy:
    - A PALPABLE nodule
    - Age < 20 or >60
    - M>F
    - History of radiation exposure
    - Familial history of thyroid cancer
    - Progressive growth on oral T-4
  - Ultrasound characteristics of TN causing concern:
    - Microcalcifications
    - Hypoechoogenicity
    - Intranodule vascularity
    - Irregular nodule margins
    - Nodule > 10mm
  - There is no strong evidence that treatment of euthyroid patients with thyroid hormone will shrink benign thyroid nodules.
  - Evaluate further if patient has normal or elevated TSH
  - Evaluate all palpable nodules
- See endocrinologist for any nodule with above risk factors or concerning

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- Gestational hyperthyroidism is the most common cause of hyperthyroidism in pregnancy (1%–3%). It is characterized by transient hyperthyroidism limited to the first half of pregnancy in the absence of serum markers of thyroid autoimmunity. It may present by hyperemesis gravidarum.
- Management of gestational hyperthyroidism depends upon the severity of symptoms. Generally, anti-thyroid medications are not required.
- Hyperthyroidism due to Grave’s disease requires treatment during pregnancy.
- Uncontrolled hyperthyroidism in pregnancy is associated with an increased risk of miscarriages, pre-eclampsia, prematurity, low birth weight, intrauterine growth restriction, stillbirth, thyroid storm, and maternal congestive heart failure.
- Propylthiouracil is recommended for the treatment of maternal hyperthyroidism through 16 weeks of pregnancy then switch to methimazole
- In all cases of hyperthyroidism, measurement of serum TSH receptor antibody around 24–28 weeks is advised for the detection of pregnancies at risk of fetal hyperthyroidism.
- Breastfeeding is safe in mothers taking anti- thyroid in moderate doses.
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### Hypothyroidism with pregnancy

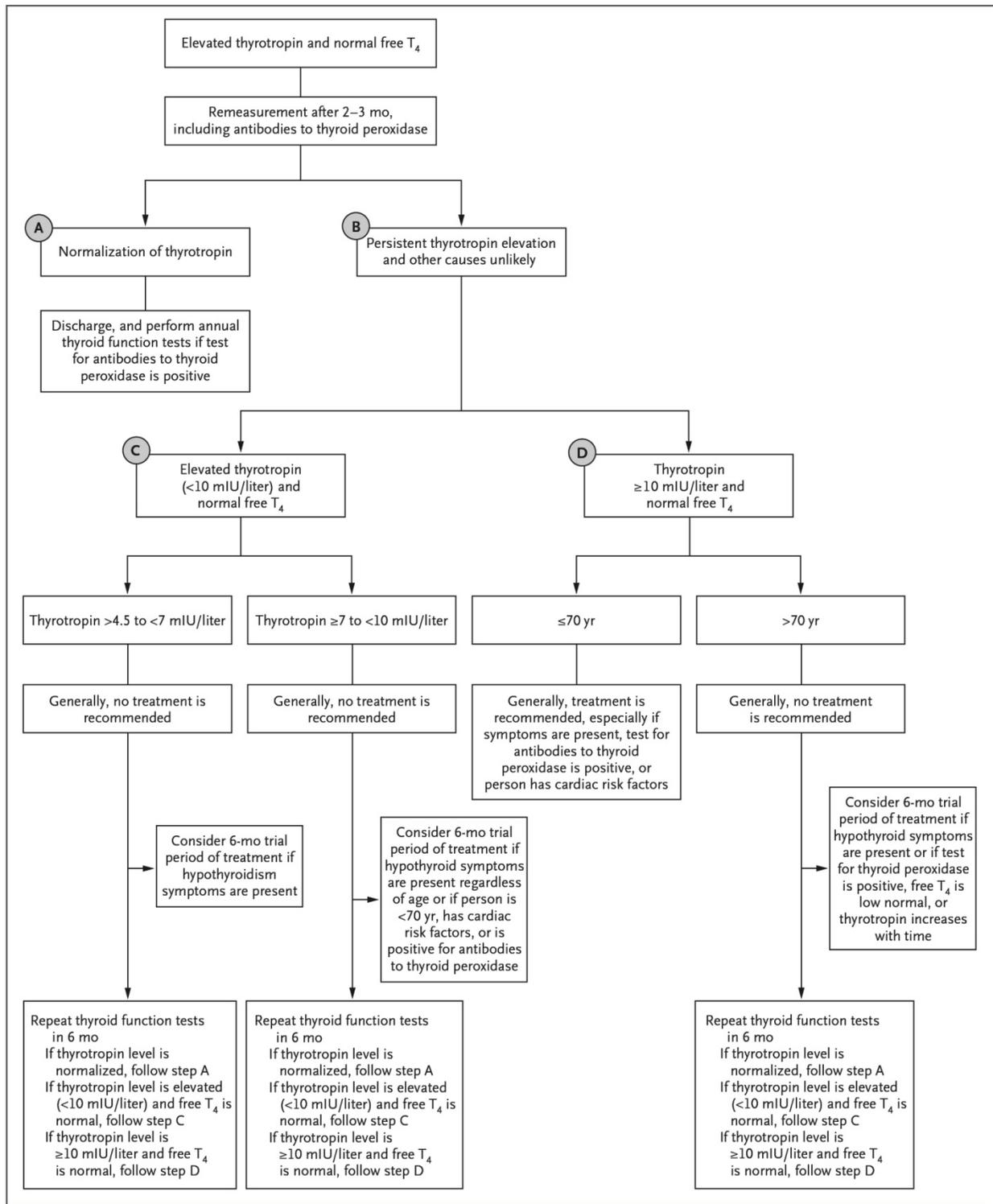
- Untreated clinical hypothyroidism is associated with an increased risk of premature birth, preeclampsia, low birth weight, and miscarriage.
- Pregnancy is a state with increased thyroid hormone requirements.
- Checking a TSH and free T4 levels every trimester and 4-6 weeks after each dose adjustment is recommended.
- Thyroid hormone supplementation doses should be adjusted to achieve a free T4 value at the upper end of the normal range and a TSH at goal (< 2.5 in the first trimester, < 3.0 in second / third trimesters).
- The pre-pregnancy dose should be resumed in the immediate postpartum period and hormone levels should be rechecked 6-8 weeks postpartum.
- There is no evidence that screening and treatment of subclinical hypothyroidism improves maternal or fetal outcomes.

### Hypothyroidism

Hypothyroidism is a syndrome that results from inadequate levels of thyroid hormone (T-4 and/or T-3). It is manifested by a set of symptoms, physical findings, and laboratory tests.

See pages 3-5 for algorithms on diagnosis and treatment of hypothyroidism and hyperthyroidism and thyroid nodule

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**Figure 1. Treatment Algorithm for Subclinical Hypothyroidism.**

This algorithm does not apply to pregnant women or to young women who may potentially seek pregnancy and is based on current U.S. and European guidelines.<sup>26,27</sup> However, the U.S. guidelines do not make an explicit distinction according to age, and neither guideline specifies differential management according to the degree of thyrotropin elevation below 10 mIU per liter.

*There are special considerations from pregnancy, both testing and replacement.*

From New England Journal of Medicine, Robin P. Peeters, M.D., Ph.D., Subclinical Hypothyroidism, Volume No. 376, Page No. 2561. Copyright © 2017 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

*Guidelines are intended to be flexible. They serve as reference points or recommendations, not rigid criteria. Guidelines should be followed in most cases, but there is an understanding that, depending on the patient, the setting, the circumstances, or other factors, care can and should be tailored to fit individual needs.*

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### Thyroid Nodule Evaluation

Thyroid nodule <1cm, repeat in 1 yr. Consider fine needle aspiration (FNA) if nodule demonstrates listed characteristics of concern.

#### Thyroid Nodule (TN) Evaluation

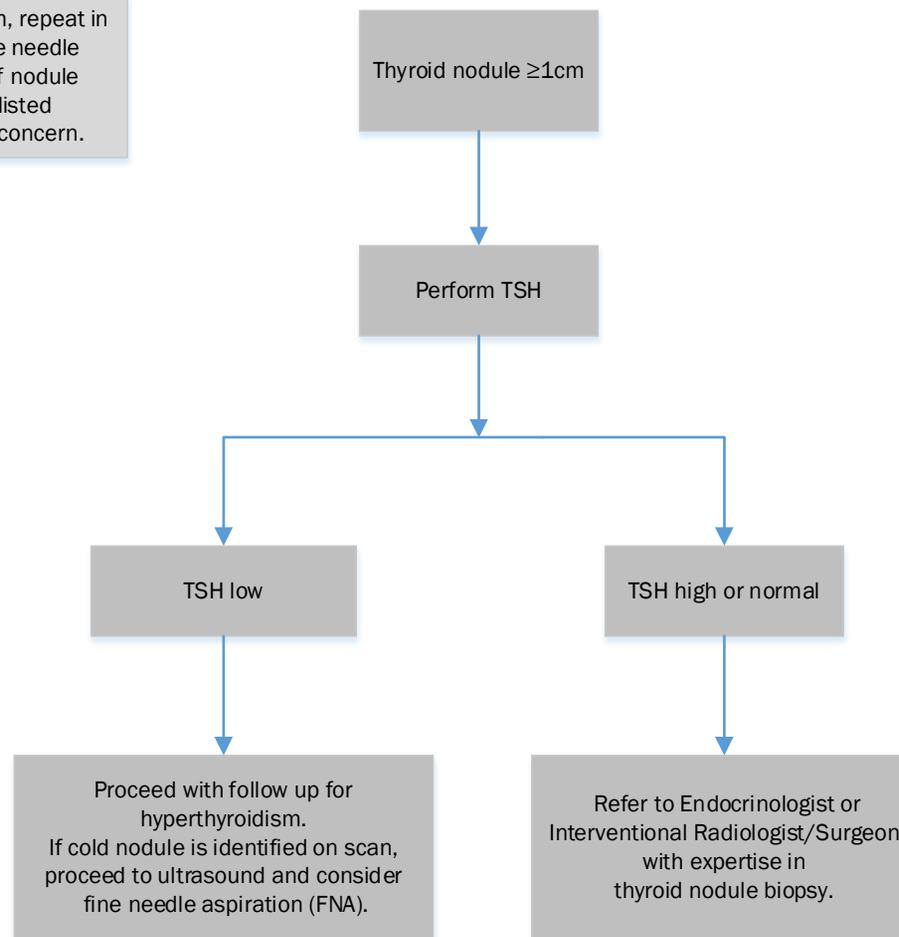
1. Rule of FIVE: 5% of your overall patient population will have palpable TNs. 5% of all palpable TNs are malignant.
2. Rule of ACTIVITY: All nodules (extremely rare exceptions) that are hyperactive are benign.
3. RISK FACTORS for malignancy:
  - A palpable nodule
  - Age <20 or >60
  - M > F
  - History of radiation exposure
  - Familial history of thyroid cancer
  - Progressive growth on oral T-4

Ultrasound characteristics that cause concern with thyroid nodules:

1. Microcalcifications
2. Hypochoogenicity
3. Intranodule vascularity
4. Irregular nodule margins
5. Nodule >10mm

#### NOTES:

- Evaluate further if patient has normal or elevated TSH.
- All palpable nodules should be evaluated.
- Nodule <1cm with abnormal ultrasound features and multinodular goiters, consider endocrine evaluation.



## Thyroid Disease

### Summary of Recommendations for Thyroid Testing from National Organizations

Organization	Core Recommendation	Recommendation – Pregnant Women
<a href="#">American Academy of Family Physicians</a>	Evidence is insufficient to recommend for or against routine screening for thyroid disease in adults. <i>(Clinical Considerations: <a href="http://www.aafp.org/patient-care/clinical-recommendations/all/thyroid.html">http://www.aafp.org/patient-care/clinical-recommendations/all/thyroid.html</a>)</i>	
<a href="#">American Association of Clinical Endocrinologists (AACE) and American Thyroid Association (ATA) Taskforce on Hypothyroidism in Adults</a>	AACE recommends routine TSH measurement in older patients – age not specified – especially women. ATA recommends screening at age 35 yrs and every 5 yrs thereafter. <i>(Jeffrey R. Garber, Rhoda H. Cobin, Hossein Gharib, James V. Hennessey, Irwin Klein, Jeffrey I. Mechanick, Rachel Pessah-Pollack, Peter A. Singer, and Kenneth A. Woeber for the American Association of Clinical Endocrinologists and American Thyroid Association Taskforce on Hypothyroidism in Adults. Thyroid. December 2012, 22(12): 1200-1235. doi:10.1089/thy.2012.0205)</i>	It remains unclear if screening for hypothyroidism in pregnancy is beneficial. A consensus statement in 2004 and clinical practice guidelines in 2007 and 2011 found insufficient data to support a 1999 and 2005 recommendation for universal screening for thyroid dysfunction during pregnancy, but rather recommended aggressive case finding. <i>(Jeffrey R. Garber, Rhoda H. Cobin, Hossein Gharib, James V. Hennessey, Irwin Klein, Jeffrey I. Mechanick, Rachel Pessah-Pollack, Peter A. Singer, and Kenneth A. Woeber for the American Association of Clinical Endocrinologists and American Thyroid Association Taskforce on Hypothyroidism in Adults. Thyroid. December 2012, 22(12): 1200-1235. doi:10.1089/thy.2012.0205)</i>
<a href="#">American College of Obstetrics and Gynecologists</a>		Thyroid testing is not a routine part of prenatal care and should be limited to women with symptoms of thyroid disease and those with a history of thyroid disease or other medical conditions associated with it, such as diabetes. <i>(Committee Opinion #381, Subclinical Hypothyroidism in Pregnancy, Obstetrics &amp; Gynecology. October 2007. Practice Bulletin Number 148: Thyroid disease in pregnancy, April 2015. Obstet Gynecol. 2015;125: 996–1005 - recommendation to not perform routine screening for thyroid disease in pregnancy has not changed.)</i>
<a href="#">The Endocrine Society</a>		The committee could not reach agreement regarding screening recommendations for all newly pregnant women. 1) Some members recommended screening of all pregnant women for serum TSH abnormalities by the ninth week or at the time of their first visit. 2) Some members recommended neither for nor against universal screening of all pregnant women for TSH abnormalities at the time of their first visit. These members strongly support aggressive case finding to identify and test high-risk women (Table 1) for elevated TSH concentrations by the ninth week or at the time of their first visit before and during pregnancy. <i>(Abalovich M, Alexander EK, Amino N, Barbour L, Cobin RH, De Groot L, et.al. Management of Thyroid Dysfunction during Pregnancy and Postpartum: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab, August 2012, 97(8):2543–2565.)</i>
<a href="#">United States Preventive Services Task Force</a>	Current evidence is insufficient to assess the balance of benefits and harms of screening for thyroid dysfunction in nonpregnant, asymptomatic adults. <i>(Released March 2015.)</i>	

Guidelines are intended to be flexible. They serve as reference points or recommendations, not rigid criteria. Guidelines should be followed in most cases, but there is an understanding that, depending on the patient, the setting, the circumstances, or other factors, care can and should be tailored to fit individual needs.



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### Resources for Patients

#### **American Thyroid Association**

- [Patients and Public – Thyroid Information](#) - Provides up-to-date online information for thyroid patients and their families and [free patient brochures about thyroid disease](#).
- [Complementary and Alternative Medicine \(CAM\)](#) - Provides information about thyroid disease and CAM, reviews types of CAM and stresses importance of patient's talking to their physician before taking CAM.

#### **Hormone Health Network**

Provides online information about hypothyroidism, hyperthyroidism, thyroid nodules, and thyroid disorder symptoms.

#### **National Institute of Diabetes, Digestive and Kidney Diseases**

Provides online information about thyroid and testing physicians may order.

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