

# **Hypothyroidism: General**

## **Background**

1. Definitions
  - Hypothyroidism
    - Clinical state marked by diminished production of thyroid hormone<sup>1</sup>
  - Subclinical hypothyroidism<sup>2</sup>
    - Slightly elevated TSH (5-10 mU/L) w/ nml free T4 & T3; symptomatic or mild Sx
2. Physiology
  - Hypothalamus secretes TRH → stimulates antr pituitary
  - Pituitary secretes TRH → stimulates antr pituitary
  - Thyroid hormones influence diverse metabolic processes
3. Guidelines
  - American Assn of Clinical Endocrinologists' Medical Guidelines for Clinical Practice for the Evaluation and Treatment of Hyper- and Hypothyroidism:  
<http://www.aace.com/pub/guidelines>
4. See also subclinical hypothyroidism

## **Pathophysiology**

1. Primary hypothyroidism
  - 95% of cases primary process in thyroid<sup>2</sup>
  - High TSH, low T4 & T3
  - Pathology<sup>2</sup>
    - Hashimoto's thyroiditis (most common cause)
      - Also known as chronic lymphocytic thyroiditis
      - Autoimmune process
        - Antibodies to thyroid peroxidase in 90% of pts
        - Antibodies to thyroglobulin in 80% of pts
  - Iatrogenic (second most common cause)<sup>2</sup>
    - Radioactive iodine Tx
    - Antithyroid drugs (propylthiouracil [PTU], methimazole)
    - Surgical removal of gland
    - Other meds
      - Lithium
      - Amiodarone
      - Interferon
    - Radiation of head & neck
  - Infiltrative dz of thyroid (less common)<sup>2</sup>
    - Sarcoid
    - Amyloid
    - Lymphoma
  - Hypothyroid phase of thyroiditis
    - Acute
    - Subacute
    - Silent<sup>2</sup>

2. Secondary hypothyroidism
  - 5% of cases<sup>2</sup>
  - Pituitary or hypothalamic process
    - Neoplasm
    - Pituitary necrosis
    - Congenital hypopituitarism
  - Low TSH, low T4 & T3
3. Myxedema<sup>1</sup>
  - Hypothyroid state w/hard edema of subcutaneous tissues and more severe Sx of hypothyroidism
4. Myxedema coma
  - Medical emergency precipitated by stress / trauma<sup>1</sup>
5. Incidence/ prevalence<sup>2</sup>
  - 0.3-0.4% of adults<sup>3</sup>
    - 4% subclinical hypothyroidism (TSH > 4.5milliunits/L; normal T4)
  - 0.5% of pregnancies
  - 2-3% of older women affected
6. Risk factors
  - Age: prevalence incr w/ age
  - Gender: women > men
  - Postpartum state
  - Hx of radiation therapy to head or neck
  - HIV infection
7. Comorbid autoimmune disorders<sup>2</sup>
  - Addison's dz
  - Diabetes mellitus
  - Pernicious anemia
  - Rheumatoid arthritis
  - Vitiligo
  - SLE
8. Assoc conditions
  - Mitral valve prolapse
  - Hypogonadism
  - Hyperlipidemia
9. Morbidity/ mortality
  - Myxedema coma
    - Hypothermia
    - Hypoglycemia
    - Hypoventilation
    - Stuporous state
    - 50-75% mortality
  - Cardiac complications
    - Heart failure
    - Pericardial effusion
    - Bradycardia
    - Hypertension

## **Diagnostics**

### 1. History

- Symptoms
  - Fatigue, lethargy
  - Apathy, decr mood
  - Dry skin
  - Cold intolerance
  - Hair loss
  - Impaired memory
  - Constipation
  - Wt gain
  - Muscle weakness, cramps
  - Dyspnea
  - Hoarseness
  - Menstrual irregularities
    - Menorrhagia
    - DUB
  - Pretibial or facial edema
- Other findings
  - Hyperlipidemia<sup>4</sup>
  - Hyponatremia<sup>5</sup>

### 2. Physical exam

- HEENT
  - Puffy face/eyelids
- Neck
  - Goiter, nodules
- Cardiac
  - Bradycardia
  - Cardiomegaly
  - Pericardial effusion
- Skin
  - Dry
  - Coarse hair
  - Pretibial non-pitting edema
- Reflexes
  - Delayed relaxation of DTRs

### 3. Diagnostic testing

- Labs
  - TSH
    - Elevated
    - Preferred test for initial evaluation of primary hypothyroidism
    - If abnormal, check free T4
  - Free T4
    - Low

- T3
    - Check T3 if TSH undetectable and free T4 nml
    - T3 often normal even if pt severely hypothyroid<sup>6</sup>
- Additional labs (optional)
  - TPOAb, thyroglobulin, and TRAb
    - Three principal thyroid antibodies
    - Can be pos in variety of autoimmune thyroid disorders
- Imaging<sup>1</sup>
  - No U/S or radioactive iodine uptake (RAIU) test indicated unless nodule present
    - If nodule present, consider U/S or RAIU, possible FNA

### Differential Diagnosis

1. Many common disorders have overlapping Sx w/hypothyroidism
  - Anemia
  - Alzheimer's dz
  - Chronic fatigue syndrome
  - Rheumatologic dz
  - Depression
2. TSH assay will establish Dx

### Therapeutics

See also subclinical hypothyroidism, severe hypothyroidism (myxedema)

1. Levothyroxine
  - Full replacement dose for adult: 1.6 mcg/kg/d<sup>1</sup>
  - Usual starting dose for adult < 50 yo: 75 mcg/d
  - Use lower dose if elderly or heart dz
    - Start w/ 12.5-50 mcg/d<sup>1</sup>
  - Use same brand throughout Tx<sup>1</sup>
  - Drug interaction<sup>7</sup>
    - Decr absorption of levothyroxine if on
      - Cholestyramine
      - Iron
      - Sucralfate
      - Calcium
      - Antacids w/aluminum hydroxide
      - Caffeine
      - Fiber supplement
    - Incr metabolism of levothyroxine if on
      - Rifampin
      - Phenobarbital
      - Carbamazepine
      - Warfarin
      - Oral hypoglycemic agents
      - Phenytoin
      - Estrogen

## Special Populations

1. Elderly
  - Full replacement dose of levothyroxine: 1 mcg/kg/d<sup>1</sup>
  - Initial Tx w/ 25-50 mcg/d, incr gradually<sup>1</sup>
2. Pregnancy
  - Must treat preg women w/hypothyroidism to prevent maternal & fetal complications
  - Check TSH every 6 wks during pregnancy<sup>1</sup>
  - Adjust levothyroxine PRN (dose requirement may incr)
    - 30% incr suggested at confirmation of pregnancy
  - Return to prepregnancy dose postpartum
3. Children
  - May require up to 4 mcg/kg/d of levothyroxine<sup>1</sup>
  - Refer to endocrinologist<sup>1</sup>

## Follow-up

1. Return to office in 6-8 wks to check TSH / adjust levothyroxine dose
2. Once TSH normal, annual levels<sup>6</sup>
3. More freq monitoring if
  - Pregnant
  - Using estrogen
  - Sig wt loss/gain
  - Return of clinical Sx
4. If TSH not normalizing, consider noncompliance
5. Refer to specialist
  - Nodule
  - Goiter
  - Age < 18 yo
  - Pregnant<sup>8</sup>
  - Not responding to Tx
  - Cardiac pt
  - Endocrine disorder
6. Admit to hospital if myxedema coma
  - Consider IV thyroid hormone replacement

## Prognosis

1. Life-long thyroid hormone replacement typically required
2. Subclinical hypothyroidism - 40% progression to hypothyroidism

## Prevention / Screening

1. Not enough evidence for or against screening<sup>9</sup>
2. Newborns routinely screened<sup>10</sup>

## Evidence-Based Inquiries

1. How should thyroid replacement be initiated?
2. Should we screen women for hypothyroidism?

3. Which lab tests are best when you suspect hypothyroidism?
4. How useful are autoantibodies in diagnosing thyroid disorders?
5. How often should you follow up on a patient with newly diagnosed hypothyroidism?

## References

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**Authors:** Tricia Hern, MD, Samer Homisha, MD, & Michele Larzelere, MD, *LSU FMRP-Kenner, LA*

**Editor:** Vince WinklerPrins, MD, *Georgetown University-Providence Hospital, Washington DC*