Hypothyroidism: General

Background

1. Definitions
    - Hypothyroidism:
        - Clinical state marked by diminished production of thyroid hormone
    - Subclinical hypothyroidism
        - 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 sn 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
    - High TSH, low T4 & T3
    - Pathology
        - 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)
        - 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)
        - Sarcoid
        - Amyloid
        - Lymphoma
    - Hypothyroid phase of thyroiditis
        - Acute
        - Subacute

        - Silent
2. Secondary hypothyroidism
    - 5% of cases
    - Pituitary or hypothalamic process
        - Neoplasm
        - Pituitary necrosis
        - Congenital hypopituitarism
    - Low TSH, low T4 & T3
3. Myxedema
    - Hypothyroid state w/ hard edema of subcutaneous tissues and more severe Sx of hypothyroidism
4. Myxedema coma
    - Medical emergency precipitated by stress / trauma
5. Incidence & prevalence
    - 0.3-0.4% of adults
        - 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
    - 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
        - Hyponatremia
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 nml even if pt severely hypothyroid
- Addl labs (optional)
    - TPOAb, thyroglobulin, and TRAb
        - Three principal thyroid antibodies
        - Can be pos in variety of autoimmune thyroid disorders
- Imaging
    - 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
    - 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
    - Use same brand throughout Tx
    - Drug interactions [7]
        - 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
    - Initial Tx w/ 25-50 mcg/d, incr gradually
2. Pregnancy
    - Must treat preg women w/ hypothyroidism to prevent maternal & fetal complications
    - Check TSH every 6 wk during pregnancy
    - 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
    - Refer to endocrinologist

Follow-up

1. Return to office in 6-8 wk to check TSH / adjust levothyroxine dose
2. Once TSH nml, annual levels
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
    - 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
2. Newborns routinely screened

References

1. AACE Thyroid Task Force. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the evaluation and treatment of hyper- and hypothyroidism. 2006 amended version. http://www.aace.com/pub/pdf/guidelines/hypo_hyper.pdf. Accessed May 20, 2010.
2. Hueston W. Treatment of hypothyroidism. Am Fam Physician. 2001;64(10):1717-24 [Erratum: 2002 Jun 15;65(12):2438. Comment: 2002 Jun 1;65(11):2212; author reply 2212, 2214.]
3. Hollowell JG, Staehling NW, Flanders WD, et al. Serum TSH, T4, and thyroid antibodies in the United States population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III). J Clin Endocrinol Metab 2002;87:489-99.
4. Diekman T, Lansberg PJ, Kastelein JJ, Wiersinga WM. Prevalence and correction of hypothyroidism in a large cohort of patients referred for dyslipidemia. Arch Intern Med 1995;155:1490-5.
5. Khaleeli AA; Gohil K; McPhail G; Round JM; Edwards RH. Muscle morphology and metabolism in hypothyroid myopathy: effects of treatment. J Clin Pathol 1983;36:519-26.
6. Vaidya B, Pearce SHS. Management of hypothyroidism in adults. BMJ 2008;337:a801.
7. Woeber K. Update on the management of hyperthyroidism and hypothyroidism. Arch Fam Med. 2000;9:743-7.
8. The Endocrine Society. Management of thyroid dysfunction during pregnancy and postpartum: an Endocrine Society clinical practice guideline. Chevy Chase. MD: Author, 2007 [See FDA's boxed warning for Propylthiouracil, 2010 Apr 21, http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm164162.htm].
9. Screening for thyroid disease: recommendation statement. U.S. Preventive Services Task Force. Ann Intern Med. 2004;140:125-7.
10. American Academy of Pediatrics; Rose SR; Section on Endocrinology and Committee on Genetics, American Thyroid Association, et al. Update of newborn screening and therapy for congenital hypothyroidism. Pediatrics. 2006;117:2290-303

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