Thyroid Disorders

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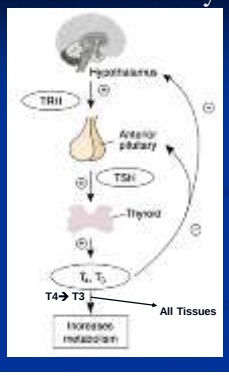
Disclosures

- Nothing to disclose

Overview
Thyroid Disorders

- Hypothyroidism
- Hyperthyroidism
- Thyroiditis
- Goiter & Thyroid nodules
- Thyroid Cancer

Hypothalamic –Pituitary- Thyroid Axis



TRH –Thyrotropin Releasing Hormone

TSH - Thyroid Stimulating Hormone

T4 conversion to biologically active T3 via deiodination

http://m.osce-aid.co.uk/

Hypothyroidism

Subclinical Hypothyroidism

- Elevated TSH but normal thyroid hormone (T4)
- Generally no symptoms but sometimes hypothyroid symptoms present
- Associated with hypercholesterolemia
- Associated with CHF
- Associated with an increased risk of CHD events and CHD mortality in those with higher TSH levels, particularly in those with a TSH concentration of 10 mIU/L or greater

Hypothyroidism

- Elevated TSH AND low thyroid hormone (T4)

JAMA. 2010;304(12):1365-1374. doi:10.1001/jama.2010.1361.

Hypothyroidism Symptoms

- Fatigue and weakness
- Dry skin
- Cold Intolerance
- Hair loss
- Difficulty in concentrating and poor memory
- Constipation
- Weight gain
- Hoarse voice
- Menorrhagia
- Paresthesias
- Impaired healing
- Water retention
- Carpal Tunnel Syndrome

Hypothyroidism Signs

- Dry skin, cool extremities
- Puffy face, hands and feet
- Delayed tendon reflex relaxation
- Bradycardia
- Diffuse alopecia
  - Scalp
  - Eyebrows
- Effusions (pleural, pericardial, ascites)
- Altered Mental Status
- Hypothermia
- Hyponatremia

Causes of Hypothyroidism

- Autoimmune hypothyroidism (Hashimoto's)
- Iatrogenic (I_{123}treatment, thyroidectomy, external irradiation of the neck)
- Aging
- Iodine deficiency
- Drugs: iodine excess, lithium, antithyroid drugs, amiodarone, nitroprusside, sulfonylureas, thalidomide, lithium, perchlorate, and interferon-alpha therapy, tyrosine kinase inhibitors (TKIs)
- Infiltrative disorders of the thyroid: amyloidosis, sarcoidosis

Evaluation of Hypothyroidism

- TSH ↑, free T4 ↓ = Hypothyroidism
  - **HIGH TSH indicates hypothyroidism (TSH > 4.0)**
  - TSH 0.35 – 4.0 normal range
- TSH ↑, free T4 normal = Subclinical Hypothyroidism
- Ultrasound of thyroid – not helpful
- Thyroid scintigraphy scan– non indicated (do not order)
- Anti thyroid antibodies – anti-TPO
- CBC: Normochromic or macrocytic anemia
- ECG: Bradycardia with small QRS complexes

Treatment of Hypothyroidism

- No serious side effects using therapeutic doses
  - Hair loss, dyspepsia, dry skin, brain fog ?
- Typical full replacement doses are 1.6mcg/kg
  - 50-150 mcg for most people
  - Dose adjustments for weight changes, estrogen use, pregnancy, menopause
- Monitor TSH, adjust q 6 weeks until stable then q 6-12 months
  - Start slowly in elderly or if underlying CAD
  - Goal TSH 1-2
- Advise patient to take thyroid hormone in the morning, empty stomach, 1 hour before eating. Take only with water. Keep coffee 1 hour away from thyroid hormone. Keep calcium, MVI, iron 4 hours away from thyroid hormone

Subclinical Hypothyroidism

- Definition: elevated TSH, normal Free T4
- Prevalence: 3-8% of the population
  - Increases with age and higher in women
  - 80% of patients have thyroperoxidase antibody
- Associations:
  - Progression to overt hypothyroidism
  - Hypercholesterolemia, systemic symptoms, psychiatric symptoms, cardiac disease all questionable
  - Higher TSH associated with CHD and Mortality

Mayo Clin Proc. 2009 Jan; 84(1): 65–71.

Subclinical Hypothyroidism: When To Treat?

- Controversial
- Consider in the following conditions:
  - Hyperlipidemia
  - Goiter/Nodules present
  - Infertility (miscarriage)
  - Symptoms compatible with hypothyroidism
  - Depression or Cognitive dysfunction
  - Ovulatory dysfunction
  - Anti-Thyroperoxidase antibody positive
- Planning pregnancy
- If TSH > 10 μU/mL

Mayo Clin Proc. 2009 Jan; 84(1): 65–71.

SwiftyPoll.com Question # 1

Hyperthyroidism

Subclinical Hyperthyroidism
Low TSH, normal Free T4

Hyperthyroidism
Low TSH and high Free T4

Usually asymptomatic

Can have mild hyperthyroid symptoms

Associated with increased risks of total, CHD mortality, and incident AF, with highest risks of CHD mortality and AF when thyrotropin level is lower than 0.10 mIU/L

Arch Intern Med. 2012 May 28;172(10):799-809

Hyperthyroidism

Antibody Stimulated
(Graves Disease)
Thyroid Stimulating Immunoglobulin (TSI) +

Subacute Thyroiditis
(acute inflammation)
Viral or antibody mediated
Post-Partum Thyroiditis

Toxic Nodule
(multiple toxic nodules)

Other Causes
HCG mediated (pregnancy)
Struma Ovarii
Factitious

Hyperthyroidism Symptoms

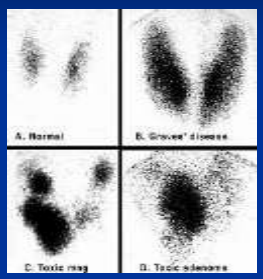
- Irritability
- Anxiety
- Heat intolerance and sweating
- Palpitations
- Fatigue and weakness
- Weight loss with increase of appetite
- Diarrhea
- Oligomenorrhea or Amenorrhea
- Hair loss

Hyperthyroidism Signs

- Tachycardia (AF)
- Tremor
- Goiter (firm rubbery)
  - Bruit over goiter
- Warm moist skin
- Proximal muscle weakness
- Lid retraction or lid lag
- Gynecomastia
- Thyroiditis - tender thyroid gland
- Graves – proptosis, scleral edema, scleral injection, periorbital edema

Diagnosis of Hyperthyroidism

Nuclear thyroid scintigraphy (I_{123})



- TSH ↓, free T4 ↑
- Thyroid auto antibodies
  - TPO (Thyroperoxidase Ab)
  - TSI (Thyroid Stimulating Immunoglobulin)

Treatment of Hyperthyroidism

- RAI (radioactive iodine 131)
- Thyroidectomy
- Thionamides
  - PTU 50mg – 100mg bid - qid dosing
    - Preferred in 1st trimester of pregnancy
    - Inhibits thyroid hormone release and T4 to T3 conversion
    - Bitter Taste
  - Methimazole 5-20mg daily or bid dosing
    - Aplasia Cutis birth defect reported
    - Inhibits thyroid hormone release

Treatment of Hyperthyroidism

- Beta-blockers
  - Propranolol
    - Preferred: can block T4 to T3 conversion
    - 10-40mg BID-QID dosing, depending on HR and BP
  - Atenolol/Metoprolol
    - Daily or BID dosing
- Side Effects
  - Thionamides: Agranulocytosis (1/300-1/500), bleeding, rash, liver inflammation (alt and alk phos elevation), liver failure

Thyroid Storm

- Presentation: fever, tachycardia, atrial fibrillation, heart failure, tremor, nausea and vomiting, diarrhea, dehydration, extreme agitation, delirium or coma
- Precipitating factors: Infections. MI, stroke, congestive heart failure, trauma, non-thyroid surgery in a hyperthyroid patient, thyroid surgery in a patient poorly prepared for surgery, radioiodine therapy, recent use of iodinated contrast

Thyroid Storm: Management

- Scoring System
- Treatment
  - PTU
  - Betablockers (propranolol)
  - IV glucocorticoids
  - SSKI drops
  - IVF hydration
  - Plasmapheresis

Thyroid Storm. Endotext.org, Leslie J De Groot, MD, Luigi Bartalena, MD, and Kenneth R Feingold, MD., December 17, 2018.

Subclinical Hyperthyroidism

- Definition: Low TSH, normal Free T4
- Prevalence:
  - 0.5-15%
  - Increases with age
  - Commonly seen in first trimester of pregnancy
- Associations:
  - CVD, osteoporosis, atrial fibrillation
  - Cognitive dysfunction and hypercoaguability
  - 5% progression to hyperthyroidism per year

Int J Endocrinol Metab. 2012 Spring; 10(2): 490–496.

Subclinical Hyperthyroidism When To Treat?

- Elderly (> 65) with TSH < 0.1 μU/mL
- Osteoporosis
- CVD disease
- Atrial Fibrillation
- Symptomatic
- Weight loss

Int J Endocrinol Metab. 2012 Spring; 10(2): 490–496.

Sick Euthyroid Syndrome

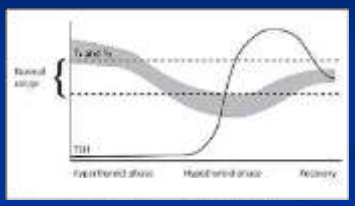
- Protective Mechanism?
- Severe Stressor
  - Infection (PNA, sepsis, MI)
  - Emotional Stressor ?
  - Interleukins, TNF-alpha, cortisol
- What's Happening?
  - TRH –Thyrotropin Releasing Hormone inhibition
    - Low normal TSH early on then rebound later
  - Inhibition of conversion of T4→ T3
    - T4 low or normal, T3 low
  - Shunting of T3 to reverse T3 (inactive)
    - Reverse T3 high

SwiftyPoll.com Question # 3

Thyroiditis

- Acute: due to suppurative infection of the thyroid
- Subacute: also termed de Quervains thyroiditis/ granulomatous thyroiditis – mostly viral origin
- Silent thyroiditis: no pain, related to post partum and antibody mediated
- Riedel's thyroiditis: chronic sclerosing replacement of the entire gland affecting nearby structures –extremely rare
- Chronic lymphocytic thyroiditis: autoimmune (Hashimoto's) – hypothyroidism
- Radiation Induced
- Medication Induced: INF, Amiodarone

Clinical Course of Sub Acute Thyroiditis



Hyperthyroid phase: lasts 1-3 months
Hypothyroid phase: lasts 9-12 months
Euthyroid phase: in 12-18 months

Management of Thyroiditis

- Hashimoto's
  - Treat with thyroid hormone if hypothyroid
- Silent
  - Monitor
- Sub Acute
  - Monitor
  - NSAID
  - Glucocorticoids
  - Thyroid hormone if hypothyroid

Goiter

- Enlarged thyroid gland
  - Iodine deficiency
  - Autoimmune mediated (check thyroperoxidase antibody)
  - Caused by to multiple nodules
  - Common in pregnancy (hcg mediated)
  - Medication related
    - Lithium
  - Management:
    - Nothing to do if asymptomatic
      - For large goiter may check for airway compression
      - PFT with flow volume loops
      - CT soft tissue of neck
    - Treat with thyroid hormone if hypothyroid

SwiftyPoll.com Question # 2

Thyroid Nodules

- Very Common
  - Incidence is high
  - About same as decade of life
  - 60% of sixty year olds will have a thyroid nodule
- Usually found incidentally on neck or chest imaging or physical exam
- <5% are malignant
- Toxic nodules are rarely malignant
- Ultrasound is best imaging for thyroid nodule
- Nuclear medicine scan not indicated unless patient is hyperthyroid

Thyroid Nodules

- Biopsy if greater than 1-2 cm in size
- Monitor if smaller than 1 cm with ultrasound
  - 1 year initially
  - 2-3 years if stable
- Concerning ultrasound characteristics
  - Microcalcifications
  - Hypoechoic or irregular border
  - Hypervascularity
  - Large size

2015 American Thyroid Association Management, Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer

The American Thyroid Association Guidelines Task Force, Thyroid Nodules and Differentiated Thyroid Cancer

Thyroid Cancer

- Papillary and Follicular – 90-95% of a cancers
  - > 98% 5 year survival
- Papillary (most common)
  - Intranuclear inclusions, psammoma bodies, papillary structures
  - Easily identifiable on FNA
  - Local spread (lymph nodes) common
  - Rarely metastastic – Lung
  - Excellent Prognosis for early stages and age < 55
- Follicular
  - Cell architecture similar to normal cells
  - Identified by capsular, vascular invasion
  - Rarely metastatic – Bone, Lung, LNs
  - Excellent Prognosis for early stages

Thyroid Cancer

- Medullary Thyroid Cancer
  - Parafollicular C-Cells Origin
  - Not very responsive to Radioactive Iodine
  - Spreads to nearby lymph nodes
  - Main treatment is surgical, follow calcitonin
  - Overall good long-term prognosis
- Anaplastic Thyroid Cancer – Undifferentiated thyroid cancers
  - Extremely poor prognosis
    - Median Survival of 6 months
  - Rapidly growing
  - Locally invasive (fat, trachea, esophagus, larynx)
  - Not responsive to RAI or external beam
  - Chemo – not very responsive
  - Newer agents - TKI, MKI (kinase inhibitors)

Thyroid Cancer

- Usually asymptomatic
- Found on exam or imaging modality for another purpose
- Ultrasound Characteristics
- Diagnosed by FNA biopsy of a thyroid nodule or biopsy of a lymph node
  - Simple office technique, small gauge needle, ultrasound guided
- Molecular marker testing for abnormal cytology
  - Testing for common mutations in thyroid cancer

Thyroid Cancer Management

- Surgery (total thyroidectomy, lymph node dissection)
- Radioactive Iodine 131 after surgery
- Thyroid hormone suppression
  - Low TSH prevents thyroid cancer growth
- Tyrosine Kinase Inhibitor therapy - rare
- Monitoring
  - Thyroglobulin
  - TSH suppression
  - Imaging (ultrasound, CT scans, PET scans, Nuclear Medicine Scans)

Conclusion

- Hypothyroidism, symptoms and signs and management
- Hyperthyroidism, symptoms and signs and management
- Thyroiditis, types and clinical course
- Goiter-Thyroid nodules
- Thyroid Cancer, types and management