Introduction

- Basic Science
- Diagnostic Issues
- Hypothyroidism
- Thyrotoxicosis
- Thyroiditis
- Interactive Case Presentation
- Controversies/New Areas of Interest
Introduction

- Nonneoplastic diseases of the thyroid affect nearly 3/4 of a billion worldwide
  - iodine deficiency common worldwide
  - iodine excess common in US
    - contribution to autoimmune diseases
- Thyroid surgery is the most common neck surgery performed by the Otolaryngologist
The thyroid is located on the anterior superior portion of the trachea near the third tracheal ring.

Arterial supply is from superior and inferior thyroid arteries.

Venous drainage from three paired thyroid veins: superior, middle, inferior.

RLN runs with inferior thyroid artery, SLN with the superior thyroid artery.
Basic Science - Histology

- Functional unit of thyroid gland is the thyroid follicle
  - cuboidal epithelial cells surrounding colloid filled lumen
  - active follicles are smaller
  - responsible for thyroid hormone synthesis

- Parafollicular “C” Cells ("Clear" cells)
  - secrete calcitonin
  - respond to serum ionized calcium levels
Basic Science - Embryology

- Thyroid gland is derived from invagination of endoderm of first branchial pouch near lingual bud
- Grows inferiorly around the hyoid to anterior trachea
  - remnant is thyroglossal duct
  - foramen cecum is remnant
- Aberrent thyroid tissue can be located anywhere along thyroglossal duct
Parafollicular Cells are of different origin than thyroid follicular cells:
- these cells originate from ultimobranchial apparatus near inferior portion of pharyngeal pouch
- ultimobranchial organ seen in lower vertebrates as a separate organ
Primary function of the thyroid gland is the secretion of thyroid hormones

- T4 is primary released hormone
- T3 at least 10 times more active
- T4 is converted to T3 peripherally

Production of thyroid hormones is regulated in normal gland by thyroid stimulating hormone (TSH) from the anterior pituitary gland
Basic Science - Physiology

- T4 and T3 act as negative feedback to the release of TSH
  - TSH response is “logarithmic”

- TSH is stimulated by thyroid releasing hormone (TRH) of the hypothalamus
  - TRH is believed to be continually secreted
  - Pituitary gland is more sensitive to negative feedback of T4 and T3 than TRH
Basic Science - Physiology

- Thyroid Hormone Secretion:
  - TSH joins follicular cell receptor, then:
  - cAMP mediates:
    - active transport of iodide
    - synthesis of thyroglobulin (TG) by ER
  - Thyroperoxidase (TPO) mediates:
    - conversion of iodide to iodine
    - coupling of iodine to tyrosine and TG (colloid)
  - Lysosomes release T4/T3
Diagnostic Issues

- No accurate test measures peripheral thyroid hormone action
- TSH, serum T4, free T4 index, T3 and RAIU are most commonly used tests
  - TSH: most useful test. Sensitive to T4/T3
  - Measures total T4. Most protein bound!
  - FT4I: \textit{mathematically estimates} FT4
  - RAIU: I123 scan. Measures activity of gland
Antimicrosomal and antithyroglobulin antibodies are seen in 90% of pts with Hashimoto’s Thyroiditis
- also seen with increasing age and nonthyroid diseases

TSH Receptor Antibodies are seen with Graves’ Disease
- may be stimulatory or competitive inhibitors
Hypothyroidism

- Physical Exam
  - Mild/Moderate Disease
    - Lethargy, hoarseness, hearing loss, thick and dry skin, constipation, cold intolerance, stiff gate
  - Sever Disease (Myxedema Coma)
    - Coma, refractory hypothermia, bradycardia, pleural effusions, electrolyte imbalances, hypoventilation, seizures
      - Tx: IV steroids, T4, ventilatory support, thermal support, antiseizure medications
Hypothyroidism

- Primary: abnormalities of the gland
- Secondary: abnormalities of the pituitary gland
- Tertiary: abnormalities of the hypothalamus (rare)
- Peripheral: end organ resistance
  - $c$-erb A gene of chromosomes 17 and 3 code for cellular hormone receptors
Hypothyroidism - Primary

- Autoimmune Diseases are the most common cause of hypothyroidism
  - Hashimoto’s Thyroiditis
  - Graves’ disease (usually hyperthyroidism)
  - Iodide excess (spina bifida, renal failure)

- Iatrogenic causes are the next most common causes
  - Surgery, radioiodine ablation, inadequate replacement, Li, Amiodarone, iodide
Hypothyroidism - Congenital

- **Cretinism**
  - severe hypothyroidism in the newborn
  - **PE:** protuberant abdomen, face, flat nose, yellow skin, constipation, lethargy, feeding difficulties, hoarse, MR
  - **Endemic:** goiter present. Maternal IgG or maternal antithyroid medications
  - **Sporadic:** thyroid agenesis (Di George syndrome most common)
Juvenile Hypothyroidism

- Usually due to hormonal synthesis defect such as TPO or to $c\text{-}erb\ A$ mutation
- PE: goiter, delayed maturation, testicular enlargement/precocious menarche
- NOT usually MR- recovery is general rule with thyroxine
Thyrotoxicosis

- **Defn:** state where exposed tissue responds to an excess of T4/T3
- **PE:** nervousness, tremors, sweating, heat intolerance, palpitations, afib, wt loss, amenorrhea, weakness
- **Etiologies:**
  - Graves’ disease most common
    - toxic multi and uninodular goiters, carcinoma and pituitary abnormalities
Thyrotoxicosis - Graves’ Dz

- Graves’ Disease
  - Autoimmune: IgG antibodies against TSH receptors. May be stimulatory (most common) or inhibitory
    - often similar to Hashimoto’s Thyroiditis, particularly when hypothyroidism present
  - Soft goiter usually present
  - Histology: “too many follicular cells, too little colloid”
Graves’ Disease - Continued

- **Treatment**
  - antithyroid medications, RAI, surgery
  - **Antithyroid medications**
    - **Iodide**: transient. Inhibits organification, proteolysis, angiogenesis
      - thyrotoxicosis in euthyroid Graves’ disease!
    - **Thionamides**: propothyouracil, methimazole
      - TPO inhibitor, peripheral T4 conversion to T3
      - Require 4-8 to work
    - **Beta blockers**: block peripheral conversion, ameliorates adrenergic side effects.
Graves’ Disease, Continued

- Radioiodine ablation
  - Most commonly used procedure in US
  - Indicated when medical therapy fails or in patients unable/unwilling to take meds
  - PTU/Iodide usually used pre-ablation as less dose is required
  - Must stop PTU/Iodide 3 days prior to avoid thyroid storm
Graves’ Disease, Continued

- Total/Subtotal Thyroidectomy
  - Less commonly used than RAI, but many feel it is the procedure of choice
  - Always procedure of choice in pregnant women requiring surgery
  - PTU/beta blockers required preoperatively to avoid thyroid storm
Toxic Adenoma

- Caused by a “Hot Nodule”
  - thyroxicosis may be caused by hot nodule, but not all hot nodules cause thyrotoxicosis
    - those larger than 3 cm usually required
  - Dx: low/absent TSH, high T4, RAIU: hot nodule
  - Tx: RAI ablation versus surgery
Toxic Multinodular Goiter

- Common in areas of iodide deficiency
- Dx: multinodular gland, sx of hyperthyroidism, low/absent TSH, high T4. RAIU: multiple hot nodules
- Tx: RAI ablation versus surgery. Exogenous T4 causes thyrotoxicity
- Histology: difficult to distinguish from adenoma
Thyrotoxicosis - Rare Causes

- Thyrotropin Induced Thyrotoxicosis is a pituitary adenoma until proven otherwise. Hyperplasia/Ca are rare.
  - high TSH, high T4, requires MRI

- Trophoblastic tumors
  - hydaditiform moles and germ cell tumors secrete thyrotropic beta HCG.
  - Tx: surgical removal
Thyroid Storm

- Exceedingly high levels of thyroid hormone
- Usually preceded by stress: infection, surgery, RAI ablation
- PE: heart failure/afib, coma, hyperthermia
- Tx: IV steroids, PTU, propanolol, ice baths
Thyroiditis

- Defn: thyroid disorders marked by infiltration of leukocytes, fibrosis or both

- Types:
  - Acute suppurative
  - Painful (de Quervain’s)
  - Postpartum
  - Hashimoto’s
  - Fibrous (Reidel’s)
Thyroiditis - Continued

- **Acute Suppurative Thyroiditis**
  - Bacterial infection, usually *S. aureus* or *S. pneumo*. Usually preceded by trauma
  - Tx: IV abx, I and D if abscess

- **Painful Thyroiditis (de Quervain’s)**
  - Unknown virus
  - Painful thyroid following URI
  - Hyperthyroidism followed by hypothyroidism - lasts 2 month
  - Tx: beta blockers/thyroxine, supportive
Postpartum Thyroiditis

- “Silent” thyroiditis of pregnancy and first few postpartum months
- Associated with Graves’ disease and other autoimmune diseases
- Tx: beta blockers/synthroid as needed
- Usually self limiting, but high titers of antibodies heralds long term disease
Thyroiditis, Continued

- Hashimoto’s Thyroiditis
  - Most common thyroiditis
  - Antimicrosomal and antithyroglobulin antibodies, but anti TSH receptor Abs seen
  - Associated with other autoimmune diseases
  - Pts usually euthyroid
  - 60-80 time increase in lymphoma
Hashimoto’s Disease, Cont.

- **Histology:** “Askanazy changes” - predominant lymphocytes with germinal centers. Scant follicles

- **Tx:**
  - Hypothyroid patients: synthroid
  - Hyperthyroid: antithyroid medications
  - Surgery reserved for failure of suppression or suspicion of lymphoma
Case

- A 32 yohf presents from Harlingen because “the doctor says my thyroid is bad.” She presents with her husband and her three children, the youngest a “FLK” newborn. Her MD is unavailable.
Case, Continued

- **PMH:** anxiety
- **PSH:** none
- **SocHx:** no tob, etoh. Home schools eldest child because “he’s lazy and won’t pay attention to the teacher or do any work.”
- **All:** NKDA
- **MEDS:** Xanax prn
Case, Continued

- **PE:** 133/77, 20, 38.1, 140
  - Thin, anxious woman
  - **HEENT:** ?slight exophthalmos. Neck: mild/mod goiter, several “nodules” palpated
  - **Neuro:** 2-12 intact, slightly tremulous
  - **Pulm:** CTA
  - **CV:** irregular, tachycardic
Labs/Studies
- TSH: 0.2 (2-10)
- FT4I: 34 (2-10)
- RAI Scan: uptake in all areas, two small hyperfunctioning nodes on left, one hypofunctioning nodule on right
- Thyroid antibodies: positive for anti TSH antibodies, antimicrosomal antibodies and antithyroglobulin antibodies
Controversies

- Treatment of Hyperthyroidism
  - Antithyroid medications versus RAI ablation versus surgery

- Indications for Surgery in goiter
  - compressive/obstructive symptoms
  - failure to suppress
  - Multinodular goiter
New Areas of Interest

- Neurodevelopment and Peripheral Resistance to Thyroid Hormones
  - Most common cause known to be malfunctioning peripheral TSH receptors
  - \textit{c-erb A} gene isolated
  - Attempts being made to "splice" \textit{c-erb A} into cells