ARTICLES FOR PRESENTATION

Having attached more articles than any provider should be expected to read in preparation for this presentation, I recommend that you tuck them away as digital resources for future reference if you so desire.
"NORMAL" CONDITIONS

Disclaimer: This presentation is not intended to apply to 100% of patients, as there are a small percentage of patients with pituitary issues, thyroid cancers, autonomous thyroid nodules, hormone-secreting tumors and/or similar conditions where diagnosis and treatment decisions are different.

The following discussion is primarily targeted at the other 99+%. 
PEARLS

1. Thyroid Testing
2. Euthyroid Sick
3. “Normal” TSH Levels
   • Subclinical Hypo- & Hyperthyroidism
4. Thyroid Dosing
5. Treatment of iatrogenic Hyperthyroidism
6. Treatment of Hyperthyroidism
7. Use of Non-Synthetic Thyroid Supplements
Regulation of thyroid hormone production

- **Hypothalamus**
  - TRH stimulates the anterior pituitary gland

- **Anterior pituitary gland**
  - Secretes TSH (Thyroid-stimulating hormone)

- **Thyroid gland**
  - Produces T4 and T3 ( Thyroxine and Triiodothyronine)

- **Liver**
  - Converts T4 to T3
  - Converts T4 and T3 to Conjugated T4 and T3

- **Intestine**
  - Absorbs T4 and T3 from the bloodstream

- **Circulatory system**
  - Transport T4 and T3 to other organs

- **Stimulatory pathway**
  - +

- **Inhibitory pathway**
  - –

- **Conjugated T4 and T3**
  - OGT
• Most of the hormone secreted from the thyroid is T4
• T4 is converted to T3 (Reverse or Active)
  • Active T3 (aT3) is far more potent than T4; formed by removal of an iodine in the outer ring of T4
  • Reverse T3 (rT3) is formed by removal of an iodine in the inner ring of T4 and is a biologically inactive metabolite of T4
  • Both are controlled by a highly regulated system involving 3 iodothyronine deiodinases (D1, D2 & D3), which selectively remove iodine atoms
• rT3 is associated with conditions characterized by a reduction in metabolic rate, including starvation; chronic HF – particularly when associated with AF; and non-thyroidal illness syndrome (aka, “euthyroid sick syndrome”). Also seen in critical illness, very elderly patients, chronic stress, myocardial infarction, and chronic inflammatory states
EUTHYROID SICK

• TSH is falsely **elevated** and frequently **misinterpreted** as hypothyroidism

• Nonthyroidal Illness leads to changes in...
  • Thyroid Hormones
  • Binding Proteins
  • TSH Concentrations

• Typical changes with nonthyroidal illness:
  • **LOW** concentrations of all 3 binding proteins
  • High concentration of FFAs that displace thyroid hormones from binding proteins
  • Acquired Central Hypothyroidism
  • Use of medications that affect thyroid function

**PEARL:** Unless thyroid disease is suspected as a contributor to the hospitalization, **wait** until the patient is at or close to baseline before checking TSH, making a diagnosis or changing thyroid supplement doses
ASSESSING THYROID FUNCTION

• Log Linear relationship between Free T4 & TSH
  • Small changes to Free T4 → Large changes in TSH

• From UpToDate: “thyroid function is best assessed by measuring serum TSH, assuming steady-state conditions and the absence of pituitary or hypothalamic disease”

• 3rd Generation TSH Assays are accurate to 0.01 and are more sensitive, specific, accurate and precise than any combination of T4, T3, Free T4, Free T3, TBI, T3RU… etc.

• Biotin interferes thyroid assays, often leading to falsely low TSH and elevated T4 and T3. Need to stop it >48 hours before testing
COMMON DRUG EFFECTS ON THE THYROID

**Biotin** interferes thyroid assays, often leading to falsely low TSH and elevated T4 / T3. **Stop it >48 hours before testing**

**Amiodarone** messes with everything thyroid.
- Destructive thyroiditis in 5-10% [↑T4/T3; ↓TSH]
- Its 37% iodine by weight provides 45X the recommended dialy intake of iodine, leading to hyperthyroidism in some and hypothyroidism in many other patients

**Lithium** causes goiter any hypothyroidism by decreasing thyroid hormone release (appx. 18% of treated patients)

COMMON DRUG EFFECTS ON THE THYROID

**Methadone** increases TBG, leading to hypothyroidism

**Glucocorticoids:**
- Inhibit conversion of T4 → T3
- Suppress Thyrotropin release (Minor clinical impact)
- Decrease TBG (minor increase in TSH)

Thyroid supplements require an acidic milieu for dissolution & absorption. **PPI** use leads to an increase in TSH

**Fe**{sup+2}, **Ca**{sup+2}, Sucralfate & Cholestyramine interfere with absorption

Use only the TSH!!!

Serum Free T4 measurements are very insensitive for assessing appropriate dose

MONITORING SECONDARY HYPOTHYROIDISM

• Use the Serum **Free T4** for pituitary or hypothalamic disease
  (eg, absent or impaired TSH release)

• Maintain Free–T4 in the upper 50% of normal
MONITORING THYROID CANCER

• Thyroid replacement is given to suppress TSH secretion to prevent recurrence of thyroid cancer or regrowth of goitrous tissue
• Should have a subnormal TSH => the 3rd generation TSH target is typically 0.05 – 0.1
• If TSH is <0.05, measure Free-T4 to guide dosage adjustment (decrease)
“NORMAL” TSH LEVELS IN SENIORS

• ‘Normal’ lab TSH Levels are based on healthy 18-40 yo males

• For patients >70, the updated Ideal Target TSH is 4-6

²Thyroid. 2014; Dec; 24[12]:1670-75
SUBCLINICAL HYPERTHYROIDISM

• Suppressed TSH with Normal T3 / T4 levels
  • Roughly TSH <1 in adults and <2 in seniors
  • 3-fold risk of AF in seniors
• Usually iatrogenic, though may be due to thyroid disease or hormone-secreting tumors
• Excess suppression of serum TSH primarily increases risk of:
  • Atrial Fibrillation
  • Anxiety
  • Osteoporosis
  • Accelerated Cognitive Decline
  • Increased Mortality

32016 ATA Guidelines for Treatment of Hyperthyroidism
• TSH is elevated with a normal Free T4
• Associated with higher CV mortality in patients <65, but no increased CV mortality in older persons
• Consensus recommendations of American Thyroid Association & American Association of Clinical Endocrinologists is to treat subclinical hypothyroidism with a TSH >10
• In those with a TSH 6-10, there appears to be no improvement in morbidity / mortality with treatment, but requires clinical judgment to decide on whether to treat or monitor
  • If there are symptoms, treatment is reasonable, though F/U shows that 1/3 have a normal TSH 1 year later without Rx changes... so it is often prudent to simply follow them and recheck in 6-12 months

4 J Clin Endocrinol Metab. 2008 Aug;93[8]:2998-3007
THYROID DOSING

• Half-life in adults is 6-7 days, but increases with age
  • Therapeutic life is about 8-11 days

• **Half-life in seniors 9-11 days**, therapeutic life 12-16 days

• Absorption easily altered if taken w/ food, drinks or oral meds

• Give entire week’s dose all at once [*Thyroid Thursdays*]

• Can safely be given weekly [10 AM? 2 PM?]
  • Decreased nursing time
  • Improved absorption
  • Avoids waking patients early every day
  • Decreased pill burden
  • Improved compliance?
**IATROGENIC HYPERTHYROIDISM**

- **TSH 0.2 – 0.4 and asymptomatic**
  - Can usually be treated by simply holding for 1-2 weeks followed by decreasing the dose; recheck 4-6 weeks after dose is reduced

- **TSH 0.1 – 0.2 and Asymptomatic**
  - NO Anxiety, tachycardia, palpitations, tremors, heat intolerance, SOB
  - Start a Beta Blocker, Hold dose for 2-4 weeks followed by reassessing dose; recheck 4-6 weeks after dose is reduced

- **TSH <0.1 OR <0.4 and Symptomatic**
  - Stop Thyroid Supplement
  - Start a Beta Blocker, Thionamide (Methimazole) and perhaps Prednisone for 2-3 weeks
  - Consider an Endocrine Consult if TSH remains <0.4 after 1 month off supplements and with the Methimazole +/- Prednisone added
NON-IATROGENIC HYPERTHYROIDISM

• Amiodarone?
• Graves?
• Nodular Goiter?
• Endocrine tumor?
• Hold the Biotin!

TREATMENT: Beta Blocker plus…
• Surgery
• Radioactive Iodine
• Pharmacologic: Methimazole +/- Steroids
USE OF NON-SYNTHETIC THYROID SUPPLEMENTS

(eg, Armour thyroid)

Don’t use them.
PEARL #1: Check the TSH only
PEARL #2: DO NOT check or trust Thyroid labs drawn during a hospitalization (for NonThyroidal Illness)
PEARL #3: An ideal TSH in seniors is 4-6
PEARL #4: A TSH <2 in seniors may represent Subclinical Hyperthyroidism associated w/ increased clinical risks
PEARL #5: Use Clinical Symptoms in Seniors to decide whether or not to change dosing in patients with a TSH 6 – 10

(Does not improve M / M)
PEARL #6: **Thyroid Thursdays**…

*consider weekly dosing*
PEARL #7: Hyperthyroidism treatment 
always starts with a Beta Blocker and 
usually includes Methimazole
BONUS PEARL: Use **ONLY** synthetic supplements