Clinical Pearls for the Treatment of Hyper- and Hypothyroidism

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What Your Tongue Tells You About Your Thyroid
Diagnosis of Primary Hypothyroidism

• Assuming normal pituitary function, the TSH is the most sensitive and dependable test for diagnosing hypothyroidism
  – “Normal” TSH is similar person to person
  – Variability lab to lab and day to day is minimal
  – Pituitary is very sensitive at detecting small changes in thyroid hormones from baseline

• Utility of T4 and T3 levels is limited to rapidly changing thyroid status
  – “Normal” levels vary significantly person to person, yet both may fall within the reference range
  – Lab variability, frequently affected by binding proteins, antibodies, medications, nutritional/health status
What is a Normal TSH?

- 0.3-3 definitely normal
- 3-5?
- 5-10?
- >10 definitely not normal: increased lipids and CVD risk long term

Exceptions:
- Pregnancy
- Aged: Octogenarians and above, optimal TSH probably closer to 3-6
• 41 yo white female presents with 4 months of fatigue, palpitations, anxiety, weight loss
• Exam is consistent with hyperthyroidism
• TSH 0.01, free T4 0.9 (0.7-1.6), free T3 2.4 (2.0-3.5), similar 2 months later
• TSI positive, diagnosed with graves disease and clinically improved on methimazole
• 4 months later, TSH normalized and T4/T3 barely lower than at presentation
TSH and T4/T3 are Discordant

• TSH and T4/T3 high
  – Pt on thyroid hormone: Non-compliance
  – Rare: TSH secreting adenoma or resistance to thyroid hormone
• TSH N/low and T4/T3 low
  – Consider pituitary disease
  – Acute nonthyroidal illness (TSH will rise later)
• TSH/T4/T3 either high or low
  – Pt on thyroid hormone: labs checked too soon
  – Rapidly changing thyroid hormones (thyroiditis, methimazole)
  – Check free T4 and T3 by equilibrium dialysis
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>1 month</th>
<th>2 months</th>
<th>4 months</th>
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<tbody>
<tr>
<td>Subacute Thyroiditis</td>
<td>TSH 0.01 Free T4 3.2 Free T3 6.8</td>
<td>TSH 0.2 Free T4 0.6 Free T3 1.2</td>
<td>TSH 24 Free T4 0.5 Free T3 1.3</td>
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<tr>
<td>Hashimoto’s</td>
<td>TSH 14 Free T4 0.7</td>
<td>TSH 9 Free T4 1.5</td>
<td>TSH 2.1 Free T4 1.5</td>
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<td>Dose increased from 100 to 125mcg</td>
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Management of Hypothyroidism

• Normal thyroid makes 90% T4 and 10% T3
  – T4 is the storage version, long half-life
  – T3 is the active version, short half-life; T4 is converted into T3 in the peripheral tissues by deiodinases
• My approach is to start with synthetic T4 alone
  – Brand versus generic
  – Timing: 1st AM vs bedtime
• Dose depends on severity of the hypothyroidism, keeping in mind that a full replacement dose is 1.6mcg/kg/day
  – Post-thyroidectomy or severe hypothyroidism: full replacement dose
  – Mild hypothyroidism: 25-50mcg/day
Special Cases: TSH Stays High

• TSH remains elevated despite escalating levothyroxine dosing
  – Confirm patient is taking it appropriately: empty stomach, wait 60 minutes to eat
  – Look at med list: calcium, iron, PPIs, bismuth sulfate
  – Look at medical history: celiac disease, malabsorptive states (bariatric surgery)
  – If compliance an issue, encourage a pill box, or even resort to dosing once a week at home or in the office
Special Cases: Pregnancy

- 36 yo female on longstanding levothyroxine for Hashimoto’s calls office to report a positive urine HCG
- Last TSH was 1.8, 6 months ago
- LT4 100mcg daily
Special Cases: Pregnancy

• If planning on pregnancy, aim for TSH<2.5 and check TSH every 3 months
• Thyroid hormone needs increase by 35-40% as early as week 5 of gestation (1 week after missed period)
• As soon as urine HCG becomes positive, patient should increase their dose by 2 extra pills per week, then come in for TSH and serum HCG
• Once TSH is back, adjust prescription accordingly:
  • If TSH in goal range (0.1-2.5 for first trimester): increase by 35-40%
• Check TSH every 4 weeks through first half of pregnancy, then every 6-8 weeks thereafter if stable
• Resume pre-pregnancy dose at time of delivery
Trimester Specific TSH Ranges

• 1\textsuperscript{st} trimester: 0.03-2.3
• 2\textsuperscript{nd} trimester: 0.03-3.1
• 3\textsuperscript{rd} trimester 0.13-3.5
Special Cases: Pregnancy

• 36 yo female on longstanding levothyroxine for Hashimoto’s calls office to report a positive urine HCG
• Last TSH was 1.8, 6 months ago
• LT4 100mcg daily

• Now TSH 2.2; levothyroxine increased to 137mcg daily
• 4 weeks later TSH 3.4, dose increased to 150mcg daily, stable remainder of pregnancy
• Dose reduced to 100mcg daily at time of delivery
Special Cases: “My TSH is Normal and I Still Feel Like Crap!”

• Consider non-thyroidal illness, especially other autoimmune conditions
• Consider pituitary disease
• Consider addition of T3
Addition of T3 (Liothyronine)

• Meta-analyses in 2006 and 2009 failed to show any clinical benefit when T3 added to T4 therapy

• Handful of RCTs have shown clinical benefit (symptoms and biochemical outcomes) to a subset of patients when T3 is added
  – Specific genetic polymorphisms might modulate effects of thyroid hormones in target tissues
Addition of T3 (Liothyronine)

• Optimize TSH first; if patient feels well, then no indication for T3 therapy
• Rule out other causes of poor well being (autoimmune)
• T4:T3 dose ratio in 10:1 to 20:1 range (avoid natural thyroid preparations, 3:1)
• Discontinue T3 if no clinical benefit is seen in 3-6 months
Hyperthyroidism

• Subacute thyroiditis: summer/fall, tender/swollen thyroid, triphasic pattern with hyperthyroid phase lasting < 8 weeks
• Graves disease: large, smooth, nontender thyroid, eye disease, personal or FH of autoimmune disease
• Toxic nodules: may or may not be palpable
• Iodine toxicity: iatrogenic, CT scan with contrast, amiodarone
Hyperthyroidism

• If TSH suppressed, check free T4 and T3
• Low threshold for beta blockade
• Observation if picture consistent with subacute thyroiditis
• If diagnosis unclear, consider I-123 scan
• Option of methimazole while referring to Endocrinology
  – 10-30mg daily
  – Caution pt’s on rash, new inflammatory joint pain, fever, signs of liver disease
Take Home Points

• Assuming normal pituitary function and steady state of thyroid hormones, TSH IS the most reliable indicator of thyroid function

• Most common cause of simultaneously elevated TSH and fT4 is a noncompliant patient on levothyroxine

• Always start with T4 therapy alone, but if clinical response unsatisfactory, okay to trial course of T3

• Once patient becomes pregnant, empirically increase levothyroxine dose by 30-40% and then check TSH
References

• 2014 Nat Rev Endocrinol 10:164. Paradigm Shift in Thyroid Hormone Replacement Therapies for Hypothyroidism
• www.thyroidmanager.org