Goal

• Provide a guide to frequently encountered problems in thyroid disease
• Follow my approach to recently encountered patients
• Focus on pathophysiology rather than algorithm driven approaches
Conflicts of Interest and Disclosures

None to disclose
Failure to Control Hypothyroidism

- 37 y.o Hispanic woman
- Excellent historian according to her Endocrinologist
- Total thyroidectomy 2009
- Current Symptoms of fatigue and cold intolerance
- Persistent elevation of TSH on 325 mcg synthroid daily
• blood pressure was 120/70 with a pulse of 76.
• screening thyroid ultrasound which revealed no thyroid tissue nor lymphadenopathy.
• Her skin was dry
• She had decreased capillary refill time.
• It was difficult to elicit deep tendon reflexes, but her ankle jerks appear to be somewhat delayed
Laboratory data

- Normal CBC
- Creatinine 1.1
- Lytes normal
- Calcium 8.6
- Normal liver function tests
- TSH 88
- T4 0.36 (0.76-1.46)
What are diagnostic possibilities?

- Taking other medication along with synthroid
- Taking synthroid at meal time
- Taking non-generic thyroid
- Non-compliance
- Thyroid hormone resistance
- TSH producing tumor
- Malabsorption of thyroid
Which possibilities can be ruled out?
Which of the following can be ruled out?

- A. Non-compliance
- B. Thyroid hormone resistance
- C. TSH producing tumor
- D. Malabsorption of thyroid
Which of the following can be ruled out?

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- B. Thyroid hormone resistance **
- C. TSH producing tumor  **
- D. Malabsorption of thyroid
My Approach

- Ask about the “three commandments” of thyroid hormone treatment
  - Takes on empty stomach yes
  - Takes without other pills yes
  - Uses non-generic l-thyroxine yes
- Ask how many pills missed per week on average none
- Ask if bottles of thyroid are outdated no
- Ask what doses she has been on previously up to 400 mcg per day
What are we left with?

• Non-compliance
• Malabsorption of thyroid
How can we confirm non-compliance?
This can be done indirectly by ruling out malabsorption
Thyroid absorption test

• 1000 mcg of l-thyroxine orally on an empty stomach
• Measure Free T4 at baseline and two hours
• Mean absorption in published is 43-61%
• Long experience has demonstrated safety of test
Test in patient

- Basal T4: 0.40
- 2 hour T4: 1.07
- 167% increase (normal 43-61%)
- Interpretation: clearly she does not malabsorb thyroxine
- This has been termed “pseudomalabsorption”
- Problem is patient compliance
Confirmation of Diagnosis

• Administer thyroxine once per week under nurse’s supervision
• Safe because half life of thyroxine is 7 days
• Increased free T4 up-regulates conversion of T4 to reverse T3 an inactivating mechanism
Follow-up Course

- Given 2000 mcg synthroid once per week at physician’s office
- TSH 1.5 after one month (confirmation of previous non-compliance)
- Asked to take once per week at home
- Follow-up 2 months TSH 34.9
- Conclusion: continued non-compliance at home
- Plan: resume once per week thyroxine in physician’s office
Multi-nodular goiter

- M C 78 y.o. female with long standing multi-nodular goiter followed over an 11 year period with normal FNA of a dominant nodule
- Serial ultrasound evaluations of multi-nodular goiter reveals stability
- TSH and free T4 levels on previous occasions normal
- Presents now with 5 pound weight loss, palpitations, decreased appetite and frequent bowel movements
- GI work up documents increased stool fat of no known etiology but with a response to pancreatic enzyme therapy
Left lobe
Pertinent Lab Data

- TSH 0.16 (nl 0.45-4.5)
- Free T4 1.01 (nl 0.7-1.5)
- Free T3 3.8 (nl 2.3-4.2)
- CBC normal
- Comprehensive metabolic panel normal
- Stool fat slightly increased
Differential Diagnosis
Differential diagnosis

- Mild sub-clinical hyperthyroidism
- Hot nodule
- Euthyroid sick syndrome
- Hypopituitarism
What can be ruled out?

- A. Mild sub-clinical hyperthyroidism
- B. Hot nodule
- C. Euthyroid sick syndrome
- D. Hypopituitarism
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- D. Hypopituitarism**
Approach

- Practical method suggested by Dr. Ken Berman, past president of the American Thyroid Association
- 6 month trial of methimazole 5-10 mg daily
- Repeat TFTs in 6 months and assess symptoms
Six month follow-up

- TSH 0.72
- Free T3 3.1
- Free T4 1.06
- Weight stabilized
- Palpitations improved
- Diarrhea improved (hyperthyroidism can cause diarrhea and fat malabsorption)
Differential Diagnosis

Differential diagnosis

• Mild sub-clinical hyperthyroidism—very likely based on response to methimazole
• Hot nodule—still possible, need to do radioactive iodine scan if suppressed TSH returns
Will now follow with repeat thyroid function tests in 3 months
• Treat subclinical hyperthyroidism if suspect that signs or symptoms related
• Six month trial of methimazole and see if TSH normalizes
• Stop methimazole and see if TSH goes back down
• If recurrent suppression of TSH, consider long term methimazole or definitive therapy
• Will need RAI uptake and scan to see if “hot nodule”
Pitfalls of treating Graves Disease

* 48 year old male working as intelligence officer in Charlottesville with classic history of hyperthyroidism

• Large goiter without nodules
• Free T4 4.5 (normal 0.7-1.5), free T3 6.8 (normal 2.3-4.2), TSH undetectable, TSI 4.5 (normal < 1.7), RAI uptake 55% at 4 hours and scan consistent with Graves disease and no nodules
Treatment

- 25 atenolol twice daily
- 20 mC RAI
- Then start on methimazole 20 mg daily
- Follow-up in 6 weeks
Followup Visit

• Missed 6 week appointment
• Finally seen 3 months later
• Complaints of difficulty concentrating, fatigue, cold intolerance, constipation, major problems with work
• PE normal except for a pulse of 50, delayed reflexes
• Free T4 0.2, Free T3 0.7, TSH 94
What would be the best approach

- A. Stop methimazole and follow for return of thyroid function
- B. Stop methimazole and start cytomel (liothyronine—T3) 12.5 mcg tid
- C. Stop methimazole and start synthroid 1.6mcg/kg or 150 mcg daily
- D. Stop methimazole and start cytomel 12.5mcg tid for two weeks and synthroid 150mcg daily
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Reasoning

• Tolerated hyperthyroidism reasonably well
• Hypothyroidism likely a combination of RAI therapy and methimazole
• Can restart thyroid replacement quickly as he is very symptomatic
• T3 has half life of 1 day, T4 has half life 7 days
• Stop methimazole and start both T3 and T4
• Close follow-up to see if he has recurrent hyperthyroidism due to stopping methimazole
Outcome

• Responded with improved symptoms on T3 and T4 therapy
• Did not develop recurrent hyperthyroidism
• Need to fine tune synthroid dose and keep TSH in the 0.5-2.5 range
Differential Diagnosis of Weight Loss

- 48 yo woman
- c/o 10 pound weight loss after wedding of son in Holland with marked increase in caloric intake during the one week wedding celebration
- Resting pulse 96
- Thyroid normal size
- No other signs or symptoms
What is the most likely diagnosis?

• A. Anxiety and reduced caloric intake
• B. Acute onset hyperthyroidism
• C. Long standing hyperthyroidism with exacerbations because of stress of foreign wedding
• D. Occult cancer
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• B. Acute onset hyperthyroidism **
• C. Long standing hyperthyroidism with exacerbations because of stress of foreign wedding
• D. Occult cancer
What would you order

• TSH  yes
• Free T3 yes
• Free T4 yes
• TSI (thyroid stimulating immunoglobulins)-later
• Anti-microsomal antibodies - later
• CBC-no
• Comprehensive metabolic panel-no
Laboratory data

- TSH undetectable
- Free T4 3.5 (0.7-1.5)
- Free T3 2.9 (2.3-4.2)
Differential diagnosis

• Production hyperthyroidism (Graves’s disease, thyroid nodule, multi-nodular goiter)
• Destruction hyperthyroidism (painless hyperthyroiditis)
Tests to establish diagnosis

- **Radioactive iodine uptake and scan**
  - High uptake equates to production hyperthyroidism
    - If hot nodule, Dx is production by nodule
    - If multinodular, Dx is multinodular goiter
    - If diffuse, Dx is Graves disease
  - Low uptake
    - Dx is painless hyperthyroiditis
    - Anti-microsomal antibodies present, Dx is Hashitoxicosis

- Alternatively thyroid stimulating immunoglobulin TSI) –if normal, no need for RAI uptake and scan
Results

- uptake 0.1% at 4 hours and 2% at 24 hours
- Anti-microsomal antibodies positive at 1:1000
- Dx, painless hyperthyroiditis and Hashimotos thyroiditis (Hashitoxicosis) type
Course of Disease

- Hyperthyroid for 4-6 weeks (release of stored thyroid hormone from gland; reason why T3 not elevated)
- Hypothyroid for 4-6 weeks (depletion of stored thyroid hormone)
- Return to normal
Treatment

- Observation
- Free T4 fell to 0.7 after 6 weeks and TSH 10
- At 12 weeks, free T4 1.2 and TSH 1.5
- Need for follow up for recurrent episodes
Course of Disease

- Recurrence two years later
- Same course
- At that time, put patient on thyroid replacement to prevent recurrences after she returned to normal
- No recurrences over the next 15 years
Hashimotos thyroiditis with neck pain

- 35 year old woman with known Hashimotos thyroiditis, thyroid gland 1.5 times above normal and normal thyroid function tests
- Calls complaining of neck pain, 4 on scale of ten and no other symptoms
What should be done?

- A. Measure free T4
- B. Measure free T3
- C. Measure TSH
- D. Obtain radioactive iodine uptake-no need
What should be done?

• A. Measure free T4
• B. Measure free T3
• C. Measure TSH **
• D. Obtain radioactive iodine uptake-no need
Rationale

• Mild pain due to inflammation is very common in patients with stable Hashimoto's thyroiditis
• TSH will rule out hypo- or hyperthyroidism
Action Needed

- Reassurance
- NSAIDs if pain significant enough
- Symptoms usually resolve
As you have seen
Some thyroid problems can be challenging

Thanks for your participation
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