

CASE 1: ALL QUESTIONS

A 25 YO woman presents to the clinic complaining that over the past few months she has difficulty performing many physical tasks due to severe muscle weakness, and frequently feels "hot and sweaty", even when the weather is cool. She also says she can feel her heart pounding all the time and has developed tremors and difficulty swallowing. Physical examination reveals a BP of 180/90, a pulse of 110 beats/min, hyperreflexia, lid lag and an enlarged thyroid gland. (estimated size, 100 g). Her TFTs are as follows: TT4 of 6 ug/dL (normal, 5-12), free T4 of 5.0 ng/dL (normal, 0.7-1.9) and TSH < 0.01 uU/mL (normal, 0.5-4.7). Tests for thyroid receptor antibodies (TSAAb, TRAb) were positive. Thyroidal uptake of 123I was 69% at 24 hours (normal, 15-23%) and the scan showed diffusely increased uptake in a symmetrically enlarged thyroid.

- **What therapeutic option(s) would be appropriate for this patient?**

Surgery: This patient is not in a "treatment of choice" group (RAI for cardiac, debilitated, elderly, drug allergy, adverse effects, etc). Surgery for difficulty in swallowing/breathing, drug allergies, malignancy and where RAI and drugs are contraindicated). Thionamides indicated for children, pregnant women, young adults and uncomplicated Graves' because of spontaneous remission. Thionamides in this patient may not be good due to size of the gland and severe disease, also their delayed onset and difficulty swallowing. Also RAI is delayed onset (see below)

- **What if this patient also presented with a blood glucose level of 290 mg/dL (normal 60-115) in addition to the symptoms and laboratory values reported above? Should insulin therapy be started?**

Thyrotoxicosis can activate or intensify diabetes (by increasing basal hepatic glucose production and the metabolism of insulin). Thus thionamides can restore control of diabetes. Evaluate BG after TFT have returned to normal

- **What therapeutic option(s) would be appropriate if this patient were three months pregnant?**

All pregnant women should be screened for TFTs and thyroid antibodies to evaluate the risk of hyperthyroidism. Treatment is crucial to prevent fetal damage and maintain the pregnancy. RAI and chronic iodide therapy is contraindicated because they cross the placenta to produce fetal goiter and athyreosis. Long-term propranolol is not appropriate because it is associated with fetal respiratory depression, a small placenta, intrauterine growth retardation, impaired response to anoxia. postnatal bradycardia and hypoglycemia. Short-term beta-blockers or iodides are safe.

Treatments of choice are surgery or thionamides in pregnancy. Surgery is safe during the second trimester. During the last trimester thionamides are preferred because surgery can precipitate spontaneous abortion. PTU is considered the thionamide of choice based on anecdotal reports of MMI causing reversible congenital scalp defects (aplasia cutis). But patients allergic to PTU can use MMI. PTU crosses the placenta less than MMI due to high plasma protein binding, but may not be a significant difference. Fetal hypothyroidism and goiter can develop when large doses of thionamides are used. To avoid fetal goiter and suppression of fetal thyroid, PTU is usually prescribed in the minimally effective dose: initiate on maximum doses of 150-300 mg/day and then tapered to 50-100 mg/day for the remainder of the pregnancy. Maintain mother in a mildly hyperthyroid state since this is

tolerated by the fetus better than maternal hypothyroidism. TFTs should be maintained in the upper range of normal because pregnancy is associated with higher levels of TBGs. Some patients can discontinue thionamides in the second half of pregnancy. In studies to date fetuses exposed to maternal PTU doses of 200 mg or less may cause reductions in neonatal serum THs, but this does not appear to cause long term problems. Doses >300 mg/day have been shown to reduce IQ. PTU is also the drug of choice in the breastfeeding mother. MMI, propranolol and iodides are excreted into breast milk and should be avoided. TH is not appropriate to the mother's regimen to prevent fetal goiter or hypothyroidism because THs do not reach the fetal circulation. This would only complicate therapy.

- **What therapeutic option(s) would be appropriate if this patient had a smaller goiter (40 g) and a history of congestive heart failure (CHF) and angina?**

This patient is a candidate for RAI (cardiac, debilitated and older pts), but must be pretreated to deplete TH stores to minimize post-RAI hyperthyroidism and thyroid storm which is caused by leakage of TH from the damaged thyroid gland. PTU has not had adequate time to deplete stores. Lugol's solution should not be given before RAI because iodides block the uptake of RAI. Iodide therapy can block RAI for several weeks. Iodides can be used within 1-7 days after RAI. To control post-treatment hyperthyroidism. Thionamides can be used before RAI, but should be discontinued 3 days before and 1-7 days after RAI for optimum RAI uptake. Thionamide onset is long. This patient shouldn't get thionamides (agranulocytosis). Beta-blockers can be used before, during and after RAI.

- **What therapeutic option(s) would be appropriate if this patient was initially treated with PTU (200 mg q8h) but the drug had to be discontinued two weeks later because she developed severe agranulocytosis?**

Answer if patient had a smaller goiter and CHF: This patient is a candidate for RAI (cardiac, debilitated and older pts), but must be pretreated to deplete TH stores to minimize post-RAI hyperthyroidism and thyroid storm which is caused by leakage of TH from the damaged thyroid gland.

- **Assume, after consultation with the patient, her physician decides to initiate PTU therapy, 200 mg q8h. Which baseline laboratory values should be obtained prior to initiating PTU therapy and how should therapy be monitored?**

Initiation of therapy. Get a baseline FT4 and TSH as well as baseline WBC with differential to help differentiate between leukopenia associated with hyperthyroidism from drug-induced leukopenia and/or agranulocytosis. Drug-induced leukopenia is usually transient and not associated with agranulocytosis (see below), and does not require drug discontinuation. Repeat FT4 and TSH after 4-6 weeks and 4-6 weeks after any change in the dosing regimen. Once a patient is euthyroid, TFTs can be obtained every 3-6 months

- **Assume, after consultation with the patient, her physician decides to initiate PTU therapy, 200 mg q8h. What concerns may you have about initiating PTU therapy if this patient was also being treated with warfarin (5 mg/day) for deep vein thrombosis?**

Caution because thionamides, especially PTU can cause hypoprothrombinemia, thrombocytopenia and bleeding (although relatively rare). Thionamides can suppress bone marrow and the synthesis of clotting factors II, VII, III, IX, X and XIII, and vitamin K and prothrombin times may remain suppressed for several months after thionamide therapy. Symptoms occur within 2 weeks to 18

months after starting thionamide therapy. Any bleeding that occurs can respond to vitamin K or blood transfusions.

- **Assume, after consultation with the patient, her physician decides to initiate PTU therapy, 200 mg q8h. How would you respond if this patient asks how long she must take this medication? What subjective and objective data in this case above would influence remission and justify a longer course of thionamide therapy?**

Length of thionamide therapy. Typically 1-2 years (although not really adequate literature support). The goal is to control symptoms until remission occurs. Spontaneous remissions occur in 25-30% of cases, but it is not known when they will occur. Some advocate short term therapy (<6 months) until patient becomes euthyroid – this is associated with about 40% remission rate. But some studies suggest short term therapy is no better than spontaneous remission. Higher remission rates (up to 85%) reported in patients with >18 months of therapy. Thionamides can be continued indefinitely if there are no side effects and RAI or surgery is not desired.

Long-term remission rates with thionamides are variable (15-75%) but relatively low. Permanent remission is rare with long follow up. Some patients who achieve long-term remission may have concurrent or subsequent Hashimoto's thyroiditis (perhaps natural course of Graves' disease). Studies have shown that Graves' antibodies fall with thionamide therapy in some patients; patients with detectable antibody titers at the end of therapy are at a higher risk of relapse within 1-2 years. Some studies suggest higher thionamide doses result in lower antibodies and less relapse. But higher doses of thionamides may mean more side effects (but not hematologic). Should consider surgery or RAI in patients on long term therapy who do not have long term remission

Clinical features that may be predictive of higher remission rates include:

- Smaller goiter
 - Reduction of goiter during treatment
 - Return of thyroid suppressibility
 - Lower antibody levels (TSI)
 - Mild symptoms of short duration
 - Genetic factors: Lower prevalence of HLA antigens? Not proven!
- **Assume, after consultation with the patient, her physician decides to initiate PTU therapy, 200 mg q8h. What adjunctive therapies may be of benefit to this patient? Why?**

Adjunctive therapy to manage symptoms of hyperthyroidism until thionamides take effect:

- Iodides:
- Beta-blockers: decrease adrenergic effects (nervousness, palpitations, fatigue, weight loss, diaphoresis, heat intolerance and tremor). Adrenergic effects from increased number of receptors (not elevated NE levels). Beta-blockers do not effect the course of the disease or thyroid hormone levels or interfere with TFTs, thionamide therapy! Use beta-blockers without ISA (atenolol, metoprolol, propranolol), but propranolol also blocks conversion of T4 to T3. Probably don't want to use beta-blockers in diabetic. Remember, there may be large differences in plasma levels of propranolol in different patients and it is reported that the clearance of propranolol is greater during the hyperthyroid phase versus the euthyroid phase (due to reduced plasma protein binding, increased metabolism). Dose based on objective signs of improvement such as reduced heart rate (<100 beats/minute).

- Calcium channel blockers (diltiazem and verapamil, not DHPs): Alternative to beta-blockers when contraindicated
- **Assume, after consultation with the patient, her physician decides to initiate PTU therapy, 200 mg q8h. Two weeks after being started on PTU therapy, she returns for a follow-up visit and complains that her symptoms have not improved. Should her therapy be modified? Is so, how?**

Inadequate amount of time for PTU to work based on mechanism of action

- **Assume, after consultation with the patient, her physician decides to initiate PTU therapy, 200 mg q8h. Should therapy be modified if this patient remains hyperthyroid (based on symptoms and TFTs) after 6 weeks of PTU therapy and admits problems with compliance? If so, how? How would you respond if she asks if she can take the PTU once a day?**

Probably not (but could consider switching to MMI 30-40 mg/day and do TFTs after 4- weeks). First consider if the dose in this patient adequate (300-800 mg/day) and higher doses at first. True resistance to thionamides is very rare. Inadequate response to PTU can result from non-compliance or delayed response due to prior loading of thyroid (patient was treated with iodides before PTU). Also, onset of PTU is slow because of mechanism of action. If this patient is compliant, it may be reasonable to increase dose schedule to 200 mg every 6 hours. Can reduce the dose when the patient becomes euthyroid. A better option may be to change to 30-40 mg methimazole once daily to enhance compliance or divided into two doses to decrease GI effects. MMI may be associated with better compliance than PTU for a number of reasons: single dose regimen, not associated with bitter taste. (But PTU has peripheral effects (block T4 to T3 conversion) which make it additionally effective in thyroid storm.).

Multiple PTU doses have been demonstrated more effective and thus are recommended for initial hyperthyroidism to achieve euthyroidism. Single doses of PTU are 300 mg (rather low). However, single doses of MMI have been demonstrated to be as effective as multiple doses. MMI is preferred for once-a-day dosing because of its longer intrathyroidal duration of action. PTU is preferred in thyrotoxic patients (thyroid storm) because it blocks the conversion of T4 to T3. Single doses of MMI are 30-60 mg,

- **Suppose this patient is euthyroid (current TFTs: FT4 of 1.0 ng/dL and TSH of 4.5 uU/mL) after two years of PTU therapy (maintenance doses of 100 mg QD) but her gland is larger than normal and has never decreased in size, even with PTU therapy. She wants to "shrink" the goiter, but refuses RAI or surgery. Could therapy be modified in some way to accommodate achieve her desire?**

Add levothyroxine (0.1 mg/day) to maintain euthyroidism and normalize TSH. This may help decrease the size of the goiter caused by TSH stimulation; lab value is high normal. If PTU doses are excessive, TH levels are suppressed and TSH secretion stimulated. A more direct solution to this problem may be to decrease PTU doses. When PTU titration has been difficult, the combination of T4 and PTU is reasonable. Addition of T4 may also increase the chance of remission when PTU is discontinued. TSH suppression decreases antigen release from the gland (reduced TSH receptor antibodies) which correlates with higher remission rates. But not all studies support that thionamides with levothyroxine is associated with higher remission rates.

- **Assume, after consultation with the patient, her physician decides to initiate PTU therapy, 200 mg q8h. After four weeks of PTU therapy the patient develops a pruritic area over the pretibial aspects of both legs, as well as several maculopapular erythematous patches. Should PTU therapy be modified or be discontinued? What would you recommend for this patient?**

May be a PTU drug rash, but may be symptoms associated with the pretibial myxedema or dermopathy associated with Grave's. Drug related (both MMI and PTU) rash is maculopapular and usually occurs early in therapy. But cross-reactivity is uncommon, so one thioamide can be substituted for another. If relatively mild, drug can be continued and the rash treated with antihistamines and topical steroids. These rashes also subside spontaneously. If the rash is urticarial or associated with systemic manifestations (fever, arthralgias), the thioamide should be stopped.

- **Assume, after consultation with the patient, her physician decides to initiate PTU therapy, 200 mg q8h. Should therapy be modified if this patient returns complaining of fever, cough and sore throat three weeks after being started on PTU therapy? Should PTU be discontinued? What would you recommend for this patient?**

May be indicative of agranulocytosis, the most severe hematologic ADR associated with thionamides. Be alert for fever (101 degree for several days), rash, malaise or other flu-like symptoms, with sore throat. If present, do a repeat WBC (compare to baseline test) and discontinue PTU. More information

- **Should therapy be modified if this patient returns complaining of nausea, vomiting, diarrhea and abdominal tenderness two months after being started on PTU therapy (200 mg q8h)? Should PTU be discontinued? What would you recommend for this patient?**

The GI effects and tenderness may be mild GI side effects from PTU or could be PTU-induced hepatitis. Transient elevations in transaminases occur in about 30% of asymptomatic patients within the first 2 months of PTU therapy. And do not require PTU discontinuation. These usually normalize within 3 months of reducing PTU doses to maintenance levels. But if clinical symptoms of hepatotoxicity are present, discontinue the drug. Overt hepatitis usually occurs within 2 months of PTU therapy. If hepatitis occurs, do not switch drugs! Go with surgery or RAI.

Check TFTs, transaminases and bilirubin in this patient. And PTU stopped until results are available. Routine monitoring of LFTs is not recommended because patient may be asymptomatic. Routine LFTs may be indicated in patients with a history of liver disease and risk factors for hepatitis (alcoholics). (Secondarily: Not hepatitis, but GI intolerance interfering with compliance)

- **Assume this patient was treated with RAI and two weeks after RAI administration she still has many symptoms of hyperthyroidism and elevated thyroid hormone levels? What should be done?**

RAI takes up to 3 months for optimal effects. At least 3 months should elapse before a second dose of RAI (some say 6 months).

- **Assume this patient was successfully treated with RAI. Three years later she presents with fatigue, dry skin, cold intolerance, a puffy face and significant weight gain (30 pounds). Explain her symptoms?**

Presentation and history compatible with hypothyroidism secondary to RAI therapy (iatrogenic hypothyroidism). Obtain a free T4 and TSH level. Treat with thyroxine.

- **Assume this patient originally refused RAI therapy and could not tolerate thionamide drugs due to severe adverse reactions, so a thyroidectomy is planned. How should the patient be prepared for this procedure? The patient inquires about possible post-operative complications associated with thyroidectomy. How would you respond?**

Wait till granulocyte levels return to normal. Patient should be euthyroid to avoid precipitation of thyroid storm and enhanced morbidity – this patient was only treated for a week or so, so they still have high TH stores. . In theory can use thionamides, iodides or beta-blockers. Combination of iodines with B-blockers may be more effective than agents alone. See operative and post-operative risks. Post-operative complications include : Hypoparathyroidism, Adhesions, Laryngeal nerve damage, Infection, Poor wound healing, Hypothyroidism

CASE 2: ALL QUESTIONS

A 26-year-old woman presents with heavy menstrual bleeding, fatigue, hoarseness, occasional muscle cramping and significant weight gain (20 pounds) over the past three months. Her normal menses occur about every 25 days and last about three days. For the past year, however, they have been as frequent as twice a month and have lasted for a week, requiring almost twice the usual number of tampons. On questioning, she acknowledged feeling cold much of the time, but she attributes this to unusually cold weather. She also reported that her hairdresser commented that her hair had become dry, coarse, and brittle. Physical examination reveals pale yellow and dry skin, puffy eyelids, delayed deep tendon reflexes and a palpable, firm thyroid. Thyroid function testing showed a serum TSH level of 85 μ U/mL (normal, 0.5-4.7) and a free T4 level of 0.4 ng/dL (normal, 0.7-1.9). The serum thyroid antiperoxidase antibody level (TPO antibodies) was 9.3 U/mL (normal, <1.0). Thyroid uptake of 123I was 1% at 24 hours (normal, 15-23%).

- **What specific therapy, if any, would be appropriate for this patient? Also develop a monitoring plan for this patient and describe appropriate patient counseling points.**

Typically use 1.6-1.7 ug/kg per day (100-125 ug). Some studies have showed that doses of 125 ug may be too high and cause a blunted TSH response. This patient may not require dose titration, but a conservative approach would employ a dosing plan such as initial doses of 50ug levothyroxine and then titrate to 100 after 1 month.

Thus all patients should be monitored for resolution of clinical signs and symptoms, as well as for maintenance of normal TSH levels as a measure the adequacy of replacement. *Many clinicians now consider serum TSH levels to be the most sensitive and specific monitoring parameter for adjustment of levothyroxine dosing.* Typically patients are monitored every 4 to 8 weeks and the thyroxine doses titrated by 25 to 50 μ g increments until resolution of symptoms and normalization of thyroid function tests. TSH assays need not be repeated until 4 to 6 weeks after initiating therapy or with dosage

changes, because of the long half-life of levothyroxine. Inadequate dosing will be reflected by continued signs and symptoms of hypothyroidism, a low T₄ level, and an elevated thyrotropin (TSH) level during periodic evaluation;. Patient compliance is probably best monitored by measuring T₄ levels. If poor patient compliance is not suspected, then levothyroxine doses are increased and the patient reevaluated at the next clinic visit in 4 to 8 weeks.

- **Would this patient's drug therapy need to be modified if she also presented with hypercholesterolemia (a total serum cholesterol level of 347 mg/dL)?**

Not necessarily. TH hormone therapy may correct this

- **Would the dosing regimen need to be modified if this patient was significantly older (65 yo) or had long-standing hypothyroidism or arteriosclerotic disease?**

Yes. These patients may be very sensitive to the effects of TH. For patients with CV disease, first assess extent of CV disease (cardiac catheterization, bypass) and start with very low doses (12.5 to 25 ug and increased every 4-6 weeks until target dose levels are achieved, usually around 50 ug/dL). Monitor ECG during titration. Stop titration if CV problems emerge. Not necessary to monitor TFTs during titration (they will remain low). Some suggest T₃ is preferred for such patients due to more rapid onset and shorter duration (effects dissipate in 3-5 days). But T₃ is more potent and dose titration is therefore more difficult. Also, high serum T₃ levels can cause more cardiac toxicity, especially angina

- **Would the dosing regimen need to be modified if this patient was significantly younger (5 yo)?**

Full dose based on weight: initial 10-15 ug/kg/day and titrate to maintain T₄ levels >10ug/dL. Decrease dose as patient ages. Adults doses at 15 yo.

- **Based on the symptoms, physical findings and TFTs, this patient was started on 100 ug of levothyroxine/day. Two weeks after starting this therapy the patient returned and continued to complain of fatigue, dry brittle hair and difficulty concentrating. Her current TFTs are: Serum TSH level of 40 μ U/mL (normal, 0.5-4.7), total T₄ of 4 ug/dL (normal 5-12), and a free T₄ level of 0.4 ng/dL (normal, 0.7-1.9). Should TH dose be increased?**

While some symptoms of hypothyroidism may resolve in 2-3 weeks, many do not improve for 4-6 weeks (anemia, skin, hair). In fact, patients with long-standing hypothyroidism may not achieve steady-state T₄ levels for 6 months. Typically TFTs are checked about 6-8 weeks after initiating therapy (measure FT₄, FT₄I and TSH) because T₄ has a half-life of 7 days and 3-4 half lives are required to achieve steady-state.

With levothyroxine therapy, plasma TSH levels begin to decrease within hours and are usually normalized within 2 weeks; however, it may take up to 6 weeks in some cases. And patients should note improvement in some symptoms (eg, weight, facial edema, palpitations speech, skin temperature, mental alertness, and physical activity) within 2 to 3 weeks, although other symptoms (eg, hoarseness, skin and hair changes) will take longer to resolve. Once the patient is euthyroid, the frequency of thyroid function test monitoring may be reduced to every 6 to 12 months. In general, many patients

remain stabilized on the same dose for years. However, physiologic changes over time (aging) or changes in concomitant drug therapy may lead to changes in levothyroxine dose.

- **Based on the symptoms, physical findings and TFTs, this patient was started on 100 ug of levothyroxine/day. Eight weeks after starting this therapy she reports resolution of all of her symptoms. Her current TFTs are: Serum TSH level of 0.5 μ U/mL (normal, 0.5-4.7), total T4 of 14 ug/dL (normal 5-12), and a free T4 level of 1.9 ng/dL (normal, 0.7-1.9). Should her drug therapy be altered?**

No. No hyperthyroid symptoms and TSH is normal! May be an artifact of the sample collection time relative to the time of drug administration. Should get a trough drug level (> 9 hours after dosing) and also get a total T3 to determine the ratio of T3:T4.

- **Based on the symptoms, physical findings and TFTs, this patient was started on 100 ug of levothyroxine/day. After several months of therapy, she discovers she is 8 weeks pregnant. Now she does not report or show any symptoms of hypothyroidism or hyperthyroidism. Her current TFTs are: Serum TSH level of 10 μ U/mL (normal, 0.5-4.7), RT3U is 25% (normal, 25-37%), total T4 of 5 ug/dL (normal 5-12) and a free T4 level of 0.7 ng/dL (normal, 0.7-1.9). How should this patient's thyroid disease be managed and why is maintenance of euthyroidism important?**

First, make sure patient is compliant and not taking other medications, etc. Women require larger dosages of T4 when they are pregnant, even though there often are no clinical signs of hypothyroidism. Most patients require approximately a 50% increase in levothyroxine dose with the goal of maintaining T4 levels in the upper limits of normal and normal TSH levels. Because TBG levels are elevated, TT4 should be kept above the normal range and TT4 levels are not the best indicator of adequate replacement. TSH levels should be monitored monthly in the first trimester. Maternal hypothyroidism is detrimental to the developing fetus (abnormal fetal development, spontaneous abortion, congenital defects, low IQ to mental retardation, increased mortality).

- **Based on the symptoms, physical findings and TFTs, this patient was started on Cytomel 50 ug TID. She is not taking any other medications. After several months of Cytomel therapy she reports for follow-up and complains of continued fatigue, and muscle aches and pains. Physical examination revealed a good physical appearance, good tendon reflexes and a palpable, but not significantly enlarged thyroid gland. Her current free T4 levels are 0.5 ng/dL (normal, 0.7-1.9). What, if anything, should be done for this patient?**

No dosage increase at this point. The free T4 levels will always be low because the patient is receiving T3. Her vague complaints may be related to hyperthyroidism. Get T3 and TSH levels (suppressed TSH and elevated T3 would indicate hyperthyroidism).

- **Based on the symptoms, physical findings and TFTs, this patient was started on 100 ug of levothyroxine/day and she became euthyroid within several months. Several years later this patient has a stroke and paralysis that prevents her from swallowing oral medications. She continued daily levothyroxine until the time of the stroke and her current TFTs are normal. Should her thyroid hormone therapy be continued and if so, how?**

Endocrine Module, Thyroid Therapy Cases and Case Questions, 2004

Because the drug has a half-life of 7 days, administration can be delayed for up to 1 week, assuming the patient would be able to take oral drugs at this time. If parenteral administration is required, the drug is available in forms for IM and IV injection. The IV route is preferred because IM absorption may be slow and unpredictable (particularly if the circulation is compromised). IV doses should be adjusted downward to account for 80% oral bioavailability of T4. Once IV replacement is successful, maintenance with once weekly IM may be appropriate.

- **Suppose this patient was on maintained on levothyroxine (100 ug/day) but six months later still suffers from heavy menses, sluggishness and cold intolerance. In addition to her thyroid medication, she is being treated with cholestyramine (Questran, 4 g QID) for hypercholesterolemia, FeSO₄ (325 mg BID) for anemia, antacids and sucralfate (1 g BID) for peptic ulcers and calcium carbonate (1 g BID) for osteoporosis (older pt). Her current TFTs are: TSH of 21 uU/mL (normal 0.5-4.7) and a free T4 of 0.6 ng/dL (normal, 0.7-1.9) and positive ATgA and TPO antibodies. Should her therapy be modified?**

Inadequate treatment possibly due to non-compliance, poor absorption, tissue resistance, abnormal (rapid) clearance. Determine time of TH administration relative to meals (absorption is optimal on an empty stomach). Assess GI status for disorders that may impair absorption or enterohepatic recycling (steatorrhea, malabsorption). Medications may also compromise absorption. Cholestyramine, iron sulfate, antacids, sucralfate and calcium carbonate all may impair TH absorption if administered at the same time. Other anticholesterol drugs such as lovastatin may also impair absorption. Change to aluminum-free antacid and an H₂-antagonist if necessary. Separate dosing of TH from cholestyramine, iron and calcium by 6 hours! Re-evaluate TFTs in 6-8 weeks.

Conditions that require Alteration of TH dosages:

Increased requirements

- Pregnancy
- Concomitant therapy with oral iron, resins (eg, cholestyramine [LoCHOLEST, Prevalite, Questran]), sucralfate (Carafate), some nonsteroidal anti-inflammatory drugs, phenytoin sodium (Dilantin), carbamazepine (eg, Tegretol), or amiodarone HCl (Cordarone)
- Excessive intake of dietary fiber or aluminum hydroxide
- Malabsorption
- Noncompliance (may falsely mimic need for high maintenance dose)
- Progression of thyroid destruction

Decreased requirements

- Aging
- Androgen therapy
- Development of thyroid-stimulating antibodies