

Hyperthyroidism/Thyrotoxicosis – Questions  
December 2003

1. Is there any difference between “thyrotoxicosis” and “hyperthyroidism”?

**Case Presentation (Questions 2a-2c):**

**A 45 year-old white female presents to your clinic with neck pain worsened by coughing & swallowing. She reports fatigue, nervousness, myalgias, and fevers to 103°. Exam reveals a moderately enlarged thyroid, exquisitely tender to palpation.**

2a. What is the most likely diagnosis?

2b. What lab abnormalities could we expect to find in this patient?

2c. What is the treatment of choice?

3. Match the subacute thyroiditis with its (most likely) etiology:

- |  |                               |
|--|-------------------------------|
| a. subacute granulomatous thyroiditis<br>(de Quervain) | 1. autoimmune                 |
| b. postpartum thyroiditis                              | 2. viral or post-viral injury |
| c. amiodarone-induced thyroiditis                      | 3. trauma                     |
| d. thyroid biopsy thyroiditis                          | 4. cellular injury            |
| e. interferon thyroiditis                              | 5. cytokines                  |

4. How do hyperthyroid symptoms differ between young and old patients?

**Case Presentation (Questions 5a-5c)**

**A 28 year-old female presents to your clinic with complaints of heat intolerance, palpitations, anxiety, and oligomenorrhea. Exam reveals mild systolic hypertension, tachycardia, proptosis, lid lag, non-pitting leg edema, and a diffusely enlarged firm painless thyroid gland.**

5a. What is the most likely diagnosis?

5b. What lab abnormalities could we expect to find in this patient?

5c. What are treatment options for this disease?

**Case Presentation (Questions 6a-6c)**

**A 65 year-old female presents to your clinic with unexplained weight loss and depression. Exam reveals a nontender goiter which has been present for many years, but now there are multiple irregular nodules palpable. Lab reveals a depressed TSH and borderline high T3 & T4.**

6a. What is the most likely diagnosis?

6b. What are the expected results from RAIU and thyroid scintigraphy?

6c. What are the treatment choices for this disease?

7. What are other causes of thyrotoxicosis?

Hyperthyroidism/Thyrotoxicosis – Answers  
December 2003

1. Is there any difference between “thyrotoxicosis” and “hyperthyroidism”?

**Yes. Thyrotoxicosis refers to a clinical syndrome characterized by elevated levels of free thyroxine (FT4), free triiodothyronine (FT3), or both. Hyperthyroidism is a subset of thyrotoxicosis that is a result of a true, sustained increase in the synthesis of thyroid hormone, thus excluding exogenous thyroid hormone intake and subacute thyroiditis.**

Case Presentation (Questions 2a-2c):

A 45 year-old white female presents to your clinic with neck pain worsened by coughing & swallowing. She reports fatigue, nervousness, myalgias, and fevers to 103°. Exam reveals a moderately enlarged thyroid, exquisitely tender to palpation.

2a. What is the most likely diagnosis?

**De Quervain subacute thyroiditis (SAT). This is the second most common cause of thyrotoxicosis (~20%) behind Graves Disease (50-60%). Although usually not necessary, the diagnosis can be confirmed by 24-hr RAIU testing, which will show low uptake.**

2b. What lab abnormalities could we expect to find in this patient?

**Abnormally high free T4, total T3.**

**Abnormally low TSH.**

**Anemia; leukocytosis; high alk phos & ferritin; elevated ESR (often exceeding 100).**

2c. What is the treatment of choice?

**NSAIDS (ie. Naproxen 500 bid or Ibuprofen 800 tid). For severe disease, glucocorticoids may be used (ie. prednisone 30mg-60mg per day for one week, then tapered over 2 weeks). Steroids are highly effective; if pain and tenderness do not disappear within 72 hours of initiating therapy, question the diagnosis. Symptomatic therapy with propranolol is often prescribed.**

**Comment: About 50% of patients with de Quervain thyroiditis will have no signs of thyrotoxicosis. When they do, this phase lasts 4-10 weeks. It's often followed by a 1-2 month period of hypothyroidism, then a return to euthyroid state. A small percentage (~5%) of patients with SAT develop permanent hypothyroidism.**

3. Match the subacute thyroiditis with its (most likely) etiology:

- |  |   |                               |
|--|---|-------------------------------|
| a. subacute granulomatous thyroiditis<br>(de Quervain) | → | 1. autoimmune                 |
| b. postpartum thyroiditis                              | → | 2. viral or post-viral injury |
| c. amiodarone-induced thyroiditis                      | → | 3. trauma                     |
| d. thyroid biopsy thyroiditis                          | → | 4. cellular injury            |
| e. interferon thyroiditis                              | → | 5. cytokines                  |

**Comment 1: The terms “subacute thyroiditis” (SAT) and “de Quervain thyroiditis” are often used interchangeably. However SAT includes many causes of thyroidal inflammation, including de Quervain (painful) and lymphocytic (painless) thyroiditis (SALT). SALT is similar to SAT in its course and low RAIU, but the gland is nontender, or “silent”, and the ESR is normal.**

**Comment 2: Watch for SAT in patients receiving interferon-alpha for chronic hepatitis. Watch for postpartum thyroiditis 1-6 months after giving birth; anti-TPO antibodies are often very high due to its autoimmune etiology. Radioiodine therapy for Graves disease may also result in transient thyroidal inflammation, causing thyroiditis. Amiodarone-induced thyroiditis (AIT) is most often caused by iodine overload in a gland with underlying abnormalities, but a direct toxic effect is observed in some patients.**

4. How do hyperthyroid symptoms differ between young and old patients?  
**Younger patients tend to exhibit more sympathetic activation, such as anxiety, hyperactivity and tremor. Older patients have more cardiovascular symptoms, such as dyspnea and atrial fibrillation, decreased bone mineral density, and unexplained weight loss.**

Case Presentation (Questions 5a-5c)

A 28 year-old female presents to your clinic with complaints of heat intolerance, palpitations, anxiety, and oligomenorrhea, Exam reveals mild systolic hypertension, tachycardia, exophthalmos, lid lag, non-pitting leg edema, and a diffusely enlarged firm painless thyroid gland.

- 5a. What is the most likely diagnosis?  
**Graves disease. Ophthalmic findings (proptosis, chemosis, periorbital edema) and non-pitting edema are classically associated with Graves.**
- 5b. What lab abnormalities could we expect to find in this patient?  
**Abnormally low TSH.  
Abnormally high free T4 and T3.  
Abnormally high anti-thyroperoxidase (anti-TPO) antibody; this level is also high with post-partum subacute thyrotoxicosis but is low in toxic multinodular goiter & toxic adenoma.  
Abnormally high thyroid-stimulating immunoglobulin (TSI) G, a TSH receptor agonist.  
Elevated alk phos, hypercalcemia, anemia & thrombocytopenia.**

5c What are treatment options for this disease?

**For symptom relief, beta-blocker therapy. If contraindicated, such as in asthmatics, calcium channel blockers can be used.**

**For reduction in T4 & T3 synthesis, methimazole & propylthiouracil are used. These are often used until definitive therapy with radioactive iodine can be performed. They also may be used in Graves disease, since some patients go into remission after treatment for 12-18 months. While methimazole is longer-acting (given qday or bid instead of tid or qid), PTU is often chosen in severe thyrotoxicosis because of its additional benefit of inhibition of T4 to T3 conversion. (T3 is 20-100 times more potent than T4.) Iodine therapy also blocks T4 to T3 conversion & release of thyroid hormone from the gland. Iodine therapy is reserved for severe thyrotoxicosis because its use prevents definitive therapy of Graves with radioactive iodine for many weeks.**

**Radioactive iodine therapy is the most common treatment of hyperthyroidism. It is administered orally as a single dose, causing fibrosis and destruction of the thyroid over weeks to months. Hypothyroidism is not an unexpected result of this therapy.**

**Surgical therapy is reserved for severe cases in children & patients intolerant of traditional therapies.**

Case Presentation (Questions 6a-6c)

A 65 year-old female presents to your clinic with unexplained weight loss and depression. Exam reveals a nontender goiter which has been present for many years, but now there are multiple irregular nodules palpable. Lab reveals a depressed TSH and borderline high T3 & T4.

6a. What is the most likely diagnosis?

**Toxic multinodular goiter (15-20%). Plummer disease occurs most commonly in the elderly and develops slowly over time. Symptoms of thyrotoxicosis are mild & thyroid hormones are only slightly elevated.**

6b. What are the expected results from RAIU and thyroid scintigraphy?

**RAIU is high and thyroid scintigraphy shows the characteristic pattern of increased & decreased activity.**

6c. What are the treatment choices for this disease?

**Radioactive iodine therapy is the treatment of choice. Thioamides (PTU, methimazole) are often given 2-8 weeks before radioactive iodine ablation to avoid precipitation of thyroid storm. Beta-blockers relieve sympathetic symptoms. Surgery is usually reserved for young individuals with large nodules or obstructive symptoms.**

7. What are other causes of thyrotoxicosis?

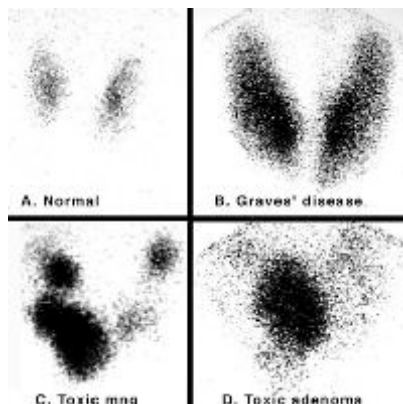
**Toxic adenoma (3-5%) is caused by a single hyperfunctioning follicular thyroid adenoma. Radioactive iodine uptake is usually normal, and the radioactive iodine scan shows only the "hot" nodule. These are non-malignant and should be treated with high-dose I<sup>131</sup> or surgery.**

**Jod-Basedow syndrome occurs in patients with excessive iodine intake such as after an iodinated radiocontrast study.**

**Struma ovarii is ectopic thyroid tissue associated with dermoid tumors or ovarian teratomas.**

**Metastatic follicular thyroid carcinoma can cause thyrotoxicosis in patients with bulky tumors.**

**Molar hydatidiform pregnancy & choriocarcinoma causes extremely high levels of bHCG that can weakly activate the TSH receptor. If bHCG levels are high enough, this can cause thyrotoxicosis.**



Closing thoughts:

Radioactive iodine uptake is useful in differentiating thyrotoxic states. A set dose of radioactive iodine (usually I<sup>123</sup>) is given, and 24 hours later, a radiation detector is placed over the thyroid to determine the percentage of the dose that was taken up by the thyroid.

Thyroid scintigraphy is useful for nodular disease. In this test, a dose of radioiodine or Tc<sup>99m</sup> is given and a scintillation scanner produces a rough picture indicating how these isotopes localize in the thyroid. Virtually all hot or cystic nodules are benign.