Stop the Thyroid Madness

Sanjay B. Dixit, M.D.
BHS Endocrinology Associates
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Welcome to the INFORMATIONAL MOTHERSHIP WEBSITE OF REPORTED "PATIENT EXPERIENCES AND WISDOM"! There's nothing more powerful than the successful experiences and wisdom of thyroid patients worldwide who've walked the path before you. I hope you find this informational site to be a great resource for your journey back to optimal health and being your own best advocate while working with your doctor! Seize the wisdom!

-- Janie A. Bowthorpe, M.Ed.

"Knowledge is power. Information is liberating."

- Kaf Amann
Did you know that the TSH lab test can look “normal”, yet you could be very hypothyroid?

Read More...

Adrenal problems are rampant thanks to being undiagnosed, dosed by the TSH, or being on T4-only, say patients.

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That once-a-day T4 thyroid pill has wreaked havoc, many patients report.

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Natural Desiccated Thyroid changes lives and has a long history of success.

Read More...

Lab work: Thyroid patients have learned what is really useful vs what is not.

Read More...

Want to talk to others who understand? Need feedback about your issues?

Read More...

Listen to Janie talk about:

- Have you been told you are “normal”, but you have continuing symptoms?? [LISTEN HERE]
- Why the TSH lab test may be the worst way to diagnose or treat by... [LISTEN HERE]
- How T4-only meds like Synthroid etc may not help you enough... [LISTEN HERE]
- What is Natural Desiccated Thyroid (NDT) about? [LISTEN HERE]
- Have you had problems with desiccated thyroid or T3-only? [LISTEN HERE]
I will not be discussing this

Adrenal problems are rampant thanks to being undiagnosed, dosed by the TSH, or being on T4-only, say patients.

Read More...
Outline of discussion

- Laboratory tests for thyroid function
- Diagnosis of hypothyroidism
- Treatment of primary hypothyroidism in adults
Lab work: Thyroid patients have learned what is really useful vs what is not.
Laboratory assessment

- Thyroxine (T4) and triiodothyronine (T3) secretion regulated by Thyroid Stimulating Hormone (TSH) secretion from pituitary gland
- TSH secretion regulated by Thyrotropin Releasing Hormone (TRH) from hypothalamus
- More importantly, TSH secretion regulated by negative feedback by T4 and T3 on both pituitary and hypothalamus
Figure 11-8, Williams Textbook of Endocrinology, 13th ed. 2016.
There is a negative log-linear relationship between serum free T4 and TSH concentrations.

What does this mean?

Very small changes in serum free T4 concentrations cause large changes in TSH values.
Figure 11-9. Williams Textbook of Endocrinology, 13th ed. 2016.
TSH assay

- TSH is the single best test for assessing thyroid function, assuming there are no confounding factors.

- These factors may include:
  - Hospitalization
  - Medications that affect thyroid function
  - Medications that affect thyroid function tests
  - Disorders of the pituitary or hypothalamus
Current TSH assay

- Current TSH assay is the “third generation” assay
  - Detection limit of 0.01 mU/L

- With that level of detection, patients who are hyperthyroid are readily apparent and differentiated from euthyroid patients

- Upper limit of normal is subject of some controversy
Differences in TSH

- Age related TSH values are important as are TSH distributions based on race
Total T4 and Total T3

- **Total T4**
  - Almost all of T4 is bound to thyroid binding globulin (TBG), transthyretin (TBPA), and albumin
  - Serum total T4 assays measure bound T4 and “free” T4

- **Total T3**
  - T3 is less tightly bound to TBG and TBPA
  - T3 is more tightly bound to albumin
Free T4 and Free T3

- “Free” refers to that portion of hormone that is readily available for each individual cell to use – compare to “bound” hormone

- None of the “free” T4 tests available can measure free T4 directly
Free T4 and Free T3

- “Direct” free T4 measurements
  - Assumption is that binding protein abnormalities are taken into account
  - No assessment of free T4 can account for all binding protein abnormalities that can occur
- Free T4 by equilibrium dialysis is considered the “best” T4 measurement
  - Most expensive
  - Result takes a long time to come back
“I want all of my levels checked”

- My practice is to check and to follow TSH only in known primary hypothyroidism
Checking T4 and T3

- Follow free T4 in secondary (central) hypothyroidism

**Hyperthyroidism**
- Check free T4 and total T3 because some assessment of these levels is needed, imprecise as they may be
- T3 dominance
  - T4 levels normal or at upper limit of normal
  - T3 levels are elevated
- But the above is also based on
  - TSH – low or suppressed
  - Clinical picture (symptoms of hyperthyroidism)
Thyroid antibodies

- Almost all patients with Hashimoto’s thyroiditis (chronic autoimmune thyroiditis) have positive antibodies to thyroglobulin and thyroid peroxidase
  - Thyroglobulin: protein made by thyroid follicular cells
  - Thyroid peroxidase: enzyme that catalyzes iodination of tyrosine residues of thyroglobulin to form monoiodotyrosine and diiodotyrosine
- TSH receptor antibodies are frequently elevated when hyperthyroidism is secondary to Graves disease
**TABLE 11-14** Prevalence of Thyroid Autoantibodies

<table>
<thead>
<tr>
<th>Group</th>
<th>TSHR-Ab (%)</th>
<th>hTg-Ab (%)</th>
<th>hTPO-Ab (%)</th>
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<tbody>
<tr>
<td>General population</td>
<td>0</td>
<td>5-20</td>
<td>8-27</td>
</tr>
<tr>
<td>Patients with Graves disease</td>
<td>80-95</td>
<td>50-70</td>
<td>50-80</td>
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<tr>
<td>Patients with autoimmune thyroiditis</td>
<td>10-20</td>
<td>80-90</td>
<td>90-100</td>
</tr>
<tr>
<td>Relatives of patients</td>
<td>0</td>
<td>40-50</td>
<td>40-50</td>
</tr>
<tr>
<td>Patients with IDDM</td>
<td>0</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>Pregnant women</td>
<td>0</td>
<td>14</td>
<td>14</td>
</tr>
</tbody>
</table>

IDDM, insulin-dependent diabetes mellitus; hTg-Ab, human thyroglobulin antibody; hTPO-Ab, human thyroid peroxidase antibody; TSHR-Ab, thyroid-stimulating hormone receptor antibody.
Hospitalized and seriously ill patients

- Euthyroid sick syndrome
  - Low serum T4
  - Low serum T3
  - Low serum TSH
- Administering thyroid hormone can actually be harmful
  - Changes in thyroid function during illness can be protective
  - Prevent excessive tissue catabolism
- Thyroid function should NOT be checked in seriously ill patients unless thyroid dysfunction is high on differential diagnosis
- In a hospitalized patient, do NOT check TSH alone
Figure 1. Thyroid function in nonthyroidal illness.

*UpToDate Online*. July 2017.
Hospitalized and seriously ill patients

- Peripheral 5’monodeiodinases produce T3 from T4 in end organ tissue (muscle, fat, etc)

- This enzymatic reaction decreases whenever
  - Caloric intake is low
  - There is a nonthyroidal illness
T4 metabolism in nonthyroidal illness

The inhibition of 5'-monodeiodinase in nonthyroidal illness leads to decreased conversion of T4 to T3 and reduced metabolism of rT3.

rT3: reverse triiodothyronine; T2: diiodothyronine; T3: triiodothyronine; T4: thyroxine.

Graphic 57919 Version 3.0
Hospitalized and seriously ill patients

- Why does the decrease in T3 production occur?
  - High endogenous serum cortisol concentrations
  - Exogenous steroid therapy
  - Inhibitors of deiodinase activity increase in illness
    - Cytokines
    - Drugs that affect 5’monodeiodinase activity
      - Amiodarone
      - Propanolol
Hospitalized and seriously ill patients

- Measure T3 in patients with low TSH
  - Differential diagnosis: hyperthyroidism v. nonthyroidal illness
    - T3 elevated in hyperthyroidism
    - T3 low in euthyroid sick syndrome

- Speaks to the importance of checking all thyroid function tests in hospitalized patients
Hospitalized and seriously ill patients

- Low T4
  - Fifteen to twenty percent of hospitalized patients have low total T4 levels
  - Total T4 is usually low because of reductions of one of the three thyroid hormone binding proteins
  - Free T4 is usually normal in patients with illness that is not severe
    - Can be low due to
      - Inability to account for all binding protein abnormalities
      - Decreased production of normal TBG
      - Production of TBG that binds T4 poorly
Hospitalized and seriously ill patients

- T4 to T3 conversion
  - Low serum T3 levels may be beneficial in critically ill patients
  - Inactivation of T4 to T3 conversion during illness may be beneficial
    - In a study of patients in an ICU, lower T3 and higher T4 levels were associated with higher likelihood of earlier discharge
    - Very low T4 levels in critically ill patients is a poor prognostic sign
Hospitalized and seriously ill patients

- TSH
  - Low but detectable
    - Almost always, TSH will be within normal limits after recovery from illness
  - Undetectable
    - Seventy five percent will have true hyperthyroidism from some etiology
  - Elevated
    - Transient elevations – even up to 20 mU/L – common during recovery from nonthyroidal illness
    - Greater than 20: usually are hypothyroid
Medications that decrease TSH secretion

- Glucocorticoids
  - Usually an acute effect
  - Those on chronic steroid treatment usually not affected because TSH secretion increases in response
  - ≥20 mg/day of prednisone or equivalent doses of other steroids
- Dopamine
- Dobutamine
- Octreotide
Medications that cause hyperthyroidism

- High doses of iodide or drugs that contain iodide may cause hyperthyroidism
  - Can occur with patients with goiter who are iodine deficient
  - Can occur in patients who are not iodine deficient if they have autonomous nodules – but only when they are exposed to large amount of iodide
  - Amiodarone can cause hyperthyroidism either because of –
    - Causing a thyroiditis
    - The high iodine load of amiodarone in patients with autonomous nodules
Medications that can cause hypothyroidism

- Iodine
  - Wolff-Chaikoff effect
  - In iodine sufficient patients
- Lithium
  - Should not be discontinued if hypothyroidism occurs
  - Treat hypothyroidism
- Tyrosine kinase inhibitors
  - Chemotherapeutic agents used for treatment of gastrointestinal stromal tumors, hepatocellular carcinoma, chronic myeloid leukemia
Euthyroid hyperthyroxinemia and hypothyroxinemia

- Medications that interfere with thyroid hormone (T4 and T3) binding in serum
- Results in a change in serum total T4 and total T3 concentrations, not in the free levels of those hormones
- Most clinically relevant situations:
  - OCPS, estrogens, selective estrogen receptor modulators
    - Increase TBG
  - Androgens, anabolic steroids, glucocorticoids
    - Lower TBG
### Drugs causing hypothyroidism

| Inhibition of thyroid hormone synthesis and/or release - thionamides, lithium, perchlorate, aminoglutethimide, thalidomide, and iodine and iodine-containing drugs including amiodarone, radiographic agents, expectorants (e.g., guaifenesin), kelp tablets, potassium iodine solutions (SSKI), Betadine douches, topical antiseptics |
| Decreased absorption of T4 - cholestyramine, colestipol, colesevelam, aluminum hydroxide, calcium carbonate, sucralfate, iron sulfate, raloxifene, omeprazole, lansoprazole, and possibly other medications that impair acid secretion, selevener, lanthanum carbonate, and chromium; malabsorption syndromes can also diminish T4 absorption |
| Immune dysregulation - interferon-alfa, interleukin-2, ipilimumab, alemtuzumab, pembrolizumab, nivolumab |
| Suppression of TSH - dopamine |
| Possible destructive thyroiditis - sunitinib |
| Increased type 3 deiodination - sorafenib |
| Increased T4 clearance and suppression of TSH - bexarotene |

### Drugs causing hyperthyroidism

| Stimulation of thyroid hormone synthesis and/or release - iodine, amiodarone |
| Immune dysregulation - interferon-alfa, interleukin-2, ipilimumab, alemtuzumab, pembrolizumab |

### Drugs causing abnormal thyroid function tests without thyroid dysfunction

| Low serum TBG - androgens, danazol, glucocorticoids, slow-release niacin (nicotinic acid), L-asparaginase |
| High serum TBG - estrogens, tamoxifen, raloxifene, methadone, 5-fluorouracil, clofibrate, heroin, mitotane |
| Decreased T4 binding to TBG - salicylates, salsalate, furosemide, heparin (via free fatty acids), certain NSAIDs |
| Increased T4 clearance - phenytoin, carbamazepine, rifampin, phenobarbital |
| Suppression of TSH secretion - dobutamine, glucocorticoids, octreotide |
| Impaired conversion of T4 to T3 - amiodarone, glucocorticoids, contrast agents for oral cholecystography (e.g., iopanoic acid), propylthiouracil, propanolol, nadolol |

T4: thyroxine; TSH: thyroid-stimulating hormone; TBG: thyroxine-binding globulin; NSAIDs: nonsteroidal anti-inflammatory drugs; T3: triiodothyronine.
Bile acid binding resins bind thyroid hormones and decrease absorption
  - E.g., cholestyramine, colestipol, colesevelam

No effect in euthyroid patients without thyroid disease

Levothyroxine should be administered at least 4 hours after administration of bile acid binding resins
Gastrointestinal absorption of thyroid hormone

- Proton pump inhibitors may affect absorption of thyroid hormone since gastric acid is required for absorption.

- Calcium and iron are notorious for binding with levothyroxine, decreasing absorption.
  - Separate calcium and/or iron containing supplements by several hours.
Biotin

- Because of the lab assays, high dose biotin supplements may cause lab values consistent with hyperthyroidism, specifically consistent with Graves disease –
  - Falsely low TSH values
  - High levels of T4, T3, and TSH receptor antibodies

- Have patients hold biotin for about two days prior to checking thyroid function tests
Did you know that the **TSH lab test** can look “normal”, yet you could be very hypothyroid?

[Read More...]
Diagnosis of hypothyroidism

- *Nonspecific* symptoms, some or all of which we *all* experience at one time or another

- Thus, diagnosis of hypothyroidism *must* also rely on lab testing
Diagnosis of hypothyroidism

- Primary hypothyroidism
  - High TSH, low serum free T4

- Subclinical hypothyroidism
  - High TSH, normal serum free T4

- Secondary (central) hypothyroidism
  - Low serum free T4, inappropriate TSH (not elevated)
Diagnosis of hypothyroidism

- More common in women (5-8 times more common)

- Some familial predisposition
Diagnosis of hypothyroidism

- Physical exam findings
  - Goiter
  - Bradycardia
  - Hypertension
  - Delayed relaxation of deep tendon reflexes

- Other lab abnormalities
  - Hyperlipidemia
  - Macrocytic anemia
  - Elevated creatine kinase
  - Hyponatremia
Primary hypothyroidism

- *Primary hypothyroidism*
  - Intrinsic to thyroid
  - Not secondary to pituitary or hypothalamus
  - Ninety-five percent of cases
Diagnosis of hypothyroidism

- TSH should be initial test
  - Elevated $\Rightarrow$ repeat TSH along with free T4
    - If repeat TSH is elevated and free T4 is low, start levothyroxine
    - If repeat TSH is still elevated but free T4 is normal, this is “subclinical hypothyroidism”
      - Decision to make about whether to treat with levothyroxine
      - Depends on
        - Individual patient factors
        - Degree of TSH elevation
  - Normal $\Rightarrow$ but patient has symptoms of hypothyroidism
    - Check free T4 to assess for secondary hypothyroidism
Secondary hypothyroidism

- Caused by problem with hypothalamus and/or pituitary
  - Specifically a problem with the *thyrotroph* cells in the pituitary that produce TSH (thyrotropin)
- TSH does not appropriately increase as T4 levels decrease
- Suspect when patient has –
  - Known hypothalamic or pituitary disease
  - Pituitary adenoma
  - History of surgery for pituitary adenoma
  - Known other hormonal deficiencies such as adrenal insufficiency or growth hormone deficiency
Thyroid antibodies in hypothyroidism

- Hashimoto’s thyroiditis
  - Most common etiology for primary hypothyroidism in the world in patients who are iodine sufficient
  - Both thyroglobulin (Tg) antibodies and thyroid peroxidase (TPO) antibodies can be elevated
  - TPO antibodies are elevated in \( \geq 90\% \) of patients with Hashimoto’s thyroiditis
Thyroid antibodies in hypothyroidism

- In most instances, it is not necessary or recommended to check thyroid antibodies
- Elevated levels of thyroid antibodies may indicate that a patient with normal TSH and normal free T4 is more predisposed to develop hypothyroidism
- Elevated levels of thyroid antibodies do not indicate –
  - When a patient may develop hypothyroidism
  - What the starting dose of levothyroxine should be
  - How often or how much to change the dose of levothyroxine
Thyroid antibodies in hypothyroidism

- Recommend checking TSH annually in patients with elevated thyroid antibodies.
- Definitely no utility in checking thyroid antibodies in patients who already have a diagnosis of primary hypothyroidism and who are on treatment.
- Check thyroglobulin antibodies as part of a thyroglobulin panel in patients who have had thyroid cancer treated by total thyroidectomy and radioactive iodine remnant ablation.
That once-a day T4 thyroid pill has wreaked havoc, many patients report.
Treatment of hypothyroidism

- T4 – levothyroxine – is treatment of choice

- T4 is a prohormone
  - Peripheral enzymatic deiodination of T4 forms T3
  - T3 is the actual thyroid hormone used in peripheral cells
Treatment of hypothyroidism

- Half life of T4 is seven days
- Half life of T3 is \( \leq \) one day
- Once daily dosing of T4 results in steady state of both T4 and T3
### Characteristics of oral thyroid hormone preparations available in the United States

<table>
<thead>
<tr>
<th>Generic name</th>
<th>Composition</th>
<th>Brand names*</th>
<th>Average adult dose/day (oral)</th>
</tr>
</thead>
</table>
| Levothyroxine ¥                      | T4                                    | Tablets Δ: Levoxyl, Synthroid, Unithroid, Unithroid Direct  
   Soft gel capsules °: Tirosint  
   Oral solution: Tirosint-Sol | 112 to 125 mcg                  |
| Liothyronine                          | T3                                    | Cytomel §                         | 37.5 mcg                    |
| Liotrix                               | 4:1 mixture of T4 and T3              | Thyrolar                          | T4 (75 mcg)/T3 (18.75 mcg) |
| Desiccated thyroid extract (Thyroid USP) | 4:1 mixture of T4 and T3 (approximately)  
   1 grain of desiccated thyroid extract (60 mg) should contain approximately 38 mcg T4 and 9 mcg T3  
   Pork or beef origin | Armour Thyroid, Nature-Throid, NP Thyroid, WP Thyroid | 90 mg                       |

T3: triiodothyronine; T4: thyroxine.  
* Generic preparations of levothyroxine and liothyronine are also available.  
¥ Best preparation.  
Δ Available in tablet strengths from 25 to 300 mcg.  
° Available in capsule strengths from 13 to 150 mcg.  
§ Available in tablet strengths of 5, 25, and 50 mcg.

Graphic 53418 Version 4.0
Dosing of levothyroxine

- Rule of thumb
  - Dose 1.6 mcg/kg/day of lean body weight
    - E.g., for 70 kg person dose would be levothyroxine 112 mcg daily
    - Again, this is an approximation
  - Can use this in young, otherwise healthy patients
    - In this population, I find levothyroxine dose of 25 mcg daily to be useless
  - In older patients and/or those with heart disease, start with levothyroxine 25 mcg – 50 mcg daily
    - Titrate slowly, based on checking TSH every 6-8 weeks
Dosing of levothyroxine

- Excessive levothyroxine replacement
  - Patients who are hyperthyroid generally feel better
  - Obviously this is not the correct treatment approach
  - Risks – the lower the TSH, the greater the risks
    - Cardiovascular – atrial fibrillation
    - Bone loss
Increased incidence of atrial fibrillation in subclinical hyperthyroidism

Cumulative incidence of atrial fibrillation in subjects over age 60 years according to the serum concentration of TSH. The risk of atrial fibrillation was increased almost threefold in the subjects with marked suppression of TSH (left panel) as compared with those who had normal serum TSH concentrations and were presumably euthyroid (right panel); patients with slightly low serum TSH concentrations (middle panel) had a lesser increase in risk.

TSH: thyroid-stimulating hormone.


Graphic 55024 Version 4.0
T3 and combined T4-T3 therapy

- I almost never advise combination T4-T3 therapy

- Remember that T4 is deiodinated to T3 in peripheral tissues
  - In most studies, serum T3 concentrations were normal in hypothyroid patients treated with levothyroxine
  - Almost all studies have concluded that combination T4-T3 therapy is not superior to T4 alone for resolution of hypothyroid symptoms
T3 and combined T4-T3 therapy

- Normal ratio of T4 to T3 in the body is 13:1 to 16:1
- The few studies in which patients stated that they felt better on combination therapy, they were receiving very high doses of T3
- One study from Lithuania in 1999 indicated improvement in mood and psychological function with combination therapy
  - Only 33 patients were studied
T3 and combined T4-T3 therapy

- Due to short half life of T3, any combination therapy of T4 and T3 is not ideal
  - Creates “pulses” of T3
  - Correct dosing may require taking very small doses of T3 several times per day (doses that are not available) or a slow release formulation of T3 (which is not available either)
- Some patients may have a polymorphism in type 2 deiodinase which results in impaired conversion of T4 → T3
T4 and combined T4-T3 therapy

- Possible treatment strategy
  - Try to mimic normal physiologic ratio of T4:T3 of 13:1 to 16:1
  - Example:
    - Patient who is taking levothyroxine 175 mcg daily and persistently has hypothyroid symptoms with normal TSH
    - Decrease levothyroxine to 150 mcg daily
    - Start T3 at dose of 5 mcg bid (10 mcg total per day)
    - Check TSH only 6-8 weeks later
    - If TSH is normal, and patient feels better → continue the T3
    - If TSH is normal, but patient does not feel better → discontinue the T3
Natural Desiccated Thyroid changes lives and has a long history of success.
T3 and combined T4-T3 therapy

- Pig thyroid gland extracts ("natural") are not appropriate treatment
  - T4:T3 ratio in these preparations is excessive
T3 and combined T4-T3 therapy

- **American Thyroid Association**
  - Levothyroxine should remain the standard of care
  - No consistently strong evidence for superiority of alternative preparations over levothyroxine only

- **European Thyroid Association**
  - “Combination therapy should be considered solely as an experimental treatment” overseen by “accredited internists / endocrinologists, and discontinued if no improvement is experienced after three months.”

- **Italian Thyroid Association**
  - Combination therapy generally not recommended
  - Trial can be considered to “improve adherence to treatment or patient well-being.”
T3 and combined T4-T3 therapy

- ABSOLUTELY avoid in pregnancy
  - Fetus uses maternal T4, not T3
  - Fetuses of women taking dessicated thyroid hormone or combination T4-T3 therapy may not have appropriate neurologic development

- ABSOLUTELY avoid in elderly
  - More susceptible to adverse effects of thyroid hormone excess
    - Atrial fibrillation
    - Osteoporotic fractures
Hypothyroidism and pregnancy

- Dose of levothyroxine in patients with preexisting hypothyroidism can increase by as much as 50% during pregnancy

- Treatment strategy
  - Check TSH every 4 weeks during pregnancy
  - Maintain mother’s TSH in population and trimester specific range; or TSH < 2.5 if those are not available
Summary

- In the outpatient setting, in almost all instances, TSH is the single best test for diagnosing hypothyroidism.
- Moreover, TSH is the best test to follow when a patient is already being treated for hypothyroidism.
- Lab testing for thyroid disorders can be affected by any number of factors, such as hospitalization and medications.
- Treatment of choice in hypothyroidism is levothyroxine.
Donald J. Trump
@realDonaldTrump

FAKE NEWS

5:19 PM - 10 Jan 2017

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42K 18K 51K