Functional Medicine University’s
Functional Diagnostic Medicine
Training Program

Module 7 * FMDT 563D

Functional Medicine Approach to Diagnosis and Treatment of
Thyroid Dysfunction

By Wayne L. Sodano, D.C., D.A.B.C.I.
&
Ron Grisanti, D.C., D.A.B.C.O., M.S.

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Please note that there is required reading for this lesson. A list of the articles and other recommended downloads may be found at the end of the table of contents.

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Recommended download:
These documents can be found on the download library at www.FunctionalMedicineUniversity.com

Functional Thyroid Scale
Adrenal Thyroid Symptom Questionnaire

Required reading
These articles can be found on the download library at www.FunctionalMedicineUniversity.com

4. Mini review: The Case or Obesogens, Felix Grun and Bruce Blumberg, Mol Endocrinol. 2009 August ; 23(8): 1127-1134
In the lesson titled “Introduction to Functional Endocrinology”, I presented a case history from one of my old patient files. I purposely left out my treatment plan in order for you to obtain a basic and advanced understanding of functional endocrinology. Please keep in mind that this case is from 2006. Treatment approaches will change as more research is conducted, however, this case will demonstrate that treating some areas of the underlying cause can have tremendous positive impact on other areas of dysfunction. Remember that all of the body systems are connected and there are multiple treatment strategies that can influence a positive treatment outcome.

The case history slides reviewed in this lesson (slides 3 through 8) may be found in Module 7 * FDMT561A Introduction to Functional Endocrinology. These slides were included in the handouts with this lesson for review.

The following illustrates what my recommendations were based on the case history and lab findings. I have also included the results of the IgG food allergy/sensitivity testing.
Dear Mrs. [Name]

The results of your physical examination and blood tests reveal the following diagnoses:

1. Hashimoto's thyroiditis (hypothyroidism) (autoimmune disease)
2. Hypercholesterolemia (high cholesterol)
3. Anemia (pernicious) B12, folic acid deficiency
4. Estrogen and progesterone deficiency
5. Suspected inflammatory bowel disease (based upon a history of cancerous intestinal polyp and irregular bowel function)

Hashimoto's thyroiditis is the most common autoimmune disease affecting the thyroid and is characterized by elevated levels of antibodies to thyroid peroxidase (TPO) and thyroglobulin. These antibodies cause inflammation of the thyroid gland, which can result in a goiter and lead to diminished production of thyroid hormone. Hashimoto's is much more common in women, has a genetic predisposition and is often associated with other autoimmune disorders.

I believe the synthroid should be of some help in the short term. I believe it is the autoimmune disease that is responsible for your joint pain. There are several areas that require treatment. We need to begin with normalizing your immune system and restoring hormone balance. The following are my initial treatment recommendations:

1. Food sensitivity test
2. [Supplement] (helps detoxify and reduce inflammation in the body)
3. [Supplement] (natural anti-inflammatory) 1 tablet three times a day
4. [Supplement] (essential fatty acids- aids the body by decreasing inflammation) 2 capsule three times a day
5. [Supplement] (probiotic for restoring health bacteria in the intestine- also acts as an anti-inflammatory agent) 2 capsule three times per day
6. [Supplement] (natural estrogen and progesterone replacement)
7. 84 ounces of water per day
8. Daily exercise- walk one mile per day

FOLLOW-UP IN 4 WEEKS

Thank you for allowing me to assist with your health care,

Dr. Wayne L. Sodano

(The patient was also advised to adjust to a gluten free diet and to use psyllium powder on a daily basis)
### Functional Medicine University’s
**Functional Diagnostic Medicine Training Program**

Module 7 FDMT 563D Functional Medicine Approach to Diagnosis and Treatment of Thyroid Dysfunction

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**Comprehensive Food Panel**

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**Provider Information**

**Wayne L Sodano DC**

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<td>SWORDFISH</td>
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<tr>
<td>YEAST (BREWER’S)</td>
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<tr>
<td>YOGURT</td>
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</table>

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Selected Natural Treatments for Herpes Simplex Virus

- Lemon Balm ointment: 70:1 lemon extract cream, applied 2 to 4 times per day
- Tincture of St. John’s Wort (Hypericum perforatum) can be helpful in relieving the pain of herpes simplex. Oily Hypericum preparations demonstrate an anti-inflammatory action due to their high flavonoid content. Advise the patient to place a few drops on a cotton ball and dab on several times a day.
- Another helpful blend is a few drops of St. John’s Wort, Olive Leaf, and Melissa mixed together. This blend can also be made into a salve with a few drops of olive oil and (pure) Shea butter, which also adds anti-bacterial and anti-inflammatory properties. Remind the patient to apply the salve with a Q-tip or while wearing gloves.
- Tincture of licorice root applied with a cotton swab or dropped directly onto the lesion, three times a day until resolution.
- Monolaurin: At first sign of infection, the patient should take 1800 to 3600 mg daily for 4 days and then reduce the dose to 600 to 1200 mg daily until lesions have resolved.
### Recommended protocols

**5/4/2006**

**Daily:**

- **Thyroid Sup #1**
  - 2 tablets 3x/day with meals

- **Thyroid Sup #2**
  - 1 tablet 3x/day with meals

- **C**
  - 4 tablets per day (chewable)

- Follow up 4-6 weeks
Recommended Treatment Protocols

(7-3-2006)

1. Begin supplement to increase estrogen metabolism
2. Continue with multivitamin, vitamin C, EFA’s, probiotics
3. Calcium supplement
4. Discontinue thyroid supplements (supplement 1 and 2) She also made the decision to stop taking the Synthroid.
5. Decrease natural progesterone and estrogen supplementation

Follow up in six to eight weeks
Module 7 FDMT 563D Functional Medicine Approach to Diagnosis and Treatment of Thyroid Dysfunction


http://www.FunctionalMedicineUniversity.com

---

**Chemistry Results**

**Progesterone**

<table>
<thead>
<tr>
<th>Reference Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Pregnant Female:</td>
</tr>
<tr>
<td>Follicular Phase: 0.2-1.4 ng/mL</td>
</tr>
<tr>
<td>Luteal Phase: 3.3-26 ng/mL</td>
</tr>
<tr>
<td>Mid-Luteal Phase: 4.4-28 ng/mL</td>
</tr>
<tr>
<td>Post-Menopausal: 0.0-7.7 ng/mL</td>
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<tr>
<td>Oral Contraceptives: 0.1-0.3 ng/mL</td>
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<tr>
<td>Pregnant Female:</td>
</tr>
<tr>
<td>First Trimester: 11-45 ng/mL</td>
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<tr>
<td>Second Trimester: 26-89 ng/mL</td>
</tr>
<tr>
<td>Third Trimester: 40-143 ng/mL</td>
</tr>
</tbody>
</table>

**T3, FREE**

270 pg/dL (230-420)

**T4, FREE, NON-DIALYSIS**

0.93 ng/dL (0.8-1.8)

**TSH**

3.4 uIU/mL (0.4-5.5)

**Estradiol**

16 pg/mL

Reference Range for Estradiol:

**Female:**

- Follicular Phase: 11 - 212 pg/mL
- Mid-Cycle: 18 - 480 pg/mL
- Luteal Phase: Less than or equal to 247 pg/mL
- Post-Menopausal: Less than or equal to 27 pg/mL

**Male:**

13 - 54 pg/mL

No pediatric reference range established. For patients less than 18 years of age, the Nichols Estradiol assay (extraction/chromatography/RIA Method) is recommended (Order Code 30289N).

**Thyroid Peroxidase Ab**

51 IU/mL (Less than 35)

---

**Chemistry Results**

**T3, FREE**

293 pg/dL (230-420)

**T4, FREE, NON-DIALYSIS**

1.12 ng/dL (0.8-1.8)

**TSH**

3.4 uIU/mL (0.4-5.5)

**Thyroid Peroxidase Ab**

34 IU/mL (Less than 35)
Functional Medicine University’s
Functional Diagnostic Medicine Training Program
Module 7 FDMT 563D Functional Medicine Approach to Diagnosis and Treatment of Thyroid Dysfunction
http://www.FunctionalMedicineUniversity.com

CONTINUATION OF REPORT - PAGE 3
For African American patients, please multiply the eGFR provided on the patient’s report by 1.21.

- Thyroid Peroxidase AB: 16 IU/mL (Less than 35)
- Thyroglobulin AB: <20 IU/mL (Less than 20)
- Hemoglobin A1C: 5.7% (<6.0)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>TSH</td>
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<td>0.03</td>
<td>3.9</td>
<td>3.4</td>
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<tr>
<td>Thyroglobulin AB</td>
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<td>&lt;20</td>
<td>&lt;20</td>
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<td>TPO AB</td>
<td>220</td>
<td>154</td>
<td>112</td>
<td>51</td>
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<td>16</td>
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<td>Free T3</td>
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<td>Free T4</td>
<td>1.11</td>
<td>2.0</td>
<td>.93</td>
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Convergence of Diseases

Many experienced functional medicine practitioners often see an overlapping signs and symptoms of metabolic, endocrine and immunological disorders as they relate to chronic disease. Blood sugar dysregulation, food allergy, hypothyroidism, hormonal imbalances, gastrointestinal disturbances and candidiasis (also called Candidiasis-related complex) appear to cause many similar symptoms.

Some of the major symptoms of chronic candidiasis include the following:
- Fatigue, lethargy
- Foggy thinking
- Constipation
- Irregular menses
- Bloating, belching or intestinal gas
- Decreases sex drive
- Mucous in stool
- Cold hands and feet

(Note: The preceding is just a short list of symptoms related to chronic candidiasis.)
Chronic mucocutaneous candidiasis describes a group of Candida infections of the skin, hair, nails and mucous membranes.¹ Most infections begin in infancy or during the first two decades. Chronic mucocutaneous candidiasis is frequently associated with endocrinopathies, such as:

- Hypoparathyroidism
- Addison disease
- Hypothyroidism
- Diabetes mellitus
- Autoimmune antibodies to adrenal, thyroid and gastric tissues
- Polyglandular autoimmune disease

Chronic mucocutaneous candidiasis (CMC) is a heterogeneous syndrome with unifying features of selective susceptibility to chronic candidiasis. Different subgroups with distinct clinical features are recognized, including autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED), CMC with hypothyroidism, and isolated CMC².

Fungal infections may have pleiotrophic effects on the endocrine system associated with pituitary, thyroid, parathyroid, pancreatic, adrenal, and reproductive organ infiltration and may lead to metabolic and electrolyte disturbances.³ Dr. Alan Gaby has stated that in his experience, patients suffering from symptoms attributed to chronic candidiasis frequently have elevated TPO antibody levels.⁴ Candidiasis should be considered as a possible contributing factor to thyroiditis in patients who have had recurrent vaginal yeast infections or a history of treatment with antibiotics, oral contraceptives or systemic glucocorticoids. ⁴

(Note: Anti-fungal prescriptive agents can cause endocrine side effects. Ketonazole may cause hypothyroidism, as well as other endocrinopathies.)³
Diagnostic Testing for Candida

**Serum Candida IgG Antibody**

<table>
<thead>
<tr>
<th>Inside Range</th>
<th>Outside Range</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Candida IgG Antibody</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

**Mycology**

*NG* NG

**KOH Results**

Few Yeast Present

**Yeast Culture Legend**

*NG NP PP P

Human microflora is influenced by environmental factors and the competitive ecosystem of the organisms in the GI tract. Pathological significance should be based upon clinical symptoms and reproducibility of bacterial recovery.
Treatment for Yeast/Fungi

Associated Conditions/Causes:

- Chronic/prolonged antibiotic use (main cause)
- High intake of sugar, milk and other dairy products and foods containing a high concentration of yeast or mold
- Hypochlorhydria
- Food allergies
- Depressed immune function
- Bowel dysbiosis

Symptoms

- Chronic fatigue
- Vaginal yeast infection
- Frequent bladder infection
- Chemical sensitivity
- Eczema
- Psoriasis
- Depression
- Rectal itching
- Bloating and gas pain
- Altered fecal transit time
- Intestinal hyperpermeability
- Opportunistic bacterial infection
- Thrush
- Thyroid dysfunction

Treatment

- Reduce intake of refined carbohydrates, sugars and fermented foods
- Stool analysis for identification and sensitivity (botanicals and pharmaceuticals)
- Probiotics (esp. S. boulardii) – crowds out yeast
- Avoid fructooligosaccharides (FOS) - feeds yeast
- Optimize GI function- (check for H. pylori) treat hypochlorhydria and pancreatic enzyme insufficiency if present.

(Note: Intestinal parasites can also decrease absorption of nutrients and can interfere with thyroid hormone synthesis. If parasites are present on the stool analysis, you will need to treat accordingly. Please refer back to the GI Module)
Celiac Disease

Celiac disease is an immune-mediated disorder clinically characterized by a multitude of symptoms and complications. The comorbidity between celiac disease and other autoimmune disorders has been clearly established. Thyroiditis has been repeatedly associated with celiac disease. A highly significant association exists between celiac disease and autoimmune thyroiditis (Greaves’ disease and Hashimoto’s thyroiditis), as evidenced by elevated EMA antibodies (Anti-Endomysial antibodies) in these thyroid conditions.

Susceptibility to celiac disease is linked to HLA class II alleles, especially the HLA-DQ region. HLA molecules are postulated to present gluten antigens to T-cell which in turn induce tissue damage. Approximately 95% of patients with celiac disease have the HLA-DQ2 heterodimer encoded by the DQA1*05 and DQB1*02 alleles, while close to 5% have the HLA-DQ8 heterodimer encoded by the DQA1*03 and DQB1*0302 alleles. The pathogenesis of co-existent autoimmune thyroid disease and celiac disease is still unclear, but these conditions share similar HLA haplotypes and are associated with gene encoding cytotoxic T-lymphocyte-associated antigen-4.

New information about the connection between celiac disease and autoimmune disease has recently been uncovered. It has been suggested that the onset of celiac disease is mediated by a skewed Th1 response. However, the participation of (T-helper cells-17) Th17 cells in the pathogenesis of the disease, a key cell population in other autoimmune diseases, appears to be a link between the celiac disease and autoimmune thyroid disease. Gliadin-specific Th17 cells are present in the mucosa of celiac disease patients having a dual role in the pathogenesis of the disease as they produce pro-inflammatory cytokines such as IL-17, IFN-γ, and IL-21. Before discussing the role of Th-17, it’s important to take a second look at a gut response to gluten intolerance and celiac disease.
Cellular and molecular induction of immune tolerance to dietary proteins (gliadin).
Depiction of immunological mechanisms underlying gluten intolerance and its immunopathological consequences.
### Table 3 - Diseases associated with low secretory IgA

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Allergy</td>
<td>• Asthma, atopy, eczema</td>
</tr>
<tr>
<td>• Autoimmunity</td>
<td>• Rheumatoid arthritis ITP, hemolytic anemia, pernicious anemia, systemic lupus erythematosus, Still's disease, transfusion reactions due to anti-IgA antibody, dermatomyositis, vitiligo, Sjogren's syndrome, Henoch-Schönlein syndrome, primary biliary cirrhosis, autoimmune hepatitis</td>
</tr>
<tr>
<td>• Respiratory tract</td>
<td>• Recurrent sinopulmonary infections, sarcoidosis, pulmonary hemosiderosis</td>
</tr>
<tr>
<td>• Gastrointestinal diseases</td>
<td>• Giardiasis, Crohn's disease, ulcerative colitis, nodular lymphoid hyperplasia, celiac disease, lactose intolerance, malabsorption villous atrophy, achlorhydria, cholelithiasis</td>
</tr>
<tr>
<td>• Neurological</td>
<td>• Seizures, migraine, sensory neuropathy, myasthenia gravis, cerebral vasculitis</td>
</tr>
<tr>
<td>• Familial history of hypogammaglobulinemia</td>
<td>• Common variable immunodeficiency</td>
</tr>
<tr>
<td>• Endocrinopathy</td>
<td>• Thyroiditis, Graves disease, idiopathic Addison's disease, diabetes mellitus, 21-hydroxylase deficiency</td>
</tr>
<tr>
<td>• Chromosomal abnormalities</td>
<td>• Chromosome 14</td>
</tr>
<tr>
<td>• Malignancy</td>
<td>• Gastric carcinoma and lymphoma</td>
</tr>
</tbody>
</table>

Reference: Reprinted with permission: Assessment of Intestinal Barrier Permeability to Large Antigenic Molecules, Aristo Vojdani, Ph.D., M.T.
Many autoimmune disorders are associated to celiac disease but the association with autoimmune thyroiditis has been more frequency documented.\(^{12}\)

The greater frequency of celiac disease in association to autoimmune thyroid disease suggests that all persons with TPO antibodies should be routinely screened for celiac disease.\(^{12}\) Tissue transglutaminase antibodies in individuals with celiac disease bind to thyroid follicles and extracellular matrix appear to contribute to thyroid dysfunction since these antibody titers correlate to TPO antibody titers.\(^{13}\) From a functional medicine perspective, I recommend that patients with known autoimmune disease of the thyroid be placed on a gluten free diet, whether or not they have celiac disease. You just saw an example of how gluten intolerance can trigger auto-antibodies. In my clinical experience, most, if not all patients with autoimmune thyroiditis has some type of gastrointestinal and/or adrenal dysfunction that can trigger and/or contribute to the autoimmune process. In Graves’s disease there are auto-antibodies to the thyroid stimulating hormone receptors and in Hashimoto’s thyroiditis, there are auto-antibodies and auto-reactive T cells to thyroglobulin and thyroid microsomal antigens.
The Major Subsets of CD4⁺ T Cells (Newly Discovered Th-17)

CD4⁺ T cells play important role in the initiation of immune responses by providing help to other cells and by taking on a variety of effector functions during immune reactions. Upon antigenic stimulation, naïve CD4⁺ T cells activate, expand and differentiate into different subsets termed Th1, Th2, Th3 (also known as T-regulatory cells) and Th17 and characterized by the production of distinct cytokines and effector functions.
The Role of Th17 Cells in Autoimmunity

For more than 30 years T-helper cells have been divided by immunologist into two functional subsets: Th1 and Th2. The role of Th17 lymphocytes in immunopathogenic processes has recently been established. The Th17 cell has been linked to a growing list of cancers, autoimmune and inflammatory diseases such as rheumatoid arthritis, systemic lupus erythematosus, multiple sclerosis, asthma, psoriasis, chronic inflammatory bowel disease and allograft rejection. The results of a recent study on the role of Th17 cells indicates that there is an increased differentiation of Th17 lymphocytes and enhanced synthesis of Th17 cytokines in autoimmune thyroid disease, in particular Hashimoto’s thyroiditis. Th17 has a role in clearing pathogens during host defense reaction. Th17 also induces tissue inflammation in autoimmune disease. As previously mentioned, Th17 up-regulation is induced by bacteria, fungus, and autoimmunity. The functional analysis of IL-17 (produced by Th17 cells) has suggested an important role for this unique cytokine in host protection against specific pathogens. The production of IL-17 and the recruitment of neutrophils seem important in host protection against gram-negative bacteria and fungal infections. It appears that the preferential production of IL-17 by the Th17 cells occurs during infections of specific pathogens such as, Klebsiella pneumonia, Bacteriodes fragilis, Borrelia burgdoferi (Lyme disease), mycobacterium tuberculosis and fungal species. A particular bacteria of interest is Yersinia enterocolitica. Yersinia has been demonstrated in lab animals to induce production of IL-17A from Th17 cells. Yersinia has also been implicated in the production of thyroid receptor antibody and is suspected in the pathogenesis of Graves’s disease through molecular mimicry. This latest research suggests another possible connection of infection and Th17 for thyroid disease. It has also been established that Gliadin-specific Th17 cells are present in the mucosa of celiac disease patients, which further establishes an additional interconnectedness to thyroid dysfunction and the gastrointestinal system.

Natural Alternatives for Reducing Inflammation in Autoimmune Conditions

- Moutan cortex (root bark of Paeonia suffruticosa)
- Perillae Fructus (perilla seed)
- Urtica dioica leaf extracts
- Ginger extract
- Artemisia annua
- Atractylenolide I

Targeting Th17

- Proper balance of 25-hydroxyvitamin D and 1,25 dihydroxyvitamin D
- Resveratrol
- Probiotics – L. casei, L. paracasei, L. rhamnosus, L. acidophilus, L. reuteri, l. brevis, B. bifidum
-ASI test- (evaluate and treat accordingly) Establishing a normal cortisol to DHEA is often overlook in the treatment autoimmune thyroiditis and non-autoimmune thyroid dysfunction, however optimal adrenal function is paramount to successful thyroid dysfunction outcomes.
**Treatment for Opportunistic Bacterial Infection**

Common causes of high levels of opportunistic bacteria present in the GI system:

- Low predominant bacteria
- Pathogen or parasite infection
- Poor diet
- Antibiotic use
- Poor gut immunity

Possible symptoms

- Diarrhea, constipation, bloating, myalgia, fatigue, and headaches
- Autoimmune – (e.g. reactive arthritis and thyroiditis may be associated with bacterial infection)

**Treatment**

- Stool analysis – to identify the cause of dysbiosis and provide a culture and sensitivity of pathogens for specific treatment agents
- Probiotics (avoid FOS if you are treating a yeast infection)
- Identify and treat for food sensitivity
- If sIgA is low, evaluate for the reason and treat accordingly

**Viral Infections and Thyroid Autoimmune Disease**

Viral infections activate both innate and adaptive immunity and have been implicated as a trigger of autoimmune diseases including Hashimoto’s thyroiditis. Viral infection are frequently cited as a major environmental factor implicated in subacute thyroiditis and autoimmune thyroid disease. Hashimoto’s thyroiditis, the most frequent tissue specific autoimmune disease in humans, is characterized by infiltration of the thyroid gland B and T lymphocytes, cellular and humeral autoimmunity, and autoimmune destruction of the thyroid. It appears that cell surface receptors, called toll-like receptors (TLR), are linked to autoimmune disorders and inflammatory disorders. These receptors protect mammals form pathogenic organisms, such as viruses, by generating an innate immune response to products of the pathogenic organism. Over expression of certain TLRs (TLR3 and TLR4), by environmental pathogens, have been associated with Hashimoto’s thyroiditis, type 1 diabetes, colitis, and atherosclerosis.

To date, no environmental reports have clearly correlated viral infections with Hashimoto’s thyroiditis. However, direct evidence of the presence of viruses or their components in the organ are available for retroviruses (HFV- Human foamy virus) and mumps in subacute thyroiditis, for retroviruses (HTLV-1, HFV, HIV and SV40) in Graves’s disease and for HTVL-1, enterovirus, rubella, mumps, HSV, EBV and parvovirus in Hashimoto’s thyroiditis. However, it remains to be determined whether they are responsible for thyroid diseases or whether they are just “innocent” bystanders.
From a functional medicine perspective, the possibility, and perhaps the probability, of a viral infection linked to thyroid diseases, as well as other diseases, must be considered as a part of the functional medicine paradigm. The total “load” on the immune system must also be considered as a part of the patient evaluation. Please read the following excerpt from the American Family Physician Journal. Even though this article is a few years old, the point is that the etiology of chronic fatigue syndrome remains unclear and that chronic fatigue syndrome is not specific to one pathogenic agent but could be a state of chronic immune activation. A recent research article conducted in 2010 highlights that there is mounting evidence that oxidative stress, especially lipid peroxidation, contributes to chronic fatigue syndrome. 23 As functional medicine practitioners, we know to look beyond the perspective of one etiological factor being the sole contributor to a specific disease. If clinically indicated, it may be worth ordering serological tests for hepatitis, Epstein-Barr virus, cytomegalovirus and herpes virus in order to assess viral exposure and activity.

‘Many patients with CFS attribute the onset of their illness to an acute influenza-like infection, and, subsequently, the role of viruses as possible causative agents for CFS has been intensively studied. In particular, an early study reported that patients with CFS presented with symptoms similar to acute infectious mononucleosis and were found to have high titers of IgG antibodies to Epstein-Barr virus (EBV). However, subsequent research refuted a correlation between titers of EBV antibodies and severity of symptoms in CFS, and showed that patients with CFS did not have significantly higher titers to EBV compared with healthy control subjects.

Although a number of other viral pathogens (such as the Coxsackie virus, human herpes virus 6, cytomegalovirus, measles, and the human T-cell lymphotropic virus [HTLV-II]) have also been implicated as etiologic agents for CFS, there is no consistent or conclusive data to suggest any causal relationships. It is now believed that CFS is not specific to one pathogenic agent but could be a state of chronic immune activation, possibly of polyclonal activity of B-lymphocytes, initiated by a virus. Patients with CFS can show different lymphocyte and cytokine profiles depending on the nature of their illness and its time of onset’. 26

**Effects of the Environment on Thyroid Function**

Since you are now aware that all of us have some level of environmental toxins in our bodies, we must take into consideration the impact that certain toxins have on the different points of regulation of thyroid hormone. These would include; the synthesis of thyroid hormone, the release, the transport through the blood, the metabolism and thyroid hormone clearance.

The ways in which chemical affect thyroid function include 24, 25

- Alteration of thyroid hormone metabolism
- Direct toxic effect on the gland, changing function and regulation
- Production of thyroid antibodies
- Interaction with thyroid protein carriers
- Blocking iodine uptake by the thyroid gland
- Increasing liver metabolism of the hormone
- Interrupting reception in cells
- Causing tumors
- Suppressing hormone production
It is important to keep in mind that many chemicals known to disrupt reproductive hormones are also suspected to cause deleterious effects on thyroid hormone.

**Endocrine Disruptors**

The Hypothalamus-Pituitary-Thyroid axis is a target of endocrine disrupting chemicals, in particular, polyhalogenated phenolic compounds such as polychlorinated biphenyls (PCBs) and polybrominated diphenyl ethers (PBDEs), probably because of their structural resemblance to thyroid hormones. These chemicals may cause disturbance of thyroid homeostasis, hypothyroidism, thyroid hyperplasia, and neoplasia. It appears that endocrine disrupting chemicals interferes on several levels of the HPT axis. These interferences appear not to conform to classic mechanism of endocrine regulation and feedback. It is possible that one compound may affect several levels of the HPT axis further complicating the situation. An example of this is genistein, one of the isoflavones. Genistein can inhibit TPO enzyme activity; inhibit thyroid hormone binding to transthyretin; and display estrogenic and anti-estrogenic effects by interacting with estrogen receptors.27

[Transthyretin is also known as thyroid-binding prealbumin. It is synthesized in the liver, as well as in the choroid plexus of the brain. The choroid plexus is where the cerebrospinal fluid in the brain is produced. It has been suggested that the choroid plexus might facilitate the transport of thyroid hormones from the blood to the brain via transthyretin synthesis in the choroid epithelial cells. Transthyretin also forms a complex with retinol-binding protein to assist with the transport of vitamin A. Transthyretin is also a negative acute phase reactant. Transthyretin, synthesized in the choroid plexus, is involved with the transport of thyroid hormone in the brain. Sequestration of lead (Pb) in the choroid plexus may lead to marked decrease in transthyretin levels in the cerebrospinal fluid.28]
Iodine is essential for thyroid hormone synthesis. Iodide enters the thyroid follicular cells via the sodium iodide symporter (NIS). Certain chemicals can interfere with the NIS causing a decrease of iodide uptake. The main chemicals of concern are; perchlorates (ClO$_4^-$), thiocyanate (SCN$^-$), and nitrate (NO$_3^-$). Thiocyanate in blood may originate from tobacco smoking, from industrial pollution of the environment, or from ingestion of certain foods. $^{29}$ Perchlorate is both a naturally occurring and manmade contaminant increasingly found in groundwater, surface water and soil. Most perchlorate manufactured in the U.S. is used as an ingredient in solid fuel for rockets and missiles. In addition, perchlorate-based chemicals are also used in the construction of highway safety flares, fireworks, pyrotechnics, explosives, common batteries, and automobile restraint systems. $^{30}$ Because of the environmental stability of perchlorate, it has become a widespread contaminant in drinking water and irrigation waters and in food, such that perchlorate contamination is nearly ubiquitous in the U.S. population. $^{31}$ Much focus has been placed on the impact of exposure to perchlorate (ClO$_4^-$) from drinking water. Recently, it has become more apparent that a significant percentage of the total ClO$_4^-$ exposure may be due to ingestion of food. $^{32}$

The organification of iodine, that is the adding of iodine to the tyrosine, is orchestrated by the enzyme thyroid peroxidase (TPO). It important to keep in mind that TPO is a heme-contain enzyme and therefore can be affected by an iron deficient state. Several substances are known to inhibit TPO, which include, 6-propyl-2-thiouracil (used to treat Graves disease) and isoflavones (e.g. genistein and coumesterol). $^{31}$ Isoflavones are polyphenolic compounds that are capable of exerting estrogen-like effects, as well as inhibiting TPO. Since soy products contain a significant amount of isoflavones, one must question the efficacy of using soy-based infant formula.
Thyroid hormones are poorly soluble in water, and therefore most of the T4 and T3 in circulation are bound to protein carriers. The principle protein carrier is thyroid-binding globulin (TBG), a glycoprotein synthesized in the liver. The other carrier proteins are albumin and transthyretin (TTR). It appears that carrier proteins allow maintenance of a stable pool of thyroid hormones from which the active, free hormones are released.

Since the liver is the production site of TBG, as well as the main source of the peripheral conversion of T4 to T3, liver dysfunction plays an important role in hormone transport and metabolism and must be a part of addressing thyroid dysfunction. The most common cause of elevated TBG is pregnancy, hormone replacement therapy, and the use of oral contraceptives. Decreased TBG is commonly associated with malabsorption, malnutrition, and nephrotic syndrome. You must also keep in mind that many drugs can either increase or decrease the production of TBG.

Drugs that increase TBG

- Estrogens
- Methadone
- Tamoxifen
- Oral contraceptives

Drugs that decrease TBG

- Steroids
- Glucocorticoids (also inhibits conversion of T4 to T3)
- Androgens
- Danazol
- Phenytion (Dilantin)
- Propanolol (also inhibits conversion of T4 to T3)

Halogenated aromatic hydrocarbons structurally resemble thyroid hormones and may compete with binding to the thyroid hormone receptors and transport proteins, possibly interfering with thyroid hormone transport and metabolism. PCBs, flame retardants, phenol compounds and phthalates competitively bind to transthyretin. Competitive binding of environmental chemicals to thyroid hormone transport protein may result in increased bioavailability of endogenous thyroid hormones. You need to keep in mind that TTR is a major thyroid hormone transport protein in the brain which is independent of the T4 homeostasis in the body. Furthermore, TTR may mediate the delivery of T4 across the blood-brain barrier and the maternal to fetal transport through the placenta. Thus, environmental chemicals bound to TTR may be transported to the fetal compartment and the fetal brain, and be able to decrease fetal brain T4 levels.
Uridine 5’-diphosphate-glucuronosyltransferases (UGT) catalyze the binding of glucuronic acid, from uridine 5’-diphosphate glucuronic acid on numerous xenobiotics or endogenous compounds including bilirubin, bile acids, steroids, thyroxine, fat-soluble vitamins and retinoids. Increase activity of these enzymes may lead to faster metabolism of thyroid hormones and therefore may influence thyroid hormone level. The chemical of note that increase this enzymes activity are dioxin-like compounds. Chemicals that can inhibit the deiodination of T4 to T3 include lead, cadmium, organochlorines, methoxychlor, octylmethoxycinnamate, and 4-methylbenzyiden-camphor (MBC).

**Environmental Chemical Influence on Thyroid Hormone Receptors**

Several recent reports show that a broad range of chemicals to which humans are routinely, and inadvertently, exposed can bind to thyroid receptors and may produce complex effects on thyroid hormone signaling. It is clear that PCBs are neurotoxic in humans and animals, and that they can interact directly with the thyroid receptor. However, the consequences of PCB exposure on thyroid hormone action appear to be quite complex. This complexity includes acting as an agonist or antagonist and may include thyroid receptor isoform selectivity. Another environmental toxin of concern is Bisphenol A (BPA). BPA is mainly used in the manufacturing of plastics. BPA has been shown to bind to the thyroid receptor. Developmental exposure to BPA in rats produces an endocrine profile similar to that observed in thyroid resistance syndrome. Polybrominated diphenylethers (PBDEs) are a particular class of flame retardant chemicals. These chemicals may also bind to the thyroid hormone receptor. There is growing evidence that PBDEs persist in the environment and accumulate in living organisms, as well as toxicological testing that indicates these chemicals may cause liver toxicity, thyroid toxicity, and neurodevelopmental toxicity. Environmental monitoring programs in Europe, Asia, North America, and the Arctic have found traces of several PBDEs in human breast milk, fish, aquatic birds, and elsewhere in the environment.
Other Environmental Toxins of Concern

Ethylenebisdithiocarbamates (EBDCs) are fungicides used on banana plantation that are linked to thyroid disease, in particular thyroid nodules. Heavy metals, such as lead and cadmium have been linked to thyroid gland dysfunction. Both lead and cadmium damage the structure and function of the thyroid gland. The mode or mechanism action by cadmium and lead on the thyroid gland and thyroid hormone metabolism were by interference in the synthesis and/or secretion of T4 by the damage of follicular cells, decrease transformation rate of T4 to T3 in peripheral tissue by inhibiting the activity of 5’-deiodinase and interference with pituitary and hypothalamus gland. Aside from cadmium damaging the thyroid gland, it is also know to damage the parathyroid glands.

Bromine is concentrated by the thyroid gland and interferes with iodine uptake, possible by competitive inhibition of iodide transport to the gland. Florine is not concentrated by the thyroid gland but has a mild antithyroid effect, possible by inhibiting iodide transport.

Agents that May Affect TSH Secretion

Increase serum TSH concentration and/or its response to TRH
- Iodine/iodide
- Lithium
- Dopamine receptor blockers
- Cimetidine (tagamet)
- Amphetamines
- Spironolactone
- L-Dopa inhibitors

Decrease serum TSH concentration and/or its response to TRH
- Thyroid hormones
- Dopaminergic agents
- Serotonin antagonists
- Glucocorticoids
- Acetylsalicylic acid
- Metformin
- Opiates

List of Thyroid Disrupting Chemicals

Persistent Organic Pollutants
- Benzenehexachloride
- Octachlorostyrene
- PBBs
- PCBs
- PBDEs
- Pentachlorophenol
Pesticides
- Acetochlor
- Alachlor
- Amitrol
- Chlofentezine
- Ethylene thiourea
- Fenbuconazole
- Fipronil
- Heptachlor-epoxide
- Karate
- Malathion
- Mancozeb
- Maneb
- Methomyl
- Metribuzin
- Nitrofen
- Pendimethalin
- Pentachloronitrobenzene
- Prodiamine
- Pyrimethanil
- Tarstar
- Thiazyzopyr
- Thiram
- Toxaphene
- Zineb
- Ziram

Other Compounds
- Perfluorooctane (PFOS)
- Resorcinol

Log on to www.scorecard.org to get an in-depth pollution report for your area of interest. Just enter the zip code.
Testing for Environmental Toxins

<table>
<thead>
<tr>
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<th>Methodology: Gas Chromatography/Mass Spectrometry</th>
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<tr>
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<tr>
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<tr>
<td>PCB 126</td>
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</tbody>
</table>

Reference: Metametrix Clinical Laboratory, 3425 Corporate Way, Duluth, GA 30096 USA

Functional Medicine Laboratory Tests to consider:

- Porphyrins Profile
- PCBs Profile
- Chlorinated Pesticides Profile
- Volatile Solvents Profile
- Phthalates & Parabens Profile
- Nutrient & Toxic Elements
- Toxic Metals
Proposed Serological Markers for Body Toxicity

**Gamma-glutamyltransferase (GGT)** – GGT is a serum marker of fatty liver, gallbladder dysfunction and oxidative stress. However, serum GGT may predict many diseases as a cumulative biomarker of various environmental chemicals. Cellular GGT is a prerequisite for metabolism of glutathione conjugates and glutathione is a critical biomolecule for conjugation of diverse chemicals.

Abstract

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**Can persistent organic pollutants explain the association between serum gamma-glutamyltransferase and type 2 diabetes?**

Lee DH, Steffes MW, Jacobs DR Jr.

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**Abstract**

The results of several epidemiological studies of serum gamma-glutamyltransferase (GGT) led us to hypothesise that associations of GGT within its normal range with type 2 diabetes may reflect detrimental effects of xenobiotics found in the environment, such as persistent organic pollutants (POPs). Epidemiological observations showed that serum GGT activity within its normal range strongly predicted future type 2 diabetes; the predictability of diabetes from obesity was low with GGT at the low end of the normal range, and GGT showed a positive association with known markers of oxidative stress or inflammation. Experimental findings on cellular GGT suggest that serum GGT levels within the normal range may reflect oxidative stress related to the re-synthesis of intracellular glutathione; however, this interpretation is not completely satisfying because, in its role of regenerating intracellular glutathione, GGT activity should be antioxidative. Alternatively, serum GGT activity may reflect amounts of glutathione conjugates formed during the metabolism of xenobiotics. Accordingly, we postulate a two-part hypothesis: that the association of serum GGT with type 2 diabetes reflects exposure to POPs, as these substances, which have a very long half-life, may influence diabetes risk by residing in adipose tissue as endocrine disruptors; and that POPs or similar substances may interact with obesity to cause type 2 diabetes. Supporting this hypothesis, cross-sectional investigation of background exposure to POPs in the National Health and Nutrition Examination Survey showed relationships similar to those observed for GGT, including a powerful association with prevalent diabetes and no association between obesity and diabetes for very low POP concentrations. Our hypothesis can be tested in both prospective studies and toxicological studies.

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**Uric acid** – elevated uric acid is a sign of oxidative stress

**Homocysteine** – elevated homocysteine is a sign of oxidative. There is also a correlation between increased homocysteine serum levels and lead exposure. Homocysteine inhibits retinoic acid synthesis. You should recall that the thyroid hormone receptor usually forms a heterodimer with retinoid X receptor at the specific thyroid hormone response element on the DNA. Low level of retinoic acid may result in a decrease effect of the DNA response to thyroid hormone.
Treatment for Environmental Toxins (Lowering Total Body Burden)

It is important to recall that once the toxins are released, they will enter the bloodstream and be metabolized by the liver. Phase I and phase II liver detoxification pathways must be supported during treatment. The kidney, the gastrointestinal system, the lungs and the skin need to be assess and treated if necessary, since these are the organ of elimination.

Four Steps to Detoxification

1. Mobilizing stored toxins
2. Supporting liver metabolism
3. Elimination from the body
4. Avoiding re-exposure to toxins

- Use the protocols listed in the Detoxification Module (Go Slow)
- Far Infrared Sauna Treatments (massage after sauna or exercise before sauna)
- Nutritional support (esp. magnesium supplementation) A good multivitamin/mineral should include: vitamin A (from mixed carotenes), B complex, C, D, E, calcium, magnesium, zinc, copper, molybdenum, iodine, selenium, choline, inositol. I recommend ordering an organic acid test prior to implementing the detoxification protocols. The organic acid test can provide patient specific nutrient needs.
- Check first morning urine pH. This will give you an idea about the body’s mineral reserves and its acid/alkaline state. A healthy zone for the first morning urine pH is between 6.5 and 7.5. If morning pH is consistently low, consider placing the patient on an alkaline diet and/or using alkaline water (www.hightechhealth.com for water alkalizer) Remember the body needs an adequate supply of mineral for overall health and for detoxification.
- Home water analysis
- Other nutritional support to consider: Whey protein, green tea, curcumin, arcticum root, taraxacum, silymarin, beetroot, artichoke, diindolylmethane (DIM), calcium-D-glucarate, N-acetylcysteine, alpha-lipoic acid, methylfolate, and methylcobalamin.

Excerpt taken from the book titled, “Clean, Green and Lean” by Dr. Walter Crinnion & John Wiley and Sons, Inc. 2010:

‘I discovered that I didn’t need to give immune-support nutrients to people with chronic viral infections of chronic fatigue. I just needed to cleanse them. When their toxic levels dropped, their white blood cells began to attack the viruses as they’re supposed to. I didn’t have to give a lot of adrenal support to people with chronic adrenal insufficiency, because their adrenal glands would begin to heal. When patients reduced their level of toxic burden, all of their organs started to work much better.’
Endocrine Disruptors as Obesogens

The root cause of obesity was thought to be prolonged positive energy balance, that is, too much food and too little exercise. Recent research implicates environmental risk factors, including nutrient quality, stress, fetal environment and pharmaceutical or chemical exposure as relevant contributing influences. Evidence points to endocrine disrupting chemicals that interfere with the body’s adipose tissue biology, endocrine hormone systems or HPA axis as suspects in derailing homeostasis mechanisms important for weight control. Adipose tissue functions as an active endocrine organ that participates in the body's feedback system that fine-tunes the regulation of appetite and the metabolic integration between organs and inflammatory responses. A variety of environmental endocrine disrupting chemicals can influence adipogenesis and obesity. Obesogens can be defined functionally as chemical agents that inappropriately regulate and promote lipid accumulation and adipogenesis.

Classification of Obesogens

Environmental Pollutants

- Tributyltin (TBT)
- Triphenyltin (TPT)
- Phthalates
- Bisphenol A (BPA)
- Perfluoroalkyl compounds (PFCs)
- Polybrominated diphenyl ethers (PBDEs)
- Dithiocarbamates
- Alkylphenols

Nutritional compounds

- Phytoestrogens
- Glycyrrhetinic acid

Pharmaceuticals

- Diethylstilbestrol (DES)
- Selective serotonin reuptake inhibitors (SSRI)
- Tricyclic antidepressants
- Thiazolidinediones (TZDs) – use to treat diabetes. Binds to PPARs (peroxisome proliferator-activated receptor
- Atypical antipsychotics
Obesogens and Programming of Metabolic Set Points

Obesogens → Hypothalamus
- Dysregulation of hypothalamus
- Regulates appetite center
- Regulates metabolic efficiency
- Establishes metabolic set point

Pituitary

Thyroid
- Carbohydrate metabolism
- Lipid metabolism
- Protein metabolism

- Depressed circulating T4 levels
- Decreased conversion of T4 to T3
- Reduced sympathetic activity

[Note: Since Obesogens can cause dysregulation of the hypothalamus and the pituitary gland, think of the impact they have on central hypothyroidism (secondary and tertiary hypothyroidism, respectively). Obesogens also influence the HPA axis]

The Effect of Weight Loss on Serum Level of POPs

It's important to note that there may be an increase in serum persistent organic pollutants with weight loss. The reason for the increase serum concentration of pollutants is due to the fact that pollutants bioaccumulate in the adipose tissue. From a functional medicine perspective, it’s important to provide nutritional detoxification support to individuals on a weight loss program.
Inverse associations between long-term weight change and serum concentrations of persistent organic pollutants

J S Lim, H-K Son, S-K Park, D R Jacobs and D-H Lee

There is emerging evidence that persistent organic pollutants (POPs) can increase the risk of various chronic diseases. As POPs mainly bioaccumulate in adipose tissue, weight change can affect serum concentrations of POPs. However, there are few population-based studies on effects of long-term weight change on serum concentrations of POPs. We examined associations between self-reported weight change over 1 year and 10 years and serum concentrations of seven POPs in 1099 adults aged ≥ 40. Serum concentrations of most POPs were higher in those with long-term weight loss, whereas they were lower in those with long-term weight gain. Adjusted correlation coefficients of each POP with weight change for 10 years were −0.23 (P<0.01) for trans-nonachlor, −0.16 (P<0.01) for p,p'-dichlorodiphenyldichloroethylene, and −0.21 (P<0.01) for β-hexachlorocyclohexane, −0.16 (P<0.01) for PCB169, −0.20 (P<0.01) for PCB180 and −0.17 (P<0.01) for 1,2,3,4,6,7,8-heptachlorodibenzo-p-dioxin. Weight change for 1 year showed similar but weaker associations, compared with those of long-term weight changes. Although both beneficial health effects after weight loss and harmful health effects after weight gain are generally expected, changes in serum concentrations of POPs in relation to weight change may act on health in directions opposite to what we expect with weight change.

The solution is to this condition is to provide proper nutritional support during a detoxification program. GO SLOW.
Response to Environmental Change: Signal Transduction

A process called “signal transduction” is how the cells of the body respond to the environment and communicate with each other in an effort to “forward the message”. Signal transduction refers to the movement of signals from outside the cell (external environment) to inside the cell (internal environment). Cells communicate by biochemical signals with the end result being an alteration in cellular function. There are two possible scenarios: a substance can enter the nucleus, bind to the DNA and affect transcription or a substance can stay in the cytoplasm and affect cellular metabolism.

There are three classifications of signal transducing receptors (aka cellular receptors):

1. Receptors that penetrate the plasma membrane and have intrinsic enzymatic activity. An example of this type of receptor is tyrosine kinase. (e.g. insulin receptor. See picture in diabetic lesson)
2. Protein-linked hormone receptors that are coupled inside the cell to GTP-binding proteins (G proteins). These receptors are also known as G-Protein coupled receptors. They use a second messenger (cAMP) to activate protein kinase and phosphatase. They can also active mitogen-activated protein kinase (MAPK). These signaling pathways can be activated by cellular stress, inflammation, apoptosis, lipopolysaccharides, IL-1, TNF-α, ionizing or ultraviolet radiation. An example of this type to receptor is the adrenergic receptors. (A mitogen is a substance that encourages cell division.)
3. Intracellular receptors – (Nuclear Hormone Receptor Family) Receptor of this class include the large family of steroid and thyroid hormone receptors.46
Cross talk between the Plasma Membrane and the Nuclear Pathways

The biological effects of steroid hormones are mediated by receptors associated with the plasma membrane, as well as located in the cytoplasm and nucleus. The steroid hormone receptors superfamily, (e.g. estrogen receptors, thyroid hormone receptors and vitamin D receptors), have been shown to function at multiple subcellular sites leading to a continuum of signals intimately linked by intracellular crosstalk. Cross talk between members of nuclear receptor superfamily appear to multiply the possible modes of gene regulation. An example of this is the activation of estrogen-dependent growth responses by a non-estrogen, such as insulin growth factor (IGF), that can promote the growth on various cell types. Cross talk between IGF and estrogens can lead to cell proliferation in breast carcinoma. Estrogen receptors and thyroid hormone receptors are ligand-dependent nuclear transcription factors that can bind to an identical half-site. The cross talk between estrogen and thyroid hormone receptor isoforms can result in differential regulation of the hypothalamus and therefore, neuroendocrine integration. From a functional medicine perspective, you must consider the potential interaction of thyroid hormones and estrogens on both nuclear receptors and the membrane-initiated molecular mechanisms of hormone signaling. In other words, you must assess for other hormonal imbalance when evaluating for thyroid dysfunction.

Non-Genomic Actions of Thyroid Hormones

Genomic refers to any action of a hormone that leads to a change in gene transcription, regardless of whether the classical nuclear receptor for that steroid is involved. Non-genomic is used for changes that occur independently of new messenger RNA transcription. Non-genomic actions are usually rapid in onset, do not require protein synthesis, and are independent of nuclear thyroid receptors. The non-genomic actions of thyroid hormone are mediated in part by signal transduction pathways. Some of the non-genomic actions of thyroid hormone include increased activity of sodium, potassium and calcium ions. Thyroid hormone is also known to cause a plasma membrane-initiated action on signal transduction by activation of mitogen-activated protein kinase (MAPK). This kinase (MAPK) is capable of causing activation of both genomic and non-genomic action. It is interesting to note that T4 is more active than T3 in stimulating the MAPK pathway in several models. This signaling pathway can cross talk with estrogen receptors contributing to estrogen-receptor activity. Therefore, the clinical states of hyperthyroidism or hyperthyroidism might impact estrogen receptors on target organs. In other words, a change in thyroid hormone level could result in functional alteration that is estrogen-like in their effects.

High Levels of Estrogen and Thyroid Hormone

High levels of estrogen (Hyperestrogenemia) increases the serum concentration of thyroid binding globulin limiting the amount of free (active) thyroid hormone to enter the target cells. Elevated TBG is associated with pregnancy, estrogen therapy, oral contraceptives, genetic predisposition and “estrogen dominance”. You also need to think about gastrointestinal dysbiosis. Dysbiotic bacteria can produce and enzyme called β-glucuronidase. This enzyme can effectively reverse detoxification that has taken place in the liver during the Phase II conjugation reactions. Excess β-glucuronidase is associated with increased risk of cancer, including estrogen related cancers. The cleavage of glucuronide from estrogen metabolites leads to their increased enterohepatic recirculation. Adequate fiber intake can assist in decreasing enterohepatic recirculation. If you suspect a liver and/or gastrointestinal dysfunction, an evaluation must be performed and treated accordingly in an effort to balance thyroid hormones as well as estrogens.
Organification (oxidation) of iodide is accomplished by $\text{H}_2\text{O}_2$ (hydrogen peroxide) catalyzed by the enzyme thyroid peroxidase, and leads to the formation of T3 and T4.\(^{54}\) Thyroid hormone synthesis requires an adequate supply of iodide and the continuous production of hydrogen peroxide.\(^{54}\) Hydrogen peroxide is toxic to the cells, can be the precursor of highly reactive peroxides, and if not properly reduced to water ($\text{H}_2\text{O}$) by intracellular defense mechanisms, can expose the thyroid to free radical damage.\(^{54}\) The thyroid gland has several mechanisms to resist oxidative stress. The thyroid cells (thyrocytes) are protected by the enzymes, catalase (CAT), glutathione peroxidase (GPx), and superoxide dismutase (SOD), both of which are selenium containing enzymes. Therefore, a selenium deficiency not only contributes to a decrease in peripheral conversion of T4 to T3, it also contributes to thyroid damage via oxidative stress. Iodine deficiency also contributes to oxidative damage to the thyroid gland. An iodine deficiency causes a compensatory increase in hydrogen peroxide in an effort to compensate for impaired thyroid hormone synthesis.\(^{54}\)
Selenium /Iodine/Zinc

Please refer to prior lessons for a complete description of iodine and selenium.

1. Module 7 (FDMT 563A) Physiology of the Thyroid Gland – Selenium
2. Module 7 (FDMT 561D) The Biochemical Effects of Iodine

Selenium

The effect of selenium on autoimmune thyroiditis, as well as many other autoimmune diseases, such as rheumatoid arthritis and lupus, is well documented. Selenium as an essential trace element is capable of exerting complex effects on the endocrine and immune system by its antioxidant capacity. The role of selenium is important because the level of free oxygen radicals is elevated in the physiological thyroid hormone synthesis. It seems that the immunomodulatory effect of this element may be more prominent than the other effects. With severe selenium deficiency there is a higher incidence of thyroiditis due to a decreased activity of selenium-dependent glutathione peroxidase activity within the thyroid cells. Selenium-dependent enzymes also have modifying effects on the immune system. Therefore, even mild selenium deficiency may contribute to the development and maintenance of autoimmune thyroid diseases. Selenium has been shown to decrease thyroid antibody titer, in particular TPO Ab. It is worth noting that selenium may be ineffective in the later stages of thyroiditis due to the atrophic phase of the pathology.

Iodine

Around 90% of dietary iodine is excreted in the urine, and variable urine volumes cause variable dilution of the iodine excreted in the urine, and thus in the concentration of iodine in the urine. In order to establish iodine status in an individual with thyroid disease or suspected thyroid disease, FMU suggests using a 24 hour iodine urine test and a serum thyroglobulin test. A 24 hour iodine test will significantly reduce the variability of iodine test results often observed with other urinary iodine tests. Thyroid volume, thyroid nodularity, or iodine excretion have close associations to serum thyroglobulin (Tg), which only originates in the thyroid. Serum Tg was found to be a suitable marker for iodine nutrition status. It is important to correlate serum Tg tests result with the condition of the thyroid gland. In general, inflammation/proliferation of the thyroid gland will cause an increase in serum Tg and suppressed activity of the thyroid gland will cause a decrease in serum Tg.

Influence of thyroid status and iodine intake on serum TG

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The Paradox of Iodine Intake and Thyroid Autoimmunity

In spite of the difficulties in interpreting and comparing results from epidemiological studies on thyroid autoimmunity, there are certain tendencies in the relationship between thyroid autoimmunity and iodine intake. A sudden increase in iodine intake in an iodine–deficient population may induce enhanced thyroid autoimmunity. A number of mechanisms have been suggested to explain the association between thyroid autoimmunity and the level of iodine intake. A sudden shift from very low to high iodine intake may induce damage to the thyroid tissue by free radicals and the enhancement of the autoimmunogenic properties of thyroglobulin by increased iodination. Excessive iodine intake reduces organic binding of iodine, resulting in hypothyroidism and goiter, thyroiditis, and autonomous thyroid nodules. Chronic intake of large amounts of iodine can limit thyroid hormone synthesis and release. FMU recommends slow titration of iodine repletion in an iodine-deficient individual. We also recommend monitoring iodine status at frequent intervals (every 4-8 weeks) early in iodine supplementation.

Zinc

Zinc is essential for many biochemical processes and also for cell proliferation. Thyroid hormones influence zinc metabolism by affecting zinc absorption and excretion. Significant relationships between thyroid volume and serum zinc levels in nodular goiter patients, between thyroid autoantibodies and zinc in autoimmune thyroid disease patients and between free T3 and zinc in subjects with normal thyroid were detected. It appears that assessing zinc status is an integral part of assessing thyroid dysfunction and is certainly part of the functional medicine spectrum of considerations.

Thyroid Hormones and Oxidative Stress

Thyroid hormones influence several mitochondrial functions including oxygen consumption and oxidative phosphorylation, and to increase the metabolic activity of almost all tissues of the body. T3 exerts significant action on energy metabolism, with the mitochondria being the major target for its calorigenic (increasing production of energy/heat and oxygen consumption) effects. Acceleration of oxygen consumption by T3 leads to an enhanced generation of reactive oxygen and nitrogen species in target tissues, with higher consumption of cellular antioxidants and inactivation of antioxidant enzymes, and thus oxidative stress. It was shown that T3 administration to rats induces a calorigenic response and liver glutathione depletion as an indication of oxidative stress, with higher levels of interleukin-6 (IL-6). You may recall that IL-6 causes the liver to produce CRP. T3 induced oxidative stress can also enhance the DNA binding of NF-kB, which is involved in the inflammatory process. Thyroid hormone has a pro-oxidant effect and increases the oxygen free radical production and hence the resultant decrease in antioxidant state in the case of hyperthyroidism when compared to the normal and hypothyroidism.
Oxidative stress is currently suggested as the mechanism underlying diabetes and diabetic complications. The level of TSH has been shown to be decreased and the levels of T4 and FT4 have been shown to be increased in diabetics. T3 and T4 are insulin antagonist that also potentiate the action of insulin indirectly. While thyroid hormones oppose the action of insulin and stimulate hepatic gluconeogenesis and glycogenolysis, they up-regulate the expression of genes such as GLUT-4 and phosphoglycerate kinase, involved in glucose transport and glycolysis respectively, thus acting synergistically with insulin in facilitating glucose disposal and utilization in the peripheral tissues. Failure to recognize the presence of thyroid dysfunction in diabetics may be a primary cause of poor management often encountered in the treatment of diabetes.

‘Thyroid Diabetes’

Hyperthyroidism and Glucose Regulation

- Highly increased intestinal glucose absorption
- Increased hepatic gluconeogenesis and glycogenolysis (This explains why glucose control deteriorates when diabetic patients develop hyperthyroidism)
- The increased glucose and post-absorptive glycemia cause an elevated fasting and/or postprandial insulin level. And apoptosis of the insulin producing cells. There is also increased peripheral tissue glucose utilization with insulin resistance.

Hypothyroidism and Glucose Regulation

- Decreased intestinal glucose absorption
- Decreased hepatic gluconeogenesis and glycogenolysis
- Reduced hepatic glucose output and post-absorptive glycemia.
- The net effect of hypothyroidism on glucose regulation is: a decrease in peripheral tissue glucose disposal and a reduced baseline plasma insulin level with increased post glucose insulin secretion.

[Glucose disposal refers to the fate of glucose taken up by the tissues. About two thirds of the glucose taken up by the tissues undergoes glycolysis, with the remainder being stored]

The impact of thyroid dysfunction on glucose metabolism has been known for a long time. Thyrotoxic patients usually lose their glucose control when thyroid decompensation is not properly solved. In other words, hyperthyroidism can lead to glucose dysregulation. Most recently, new pathways of thyroid hormone action at the tissue level have been unveiled and may be of relevance to understanding of insulin resistance present in both hypothyroid and hyperthyroid states.

It is recommended that patients with glucose dysregulation and diabetes be assess for thyroid dysfunction (as well as for oxidative stress) due to the high prevalence of both endocrinopathies.
From a functional medicine perspective, it is especially important to assess antioxidant status and oxidative stress in patients who are in a hypermetabolic state, as in hyperthyroidism, in patients who are on thyroid replacement hormone(s) and in patients with glucose dysregulation (insulin resistance/diabetes).

The following functional medicine tests will assist in assessing antioxidant status and oxidative stress:

- Organic acid test
- Nutrient element test
- Antioxidant Vitamin test (vitamins A, beta-carotene, Coenzyme Q10)

Abstract: L-Carnitine Improves Glucose Disposal in Type 2 Diabetic Patients

Objective: Aim of the present study is to evaluate the effects of L-carnitine on insulin-mediated glucose uptake and oxidation in type II diabetic patients and compare the results with those in healthy controls.

Design: Fifteen type II diabetic patients and 20 healthy volunteers underwent a short-term (2 hours) euglycemic hyperinsulinemic clamp with simultaneous constant infusion of L-carnitine (0.28 μmole/kg bw/minute) or saline solution. Respiratory gas exchange was measured by an open-circuit ventilated hood system. Plasma glucose, insulin, non-esterified fatty acids (NEFA) and lactate levels were analyzed. Nitrogen urinary excretion was calculated to evaluate protein oxidation.

Results: Whole body glucose uptake was significantly (p<0.001) higher with L-carnitine than with saline solution in the two groups investigated (48.66±4.73 without carnitine and 52.75±5.19 μmoles/kg fmin/minute with carnitine in healthy controls, and 35.90±5.00 vs. 38.90±5.16 μmoles/kg fmin/minute in diabetic patients). Glucose oxidation significantly increased only in the diabetic group (17.61±3.33 vs. 16.45±2.95 μmoles/kg fmin/minute, p<0.001). On the contrary, glucose storage increased in both groups (controls: 26.36±3.25 vs. 22.79±3.46 μmoles/kg fmin/minute, p<0.001; diabetics: 21.28±3.18 vs. 19.66±3.04 μmoles/kg fmin/minute, p<0.001). In type II diabetic patients, plasma lactate significantly decreased during L-carnitine infusion compared to saline, going from the basal period to the end-clamp period (0.028±0.0191 without carnitine and 0.0759±0.0329 with carnitine, p<0.0003).

Conclusions: L-carnitine constant infusion improves insulin sensitivity in insulin resistant diabetic patients; a significant effect on whole body insulin-mediated glucose uptake is also observed in normal subjects. In diabetics, glucose, taken up by the tissues, appears to be promptly utilized as fuel since glucose oxidation is increased during L-carnitine administration. The significantly reduced plasma levels of lactate suggest that this effect might be exerted through the activation of pyruvate dehydrogenase, whose activity is depressed in the insulin resistant status.

You must use caution when prescribing L-carnitine in individuals experiencing thyroid dysfunction. L-carnitine inhibits both T3 and T4 entry into the cell nuclei. A clinical observation proved the usefulness of L-carnitine in the most serious form of hyperthyroidism: thyroid storm. Between 2 and 4 grams per day of oral L-carnitine are capable of reversing hyperthyroid symptoms, as well as the appearance of hyperthyroid symptoms.
The initial steps of thyroid hormone synthesis are catalyzed by heme-containing thyroid peroxidase (TPO). Iron deficiency may lower thyroperoxidase activity and interfere with the synthesis of thyroid hormones. Iron deficiency has been shown to impair response to iodine supplementation. Studies in humans have shown that moderate to severe iron deficiency significantly lowers both T3 and T4 (although T3 to a greater extent) and reduces TSH responsiveness. The mechanisms by which iron status influences thyroid metabolism:

- Impairment of thyroid metabolism through anemia and lowered oxygen transport
- Alter central nervous system control of thyroid metabolism and nuclear t3 binding
- Impairment of thyroid peroxidase activity (By reducing TPO activity, iron deficiency may decrease iodine incorporation into thyroglobulin and subsequent coupling of iodotrysosines to form thyroid hormone.

Note: Vitamin C has a role in iron absorption. Vitamin C prevents the formation of insoluble and unabsorbable iron compounds and cause the reduction of ferric to ferrous iron, which is the form of iron that is required for uptake by the mucosal cells.
Iron Panel Blood Test Interpretation

<table>
<thead>
<tr>
<th></th>
<th>FERRITIN</th>
<th>IRON</th>
<th>TIBC</th>
<th>%TRANSFERRIN SATURATION</th>
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<tr>
<td>CHRONIC BLOOD LOSS</td>
<td>L</td>
<td>L</td>
<td>H</td>
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<td>N</td>
<td>L</td>
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<tr>
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<td>L</td>
<td>L</td>
<td>E</td>
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<tr>
<td>HEMOLYTIC ANEMIA</td>
<td>H</td>
<td>H</td>
<td>L</td>
<td>H</td>
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<tr>
<td>CHRONIC DISEASE</td>
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<td>L</td>
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<td>H</td>
<td>L</td>
<td>H</td>
</tr>
<tr>
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<td>L</td>
<td>L</td>
<td>H</td>
<td>L</td>
</tr>
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<td>H</td>
<td>H</td>
<td>L</td>
</tr>
<tr>
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<td>H</td>
<td>N</td>
<td>L</td>
<td>H</td>
</tr>
<tr>
<td>IRON TOXICITY</td>
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<td>H</td>
<td>N</td>
<td>H</td>
</tr>
<tr>
<td>IRON EXCESS</td>
<td>N(optimal)</td>
<td>N(optimal)</td>
<td>N(optimal)</td>
<td>H (Greater than 45%)</td>
</tr>
<tr>
<td>IRON DEPLETION</td>
<td>L (20ug/L) Low optimal</td>
<td>N (ref)</td>
<td>N(ref)</td>
<td>N (optimal)</td>
</tr>
<tr>
<td>IRON DEFICIENCY WITHOUT ANEMIA</td>
<td>L(optimal) N (ref)</td>
<td>L (optimal) N(ref)</td>
<td>H (optimal) N (ref)</td>
<td>L(optimal) N (ref)</td>
</tr>
</tbody>
</table>

Change optimal serum iron to 65 – 115 ug/dL.

Notes on iron

1. The first major indicator of iron excess is a % transferring saturation greater than 45
2. The three stages of iron-deficiency anemia – the first stage, called iron depletion, is characterized by a progressive reduction in the amount of storage iron in the liver. Serum ferritin will be 20 ug/L or less. The second stage, called iron deficient erythropoiesis (also known as iron deficiency without anemia), is characterized by low iron supply to the erythopoietic cells and a decrease in % transferring saturation. The third and final stage is iron deficiency anemia. This stage show frank microcytic, hypochromic anemia. There will be a decrease in hemoglobin at this stage. Hemoglobin is an insensitive biomarker of iron deficiency since its concentration only falls during the last stage of iron deficiency.
3. Iron deficiency is often associated with iodine deficiency. Iron deficiency has been shown to impair the response to iodine supplementation. Iron deficiency can affect thyroid function even in the absence of iodine deficiency. Moderate to severe iron deficiency can significantly lower T4 and T3 and reduce TSH response. T3 is generally reduced to a greater extent.
Peroxisome proliferator–activated receptors (PPARs) and thyroid hormone receptors (TRs) are members of the nuclear receptor superfamily. Recent studies have indicated that PPARs and TRs can crosstalk to affect diverse cellular functions. You should recall that the ligands for PPARs are fatty acids, in particular the omega-6 and omega-3 fatty acids. This relationship suggests that fatty acids play a role in thyroid function and the important of optimizing essential fatty acid status. As you can visualize in the illustration depicting retinol, vitamin D, vitamin A and thyroid hormone, the retinoid X-receptor forms a heterodimer with thyroid hormone receptor, PPAR, vitamin D receptor and retinoic acid receptor. Vitamin A, in particular 9-cis-retinoic acid, is the ligand for the retinoid X-receptor, and is therefore an important constituent in the activation of the receptor and the heterodimer it combines to. In other words, vitamin A is needed for gene regulation of vitamin D receptor, thyroid hormone receptor, PPARs and retinoic acid receptor. There also appears to be a crosstalk between vitamin D receptors and thyroid hormone receptor signaling pathways.
The Physical Signs of Vitamin A Deficiency Include:

- Dry, scaly skin
- Follicular hyperkeratosis
- Night blindness
- Xerophthalmia
- Psoriasiform rash

(If these signs are present, you need to question whether or not there is a liver/gallbladder dysfunction)

Vitamin D and Autoimmunity

The vitamin D-mediated endocrine system plays a role in the regulation of calcium homeostasis, cell proliferation, and (auto) immunity.\textsuperscript{71} 1,25 dihydroxyvitamin D is the active metabolite that can help prevent the development of autoimmune thyroiditis in an animal model and inhibits HLA class II expression on endocrine cells.\textsuperscript{71} 1, 25 dihydroxyvitamin D exerts its immunomodulatory effects by down-regulating the expression of HLA class II molecules on thyrocytes and inhibiting lymphocyte proliferation as well as secretion of inflammatory cytokines.\textsuperscript{72} Polymorphic sites tested at the vitamin D receptors were found to be associated with a higher risk of Hashimoto’s thyroiditis.\textsuperscript{71,73}
In an earlier lesson in this module there was an explanation of the rational of assessing serum level of both 25-hydroxyvitamin D and 1, 25 dihydroxyvitamin D with regard to chronic inflammation and autoimmune disease. It is known that the vitamin D receptor play a role in activating the innate immune response (first line of defense) and recent research indicates that dysregulation of the vitamin D receptor (VDR) may be central to the pathogenesis of autoimmune disease. It appears that certain bacteria are capable of dysregulating the VDR leading to hormonal imbalances and autoimmunity. The normal VDR activates an enzyme responsible for the breakdown of 1, 25 dihydroxyvitamin into inactive metabolites, which establishes a balance, via a negative feedback system, in order to maintain an optimal 1, 25 dihydroxyvitamin D level. The dysregulation of the VDR causes a decrease in catabolism of 1, 25 dihydroxyvitamin D and therefore, an increase in serum concentration. 1, 25 dihydroxyvitamin D appears to have a high affinity for the alpha thyroid receptor, which can displace T3 and result in a condition called thyroid hormone resistance. Another mechanism of 1, 25 dihydroxyvitamin D and VDR dysregulation is through the inhibitory effects of NF-kB. The inflammatory cytokine, tumor necrosis factor-α is produced by NF-kB and has been shown to decrease osteoblast transcriptional responsiveness to vitamin D and to inhibit the binding of the vitamin D receptor and its nuclear partner the retinoid X receptor to DNA.

(Biofilm: Microorganisms commonly attach to living and nonliving surfaces and form extracellular polymers. The organisms in biofilms are difficult to treat with antimicrobial agent. Bacteria living in biofilms can have significantly different properties than free-floating bacteria, making them more resistant to treatment. Dental plaque is a prime example of biofilm.)

[There are new products on the market that contain enzymes that disrupt the biofilm matrix and encourage healthy microbial communities. (Klaire Labs – Interfase/Interfase Plus)]

Functional Medicine Testing for Fat-Soluble Vitamin
(REMEMBER to include 1, 25-dihydroxyvitamin D)
HPA-HPT Axes

Reprinted with permission: BioHealth Diagnostics, 2929 Canon Street, San Diego, CA 92106
The Thyroid - Adrenal Connection

Low Metabolic Energy

Low metabolic energy is commonly caused by thyroid dysfunction and/or adrenal dysfunction with a common scenario being a combination of the two. Environmental toxins and other hormonal imbalance also contribute to low metabolic energy. From a functional medicine perspective, restoring metabolic energy helps the body help itself by letting the self repair mechanisms function properly and thereby, restoring health.
Contributors to low metabolic energy include:

- Thyroid dysfunction
- Adrenal dysfunction – If adrenal dysfunction and thyroid dysfunction coexist, it’s important to treat the adrenal dysfunction first while supporting the thyroid gland. The individual with hypothyroidism may be unable to tolerate even sub-therapeutic amounts of thyroid hormone due to adrenal fatigue. 77 “In their attempt to raise the energy of the body and compensate for the under-activity of the thyroid gland, the adrenals have overworked and are now exhausted.” 77 Optimizing adrenal function is an important component in the treatment of autoimmune disease. If clinically indicated, order an ASI test and treat accordingly. I personally recommend ordering an ASI on all patients with thyroid dysfunction, not only to assess cortisol levels, but also to assess DHEA. DHEA appears to potentiate the action of thyroid hormone. 4,78 Patients receiving both thyroid hormone and DHEA should therefore be monitored closely. 4

Some of the signs and symptoms of adrenal fatigue include:

- low blood glucose
- low blood pressure
- dizziness or lightheadedness upon standing
- muscle and joint pain
- recurrent infection, allergies
- irregular menstrual cycles
- infertility
- low libido
- hair loss
- headaches
- dry skin
- cold and heat intolerance
- depression and anxiety

Some of the signs and symptoms of hypothyroidism include:

- Depression
- difficulty losing weight
- dry skin
- headaches
- fatigue
- memory problems
- menstrual problems
- recurrent infections
- sensitivity to cold and hyperlipidemia.

Based on the overlapping of signs and symptoms, adrenal function and thyroid function must both be assessed to achieve optimal patient outcomes.

- Nutritional deficiency
- Oxidative Stress
- Environmental toxins
- Other Hormonal imbalances – High levels of estrogen cause the liver to increase production of thyroid binding globulin. This causes a decrease availability of the free (active) thyroid hormones, and therefore symptoms of hypothyroidism. (This a type of “functional hypothyroidism”)

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Functional Medicine University’s
Functional Diagnostic Medicine Training Program
Module 7 FDMT 563D Functional Medicine Approach to Diagnosis and Treatment of Thyroid Dysfunction
http://www.FunctionalMedicineUniversity.com
Adrenal Thyroid Symptom Questionnaire

This questionnaire can be located in the download library at www.FunctionalMedicineUniversity.com

Assessing Metabolic Energy via Temperature Graph Plotting

Functional thyroid activity can be estimated by measuring basal body temperature, which is an indicator of basal metabolic rate. Hypofunction of the thyroid gland and adrenal function are common causes of low metabolic energy. Both are present with low body temperature and although some signs and symptoms are shared by both, some are not. Low basal metabolic rate can also indicate nutritional deficiencies and inadequate physical activity. Infections, hormonal imbalance, side effects of medication, and some autoimmune/inflammatory diseases (e.g. rheumatoid arthritis, lupus, Crohn’s disease) and cancer can increase body temperature. Keep in mind that while Hashimoto’s thyroiditis can be a cause of hypothyroidism which decreases basal body temperature, there is a high incidence of co-morbidity in individuals with Hashimoto’s thyroiditis with other autoimmune diseases that may raise body temperature.

(Please keep in mind that low basal body temperature plotting is not an exact science. Patients may present with normal body temperature and still have hypothyroidism due to adrenal compensation. The temperature graph is not a substitute for a comprehensive history, physical exam and lab testing.)
There are two ways to assess basal body temperature:

1. **Axillary temperature** (positive test result is a temperature below 97.4) - This is done first thing in the morning. The thermometer need to be shaken down the night before and placed on the night table. As soon as the individual wakes up, the thermometer is placed in the axilla for 10 minutes. The reading is then recorded. This is performed for five consecutive days. Men and postmenopausal women can perform this at any time. It is recommended that cycling women start this test on the second day of menstruation. (This is the time at which the temperature is the lowest)

2. **Functional Temperature Assessment using the metabolic temperature graph**
   - Have your patient measure their temperature (orally) two or three times per day at the same time every day. (preferably before or two hours after meals) Take the average of the temperature and plot on the graph.
   - Have your patient keep a journal while plotting their graph. Ask them to log in how they are feeling and list coexisting symptoms. (e.g. I feel very tired today - I have a viral infection - I am also started menstruating) (temperature will increase upon ovulation)

   (Oral temperatures can vary due to sinus infections and mouth breathing)
Interpreting the Temperature Graph as a Guideline

- **Stable but low temperature**
  - Patients with low functioning thyroid or hypothyroidism typically have very stable, but low temperatures.

- **Considerable variability and instability (sharp and spiking)**
  - Adrenal types i.e. people with low adrenal function or adrenal fatigue show considerable variability and instability in their temperatures. Adrenal types are hot in the heat and cold in the cold. As adrenal patients begin to heal, a pattern of contraction is noticed in their highs and lows i.e. the differences between their highs and lows are not as extreme. This is a sign that healing is taking place and stabilization will show in the pattern.

- **Rising in average temperatures (stable or unstable)**
  - As the metabolic energy increases a rising in the average temperatures may be noticed.

- **Increase in variability – an expansion pattern**
  - Greater stress on the adrenals or an increase in thyroid stimulation causes the temperatures to be less stable. This pattern shows that the patient is unable to handle the increasing stress on the body.

- **Contracting/Rising pattern – a sign of improvement**
  - This is a sign of improvement. The highs and lows get closer together and there is a general rise in body temperature.

Using the Metabolic Temperature Graph is an excellent way to monitor your patient’s response to treatment and provide a daily log of their signs and symptoms. I recommend having the patient use the graph daily for the first three months of treatment. Instruct them to bring it with them on all follow-up office visits for your review.
Sample Temperature Graph of Proper Adrenal Support

Reprinted with permission: Dr. Bruce Rind, MD

Diagram Legend:

A. Unstable temperatures: adrenal fatigue. Core temperatures have wide variations.
B. Decreasing variability with adrenal support. The adrenals are improving. Decrease in temperature variations.
C. Low but stable temperatures.
D. Stable and rising temperatures: After a period of being stable, the next phase of improvement is a gradual rise in the average temperature.
E. Stable normal temperature
Sample Temperature Graph of Proper Thyroid Support

(Keep in mind that temperature improvement can occur without thyroid replacement therapy. A proper detoxification program and/or optimizing adrenal function can normalize the temperature.)

Diagram Legend:

A. Stable but low
B. Stable and rising
C. Stable but leveled off
D. Stable and normal temperature
Functional Medicine University’s
Functional Diagnostic Medicine Training Program
Module 7 FDMT 563D Functional Medicine Approach to Diagnosis and Treatment of Thyroid Dysfunction
http://www.FunctionalMedicineUniversity.com

Proposed Functional Etiology of Thyroid Dysfunction

Functional/Preventive Intervention

Iodine deficiency
Selenium deficiency
Low antioxidants
Other nutritional deficiencies
Environmental factors

H₂O₂ (Free radicals)

Hyperplasia

Mutagenesis

Single cell
Somatic mutations

Goiter

Cold or hot nodules

Autoimmune Disease of the Thyroid Gland

Graves’ Disease
- Stress
- Smoking
- Genetic factors (HLA)
- Vitamin D-binding protein polymorphism
- Immune dysregulation

Thyroid Antibodies

*TSI
TR-Ab
Tg-Ab

Stimulating

T-helper cells increases
B-cells produce TSH receptor antibodies
T cells produce inflammatory cytokines

(Anti TSH receptor IgG)
(TSH receptor)

Release of Thyroid Hormone

Hashimoto’s Thyroiditis
- Iodine
- Infection(s)
- Genetic predisposition
- Celiac Disease
- Immune dysregulation

Thyroid Antibodies

*TPO-Ab
Tg Ab

Destructive

T-helper cells
T-cytotoxic cells
B-cells antibodies

Immune cells in gland

Apoptosis of thyrocytes

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Hypothyroidism

Primary (Overt) Hypothyroidism

About 95% of all case of hypothyroidism are primary. In primary hypothyroidism the problem is in the thyroid gland itself, which fails to produce thyroid hormone.

- Autoimmune – the most frequent cause of hypothyroidism is autoimmune thyroiditis, also called Hashimoto’s thyroiditis. Most individuals have circulating antibodies to the thyroid gland found in the blood. Anti-thyroid peroxidase (TPO-Ab) and anti-thyroglobulin antibodies (TG-Ab) with TPO-Ab usually in higher concentration.
- Postpartum hypothyroidism (thyroiditis) – This condition is usually transient, but may require treatment.
- Iodine deficiency or excess
- Subclinical hypothyroidism
- Thyroidectomy
- Radioactive iodine – from a nuclear reactor breach or medicinally (used to treat Graves disease)

Central Hypothyroidism (secondary or tertiary)

Secondary hypothyroidism is due to anterior pituitary hypofunction, which fails to produce optimum levels of TSH to stimulate the thyroid. In tertiary hypothyroidism, the hypothalamus shuts down protectively in response to stress, producing low levels of TSH, T4, and T3. This is often linked to chronic fatigue syndrome and fibromyalgia.

Other causes of central hypothyroidism to consider include;

- Pituitary adenoma
- Other brain tumors
- Genetic disorders
- Drug induced (e.g. lithium and dopamine)
- Chronic Stress
- Environmental toxins

Subclinical Hypothyroidism and Sub-Laboratory Hypothyroidism

Subclinical hypothyroidism (SCH), also called thyroid failure, is diagnosed when peripheral thyroid hormone levels are within normal reference laboratory reference range but serum thyroid-stimulating hormone (TSH) levels are mildly elevated. Individuals with subclinical hypothyroidism do not present with symptoms. This condition occurs in 3% to 8% of the general population. It is more common in women than men, and its prevalence increases with age. Of patients with SCH, 80% have a serum TSH of less than 10 mIU/L. The most important implication of SCH is a high likelihood of progression to clinical hypothyroidism.
Risk Factors for developing Subclinical Hypothyroidism:\textsuperscript{80}

- Hashimoto’s thyroiditis
- Recent treatment with radioactive iodine (use to treat hyperthyroidism), interferon-\(\alpha\) (anticancer drug), and interleukin 2 (used to treat kidney cancer)
- Irregular heart rhythm treatment with amiodarone
- Treatment with lithium
- Recent pregnancy and child delivery

Other potential causes of subclinical hypothyroidism include:

- Inflammatory bowel disease (any malabsorption should be considered)
- Medication
- Nutritional deficiencies
- Iodine excess

Sub-Laboratory refers to a patient who presents with a clinical history, physical examination and altered basal body temperature indicating thyroid dysfunction; however their laboratory tests are normal. In the typical patient complaining of fatigue or depression, the presence of additional symptoms such as cold extremities, dry skin, hair loss, decreased mental concentration, poor memory, constipation or menstrual irregularities increases the index of suspicion for hypothyroidism.\textsuperscript{4} A clinical decision needs to be make on whether or not to treat patients with sub-laboratory hypothyroidism with thyroid hormone replacement therapy or not. It may be prudent to use low-dose thyroid hormone, while investigating the underlying cause of the patient’s clinical presentation.

**Nonthyroidal Illness Syndrome**

The evaluation of altered thyroid function parameters in systemic illness and stress remains complex because changes occur at all levels of the hypothalamic-pituitary-thyroid axis.\textsuperscript{81} The so-called ‘nonthyroid illness syndrome” (NTIS), also known as the low T3 syndrome or euthyroid sick syndrome, is not a true syndrome but rather reflects alterations in thyroid function tests in a variety of clinical situations that commonly include a low T3, normal to low T4 and high reverse T3.\textsuperscript{81}

**Alterations in Lab Tests with (NTIS)**

- Low T3 – (the most common manifestation of NIS) Inhibition of 5’-deiodinase
- T4 – Generally decreases due to hypothalamic-pituitary suppression, disorder of iodine uptake, abnormal peripheral metabolism (free T4 may be normal)
- Reverse T3 – rT3 is usually elevated. \textit{“Previously, measurements of rT3 were said to be useful to differentiate nonthyroidal illness (with high rT3) form hypothyroidism (which is associated with low rT3), but subsequent studies have shown that rT3 does not accurately distinguish the two states.”} \textsuperscript{81}
- TSH – TSH is usually within normal reference range, however TSH may be transiently elevated during nonthyroidal illness recovery.
Thyroid hormone dysregulation in specific clinical conditions:

- Starvation and fasting – suppression of the HPT axis. Thyroid function is affected not only by caloric content but also by dietary composition.  
- Infectious disease – “The development of nonthyroidal illness syndrome during infection and sepsis involves central and peripheral mechanisms, including decreased TSH secretion from the pituitary, reduced thyroidal secretion of T4 and t3, and impaired peripheral T4 to t3 conversion. These changes contribute to low T4, free T4, T3 and TSH. Because increased cytokine release is predominantly observed in sepsis as compared with nonsepsis diseases, attention has recently been focused on the role of cytokines in the development of nonthyroidal illness syndrome in the setting of sepsis and severe inflammatory states. Evidence suggests that the cytokines interleukin-1β, soluble IL-2 receptor, IL-6, TNF-α, and nuclear factor kB (NF-kB) have roles in the direct suppression of TSH in sepsis.” Cytokines such as tumor necrosis factor α, which are produced by the immune system during severe illness, may inhibit thyroid function directly and be responsible for the changes in pituitary-thyroid function.
- Cardiac disease - Low T3 has been prospectively shown to be an independent predictor of mortality in hospitalized cardiac patients.
- Renal disease – The kidney has a role in metabolism and excretion of thyroid hormone.
- Hepatic disease – normal liver function is important to thyroid metabolism. The liver is the principle site of peripheral conversion of T4 to T3 and for the formation of thyroid binding globulin.

[The diagnosis of “Wilson’s Temperature Syndrome” remains controversial and is not accepted as a “medical” diagnosis. I recommend you search for the underlying cause of the thyroid hormone abnormality, and not be concerned with this controversy.]
Subclinical Hyperthyroidism

Subclinical hyperthyroidism is characterized by a low or undetectable TSH with free T3 and free T4 in the normal reference ranges. The view that individuals with an undetectable serum TSH level suffer from a mild form of tissue hyperthyroidism is supported by the finding of relevant changes in cardiovascular measures and in bone structure and metabolism in these individuals.

Subclinical hyperthyroidism may be caused by exogenous or endogenous factors:

- Endogenous – Graves’ disease, autonomously functioning thyroid adenoma or multinodular goiter
- Exogenous – excessive thyroid hormone replacement or intentional thyroid hormone suppression therapy

Signs and Symptoms
- Increased prevalence of palpitations
- Heat intolerance
- Nervousness
- Anxiety
- Inability to concentrate
- Hostility
- Increase in dementia and Alzheimer’s disease
The allopathic approach to addressing subclinical hyperthyroidism is based on the level of TSH and other factors. The treatment of choice is usually radioiodine. The most likely patients to receive treatment have a TSH of <0.1 or between 0.1 – 0.4, postmenopausal, over the age of 60 and have a history of heart disease and osteoporosis. From a functional medicine perspective, it seems reasonable to perform a nutritional assessment (e.g. antioxidants, iron, selenium, etc.), and assess for oxidative stress and environmental toxins.

**Thyroid Hormone Resistance (THR)**

Resistance to thyroid hormone has been classified as a rare autosomal dominant inherited syndrome of reduced end-organ responsiveness to thyroid hormone. Mutations in the thyroid receptor appear to be involved. Some authorities classify THR as a condition similar to insulin resistance. The common clinical presentation of THR includes:

- Elevated free T4 and free T3, and normal to slightly elevated TSH
- Goiter
- Absence of the usual symptoms and metabolic consequences of thyroid hormone excess

The differential diagnosis of THR includes a TSH-secreting pituitary adenoma and the presence of endogenous antibodies against T4 and T3. The allopathic treatment of THR consists of thyroid hormone replacement therapy, while closely monitoring TSH. The functional medicine approach for the treatment of THR includes:

- Initially prescribe thyroid hormone replacement therapy to overcome the mitochondrial and thyroid receptor dysfunction (The patient must be closely monitored by checking TSH, metabolic temperature plotting and symptom survey.) As the mitochondrial become more efficient and the body is able to perspire out some of the toxins, the need for thyroid hormone replace should decrease. As the more toxins are eliminated, the better the cells, including the mitochondrial and the hormone receptors will function.
- Detoxification – liver detoxification and far infrared sauna
- Nutritional support - Organic acid test
- Adrenal glandular support – ASI test
Laboratory Thyroid Assessment

It is always important that the clinical situation be taken into consideration when thyroid function tests are interpreted. In other words, treat the patient not the lab test. Total hormone concentrations are dependent on binding protein levels, which are variable and influenced by some physiological states and many drugs. Therefore, free hormone levels are preferable when using thyroid function tests to diagnose thyroid disease, although they also have limitations.

Reference: Reprinted with permission: Genova Diagnostics, 63 Zillico Street, Asheville, NC 28801

Thyroid Panel

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<thead>
<tr>
<th></th>
<th>Lab Range</th>
<th>Optimal Range</th>
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</thead>
<tbody>
<tr>
<td>TSH</td>
<td>0.4 – 5.5 mIU/L</td>
<td>1.3 – 2.0 mIU/L</td>
</tr>
<tr>
<td>Total T4</td>
<td>4.5 – 12.5 µg/dL</td>
<td>6.0 – 11.9 µg/dL</td>
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<tr>
<td></td>
<td>57 – 148 nmol/L</td>
<td>77 – 154 nmol/L</td>
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<tr>
<td>Total T3</td>
<td>80 – 230 ng/dL</td>
<td>90 – 168 ng/dL</td>
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<tr>
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<td>1.23 – 3.53 nmol/L</td>
<td>1.4 – 2.6 nmol/L</td>
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<tr>
<td>Free T3</td>
<td>2.3 – 4.8 ng/dL</td>
<td>3.0 – 3.25 ng/dL</td>
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<tr>
<td></td>
<td>230 – 480 pg/dL</td>
<td>300 – 325 pg/dL</td>
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<td>Free T4</td>
<td>0.7 – 2.4 ng/dL</td>
<td>1.0 – 1.5 ng/dL</td>
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<tr>
<td></td>
<td>9 – 30 pmol/L</td>
<td>12.9 – 19.3 pmol/L</td>
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<td>11 – 32 ng/dL</td>
<td>14.9 – 26.7 ng/dL</td>
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<tr>
<td></td>
<td>0.11 – 0.32 ng/ml</td>
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(Note: These values are subject to change)
General Interpretation of Thyroid Function Test

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<tr>
<th>Condition</th>
<th>TSH</th>
<th>Free T4 or Free T3</th>
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<tr>
<td>Thyroid hormone resistance</td>
<td>N</td>
<td>H</td>
<td></td>
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</tr>
<tr>
<td>Recent ingestion of thyroid hormone</td>
<td>N</td>
<td>H</td>
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<td></td>
</tr>
<tr>
<td>Euthyroid</td>
<td>N</td>
<td>N</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pituitary hyperthyroidism</td>
<td>H</td>
<td>H</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subclinical hypothyroidism</td>
<td>H</td>
<td>N</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary hypothyroidism</td>
<td>H</td>
<td>L</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pituitary hypothyroidism</td>
<td>N</td>
<td>L</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonthyroidal illness</td>
<td>N</td>
<td>L</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary Hyperthyroidism</td>
<td>L</td>
<td>H</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subclinical Hyperthyroidism</td>
<td>L</td>
<td>N</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medication (Dopamine)</td>
<td>L</td>
<td>N</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medication (Glucocorticoids)</td>
<td>L</td>
<td>N</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Free T4: Free T3

Both TRH and TSH are subject to negative feedback of T4 and T3 on the hypothalamus and pituitary respectively. The “normal” serum ratio of T4 to T3 is 4-5:1 (peripheral conversion of T4 to T3 is factored into the ratio of T4 to T3).

[ Note: free T4 is measured in nanograms/dL and free T3 is measured in pictograms/dL. Nanograms must be converted to pictograms to obtain the correct values to compare the T4:T3 ratio. One nanogram equals 1000 picograms. Example:

T4 labs results (1.2 ng/dL)

T3 lab results (240 pg/dL)

Calculations;

1. 1.2 ng/dL times 1000 pg/1 ng equals 1200 pg/dL of Free T4
2. 1200 pg/dL of T4 divided by 240 pg/dL equals 5
3. 5:1 ratio of free T4 to free T3

<table>
<thead>
<tr>
<th>State of Health</th>
<th>Normal 4-5:1 ratio of T4:T3</th>
<th>Increased T4:T3 ratio</th>
<th>Decreased T4:T3 ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>optimal</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonthyroidal illness</td>
<td>x</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Iodine deficiency</td>
<td></td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>T3 thyrotoxicosis</td>
<td></td>
<td></td>
<td>x</td>
</tr>
<tr>
<td>Amiodarone (antiarrhythmic medication)</td>
<td></td>
<td></td>
<td>x</td>
</tr>
</tbody>
</table>
The Functional Medicine Thyroid Scale

<table>
<thead>
<tr>
<th>Test</th>
<th>Low</th>
<th>Optimal Range</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH</td>
<td>0.5</td>
<td>1.3 – 1.8</td>
<td>5.0</td>
</tr>
<tr>
<td>Free T4</td>
<td>0.8</td>
<td>1.2 – 1.3</td>
<td>1.8</td>
</tr>
<tr>
<td>Free T3</td>
<td>230</td>
<td>320 – 330</td>
<td>420</td>
</tr>
<tr>
<td>Free T3*</td>
<td>2.3</td>
<td>3.2 – 3.3</td>
<td>4.2</td>
</tr>
</tbody>
</table>

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(*Some labs divide FT3 results by 100)

The Thyroid Scale is a tool that analyses TSH, Free T4 and Free T3 from a functional medicine perspective. Each analyte is plotted on the scale and compared to one another. By relating the analytes, they can be view under the functional medicine “lens”.

![Thyroid Scale Diagram](image-url)
**Functional Medicine University’s**  
**Functional Diagnostic Medicine Training Program**

**Module 7 FDMT 563D Functional Medicine Approach to Diagnosis and Treatment of Thyroid Dysfunction**  
[http://www.FunctionalMedicineUniversity.com](http://www.FunctionalMedicineUniversity.com)

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### Thyroid Scale Diagram - Healthy

<table>
<thead>
<tr>
<th>Labs</th>
<th>-8</th>
<th>-7</th>
<th>-6</th>
<th>-5</th>
<th>-4</th>
<th>-3</th>
<th>-2</th>
<th>-1</th>
<th>0</th>
<th>+1</th>
<th>+2</th>
<th>+3</th>
<th>+4</th>
<th>+5</th>
<th>+6</th>
<th>+7</th>
<th>+8</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH</td>
<td>0.26–0.33</td>
<td>0.34–0.41</td>
<td>0.42–0.49</td>
<td>0.50–0.65</td>
<td>0.66–0.81</td>
<td>0.82–0.97</td>
<td>0.98–1.13</td>
<td>1.14–1.29</td>
<td>1.30–1.80</td>
<td>2.20–3.20</td>
<td>2.21–3.00</td>
<td>3.01–4.00</td>
<td>4.01–5.00</td>
<td>5.01–6.00</td>
<td>6.01–8.00</td>
<td>8.01–10.00</td>
<td></td>
</tr>
<tr>
<td>FT4</td>
<td>0.40–0.49</td>
<td>0.50–0.59</td>
<td>0.60–0.69</td>
<td>0.70–0.79</td>
<td>0.80–0.89</td>
<td>0.90–0.99</td>
<td>1.00–1.09</td>
<td>1.10–1.19</td>
<td>1.20–1.30</td>
<td>1.31–1.40</td>
<td>1.41–1.50</td>
<td>1.51–1.60</td>
<td>1.61–1.70</td>
<td>1.71–1.80</td>
<td>1.91–2.00</td>
<td>2.01–2.10</td>
<td></td>
</tr>
</tbody>
</table>

---

### Thyroid Scale Diagram - Hypothyroid

<table>
<thead>
<tr>
<th>Labs</th>
<th>-8</th>
<th>-7</th>
<th>-6</th>
<th>-5</th>
<th>-4</th>
<th>-3</th>
<th>-2</th>
<th>-1</th>
<th>0</th>
<th>+1</th>
<th>+2</th>
<th>+3</th>
<th>+4</th>
<th>+5</th>
<th>+6</th>
<th>+7</th>
<th>+8</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH</td>
<td>0.26–0.33</td>
<td>0.34–0.41</td>
<td>0.42–0.49</td>
<td>0.50–0.65</td>
<td>0.66–0.81</td>
<td>0.82–0.97</td>
<td>0.98–1.13</td>
<td>1.14–1.29</td>
<td>1.30–1.80</td>
<td>2.20–2.60</td>
<td>2.21–3.00</td>
<td>3.01–4.00</td>
<td>4.01–5.00</td>
<td>5.01–6.00</td>
<td>6.01–8.00</td>
<td>8.01–10.00</td>
<td></td>
</tr>
<tr>
<td>FT4</td>
<td>0.40–0.49</td>
<td>0.50–0.59</td>
<td>0.60–0.69</td>
<td>0.70–0.79</td>
<td>0.80–0.89</td>
<td>0.90–0.99</td>
<td>1.00–1.09</td>
<td>1.10–1.19</td>
<td>1.20–1.30</td>
<td>1.31–1.40</td>
<td>1.41–1.50</td>
<td>1.51–1.60</td>
<td>1.61–1.70</td>
<td>1.71–1.80</td>
<td>1.91–2.00</td>
<td>2.01–2.10</td>
<td></td>
</tr>
</tbody>
</table>

*Note: A complete thyroid scale diagram is located on the download library at [www.FunctionalMedicineUniversity.com](http://www.FunctionalMedicineUniversity.com)*
Interpretive Guide for the Thyroid Scale

<table>
<thead>
<tr>
<th>State of Health</th>
<th>TSH</th>
<th>Free T4</th>
<th>Free T3</th>
<th>Temperature Pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy</td>
<td>optimal</td>
<td>optimal</td>
<td>optimal</td>
<td>Stable /normal</td>
</tr>
<tr>
<td>Adrenal Fatigue</td>
<td>low</td>
<td>low</td>
<td>low</td>
<td>Low, very unstable</td>
</tr>
<tr>
<td>Estrogen dominance</td>
<td>low</td>
<td>low</td>
<td>low</td>
<td>Low, very unstable</td>
</tr>
<tr>
<td>Primary hypothyroidism</td>
<td>High</td>
<td>Low</td>
<td>Low but to the right of T4</td>
<td>Low and stable</td>
</tr>
<tr>
<td>Hypothyroidism due to pituitary dysfunction</td>
<td>Low</td>
<td>Low</td>
<td>Low but to the right of T4</td>
<td>Low and stable</td>
</tr>
<tr>
<td>Late Hashimoto’s Thyroiditis or Hypothyroidism and adrenal fatigue</td>
<td>Optimal to high</td>
<td>low</td>
<td>Low and mildly to the right of T4</td>
<td>Low and unstable</td>
</tr>
<tr>
<td>Early Hashimoto’s Thyroiditis</td>
<td>Very low</td>
<td>high</td>
<td>High but to the left of T4</td>
<td>Variable</td>
</tr>
<tr>
<td>Grave’s Disease</td>
<td>Very low</td>
<td>Very high</td>
<td>Very high and to the right of T4</td>
<td>Tends to be high and stable early and then becomes low and unstable</td>
</tr>
<tr>
<td>Thyroid hormone resistance</td>
<td>Mildly high</td>
<td>high</td>
<td>High and to the right of T4</td>
<td>Low and mostly stable. Assess for nutritional deficiency, toxic burden, mitochondrial cytopathy</td>
</tr>
<tr>
<td>Chronic infection</td>
<td>Optimal to mildly high</td>
<td>Optimal to mildly high</td>
<td>Optimal to mildly high</td>
<td>Mildly elevated</td>
</tr>
<tr>
<td>Iron deficiency</td>
<td>high</td>
<td>low</td>
<td>low</td>
<td>Iron deficiency is thought to impair thyroid peroxidase activity causing a decrease in synthesis of thyroid hormones.</td>
</tr>
</tbody>
</table>

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Thyrotropin-Releasing Hormone Stimulation Test

TRH stimulation test is useful in the diagnosis of central hypothyroidism, especially in whom free T4 and/or TSH is low-normal and known to have hypothalamic-pituitary pathology. The TRH test must be performed by a physician experienced in the procedure. A TSH baseline is first established, after which the patient is given an injection of TRH. About thirty minutes later, a second blood draw is performed to assess TSH. To my knowledge, it appears that Dr. Raphael Kellman is fronting the resurgence of this test. Accord to Dr. Kellman, the patients that can benefit from this test are those who have the symptoms of hypothyroidism and normal to optimal lab findings, and the elderly population who experience fatigue, depression and dementia. He is also a proponent of using this test on autistic patients, due to the thyroid-autism connection (possible due to endocrine disruptor).
Thyroid Hormone Replacement

- Synthroid
  - Synthetic T4
  - Narrow therapeutic index
  - Contraindicated for adrenal insufficiency; underlying CVD
  - Many drug interactions
  - May still have problems with peripheral conversion of T4 to T3

- Cytomel (Liothyronine Sodium) (T3)
  - 25 mcg is equal to approx 1 grain of desiccated thyroid

- Armour Thyroid (thyroid tablets USP)
  - Non-synthetic
  - T4 and T3 (4.2 parts T4 to one part T3)
  - For some patients - best taken in two divided doses

Side Effects, Interventions, Contraindications, & Absorption Issues

- All thyroid medications have similar actions in the body

- Look for signs/symptoms of hyperthyroidism
  - Tremor
  - Heat intolerance
  - Cardiovascular
  - Gastrointestinal
  - Hair loss

- Drug interactions
  - Estrogens
  - Anticoagulants
  - Beta blockers
  - Theophylline
  - Cholestyramine

- Contraindications
  - Obesity
  - CVD
  - Hyperthyroidism
  - Addison’s disease/adrenal insufficiency

- Absorption impaired by
  - Antacids
  - Hydroxides
  - Calcium carbonate
  - Ferrous sulfate
  - Bile acid sequestrants
Precautions of Thyroid HRT

Side Effects may include:
- Anxiety
- Nervousness
- Insomnia
- Palpitations
- Rapid pulse
- Pain or tightness in the chest

Thyroid Hormone and Hypoadrenalism
In patients in whom hypothyroidism and severe hypoadrenalism coexist, administration of thyroid hormone prior to correcting adrenal insufficiency can trigger an “adrenal crisis”.

Licorice root (Glycyrrhiza glabra): 2 – 6 drops twice a day of 1:1 or 1:2 tincture or 6 – 10 drops 2 – 3 times per day of 1:3 tincture. Licorice root delays the breakdown of adrenal hormones in the liver, and was considered the treatment of choice for adrenal failure prior to the discovery of adrenal steroid hormones. Some patients may need cortisol replacement.
Functional Medicine Approach to Treating Thyroid Dysfunction and Balancing the HPT and HPA Axes

Check List:

1. Nutritional status: Is there an adequate supply of thyroid hormone precursors (raw material) to synthesis thyroid hormones? (Tyrosine, iodine, iron, selenium, and zinc)
2. Gastrointestinal Status: Hypochlorhydria, H. Pylori, celiac disease, bowel dysbiosis (esp. Candida)
3. Adrenal Gland status: Is the proper amount and ratio of cortisol to DHEA present?
4. Liver status (peripheral conversion problem of T4 to T3 and decreased absorption of fat soluble vitamins): Is there signs, symptoms and lab tests that indicate liver/gallbladder dysfunction? (Remember that fat soluble vitamins are needed for nuclear hormone receptors activity)
5. Immune status: Are thyroid antibodies present? Is there a history of chronic inflammation or other autoimmune diseases?
6. Environmental toxin exposure: Do you suspect the presents of a significant amount of endocrine disrupting chemicals? Are there indications of heavy metal toxicity?
7. Oxidative Stress Status: Does the patient have diabetes mellitus? Are there signs of mitochondrial dysfunction?
8. Medications: Is the patient taking medication(s) that interfere with thyroid hormone function?
9. Thyroid Medication: Is the patient currently taking medication and/or supplementation for a thyroid disorder? If so, what type, how long and what dosage(s).
Summary

As you know by now, there is no “one-size-fits-all”, when it comes to the assessment and treatment of functional disorders. As functional medicine practitioners, we know to treat the patient not the laboratory tests. The lab tests serve as compass to guide and monitor our treatment protocols; however they may not disclose the underlying cause of the dysfunction. Remember, every patient is an experiment with no controls. You now know the tools and have the investigative skills to assess and treat thyroid dysfunction from a functional medicine perspective.
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