Thyroid Dysfunction: The Role of Nutrients, Toxins and Stress

Patrick Hanaway, MD
Genova Diagnostics
Clinical Questions will be answered during the final fifteen (15) minutes of the webinar.
Clinical Concerns – Hormonal Assessment

- Sex Hormones
- Thyroid
- Adrenals
STRESS

HPA Axis

Hypothalamus & Pituitary

ACTH

Adrenal Cortex

DHEA (anabolic)

Cortisol (catabolic)
Cortisol & DHEA derive from same precursors.
**Salivary Cortisol and DHEA**

**Cortisol**
Reference Range
1 Hour After Rising
7AM - 9AM:
0.27-1.18 mcg/dL
11AM - 1PM:
0.10-0.41 mcg/dL
3PM - 5PM:
0.05-0.27 mcg/dL
10PM - 12AM:
0.03-0.14 mcg/dL

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<th>Hormone</th>
<th>Reference Range</th>
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<tr>
<td>DHEA 7am - 9am</td>
<td>568</td>
<td>71-640 pg/mL</td>
</tr>
<tr>
<td>DHEA: Cortisol Ratio/10,000</td>
<td>575</td>
<td>115-1,188</td>
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Salivary Cortisol and DHEA

Stage - One

Cortisol
Reference Range
1 Hour After Rising
7AM - 9AM:
0.27-1.18 mcg/dL
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DHEA 7am - 9am
Reference Range: 71-640 pg/mL

DHEA: Cortisol Ratio/10,000
Reference Range: 115-1,188

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Stage - Two

Salivary Cortisol and DHEA

Cortisol
Reference Range
1 Hour After Rising
7AM - 9AM:
0.27-1.18 mcg/dL
11AM - 1PM:
0.10-0.41 mcg/dL
8PM - 5PM:
0.05-0.27 mcg/dL
10PM - 12AM:
0.03-0.14 mcg/dL

DHEA
Hormone
Reference Range
7am - 9am
70
71
71-640 pg/ml

DHEA:
Cortisol Ratio/10,000
115-1,188
Factors that Affect Thyroid Function

Factors that contribute to proper production of thyroid hormones
- Nutrients: iron, iodine, tyrosine, zinc, selenium
- Vitamin E, B2, B3, B6, C, D

Factors that inhibit proper production of thyroid hormones
- Stress
- Infection, trauma, radiation, medications
- Fluoride (antagonist to iodine)
- Toxins: pesticides, mercury, cadmium, lead
- Autoimmune disease: Celiac

Factors that increase conversion of T4 to RT3
- Stress
- Trauma
- Low-calorie diet
- Inflammation (cytokines, etc.)
- Toxins
- Infections
- Liver/kidney dysfunction
- Certain medications

Factors that increase conversion of T4 to T3
- Selenium
- Zinc

T3 and RT3 compete for binding sites

Factors that improve cellular sensitivity to thyroid hormones
- Vitamin A
- Exercise
- Zinc

Courtesy of IFM
Thyroid Questionnaire

Put a check by the following statements that apply to your family history, your personal history and the symptoms that you have:

**History**
- ___ My family (parent, sibling, child) has a history of thyroid disease
- ___ I've had a thyroid problem (i.e., hyperthyroidism, Graves' disease, Hashimoto's thyroiditis, postpartum thyroiditis, goiter, nodules, thyroid cancer) in the past
- ___ A member of my family or I have currently or in the past been diagnosed with an autoimmune disease
- ___ I have had radiation treatment to my head, neck, chest, tonsil area, etc.
- ___ I grew up, live, or work near or at a nuclear plant
- ___ Women: I have a history of infertility or miscarriage

**Signs and Symptoms**
- ___ I am gaining weight for no clear reason or am unable to lose weight with a diet and exercise program
- ___ My "normal" body temperature is low (below 98.2° when I take it)
- ___ My hands and feet are cold to the touch and I frequently feel cold when others do not
- ___ I feel fatigued or exhausted more than normal
- ___ I have a slow pulse, and/or low blood pressure
- ___ I have been told I have high cholesterol
Signs of Low Thyroid Function

- Dry skin, elbow keratosis, brittle nails
- Diffuse hair loss
- Puffy face, swollen eyelids; edema in legs, feet, hands
- Elevated cholesterol, generally LDL
- Easy bruising
- Prolonged Achilles tendon reflex
- Keratoderma
- Enlarged thyroid gland
Symptoms of Low Thyroid Function

- Fatigue, usually persistent, especially on waking; less toward the evening
- Cold intolerance, with cold extremities
- Slow speech, movement, heart rate
- Morning stiffness, arthralgias, muscle pain/cramps, particularly in calves, thighs, and upper arms
Symptoms of Low Thyroid Function

- Memory and concentration problems
- Diffuse headache, migraines
- Depression; melancholia
- Constipation: hard bowel movements and decreased frequency
- Low libido
- Reactive hypoglycemia
Top 10 Signs and Symptoms when Suspecting Suboptimal Thyroid Function

1. Fatigue
2. Weight Gain
3. Feeling Cold
4. Dry Hair and Skin
5. Hair Loss
6. Menstrual Irregularities
7. Edema
8. Muscle Aches and Joint Pain
9. Constipation
10. Depression
Comprehensive Thyroid Assessment

Central Thyroid Regulation & Activity
- TSH
  - Ref Range: 0.40 - 2.50 µIU/mL
  - Value: 4.12
- Free T4
  - Ref Range: 0.8 - 1.9 ng/dL
  - Value: 1.2

Histograms represent idealized data based upon large populations.

Peripheral Thyroid Function
- Free T3
  - Ref Range: 1.80 - 4.20 pg/mL
  - Value: 2.86
- Reverse T3
  - Ref Range: 9.0 - 35.0 ng/dL
  - Value: 22.6

Histograms represent idealized data based upon large populations.

Thyroid Auto Immunity
- Anti-TG Antibody Titer
  - Ref Range: <= 40 IU/mL
  - Value: <32
- Anti-TPO Antibody Titer
  - Ref Range: <= 34 IU/mL
  - Value: <14

Histograms represent idealized data based upon large populations.
What is the ‘optimal’ level of TSH?

a) 0.4 – 4.5
b) 0.4 – 3.0
c) 0.4 – 2.5
d) 0.4 – 2.0
e) 1.3 – 1.8
TSH Controversy

What is the Reference Range?

In 2002, the National Academy of Clinical Biochemistry (NACB) issued new guidelines for the diagnosis and monitoring of thyroid disease.

- TSH reference range may be too wide.
- Newer research suggested that these older ranges included individuals with borderline thyroid disease.
- When more sensitive screening was performed, 95% of the population tested actually had a TSH level between 0.4 and 2.5 uIU/ml.
TSH Controversy

THEN, American College of Clinical Endocrinologists (AACE) suggested that a new reference range of 0.3–3.0 uIU/ml should be adopted.

TSH Controversy

- In NHANES III, of over 17,000 people evaluated, more than 80% had a serum TSH below 2.5 mIU/L.
- TPOAb prevalence was lowest (<3%) with TSH 0.1 – 1.5 mIU/L in women and 0.1 – 2.0 mIU/L in men and progressively increased to above 50% when TSH exceeded 20 mIU/L.
- TSH upper reference limits may be skewed by TPOAb-negative individuals with occult autoimmune thyroid dysfunction.


Clinical Concerns – Hormonal Assessment

- Sex Hormones
- Thyroid
- Adrenals

Comprehensive Thyroid Assessment
How to Review a Report

Adrenocortex Stress Profile
How to Review a Report

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Adrenocorticol Hyperactivity

- Life-saving in the short-term! (catabolism frees up energy reserves)
- Persistent cortisol production → immune suppression, hyperglycemia, insulin resistance, central adiposity, hypertension, memory impairment (hippocampal damage), hyperlipidemia, impaired hepatic T4 → T3 conversion
Reverse T3 (rT3)

- T4 is also converted to rT3 which is metabolically inactive but binds to the same nuclear receptors as T3

- In Euthyroid Sick Syndrome (ESS) and in Low T3 Syndrome,
  - T4 is normal or high,
  - TSH is normal or slightly low,
  - but T3 is low,
  - and rT3 levels are high,
Adrenocorticol Hypoactivity

• High CRH is also possible in adrenal hypoactivity (lack of inhibitory cortisol feedback → persistent output of CRH → excessive adrenalin production)

• Low cortisol → fatigue, hypotension, hypoglycemia, sugar cravings, increased inflammatory response, ↑↑↑ conversion T4 to T3.
Hypothalamus → TRH → Pituitary → TSH → Thyroid Gland

Liver or Kidney → 95% T4 → Thyroid Gland

Chronic Stress → rT3 (Inactive) → T3 (Active) → Cell Nucleus

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Factors Promoting Conversion of T₄ to T₃

**Micro-nutrients:**
- selenium, potassium, iodine, iron, zinc

**Vitamins:**
- A, E, riboflavin

**Hormones:**
- cortisol (physiologic doses)
- growth hormone, testosterone
- insulin, glucagon
- melatonin
Other 5’-Deiodinase Inhibitors

- Excess cortisol, catecholamines
- Selenium deficiency
- Deficient protein, excess sugar
- Chronic illness (cytokines, free radicals)
- Compromised liver or kidney function
- Cd, Hg, Pb toxicity
- Herbicides, pesticides
- Polycyclic aromatic hydrocarbons
- Oral contraceptives, excess estrogen
Thyroid’s Relationship to Other Hormones

- High adrenal activity impairs 5’ deiodinase → higher T4, lower T3, normal or elevated TSH
- Low adrenal activity may result in lower T4, higher T3, normal or elevated TSH
- With Low Cortisol and elevated CRH → XS adrenalin desensitizes T3 receptors → T3 resistance AND higher T3, despite symptoms of hypothyroid
- XS adrenalin → lowering T4 → symptoms of hypothyroid → patient intolerant of thyroid supplementation (balance adrenals first!)
Thyroid’s Relationship to Other Hormones

• Hypothyroidism associated with less deactivation of cortisol to cortisone (hyperthyroidism $\Rightarrow$ opposite)
• Hypothyroidism stimulates CYP3A4 $\Rightarrow$ increased production of $16\alpha$OHE1
• Hypothyroid decreases concentration of SHBG $\Rightarrow$ more bioavailable E2 and testosterone
• Hyperthyroid increases SHBG $\Rightarrow$ less bioavailable E2 and testosterone
(Serum)...

**Case Study**

**Central Thyroid Regulation & Activity**
- **TSH**
  - Ref Range: 0.40 - 2.50
  - Value: 4.99
  - Description: High
- **Free T4**
  - Ref Range: 0.8 - 1.9
  - Value: 1.0
  - Description: Normal

**Peripheral Thyroid Function**
- **Free T3**
  - Ref Range: 1.80 - 4.20
  - Value: 4.22
  - Description: High
- **Reverse T3**
  - Ref Range: 9.0 - 35.0
  - Value: 18.3
  - Description: High

**Thyroid Auto Immunity**
- **Anti-TG**
  - Ref Range: <32
  - Value: <32
  - Description: Negative
- **Anti-TPO**
  - Ref Range: <31
  - Value: 312
  - Description: Elevated

**TSH = high**
**Free T3 = high normal**
**Anti-TPO antibodies elevated**
Case Study

(Saliva)…

Cortisol = Normal  DHEA = Low Normal (age-adjusted)
Auto-Immunity and Thyroiditis

Three major thyroidal auto-antigens:

- Thyroglobulin (Tg)
- Thyroidal peroxidase (TPO)
- TSH receptor (TSH-R)
What % of Americans have auto-immune Thyroid Ab?

a) 2.5%
b) 5.0%
c) 7.5%
d) 10.0%
e) 12.5%
Why Test Thyroid Antibodies?

• It is the most common autoimmune disease in the United States.
• It is the most common cause of hypothyroidism in the United States.
• It affects women four times more than men:
  – Up to 20% of menopausal women
  – Up to 24% of allergic women
  – 5–10% of postpartum women
Autoimmune Thyroid Disease

- Anti-TPO: attacks thyroid peroxidase, which is important in the production of thyroid hormones.
- TgAb: attacks thyroglobulin, which is essential in the production of the T4 and T3 thyroid hormones.
Anti-Tg and Anti-TPO Antibodies (formerly known as microsomal antibody)

- Most sensitive measure to diagnose chronic thyroiditis
- Elevated in 85-90% of chronic thyroiditis patients
- Elevated in 97% of patients with Graves disease or Hashimoto’s thyroiditis
- Titers will fall with successful treatment of either Graves or Hashimoto’s
- CHECK FOR OTHER AUTOIMMUNE Dz
Diet: Gluten, Celiac Disease and Thyroid Function

Study of 241 untreated celiac disease patients vs. 212 controls confirmed that patients with celiac disease are at increased risk for developing thyroid disease with an overall threefold higher frequency than in controls (30% vs. 11%).

After 1 year on a gluten-free diet:

- Subclinical hypothyroidism normalized in 10 of 14 (71%) patients with non-autoimmune disease.
- In three of five (60%) patients with autoimmune thyroid disease (AIT), there was a shift to AIT with euthyroidism.
- In four of five subjects with no improvement in thyroid function, compliance with the diet was poor.

“Molecular mimicry has long been implicated as a mechanism by which microbes can induce autoimmunity.”

1. Introduction

Traditionally, it was assumed that infectious agents induced disease by causing direct tissue damage (for example via secretion of exotoxins and endotoxins). However, we now know only too well that infectious agents play a role in the induction of non-infectious consequences, including malignancies (for example Epstein-Barr virus and Burkitt's lymphoma), HTLV-I, and adult T cell leukemia), acquired immunodeficiency syndrome (human immunodeficiency virus), peptic ulcer (Helicobacter pylori), and autoimmune diseases. Infectious agents have been implicated in the pathogenesis of a variety of autoimmune diseases, namely, rheumatic fever, Reiter's syndrome, systemic lupus erythematosus (SLE), myasthenia gravis, insulin-dependent diabetes mellitus, Sjogren's syndrome, and the autoimmune thyroid diseases. This review examines the pertinent data relating to the possible role of infecting organisms in the development of autoimmune thyroid diseases (AITD), with an emphasis on thyroiditis. Clinically the disease has several characteristics typical of viral infections including a typical viral prodrome with myalgia, malaise and fatigue, absence of leukocytosis, and usually a self-limited course. Additionally, clusters of the disease have been reported during outbreaks of viral infection (4). A higher prevalence of subacute thyroiditis has also been reported during the summer, coinciding with the seasonal distribution of the enteroviruses (5), and in Holland an epidemic of subacute thyroiditis affecting 23 individuals has been described (6). Eylan and colleagues (7) reported 11 patients with subacute thyroiditis diagnosed during a mumps epidemic. These 11 patients were found to have circulating anti-mumps antibodies without clinical evidence of mumps. In two patients the mumps virus was cultured from thyroid tissue obtained at biopsy. Others have also reported an association between mumps virus and subacute thyroiditis (8–10). Different viruses reportedly associated with subacute...
Thyroid Auto-Immunity and Bacterial Overgrowth

• Small Intestinal Bacterial Overgrowth (SIBO) is an abnormally high bacterial population in the small intestine
• Luminal bacterial modulate gastrointestinal symptoms and interfere with T4 absorption
• 54% of patients with hypothyroidism due to autoimmune thyroiditis were positive for SIBO.
Thyroid Autoimmunity – Clinical Approach

• Rule out antigenic and inflammatory triggers:
  – Celiac/gluten sensitivity (may promote multiple autoimmune endocrinopathies)
  – Food hypersensitivities
  – Dysbiosis, leaky gut
  – Heavy metal toxicity

• Rule out adrenal insufficiency (low cortisol)

• Anti-inflammatory measures, e.g., fatty acid balancing

• Correct nutrient imbalances
Factors that Affect Thyroid Function

Factors that contribute to proper production of thyroid hormones
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Factors that inhibit proper production of thyroid hormones
- Stress
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T3 and RT3 compete for binding sites

Factors that improve cellular sensitivity to thyroid hormones
- Vitamin A
- Exercise
- Zinc

Nucleus/Mitochondria

Cell

Courtesy of IFM
Questions & Answers

Register for upcoming LiveGDX Webinars online @ www.gdx.net

As part of our continued commitment to medical education, we are proud to announce an exciting new webinar series “Heart Health.” The insightful four-part series begins Wednesday, May 4, 2011, as Chief Medical Officer Patrick Hamawey, M.D., presents “Patient’s Progress to Developing Diabetes,” an in-depth look at how medical testing can help physicians identify the 80% of patients at risk of developing diabetes who are missed by traditional diagnostics.

Then on the first Wednesday of the following three months, we will offer online seminars on “New Heart Disease Risk Factors,” “Pre-Diabetes, Hypertension, and Heart Disease,” and “Genomic Risk of Heart Disease.” You can register for any or all of the four online presentations. Those registrants who attend all four parts of the “Heart Health” series will be entered into a drawing for an Apple iPad!”

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Introducing Genova's new LiveGDX webinar series, **Sick & Tired: Understanding the Root Cause of Fatigue**. Our first webinar titled, Adrenal Stress & Nutrient Deficiency with Dr. Patrick Hanaway and Dr. Kathleen O’Neil-Smith is scheduled for September 21, 2011 12:00pm & 8:00 EST. [Click here](#) to register today.

Previously Recorded Webinars include:

- **Patients Progress to Developing Diabetes** recorded on May 4, 2011
- **New Heart Disease Risk Factors** recorded on June 1, 2011
- **Pre-Diabetes, Hypertension and Heart Disease** recorded on June 6, 2011
- **Genomic Risk of Heart Disease** recorded on August 3, 2011

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Enhanced Nutrition Report Design

The following LearnGDX modules are focused on giving clinicians insight into our newly redesigned and enhanced patient results.

Report Review
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- Essential & Metabolic Fatty Acids Analysis
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- Oxidative Stress - Biomarkers
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- Amino Acids Plasma - Biomarkers
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Upcoming LiveGDX Webinars

The Endocrine Pyramid

• 6/27/12 – Sex Hormone Dysfunction: 
  » The Role of Stress, Nutrients & Inflammation

• 7/23/12 – Cortisol Steal & A/C Balance: 
  » Stress and Steroid Metabolism

• 8/22/12 – Essential Estrogens 
  » Diet and Cancer Risk