The Thyroid and How it Works
Biomedicine: 5 ceu’s

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THE THYROID AND HOW IT WORKS

Derived from the Greek word meaning *shield*, the thyroid gland is an important part of the Endocrine System. The thyroid gland normally weighs less than one ounce. It is situated in the anterior neck below the skin and muscle layers. It is made up of two halves, called lobes, that lie along the trachea and are joined together by a narrow band of thyroid tissue, known as the isthmus. (an Isthmus is a passage connecting two larger structures.) Some say the gland is shaped similar to a butterfly with two wings (the thyroid lobes), that wrap around the trachea.

The thyroid is situated just below your "Adams apple" or larynx. While developing in utero, the thyroid gland originates in the back of the tongue, but it normally migrates to the front of the neck before birth. In rare circumstances, it fails to migrate properly and is located high in the neck or even in the back of the tongue (lingual thyroid) or it may migrate too far and ends up in the chest.
The function of the thyroid gland is to take the iodine from food we eat, and convert it into thyroid hormones: thyroxine (T4) and triiodothyronine (T3). Thyroid cells are the only cells in the body that can absorb iodine. These cells combine iodine and the amino acid tyrosine to make T3 and T4. These are then released into the bloodstream and are transported throughout the body where they control metabolism, converting oxygen and calories to energy. Every cell in the body depends upon thyroid hormones for regulation of their metabolism.

Thyroxine is called T4 because it contains four iodine atoms and Triiodothyronine is called T3 because it has three iodine atoms. The normal thyroid gland produces about 80% T4 and about 20% T3. However, T3 is actually the major active thyroid hormone. T4 is produced within the thyroid gland and is later converted to the active T3 outside the thyroid gland in peripheral tissues.

The thyroid gland is under the control of the pituitary gland. When the level of T3 & T4 drops too low, the pituitary gland produces Thyroid Stimulating Hormone (TSH) which stimulates the thyroid gland to produce more hormones. Under the influence of TSH, the thyroid will manufacture and secrete T3 and T4 and raise their levels in the blood. The pituitary senses this and responds by decreasing its TSH production. The pituitary gland itself is regulated by another gland, the hypothalamus. The hypothalamus is part of the brain and produces TSH Releasing Hormone (TRH) which tells the pituitary gland to stimulate the thyroid gland (release TSH).

Modern measurement of thyroid hormones is done using a technique called radioimmunoassay (RIA). It was discovered by Dr. Solomon Berson and Dr. Rosalyn Yallow. They were awarded the 1977 Nobel Prize in Medicine for this discovery. To perform a radioimmunoassay, a known quantity of an antigen is made radioactive, frequently by labeling it with gamma-radioactive isotopes of iodine attached to tyrosine. This radiolabeled antigen is then mixed with a known amount of antibody for that antigen, and as a result, the two chemically bind to one another. Then, a sample of serum from a patient containing an unknown quantity of that same antigen is added. This causes the unlabeled (or "cold") antigen from the serum to compete with the radiolabeled antigen ("hot") for antibody binding sites. As the concentration of "cold" antigen is increased, more of it binds to the antibody, displacing the radiolabeled variant, and reducing the ratio of antibody-bound radiolabeled antigen to free radiolabeled antigen. The bound antigens are then separated from the unbound ones, and the radioactivity of the free antigen remaining in the supernatant is measured using
a gamma counter. Using known standards, a binding curve can then be generated which allows the amount of antigen in the patient's serum to be derived.

Commonly used thyroid tests

Measurement of Serum Thyroid Hormones: T4 by RIA
T4 by RIA (radioimmunoassay) is the most used thyroid test of all. It is frequently referred to as a T7 which means that a resin T3 uptake (RT3u) has been done to correct for certain medications such as birth control pills, other hormones, seizure medication, cardiac drugs, or even aspirin that may alter the routine T4 test. The T4 reflects the amount of thyroxine in the blood. If the patient does not take any type of thyroid medication, this test is considered a good measure of thyroid function.

Measurement of Serum Thyroid Hormones: T3 by RIA
Thyroxine (T4) represents 80% of the thyroid hormone produced by the normal gland and generally represents the overall function of the gland. The other 20% is triiodothyronine measured as T3 by RIA. Sometimes the diseased thyroid gland will start producing very high levels of T3 but still produce normal levels of T4. Measurement of both hormones provides an even more accurate evaluation of thyroid function.

Thyroid Binding Globulin
Most of the thyroid hormones in the blood are attached to a protein called thyroid binding globulin (TBG). If there is an excess or deficiency of this protein it alters the T4 or T3 measurement but it does not affect the action of the hormone. If a patient appears to have normal thyroid function, but an unexplained high or low T4, or T3, it may be due to an increase or decrease of TBG. Direct measurement of TBG can be done and will explain the abnormal value. Excess TBG or low levels of TBG are found in some families as a hereditary trait. It causes no problem except falsely elevating or lowering the T4 level. These people are frequently misdiagnosed as being hyperthyroid or hypothyroid, but they have no thyroid problem and need no treatment.

Measurement of Pituitary Production of TSH
Pituitary production of TSH is measured by a method referred to as IRMA (immunoradiometric assay). Normally, low levels (less than 5 units) of TSH are sufficient to keep the normal thyroid gland functioning properly. When the thyroid gland becomes inefficient, the TSH becomes elevated even though the T4 and T3 may still be within the "normal" range. This rise in TSH represents the pituitary gland's response to a drop in circulating thyroid hormone and it is usually the first indication of thyroid gland failure. Since TSH is normally low when the thyroid gland is
functioning properly, the failure of TSH to rise when circulating thyroid hormones are low is an indication of impaired pituitary function. The new "sensitive" TSH test will show very low levels of TSH when the thyroid is overactive (as a normal response of the pituitary to try to decrease thyroid stimulation). Interpretations of the TSH level depends upon the level of thyroid hormone so the TSH is usually used in combination with other thyroid tests such as the T4 RIA and T3 RIA.

**TRH Test**

Normally, TSH secretion from the pituitary can be increased by giving a shot containing TSH Releasing Hormone (TRH, the hormone released by the hypothalamus which tells the pituitary to produce TSH). A baseline TSH of 5 or less usually goes up to 10-20 after giving an injection of TRH. Patients with too much thyroid hormone (thyroxine or triiodothyronine) will not show a rise in TSH when given TRH. This "TRH test" is presently the most sensitive test in detecting early hyperthyroidism. Patients who show too much response to TRH (TSH rises greater than 40) may be hypothyroid. This test is also used in cancer patients who are taking thyroid replacement to see if they are on sufficient medication. It is sometimes used to measure if the pituitary gland is functioning. The new "sensitive" TSH test has eliminated the necessity of performing a TRH test in most clinical situations.

**Iodine Uptake Scan**

A means of measuring thyroid function is to measure how much iodine is taken up by the thyroid gland (RAI uptake). Hypothyroid patients usually take up too little iodine and hyperthyroid patients take up too much iodine. The test is performed by giving a dose of radioactive iodine on an empty stomach. The iodine is concentrated in the thyroid gland or excreted in the urine over the next few hours. The amount of iodine that goes into the thyroid gland can be measured by a "Thyroid Uptake". Of course, patients who are taking thyroid medication will not take up as much iodine in their thyroid gland because their own thyroid gland is turned off and is not functioning. At other times the gland will concentrate iodine normally but will be unable to convert the iodine into thyroid hormone; therefore, interpretation of the iodine uptake is usually done in conjunction with blood tests.

**Thyroid Scan**

Taking a "picture" of how well the thyroid gland is functioning requires giving a radioisotope to the patient and letting the thyroid gland concentrate the isotope. It is usually done at the same time that the iodine uptake test is performed. Although other isotopes, such as technetium, will be concentrated by the thyroid gland; these isotopes will not measure iodine uptake. It has also been found that thyroid nodules that
concentrate iodine are rarely cancerous; this is not true if the scan is done with technetium. Therefore, all scans are now done with radioactive iodine.

Two types of thyroid scans are available. A camera scan is most common, using a gamma camera operating in a fixed position viewing the entire thyroid gland at once. This type of scan takes only five to ten minutes.

**Computerized Rectilinear Thyroid (CRT)** utilizes computer technology to improve the clarity of thyroid scans and enhance thyroid nodules. It measures both thyroid function and thyroid size. A life-sized 1:1 color scan of the thyroid is obtained giving the size in square centimeters and the weight in grams. The precise size and activity of nodules in relation to the rest of the gland is also measured. In addition to making thyroid diagnosis more accurate, the CRT scanner improves the results of thyroid biopsy. The accurate sizing of the thyroid gland aids in the follow-up of nodules to see if they are growing or getting smaller in size. Knowing the weight of the thyroid gland allows more accurate radioactive treatment in patients who have Graves' disease.

**Thyroid Ultrasound**
Thyroid ultrasound refers to the use of high frequency sound waves to obtain an image of the thyroid gland and identify nodules. It tells if a nodule is "solid" or a fluid-filled cyst, but it cannot tell if a nodule is benign or malignant. Ultrasound allows accurate measurement of a nodule's size and can determine if a nodule is getting smaller or is growing larger during treatment. Ultrasound aids in performing thyroid needle biopsy by improving accuracy if the nodule cannot be felt easily on examination.

**Thyroid Antibodies**
The body normally produces antibodies to foreign substances. Some people are found to have antibodies against their own thyroid tissue. A condition known as Hashimoto's Thyroiditis is associated with a high level of these thyroid antibodies in the blood. Whether the antibodies cause the disease or whether the disease causes the antibodies is not known. A finding of a high level of thyroid antibodies is strong evidence of this disease. Occasionally, low levels of thyroid antibodies are found with other types of thyroid disease. When Hashimoto's thyroiditis presents as a thyroid nodule rather than a diffuse goiter, the thyroid antibodies may not be present.

**Thyroid Needle Biopsy**
This has become the most reliable test to differentiate the "cold" nodule that is cancerous from the "cold" nodule that is benign. "Hot" nodules are rarely cancerous. It provides information that no other thyroid test will provide. While not perfect, it will provide definitive information in 75% of the nodules biopsied.
Thyroid Function Tests

Normal Laboratory Values

<table>
<thead>
<tr>
<th>Test</th>
<th>Abbreviation</th>
<th>Typical Ranges</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum thyroxine</td>
<td>T4</td>
<td>4.6-12 ug/dl</td>
</tr>
<tr>
<td>Free thyroxine fraction</td>
<td>FT4F</td>
<td>0.03-0.005%</td>
</tr>
<tr>
<td>Free Thyroxine</td>
<td>FT4</td>
<td>0.7-1.9 ng/dl</td>
</tr>
<tr>
<td>Thyroid hormone binding ratio</td>
<td>THBR</td>
<td>0.9-1.1</td>
</tr>
<tr>
<td>Free Thyroxine index</td>
<td>FT4I</td>
<td>4-11</td>
</tr>
<tr>
<td>Serum Triiodothyronine</td>
<td>T3</td>
<td>80-180 ng/dl</td>
</tr>
<tr>
<td>Free Triiodothyronine l</td>
<td>FT3</td>
<td>230-619 pg/d</td>
</tr>
<tr>
<td>Free T3 Index</td>
<td>FT3I</td>
<td>80-180</td>
</tr>
<tr>
<td>Radioactive iodine uptake</td>
<td>RAIU</td>
<td>10-30%</td>
</tr>
<tr>
<td>Serum thyrotropin</td>
<td>TSH</td>
<td>0.5-6 uU/ml</td>
</tr>
<tr>
<td>Thyroxine-binding globulin</td>
<td>TBG</td>
<td>12-20 ug/dl T4 +1.8 ugm</td>
</tr>
<tr>
<td>TRH stimulation test Peak</td>
<td>TSH</td>
<td>9-30 uIU/ml at 20-30 min</td>
</tr>
<tr>
<td>Serum thyroglobulin l</td>
<td>Tg</td>
<td>0-30 ng/m</td>
</tr>
<tr>
<td>Thyroid microsomal antibody titer</td>
<td>TMAb</td>
<td>Varies with method</td>
</tr>
<tr>
<td>Thyroglobulin antibody titer</td>
<td>TgAb</td>
<td>Varies with method</td>
</tr>
</tbody>
</table>

Diseases and Disorders of the Thyroid

Diseases and disorders associated with the thyroid can develop at any age and can result from a variety of causes— injury, disease, or dietary deficiency. Most cases, can be traced to the following problems:

- Too much or too little thyroid hormone
- Abnormal thyroid growth
- Nodules or lumps within the thyroid
- Thyroid cancer

Patients with a family history of thyroid cancer or who had radiation therapy to the head or neck as children for acne, adenoids, or other reasons are more prone to develop thyroid malignancy.
### Signs and Symptoms of Thyroid Imbalance

<table>
<thead>
<tr>
<th>Common symptoms and signs of hypothyroidism</th>
<th>Common symptoms and signs of hyperthyroidism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extreme fatigue, lack of energy</td>
<td>Palpitations</td>
</tr>
<tr>
<td>Unexplained weight gain</td>
<td>Heat intolerance</td>
</tr>
<tr>
<td>Depression and depressed mood</td>
<td>Nervousness</td>
</tr>
<tr>
<td>Joint and muscle pain, headaches</td>
<td>Insomnia</td>
</tr>
<tr>
<td>Paleness, dry skin</td>
<td>Breathlessness</td>
</tr>
<tr>
<td>Brittle nails that break easily</td>
<td>Increased bowel movements</td>
</tr>
<tr>
<td>Brittle hair, itchy scalp, hair loss</td>
<td>Light or absent menstrual periods</td>
</tr>
<tr>
<td>Irregular periods</td>
<td>Fatigue</td>
</tr>
<tr>
<td>PMS symptoms</td>
<td>Fast heart rate</td>
</tr>
<tr>
<td>Breast milk formation</td>
<td>Trembling hands</td>
</tr>
<tr>
<td>Cold/heat intolerance (especially when everyone else is comfortable)</td>
<td>Weight loss</td>
</tr>
<tr>
<td>Hands &amp; Feet cold to touch</td>
<td>Muscle weakness</td>
</tr>
<tr>
<td>Constipation</td>
<td>Warm moist skin</td>
</tr>
<tr>
<td>Sleepiness</td>
<td>Hair loss</td>
</tr>
<tr>
<td>Low sex drive</td>
<td>Staring gaze</td>
</tr>
<tr>
<td>Heart palpitations /Hypertension</td>
<td>Bulging eyes</td>
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<tr>
<td>Swelling, tenderness or a feeling of tightness in Neck or Throat</td>
<td></td>
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<tr>
<td>Hoarseness or coughing</td>
<td></td>
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<tr>
<td>Difficulty swallowing or breathing</td>
<td></td>
</tr>
<tr>
<td>Thick /Swollen tongue</td>
<td></td>
</tr>
<tr>
<td>Bruising/clotting problems</td>
<td></td>
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<tr>
<td>Allergies</td>
<td></td>
</tr>
<tr>
<td>Slowness or slurring of speech</td>
<td></td>
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<tr>
<td>Memory loss, fuzzy thinking</td>
<td></td>
</tr>
<tr>
<td>Puffiness in face under eyes</td>
<td></td>
</tr>
<tr>
<td>Outer part of eyebrow missing</td>
<td></td>
</tr>
<tr>
<td>Could be over or underweight</td>
<td></td>
</tr>
<tr>
<td>Slow reflexes</td>
<td></td>
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</tbody>
</table>
Conventional medicine diagnoses hypothyroidism almost exclusively from the blood tests listed above. If a patient has a normal TSH and a normal free T4, they are told that hypothyroidism is not a factor, no matter how many signs and symptoms are present. These tests only pick up the most severe cases of hypothyroidism and miss most of the milder cases.

Prior to the extensive use of blood tests, hypothyroidism was diagnosed by obtaining an extensive medical history, including family history and a complete physical examination. Later basal metabolic rates were measured using special equipment. Then blood tests were relied upon exclusively.

What should be considered when looking at family medical history? Some or all of these may exist in the patient or family members:

Infancy:
A high birth weight of over 8 lbs. may suggest low thyroid.

Childhood & Adolescence:
Early or late teething, late walking or late talking suggests a low functioning thyroid in the child.
Frequent ear infections, colds, pneumonia, bronchitis or other infections
Problems in school including difficulty concentrating, abnormal fatigue--especially having difficulty getting up in the morning and poor athletic ability all suggest a low thyroid.
Adolescent girls suffer from menstrual irregularity, premenstrual syndrome and painful periods.
Drug and alcohol abuse are common.

Throughout life, disorders associated with hypothyroidism include headaches, migraines, sinus infections, post-nasal drip, visual disturbances, frequent respiratory infections, indigestion, gas, flatulence, constipation, diarrhea, frequent bladder infections, infertility, reduced libido and sleep disturbances, with the person requiring 12 or more hours of sleep at times, intolerance to cold and/or heat, poor circulation, Raynaud's Syndrome (which involves the hands and feet turning white in response to cold) allergies, asthma, heart problems, benign and malignant tumors, cystic breasts and ovaries, fibroids, dry skin, acne, fluid retention, loss of memory, depression, mood swings, fears, and joint and muscle pain.

A family history of Tuberculosis suggests the possibility of low thyroid.
Conventional Treatments for Hypothyroidism:

Synthetic thyroid
Armour desiccated pig thyroid

Hyperthyroidism is a condition caused by the effects of too much thyroid hormone on tissues of the body. Although there are several causes of hyperthyroidism, most of the symptoms patients experience are the same regardless of the cause.
Because the body's metabolism is increased, patients often feel hotter than those around them and can slowly lose weight even though they may be eating more. Some patients gain weight because of an increase in their appetite.
Patients with hyperthyroidism usually experience fatigue at the end of the day, but have trouble sleeping. Trembling of the hands and a hard or irregular heartbeat may develop. These individuals may become irritable and easily upset.
When hyperthyroidism is severe, patients can suffer shortness of breath, chest pain, and muscle weakness. Usually the symptoms of hyperthyroidism are so gradual in their onset that patients don't realize the symptoms until they become more severe. In older people, some or all of the typical symptoms of hyperthyroidism may be absent, and the patient may just lose weight or become depressed.

The most common underlying cause of hyperthyroidism is Graves' disease.
An enlarged thyroid / goiter is producing way too much thyroid hormone. Only a small percentage of goiters produce too much thyroid hormone, most become large because they are not producing enough thyroid hormone.
Graves' disease is classified as an autoimmune disease. Antibodies attach to specific activating sites on the thyroid gland, and that in turn causes the thyroid to make more hormone.
Graves' disease affects women much more often than men, about 8:1 ratio.
Graves' disease is uncommon over the age of 50, it is more commonly diagnosed in the 30’s and 40’s.
Graves' disease tends to run in families
There are three distinct parts of Graves' disease:
overactivity of the thyroid gland (hyperthyroidism)
inflammation of the tissues around the eyes, causing swelling
thickening of the skin over the lower legs (pretibial myxedema).
Most patients with Graves' disease have no obvious eye involvement. Their eyes may
feel irritated or they may look like they are staring. About one out of 20 people with
Graves' disease will suffer more severe eye problems, which can include bulging of the
eyes, severe inflammation, double vision, or blurred vision. If these serious problems
are not recognized and treated, they can permanently damage the eyes and even cause
blindness.

Less Common Causes of Hyperthyroidism

Hyperthyroidism can also be caused by a single nodule within the thyroid instead of
the entire thyroid.
**Thyroid nodules** usually represent benign lumps or tumors in the gland. These
nodules sometimes produce excessive amounts of thyroid hormones. This condition is
called "toxic nodular goiter."

**Inflammation of the thyroid gland**, called thyroiditis, can lead to the release of
excess amounts of thyroid hormones that are normally stored in the gland.
In sub-acute thyroiditis, the painful inflammation of the gland is believed to be caused
by a virus, and the hyperthyroidism lasts a few weeks.
A more common painless form of thyroiditis occurs in one out of 20 women, a few
months after delivering a baby and is, therefore, known as postpartum thyroiditis.

Hyperthyroidism can also occur in patients who take excessive doses of any of the
available forms of thyroid hormone. This is a particular problem in patients who take
forms of thyroid medication that contains T3, which is normally produced in relatively
small amounts by the human thyroid gland.

Thyroid-stimulating hormone (TSH) produced by the pituitary will be decreased in
hyperthyroidism. Thus, the diagnosis of hyperthyroidism is nearly always associated
with a low TSH level. If the TSH levels are not low, then other tests must be run.
Thyroid hormones themselves (T3, T4) will be increased. For a patient to have
hyperthyroidism, they must have high thyroid hormone levels. Sometimes all of the
different thyroid hormones are not high and only one or two of the different thyroid
hormone measurements are high. Most people with hyperthyroidism will have all of
their thyroid hormone measurements high (except TSH).
Iodine thyroid scan will show if the cause is a single nodule or the whole gland. Untreated hyperthyroidism can lead to serious complications, mainly related to the heart.

Some possible heart-related complications of uncontrolled hyperthyroidism are:
- Arrhythmia
- Cardiac dilation and congestive heart failure
- Sudden cardiac arrest
- Hypertension

**Osteoporosis:**
Gradually bone mineral density loss occurs because uncontrolled hyperthyroidism can cause the body to pull calcium and phosphate out of the bones and to excrete too much calcium and phosphorous through urine and stool.

**Conventional Treatment:**

- Anti Thyroid medication
- There are 2 types of anti-thyroid medications used in the U.S.:
  - Propylthiouracil (PTU) and methimazole (also known as Tapazole).
- Radioactive Iodine to destroy the gland
- Surgery to remove the gland

Credits:
Dr. Broda O. Barnes. Hypothyroidism: the Unsuspected Illness.
Michael B. Schachter, M.D. Schachter Center for Complementary Medicine
Mayo Clinic Book of Health