

Thyroid Regulation

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The thyroid gland is a butterfly-shaped organ located in the neck. Its main function is to produce thyroid hormones, which control the body's metabolic rate.

The thyroid gland uses iodine (mostly available from the diet in foods such as seafood, bread, and salt) to produce thyroid hormones. The two most important thyroid hormones are thyroxine (T4) and triiodothyronine (T3). While a small amount of T3 is actually made in the thyroid gland, most of it is converted in the tissues from the T4 released from the thyroid gland into the blood. T3 is the active hormone that affects the metabolism of cells.

An excess of thyroid hormones (hyperthyroidism) overstimulates the body, resulting in increased heart rate, anxiety, and weight loss, while a lack of thyroid hormones (hypothyroidism) can cause depression, sluggishness, weight gain, and heart failure. Hyperthyroidism is rare (affecting about 1 percent of the population), while mild, subclinical hypothyroidism may be much more common than most people think.

Subclinical hypothyroidism is estimated to occur in a significant percentage of the adult American population (Hollowell JG et al 2002). One side effect of thyroid deficiency is high cholesterol. It is very possible that many people are being prescribed cholesterol-lowering statin drugs while their underlying problem—low thyroid function—goes unaddressed.

The most common cause of overt hypothyroidism in the United States is an autoimmune disorder known as Hashimoto's thyroiditis (Lorini R et al 2003). This condition is characterized by an overactive immune system response that floods the thyroid gland with white blood cells that attack the gland. Hashimoto's thyroiditis is more common in women than in men, and there is a genetic component to the disease.

Worldwide, a lack of dietary iodine is the leading cause of hypothyroidism (Delange F 1998). Iodine is necessary for the synthesis of thyroid hormones. Since table salt was iodized in the United States, lack of dietary iodine has not been a major problem, though cases of iodine deficiency are still reported. Besides iodine, thyroid function can be affected by a number of nutrients, including zinc and selenium. Deficiencies in either of these have been shown to increase the risk of hypothyroidism.

There is evidence that the standard blood test reference ranges may cause many cases of hypothyroidism to be missed. Based on published clinical data, Life Extension advocates a more complete thyroid evaluation to rule out thyroid deficiency as a cause of common age-associated maladies such as depression, fatigue, and unwanted weight gain.

Hypothyroidism is typically treated with supplemental thyroid hormones. There are a number of approaches to increasing thyroid hormone, including use of synthetic hormones (both T3 and T4) and natural desiccated thyroid hormone from animals. New combination drugs provide fixed ratios of T3 and T4. The choice of which form of thyroid hormone to use is an individual decision, to be made on the basis of blood tests and effectiveness of therapy.

CONSEQUENCES OF LOW THYROID HORMONE

The vast majority of the thyroid hormone produced by the thyroid gland is T4. However, T4 has only a slight effect on the body's metabolic rate. The more active hormone is T3. To supply the necessary T3, the liver and other tissues convert T4 into T3.

T4 and T3 are essential for regulating metabolic processes throughout the body, including (1) maintaining the basal metabolic rate; (2) making more glucose available to meet the elevated metabolic demands; (3) stimulating new protein synthesis; (4) increasing metabolism of lipids and conversion of cholesterol into bile acids, activating lipoprotein lipase, and increasing sensitivity of adipose tissue to hormones that stimulate the breakdown of fat; (5) increasing cardiac output and blood flow; and (6) increasing neural transmission.

If untreated, chronic hypothyroidism can result in myxedema, a rare, life-threatening condition. Mental dysfunction, stupor, cardiovascular collapse, and coma can develop after the worsening of chronic hypothyroidism. Patients may pass into a hypothermic stuporous coma and die (Jordan RM 1995; Smallridge RC 1992).

Additional possible complications of chronic hypothyroidism include the following:

- **Depression and psychiatric disorders.** Panic attacks, anxiety, depression, phobias, and obsessive compulsive disorders are commonly encountered in hypothyroidism and hyperthyroidism (Romaldini JH et al 2004). Subclinical hypothyroidism is the most commonly encountered organic cause of depression (Saddock BJ 2000).
- **Reduced cardiac output.** In overt hypothyroidism, cardiac contractility and cardiac output are decreased, and vascular resistance is increased. These changes also affect people with subclinical hypothyroidism, but to a lesser degree (Danzi DS et al 2004).
- **High blood pressure.** Hypothyroidism is often accompanied by diastolic hypertension that, in conjunction with elevated cholesterol (see below), may promote atherosclerosis (Duntas LH 2002). Hypertension is relatively common among patients with laboratory evidence of hypothyroidism; in one study, 14.8 percent of patients with hypothyroidism were hypertensive, compared with 5.5 percent of people with normal thyroid function (Saito I et al 1983).
- **High cholesterol.** Hypothyroidism is characterized by hypercholesterolemia and a marked increase in low-density lipoproteins and apolipoprotein A. These changes accelerate atherosclerosis, which causes coronary artery disease (O'Brien T et al 1993). Subclinical hypothyroidism has been associated with endothelial dysfunction, aortic atherosclerosis, and myocardial infarction (Duntas LH 2002). Thyroid hormone replacement therapy may slow the progression of coronary artery disease (Perk M et al 1997) because of its beneficial effects on lipids (Duntas LH 2002; Althaus B et al 1988; Fowler PB et al 1996).
- **Elevated C-reactive protein.** Clinical and subclinical hypothyroidism are associated with increased levels of low-grade inflammation as indicated by elevated C-reactive protein and may be a risk factor for development of cardiovascular disease in younger males (Kvetny J et al 2004).
- **Musculoskeletal system.** Hypothyroid patients may exhibit joint aches and effusions and pseudogout (Westphal SA 1997).
- **Reproductive system problems.** In women, hypothyroidism is associated with menstrual irregularities, absence of ovulation, and infertility (Joshi JV et al 1993). In men, hypothyroidism is associated with abnormalities of gonadal function (Wortsman J et al 1987).
- **Pregnancy complications.** Subclinical and postpartum hypothyroidism are gaining recognition as serious health problems among women. In pregnancy, the fetus is dependent on the mother for adequate thyroid hormone. Postpartum thyroiditis, or chronic inflammation of the thyroid gland, may develop in as many as one out of 10 women after giving birth.

RETHINKING THYROID HORMONE MEASUREMENTS

The most common test used to measure thyroid function is determination of thyroid-stimulating hormone (TSH) levels. TSH is produced by the pituitary gland; it stimulates the thyroid gland to secrete T3 and T4. TSH is elevated in response to low thyroid hormone levels, while TSH levels are low in response to elevated thyroid hormone levels.

While this test is commonly used, and recent improvements have made it more sensitive, there is a good chance that the standard reference ranges used by many laboratories are so wide that many people with subclinical hypothyroidism are not correctly diagnosed. This means that potentially tens of thousands of people suffering from depression, heart disease, or weight gain may be unaware that their conditions are actually due to low thyroid hormone.

The standard reference range for TSH is between 0.2 and 5.5 mU/L. Any reading more than 5.5 mU/L would signal low thyroid hormone and possible hypothyroidism. Unfortunately, this TSH reference range is very broad. Many clinicians and scientists believe that the upper limit of the established "normal" range is too high to permit detection of people with significantly low thyroid function.

In reality, a TSH reading of more than 2.0 may indicate lower-than-optimal thyroid hormone levels. Patients in this group have an increased chance of developing frank hypothyroidism (a TSH greater than 5.5) and may also suffer from symptoms such as depression and weight gain. One study found that TSH levels of more than 4.0 are associated with increased risk of heart disease (Hak AE et al 2000).

According to a study reported in *Lancet*, one of the world's leading medical journals, various "normal" TSH ranges may actually be associated with adverse health outcomes (Dayan CM et al 2002):

- TSH greater than 2.0: increased 20-year risk of hypothyroidism and increased risk of thyroid autoimmune disease
- TSH greater than 4.0: greater risk of heart disease
- TSH between 2.0 and 4.0: cholesterol levels decline in response to T4 therapy

Hashimoto's thyroiditis is diagnosed by tests to detect the presence of autoimmune antibodies to thyroid tissue.

Direct tests of thyroid function include measurement of thyroid hormones themselves. Both T3 and T4 can be determined in blood, though it is the level of free (not protein-bound) hormone that is biologically active and therefore relevant. Levels of free T3 and T4 will be below normal in hypothyroidism. Measurement of these hormones is commonly done only when TSH levels are known to be abnormal.

Invasive procedures, such as biopsy or enzymatic studies, are occasionally required to establish a definite diagnosis. Gross abnormalities of the thyroid gland, detected by palpation, can be assessed by scintiscanning and by ultrasonography (Surks MI et al 1990).

THYROID HORMONE REPLACEMENT: SYNTHETIC VERSUS NATURAL

The most common treatment for low thyroid hormone levels consists of thyroid hormone drug replacement therapy. The goals of thyroid hormone replacement are to relieve symptoms and to provide sufficient thyroid hormone to decrease elevated TSH levels to within the normal range (Hennessey JV et al 1986).

Conventional treatment almost always begins with synthetic T4 drugs, including Synthroid® and Levothyl® (levothyroxine). Low doses are usually used at first because a rapid increase in thyroid hormone may result in cardiac damage (Arnoff WS 1995).

In a study of thyroidectomized rats (rats whose thyroid glands had been surgically removed) treated with levothyroxine alone, no single dose was able to restore normal concentrations of TSH, T4, and T3 in the blood and normalize T4 and T3 levels in all tissues and organs analyzed (Escobar-Morreale HF et al 1995). In most tissues, the dose of levothyroxine required to produce normal T3 levels resulted in significantly elevated T4 levels.

For some patients, hypothyroidism symptoms persist despite standard thyroxine or levothyroxine replacement therapy. T4 therapy may be no more effective than placebo in improving cognitive function and psychological well-being in patients with symptoms of hypothyroidism, despite thyroid function test scores well within the reference range (Pollock MA et al 2001; Walsh JP et al 2001).

Instead, only combination therapy, using levothyroxine administered at the same time as T3, is able to restore natural thyroid hormone levels. One such combination option is a drug called Thyrolar, which combines synthetic T3 and T4 in a fixed 4:1 ratio. Caution should be used, however, in administering T3 to people over age 50 because of the increased risk of cardiac problems due to increased levels of T3.

Another T3 option is a drug called Cytomel®, which is a synthetic form of T3 and which can be used in combination with T4. A recent study reported that in some hypothyroid patients, the combination of T4 and T3 resulted in improved mood and psychological function compared with monotherapy with T4 (Bunevicius R et al 1999). Other studies have failed to demonstrate any advantage of the combination therapy, although the results do suggest the possibility of a subset of hypothyroid patients who would benefit from combination therapy (Sawaka AM et al 2003; Walsh JP et al 2003).

ARMOUR THYROID

Armour thyroid (Thyrar), Nathroid, and Westroid are prescription medications that contain desiccated thyroid derived from the thyroid gland of the pig. Natural thyroid extracts have been used since 1892 and were approved by the Food and Drug Administration in 1939. Armour thyroid and most other natural glandular preparations are made to standards approved by the United States Pharmacopoeia.

Natural thyroid extracts were largely replaced in clinical medicine by levothyroxine (Synthroid®) because the natural extracts have a reputation for being impure and inconsistent from dose to dose.

Armour thyroid (desiccated thyroid) is preferred by some clinicians because it may achieve better results for a wider range of symptoms than levothyroxine alone (Gaby AR 2004). While levothyroxine consists solely of T4, desiccated thyroid contains approximately 80 percent T4 and 20 percent T3, as well as other iodinated compounds (diiodotyrosine and monoiodotyrosine). Patients with hypothyroidism show greater improvements in mood and brain function if they receive treatment with Armour thyroid rather than Synthroid®. Researchers found that substituting Armour thyroid led to improvements in mood and in neuropsychological functioning.

Ultimately, there may not be a single correct approach to low thyroid hormone levels. Instead, the best option may be to monitor thyroid levels through regular blood testing and experiment with various approaches to see what yields the best blood results and resolves any symptoms. Some people may prefer to begin with desiccated thyroid, while others may find it preferable to begin with T4 supplementation, then move to a combination T3-T4 therapy if they experience no improvement from T4 alone.

NUTRIENTS TO ENHANCE THYROID FUNCTION

Iodine and minerals. Iodine is required by the body to form thyroid hormone, and iodine deficiency can lead to goiter (abnormal enlargement of the thyroid gland) and hypothyroidism. Currently, most cases of iodine deficiency occur in developing nations. In industrialized countries where iodized salt is used, iodine deficiency has become rare (Stewart JC et al 1976).

Vegetarians, however, are at risk of developing iodine deficiency, especially if they live in areas where the soil is low in iodine. Vegans, who do not eat iodine-enriched dairy products, are at an even higher risk (Remer T et al 1999).

Other minerals, including iron and zinc, are essential for normal thyroid hormone metabolism. Coexisting deficiencies of these elements can impair thyroid function. Iron deficiency impairs thyroid hormone synthesis by reducing activity of iron-dependent thyroid peroxidase. Iron supplementation improves the efficiency of iodine supplementation. A study found that TSH has a significant effect on the concentration of iodine, selenium, and zinc in normal and altered human thyroid (Bellisola G et al 1998). The roles of iron, zinc, and copper in the thyroid are less well defined, but reduced intake of all these elements can damage thyroid hormone metabolism (Arthur JR 1999).

Zinc. In animal studies, single and multiple deficiencies of iodine, selenium, and zinc have distinct effects on thyroid metabolism and structure (Ruz M et al 1999). In animal studies, zinc deficiency was associated with decreased concentrations of T3 and free thyroxine in serum by approximately 30 percent when compared with zinc-adequate controls (Kralik A et al 1996). Zinc may play a role in thyroid hormone metabolism in patients with low T3 and may contribute to conversion of T4 to T3 in humans (Nishiyama S et al 1994).

Selenium. Selenium is required for appropriate thyroid hormone synthesis, activation, and metabolism. Adequate selenium supports efficient thyroid hormone synthesis and metabolism and protects the thyroid gland from damage caused by excessive exposure to iodide (Zimmerman MB 2002). Long-term selenium deficiency in experimental animal models led to thyroid cell death and scarring after high iodide loads (Kohrle J 1999). Selenium deficiency may seriously influence the generation of free radicals, the conversion of thyroxine T4 to T3, and the autoimmune process (Kohrle J 1999).

One study also found that selenium deficiency decreased the inflammation that is associated with autoimmune thyroiditis. During this study, female patients with autoimmune thyroiditis and elevated antithyroid antibodies were given selenium. At the end of the study, researchers found that a significant percentage of the patients had normalized their antibody concentrations (Gartner R et al 2002).

Vitamins. Newer research has suggested that antioxidant vitamins, such as vitamin C and vitamin E, can reduce the oxidative stress caused by hypothyroidism. In one animal study, vitamin E was shown to protect animals from increased oxidation and thyroid cell damage (Sarandol E et al 2005). Another study found that vitamin E reduced proliferation of goiter cells and auto-antibodies (Oner J et al 2003). Finally, an antioxidant mix containing vitamins C and E, along with turmeric extract, reduced hypothyroidism in animals (Deshpande UR et al 2002).

Dietary Recommendations

Some foods contain goitrogenic substances that prevent the utilization of iodine. These foods include canola oil, Brassica vegetables (e.g., cabbage, Brussels sprouts, broccoli, and cauliflower), corn, cassava, sweet potatoes, lima beans, and pearl millet. The actual content of goitrogens in these foods is quite low, however, and cooking destroys it.

Hypothyroid patients should also avoid soy supplements (Bell DS et al 2001; Jabbar MA et al 2001).

LIFE EXTENSION FOUNDATION RECOMMENDATIONS

People with low thyroid are often placed on synthetic hormone preparations, such as Synthroid® and Unithroid® (synthetic T4), or Cytomel® (synthetic T3). A combination synthetic T3 and T4 is available (Thyrolar). Ultimately, which of these drug regimens is best depends on each person's response.

Natural glandulars, such as Armour Desiccated Thyroid Hormone, Nathroid, and Westroid, derived from the thyroid gland of the pig, contain T3 and T4 and most closely resemble human thyroid hormone.

The following supplements have been shown to enhance thyroid function:

- **Iodine**—150 micrograms (mcg) to 1.5 milligrams (mg) daily (Note: Take milligram doses of iodine only under a physician's supervision.)
- **Zinc**—30 to 60 mg daily
- **Copper**—1 to 2 mg daily
- **Selenium**—200 to 400 mcg daily
- **Vitamin E**—400 international units (IU) daily (with at least 200 mg gamma tocopherol)
- **Vitamin C**—2 to 3 grams (g) daily

In addition, patients with low thyroid hormone may be deficient in DHEA, a vital hormone that serves as a precursor of sex hormones

such as estrogen and testosterone (Tagawa N et al 2000). A normal beginning dose is 15 to 75 mg, followed by blood testing.

PRODUCT AVAILABILITY

All the nutrients and supplements discussed in this section are available through the Life Extension Foundation Buyers Club, Inc. For ordering information, call anytime toll-free 1-800-544-4440, or visit us online at www.LifeExtension.com.

The blood tests discussed in this section are available through Life Extension National Diagnostics, Inc. For ordering information, call anytime toll-free 1-800-208-3444, or visit us online at www.LifeExtension.com.

THYROID DEFICIENCY SAFETY CAVEATS

An aggressive program of dietary supplementation should not be launched without the supervision of a qualified physician. Several of the nutrients suggested in this protocol may have adverse effects. These include:

Copper

- Do not take copper supplements if you have Wilson's disease.
- Consult your doctor if you take copper supplements and have chronic liver failure and/or chronic kidney failure.
- Do not take high doses of copper. High doses of copper are extremely toxic.
- Copper can cause gastrointestinal symptoms such as nausea and diarrhea.

Potassium iodide

- Potassium iodide can cause hyperthyroidism in older people with nodular goiters.
- Potassium iodide may exacerbate symptoms of autoimmune thyroiditis.
- Potassium iodide may cause rashes, arrhythmias, central nervous system effects (confusion, numbness, tingling, weakness in the hands or feet), hypothyroidism, hyperthyroidism (Jod-Basedow phenomenon), parotitis (iodide mumps), thyroid adenoma and small bowel lesions.
- Potassium iodide may cause hypersensitivity reactions including angioedema, symptoms resembling serum sickness (fever, arthralgia, eosinophilia, lymphadenopathy), cutaneous and mucosal hemorrhages, urticaria, thrombotic thrombocytopenia purpura (TTP), and fatal periarteritis.
- Enteric-coated potassium iodide may cause nonspecific small bowel lesions manifested by stenosis with or without ulcerations. These lesions may cause hemorrhage, obstruction, perforation and death.
- Chronic intake of pharmacological doses of iodides (>2 mg) can lead to iodism characterized by frontal headache, pulmonary edema, coryza (head cold), eye irritation, skin eruptions, gastric disturbances, as well as inflammation of the tonsils, larynx, pharynx, and submaxillary and parotid glands.

Selenium

- High doses of selenium (1000 micrograms or more daily) for prolonged periods may cause adverse reactions.
- High doses of selenium taken for prolonged periods may cause chronic selenium poisoning. Symptoms include loss of hair and nails or brittle hair and nails.
- Selenium can cause rash, breath that smells like garlic, fatigue, irritability, and nausea and vomiting.

Vitamin C

- Do not take vitamin C if you have a history of kidney stones or of kidney insufficiency (defined as having a serum creatine level greater than 2 milligrams per deciliter and/or a creatinine clearance less than 30 milliliters per minute).
- Consult your doctor before taking large amounts of vitamin C if you have hemochromatosis, thalassemia, sideroblastic anemia, sickle cell anemia, or erythrocyte glucose-6-phosphate dehydrogenase (G6PD) deficiency. You can experience iron overload if you have one of these conditions and use large amounts of vitamin C.

Vitamin E

- Consult your doctor before taking vitamin E if you take warfarin (Coumadin).
- Consult your doctor before taking high doses of vitamin E if you have a vitamin K deficiency or a history of liver failure.
- Consult your doctor before taking vitamin E if you have a history of any bleeding disorder such as peptic ulcers, hemorrhagic stroke, or hemophilia.

- Discontinue using vitamin E 1 month before any surgical procedure.

Zinc

- High doses of zinc (above 30 milligrams daily) can cause adverse reactions.
- Zinc can cause a metallic taste, headache, drowsiness, and gastrointestinal symptoms such as nausea and diarrhea.
- High doses of zinc can lead to copper deficiency and hypochromic microcytic anemia secondary to zinc-induced copper deficiency.
- High doses of zinc may suppress the immune system.

For more information see the Safety Appendix

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