

## Hypothyroidism

### **Pronunciations:** ([Hypothyroidism](#))

Hypothyroidism (under active thyroid) is a condition where the thyroid gland fails to secrete enough of the thyroid hormones thyroxine (T4) and triiodothyronine (T3). The most common cause of hypothyroidism is autoimmune thyroiditis (Hashimoto's disease) which damages the thyroid gland and creates insufficient thyroid production.

### **Causes**

Inadequate iodine intake is the most common cause of primary hypothyroidism in the world, whereas in the United States Hashimoto's thyroiditis remains most common. Iodine deficiency creates a marked rise in TSH production because of insufficient thyroid hormone production, leading to enhanced iodine trapping and goiter. In Hashimoto's disease the thyroid gland is damaged by CD8+ lymphocytes and antibodies such as thyroid stimulation-blocking antibody (TSBAb) are present. TSBAb binds to a region on the thyrotropin (TSH) receptor, thereby blocking TSH to bind and stimulate thyroid hormone production. Schmidt's syndrome is often found with Hashimoto's disease. Other primary causes of hypothyroidism include lithium therapy, dietary goitrogen consumption, mutations in thyroglobulin, Na<sup>+</sup>/I<sup>-</sup> symporter, and thyroid peroxidase, surgery, nitrate and thiocyanate consumption, and radiothyroidectomy. Secondary causes of hypothyroidism may result if hypothalamic/pituitary disorders are present such as pituitary cancer which prevents TSH release. Tertiary causes are due to lack of thyrotropin releasing hormone (TRH) secretion. An estimated 4.6% of Americans have hypothyroidism, with more of those cases being women. The risk for hypothyroidism increases with age and obesity. Congenital hypothyroidism in infants is a fairly common occurrence in the United States affecting 1 out of 4000.

### **Diagnosis**

#### *Symptoms:*

Symptoms of hypothyroidism are usually subtle in its early stages. Early symptoms include weakness, fatigue, modest weight gain or difficulty losing weight, and hypothermia. Chronic symptoms are usually dull facial expression, droopy eyelids, slow and hoarse speech, hair thinning and sparseness, dry, course, and thick skin, myxedema, and menstrual disorders such as menorrhagia in women.

#### *Other symptoms:*

Constipation  
Depression  
Thin and brittle nails  
Paleness  
Hypercarotenemia of soles and palms  
Paresthesias of hands and feet

## Interpretation of Laboratory Tests

The following methods are frequently used to help reach a diagnosis for hypothyroidism. Selecting the type of test to order may depend on the severity of symptoms, confirming previously ordered tests, or availability of resources.

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<b>LABORATORY TESTS</b>		
<b>Test Name</b>	<b>Normal values</b>	<b>Indicators</b>
Serum TSH	0.2-4.7 mcU/ml Reference ranges vary between assays.	Higher than normal levels are usually present with primary hypothyroidism. Secondary hypothyroidism usually present low levels, but normal and high levels may also be observed.
Plasma Total T4	4.5 to 11.2 µg/dl Reference ranges vary between assays.	Lower than normal levels are usually present with this disorder.
Serum Free T4	0.8 – 2.0 ng/dl Reference ranges vary between assays.	Lower than normal levels are usually present with this disorder.
Plasma Total T3	86 – 187 ng/dl Reference ranges vary between assays.	Lower than normal levels are usually present with this disorder. Normal levels may also be observed.
Serum Free T3	1.4 – 4.4 pg/ml Reference ranges vary between assays.	Lower than normal levels are usually present with this disorder. Normal levels may also be observed.
TRH Test	500 µg IV of TRH should increase TSH to 5 to 25 µU/ml, peaking at 30 minutes and return to normal after 2 hours	Higher response seen in primary hypothyroidism. A delayed or impaired response is usually seen with secondary hypothyroidism.
<b>OTHER BLOOD TESTS</b>		
<b>Test Name</b>	<b>Normal values</b>	<b>Indicators</b>
Thyroid Autoantibodies		Thyroid peroxidase and less commonly thyroglobulin antibodies present in Hashimoto's disease.

Serum Cholesterol	Total Cholesterol: < 200 mg/dL (desirable) (< 180 optimal) LDL Cholesterol: < 100 mg/dL (optimal) 100-129 mg/dL (near optimal/above optimal)	Usually elevated in primary hypothyroidism.
Partial Pressure of Oxygen (Pao <sub>2</sub> )	75 to 100 mm Hg	Levels are low (hypoxemia) in myxedema coma.
<b>IMAGING TESTS</b>		
Test Name	Indicators	
Radioactive Iodine Uptake (RAIU)	100-200 µCi of <sup>123</sup> I is orally administered and radioactivity is measured on scintillation counter 6 to 24 hours after ingestion. RAIU will be low in hypothyroidism. It is most useful in determining the etiology of thyrotoxicosis (i.e., hyperthyroidism).	
Radioimaging	Reveals the shape and size of the thyroid gland and where iodine is distributed (hot vs cold nodules). The test requires ingestion of 200-300 µCi of <sup>123</sup> I sodium iodide. <sup>99m</sup> TcO <sub>4</sub> <sup>-</sup> pertechnetate is also used for radioimaging.	
Perchlorate Washout Test	Can be used in the diagnosis of an organification defect. The test is conducted during a RAIU test, when after 3 hours potassium perchlorate is given, a known inhibitor of NIS. Decreased radioactivity suggests an organification defect.	

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Serum TSH is the most sensitive index for diagnosing primary hypothyroidism. Low serum TSH levels are usually present with secondary hypothyroidism, but elevated with primary hypothyroidism because feedback inhibition is not functioning. T3 levels may be normal because of enhanced TSH stimulation leading to enhanced release of the more active thyroid hormone. It is very important to review the patient's clinical and medical history when diagnosing hypothyroidism. Several factors such as protein-energy malnutrition, chronic illness, fasting, diabetic ketoacidosis, drugs (i.e., glucocorticoids), and many others can lead to altered thyroid hormone test results.

### Common Current Treatments

Treatment of hypothyroidism requires life-long medication of synthetic T4 (L-thyroxin [Levothyroxine]) to replace deficient thyroid hormones. The lowest dose possible that normalizes serum TSH levels and relieves symptoms is commonly used. Monthly blood tests should be conducted initially to assess thyroid hormone levels, which should be followed by yearly follow-ups.

#### *Medications*

The following table lists some classes and examples of medications commonly prescribed for patients with hypothyroidism. Commonly synthetic T4 (L-thyroxine), triiodothyronine (Liothyronine sodium), or a combination of both, and desiccated thyroid

are used for treatment than iodine replacement. L-thyroxine is effective in correcting iodine deficiency, although this method is more costly. The standard dosage for L-thyroxine is 50µg/day orally, which should be increased by 25-50 µg/day every 4 to 8 weeks until a maintenance dose (50-200 µg/day) is reached. The drug is best taken in the morning on an empty stomach. The initial dosage for Liothyronine is 5 µg/day orally which should be increased by 5-10 µg/day until a maintenance dose (25 to 50 µg/day) is reached. The initial dosage for desiccated thyroid hormone is 30 mg/day orally which should be increased until a maintenance dose (60-180 mg/day) is achieved. A maintenance dose the minimum drug dose that normalizes T4 and T3 levels or lowers TSH to the low end of the reference range. Myxedema coma may be present, although rare, in hypothyroidism and the initial treatment requires an intravenous infusion of large amounts of L-thyroxine (400-500 µg) and L-triiodothyronine (40 µg) which is followed by a maintenance dose of 50-100 µg/day IV of L-thyroxine and 10-20 µg/day IV of L-triiodothyronine until oral L-thyroxine can be given. Dosages may need to be adjusted when other drugs (i.e., cholestyramine) are given simultaneously that are known to affect absorption or drug metabolism.

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<b>THYROID HORMONE MEDICATIONS</b>		
<b>Indication</b>	<b>Class/Examples</b>	<b>Notes</b>
Thyroid hormone deficiency	L-thyroxine: Levothyroxine	Monitor for cardiac problems and adrenal crisis.
Thyroid hormone deficiency	Liothyronine sodium	Monitor for cardiac problems and adrenal crisis.
Thyroid hormone deficiency	Desiccated thyroid	Monitor for cardiac problems and adrenal crisis. Rarely used in the United States.
<b>IODINE</b>		
<b>Indication</b>	<b>Class/Name</b>	<b>Notes</b>
Iodine deficiency	Potassium Iodide	Patients with iodine deficiency goiter may develop thyrotoxicosis with large doses. Doses > 1000 µg/day may increase the risk for lithium toxicity. Use of this is not very practical.
<b>CORTICOSTEROIDS</b>		
<b>Indication</b>	<b>Class/Name</b>	<b>Notes</b>
Myxedema Coma	Corticosteroid: Hydrocortisone (intravenous)	

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## **Dietary Interventions**

If iodine deficiency is the main cause of hypothyroidism, ingestion of 100-150 µg/day of dietary iodine in adults and adolescents is sufficient to reverse deficiency. Pregnant and lactating women are recommended to ingest 200 µg/day, whereas the recommended dose for children 1 to 11 is 90-120 µg/day and 50-90 µg/day in infants < 1 year. Patients should be advised to use iodized salt in cooking and to sprinkle the salt on food. In addition, consumption of marine foods (i.e., saltwater fish), milk, and egg yolks should be recommended. There are no dietary recommendations for primary and secondary hypothyroidism, however, if weight gain has ensued from thyroid production failure, then increasing fiber and decreasing calories may help with weight loss. Constipation is often associated with hypothyroidism therefore increasing fiber to the recommended levels (20-35 grams/day) will reduce this occurrence and the satiety promoting effects may enhance weight loss through decreased calorie consumption. It is important that the patient drink adequate amounts of fluids, otherwise constipation may be increased. Fiber consumption is easily increased by eating more fruits, vegetables, whole grains, legumes, and cereals. Physical activity should also be increased.

## **Orders**

**Drug therapy should be administered promptly once the cause of hypothyroidism is discovered.**

When T4, T3, and TSH levels normalize, the patient should receive annual TSH screenings. If weight gain has occurred, the patient should start a weight loss program by decreasing calories and increasing activity level. Fiber intake may also need to be increased which can be easily implemented.

## **What to Tell the Patient and Family**

It is important to discuss that hypothyroidism is a life-long disease that will require life-long therapy. The patient and their family should be informed on the proper way to administer medications, contraindications associated with the medications, and be willing to have TSH levels tested annually once a maintenance dose has been established.