Hypothyroidism in Adults

**Description/Etiology**

Hypothyroidism is an endocrine disorder characterized by a hypometabolic state secondary to insufficient circulating levels of the thyroid hormones (THs) thyroxine (T<sub>4</sub>) and triiodothyronine (T<sub>3</sub>; active thyroid hormone). Hypothyroidism is caused by reduced TH production or, in rare cases, by impaired T<sub>4</sub> synthesis by thyroid follicle cells. TH is released through a negative feedback mechanism composed of the hypothalamus, anterior pituitary, and thyroid gland. Thyrotropin-releasing hormone (TRH) in the hypothalamus stimulates secretion of thyroid-stimulating hormone (TSH) from the anterior pituitary. TSH stimulates synthesis and release of T<sub>4</sub> and T<sub>3</sub>. THs regulate protein, fat, and carbohydrate catabolism, metabolic rate, and body heat production; maintain growth hormone secretion, cardiac rate and force, and calcium mobilization; affect respiratory rate, oxygen utilization, and RBC production; and stimulate lipid turnover and cholesterol synthesis. Interruption of production or tissue absorption of T<sub>4</sub> and T<sub>3</sub> affects all body systems, reducing energy metabolism and heat production and is manifested by feeling cold, low basal body temperature, and mental, physical, and physiologic sluggishness.

*Primary* hypothyroidism is caused by thyroid gland failure, reducing TH production. In response to reduced TH levels, TSH secretion increases and can cause goiter. Worldwide, iodine deficiency is the most common cause of primary hypothyroidism; in regions with sufficient dietary iodine, primary hypothyroidism is usually secondary to Hashimoto thyroiditis, an autoimmune disease that progressively destroys thyroid tissue. Other causes of primary hypothyroidism include surgical or radiation-induced thyroid gland destruction, and congenital or idiopathic myxedema. *Secondary* hypothyroidism is caused by deficient pituitary TSH production, and *tertiary* hypothyroidism by deficient hypothalamic TRH production; secondary and tertiary hypothyroidism are classified as central hypothyroidism. *Transient* hypothyroidism can be caused by subacute or postpartum thyroiditis. Rarely, hypothyroidism is caused by increased tissue resistance to TH.

Symptoms and complications range in severity from fatigue and cold intolerance to myxedema coma/crisis, a life-threatening medical emergency characterized by reduced consciousness, hypothermia, hypoventilation, hypotension, hypoglycemia, and lactic acidosis (see *Quick Lesson About ... Myxedema Coma/Crisis*). Other complications include hypercholesterolemia, arteriosclerosis, ischemic heart disease, cardiomegaly, heart failure, achlorhydria (i.e., no gastric acid production), anemia, lowered immunity, depression, hair loss, and miscarriage. Severe hypothyroidism can cause organic psychoses with paranoid delusions (“myxedema madness”) in some patients.

Diagnosis is based on laboratory studies that measure serum hormonal levels. Because the clinical presentation of hypothyroidism can be vague and develop over months to years, it can be confused with a number of other medical and psychological conditions. The differential diagnosis includes chronic fatigue syndrome, depression, dementia from other causes, heart failure, irregular vaginal bleeding, anemia secondary to other causes, nephrotic syndrome, amyloidosis, and prolactin-secreting pituitary adenoma. Unless hypothyroidism is transient, treatment consists of lifelong TH replacement therapy to restore normal metabolism. As hypothyroidism has a wide range of physical and mental symptoms, supportive therapy and emotional and psychological support are important components of
the treatment plan. For more information about the disorder in children (see Quick Lesson About ... Hypothyroidism in Children).

Facts and Figures
Subclinical hypothyroidism (see Laboratory Tests for definitions) affects 1–10% of United States residents; overt hypothyroidism is reported at 0.3–0.4%. Hypothyroidism is more common in women, and incidence increases with age. Widespread use of iodized salt has reduced global hypothyroidism incidence over the past century.

Risk Factors
Risk factors for hypothyroidism include increased age, female gender, obesity, iodine deficiency or excess, diabetes mellitus type 1, genetic defects, smoking, prior hyperthyroidism treatment, neck irradiation from prior X-rays and/or radiation therapy, drugs that affect the thyroid (e.g., lithium carbonate, amiodarone, propylthiouracil), and family history of hypothyroidism.

Signs and Symptoms/Clinical Presentation
Classic signs and symptoms of hypothyroidism include cold intolerance, reduced sweating, coarse skin and/or hair, hair loss, jaundice, edema, slowed movements, fatigue or weakness, weight gain, forgetfulness, slowed speech, constipation, and menstrual irregularities. Many patients are asymptomatic.

Assessment
› Patient History
• Assess onset, duration, and severity of signs and symptoms
• Obtain full medical and surgical history; assess for family history of hypothyroidism and for other risk factors
› Physical Findings of Particular Interest
• Presence of goiter and delayed relaxation of deep tendon reflexes can help establish clinical diagnosis
› Laboratory Tests
• Serum TSH and free T$_4$ tests might reveal ↑ TSH and normal free T$_4$ (subclinical hypothyroidism) or ↑ TSH and ↓ free T$_4$ (overt hypothyroidism)
• Serum chemistry studies might reveal ↓ sodium, ↑ LDL-cholesterol, ↑ alkaline phosphatase, ↑ liver enzymes, ↑ creatine kinase, ↑ cholesterol, ↑ prolactin
• CBC might reveal normocytic anemia
› Other Diagnostic/Imaging Tests/Studies
• Skull X-rays or MRI/CT scan can be ordered to evaluate for pituitary and/or hypothalamic lesions and/or retarded bone growth
• Chest X-ray can be performed to evaluate for enlarged heart or pleural effusion
• Neck and thyroid ultrasonography can detect thyroid nodules or infiltrative disease
• Abdominal ultrasonography can reveal ascites
• ECG can reveal bradycardia, low amplitude QRS complexes, or flattened or inverted T waves

Treatment Goals
› Provide Supportive Care and Reduce Risk for Complications
• Assess vital signs and all physiologic systems; review results of thyroid function tests and other laboratory/diagnostic studies, and verify that the treating clinician is aware of results
• Administer prescribed levothyroxine with water 30–60 minutes before a meal, as ordered; educate patient on self-administration for long-term management, as appropriate
  – Monitor for and educate on potential adverse reactions of levothyroxine
• Monitor vital signs, intake and output, frequency of bowel movements, and daily weight; monitor bowel sounds and for edema, abdominal distension, and cardiovascular, pulmonary, mental, and neurologic status changes
• Promote regular exercise and nutritious dietary intake
› Provide Emotional/Psychological Support and Educate
• Listen to patient and family concerns with empathy, understanding that hypothyroidism can markedly alter mental and emotional status; advocate for referral to a mental health professional for additional counseling, if necessary
• Encourage adequate sleep and rest periods for optimal mental and physical well-being
Food for Thought
› Authors of a case report, describing an incident of fenofibrate monotherapy inducing rhabdomyolysis in a patient with hyperthyroidism, report that this is not a rare incident and that fenofibrate monotherapy should be avoided, if possible, for patients with hypothyroidism (Wang et al., 2018)
› Authors in a systematic review of 50 observational studies evaluating the effects of excessive iodine intake on thyroid disease found that rural populations exposed to high amounts of iodine via poorly-regulated salt and water sources are at increased risk for developing hypothyroidism (Katagiri et al., 2017)
› Authors of a retrospective population-based cohort study including 2,630 patients with hypothyroidism in Spain found that most (90.3%) were women, a fifth had inadequate hormone replacement therapy during the first year, and that dosing (medium, or 75–125 mcg) and older age contributed to stable TSH levels (Caty, 2017)
› Authors of a study evaluating the effects of excess iodine intake described how it can cause excessive thyroid hormone synthesis and release, which can consequently induce the autonomic thyroid function and lead to hyperthyroidism. One example of a drug with high iodine content is the anti-arrhythmic agent amiodarone, which can induce hypo- or hyperthyroidism (Koukkou et al., 2017)
› Authors of a case review outlining the first report of nivolumab (a monoclonal IgG antibody) inducing hypothyroidism and isolated ACTH deficiency recommend careful monitoring of laboratory values (glucose, sodium, thyroid function) and blood pressure when cancer immunotherapies are administered in this population (Zeng et al., 2017)
› The American Society for Reproductive Medicine (ASRM) issued recent guidelines for the treatment of subtle thyroid abnormalities in infertile women attempting pregnancy; the guidelines can be accessed at https://guideline.gov/summaries/summary/50074

Untreated hypothyroidism in pregnancy increases risk for miscarriage, premature delivery, preeclampsia, low birth weight, and fetal intellectual and/or psychomotor development impairment
• In a large, population-based study, researchers found that perinatal outcomes of women with treated overt hypothyroidism were similar to those in pregnant women with normal thyroid function. Screening results that suggested hypothyroidism but were not confirmed predicted pregnancy risks similar to those associated with subclinical hypothyroidism, specifically preeclampsia, but this was only true in women with an initial TSH level > 4.5 mU/L (Bryant et al., 2015)

Red Flags
› Myxedema coma/crisis is a medical emergency that can require mechanical ventilation, close cardiac monitoring, and IV levothyroxine and corticosteroids until normal adrenal function is restored
› Switching between brand-name or generic levothyroxine can produce clinically significant differences in TSH and T4 levels

What Do I Need to Tell the Patient/Patient’s Family?
› Educate the patient and family about the disorder and its management; reinforce that replacement therapy gradually restores proper metabolic function and quality of life
› Emphasize the importance of adherence to the prescribed levothyroxine regimen and continued medical surveillance to check TH levels and adjust dose if necessary
› Instruct the patient and/or family to contact emergency services if S/S of myxedema coma/crisis develop (e.g., mental deterioration [e.g., apathy, confusion, psychosis], severe breathing difficulty, bradycardia [< 60 beats per minute], hypothermia [< 95ºF/35ºC], extreme weakness and fatigue)

References

