HYPOTHYROIDISM

Hypothyroidism is a clinical syndrome caused by deficiency of thyroid hormones. In infants and children, hypothyroidism causes retardation of growth and development and may result in permanent motor and mental retardation. Congenital causes of hypothyroidism include agenesis (complete absence of thyroid tissue), dysgenesis (ectopic or lingual thyroid gland), hypoplastic thyroid, thyroid dyshormogenesis, and congenital pituitary diseases. Adult-onset hypothyroidism results in a slowing of metabolic processes and is reversible with treatment. Hypothyroidism is usually primary (thyroid failure), but it may be secondary (hypothalamic or pituitary deficiency) or rarely the result of resistance at the thyroid hormone receptor (Table 63-5).

In adults, autoimmune thyroiditis (Hashimoto's thyroiditis) is the most common cause of hypothyroidism. This condition may be isolated, or it may be part of polyglandular failure syndrome type II (Schmidt's syndrome), which also includes insulin-dependent diabetes mellitus, adrenal insufficiency, pernicious anemia, vitiligo, gonadal failure, hypophysitis, celiac disease, myasthenia gravis, and primary biliary cirrhosis. Iatrogenic causes of hypothyroidism include ^{131}I therapy, thyroidectomy, and treatment with lithium or amiodarone. Iodine deficiency or excess can also cause hypothyroidism.

Clinical Presentation

The clinical presentation of hypothyroidism (Table 63-6) depends on the age at onset and the severity of the thyroid deficiency. Infants with congenital hypothyroidism (also called *cretinism*) may exhibit feeding problems, hypotonia, inactivity, an open posterior fontanelle, and edematous face and hands. Mental retardation, short stature, and delayed puberty occur if treatment is delayed.

Hypothyroidism in adults usually develops insidiously. Patients often complain of fatigue, lethargy, and gradual weight gain for years before the diagnosis is established. A delayed relaxation phase of deep tendon reflexes (*hung-up* reflexes) is a valuable clinical sign that is characteristic of severe hypothyroidism. Subcutaneous infiltration by mucopolysaccharides, which bind water, causes the edema; this condition, termed *myxedema*, is responsible for the thickened features and puffy appearance of patients with severe hypothyroidism.

Severe untreated hypothyroidism can result in myxedema coma, which is characterized by hypothermia, extreme weakness, stupor, hypoventilation, hypoglycemia, and hyponatremia and is often precipitated by cold exposure, infection, or psychoactive drugs.

Diagnosis

Laboratory abnormalities in patients with primary hypothyroidism include elevated serum TSH and low total and free T_4. A low or low-normal morning serum TSH level in the setting of hypothalamic or pituitary dysfunction characterizes secondary hypothyroidism. Often, the serum total and free T_4 levels are at the lower limits of normal.

Hypothyroidism is often associated with hypercholesterolemia and elevated creatine phosphokinase skeletal muscle (MM) fraction (the fraction representative of skeletal muscle). Anemia is usually normocytic and normochromic but may be macrocytic (with vitamin B_{12} deficiency resulting from associated pernicious anemia) or microcytic (caused by nutritional deficiencies or menstrual blood loss in women). Because TPO Ab is usually positive in Hashimoto's thyroiditis, the major cause of hypothyroidism in adults, its measurement is helpful in deciding whether levothyroxine treatment is appropriate in patients with subclinical hypothyroidism (discussed later).

Differential Diagnosis

Because the initial manifestations of hypothyroidism are subtle, early diagnosis demands a high index of suspicion in patients with one or more of the signs and symptoms (see Table 63-6). Early symptoms that are often overlooked include menstrual irregularities (usually menorrhagia), arthralgias, and myalgias.

Laboratory diagnosis may be complicated by the finding of a low total T_4 level in euthyroid states associated with low TBG, such as nephrotic syndrome, cirrhosis, or TBG deficiency. TSH and free T_4 levels are normal in these instances. A low total T_4 level may also be found with nonthyroidal illness (*euthyroid sick syndrome*), a condition occurring in acutely ill patients. In such patients, total and occasionally free T_4 levels are low' the serum TSH level is usually normal but may be mildly elevated. This condition can be differentiated from primary hypothyroidism by absence of a goiter, negative antithyroid antibodies, and elevated serum reverse T_3 levels as well as by the clinical presentation.

TABLE 63-5 CAUSES OF HYPOTHYROIDISM

PRIMARY HYPOTHYROIDISM	Hypoplastic thyroid
Autoimmune	Biosynthetic defects
Hashimoto's thyroiditis	**SECONDARY HYPOTHYROIDISM**
Part of polyglandular failure syndrome, type II	**Hypothalamic Dysfunction**
Iatrogenic	Neoplasms
^{131}I therapy	Tuberculosis
Thyroidectomy	Sarcoidosis
Drug-Induced	Langerhans cell histiocytosis
Iodine deficiency	Hemochromatosis
Iodine excess	Radiation treatment
Lithium	**Pituitary Dysfunction**
Amiodarone	Neoplasms
Antithyroid drugs	Pituitary surgery
Congenital	Postpartum pituitary necrosis
Thyroid agenesis	Idiopathic hypopituitarism
Thyroid dysgenesis	Glucocorticoid excess (Cushing's syndrome)
	Radiation treatment to the pituitary

TABLE 63-6 CLINICAL FEATURES OF HYPOTHYROIDISM

CHILDREN	Weight gain
Learning disabilities	Constipation
Mental retardation	Menstrual irregularities
Short stature	Dry, coarse, cold skin
Delayed bone age	Periorbital and peripheral edema
Delayed puberty	Delayed reflexes
ADULTS	Bradycardia
Fatigue	Arthralgias, myalgias
Cold intolerance	