The thyroid hormone levels return to normal with resolution of the acute illness, and patients do not require levothyroxine therapy.

Treatment

Hypothyroidism should be treated initially with synthetic levothyroxine. Administration of levothyroxine results in physiologic levels of bioavailable T_3 and T_4. Levothyroxine has a half-life of 8 days; consequently, it needs to be given only once a day. The average replacement dose of levothyroxine for adults is 75 to 150 µg/day. In healthy adults, 1.6 µg/kg/day is an appropriate starting dose. In some older patients and patients with cardiac disease, levothyroxine should be increased gradually, starting at 25 µg/day and increasing the dose by 25 µg every 2 weeks; however, most patients can safely be started on a full replacement dose. The therapeutic response to levothyroxine therapy should be monitored clinically and with measurement of serum TSH levels 6 weeks after a dose adjustment. TSH levels between 0.5 and 2 mU/L are optimal. Because TSH measurements are not a useful guide in patients with secondary hypothyroidism (pituitary or hypothalamic dysfunction), these patients should be given levothyroxine until their free T_4 is in the mid-normal range.

Recent studies have suggested that a percentage of patients treated with levothyroxine for hypothyroidism continue to have hypothyroid symptoms despite normalization of TSH. Furthermore, a large study found that more than 20% of athyreotic patients treated with levothyroxine replacement did not maintain free T_3 or free T_4 values in the normal range despite normal TSH levels. This reflects the inadequacy of peripheral deiodination to compensate for the absent T_3 secretion. Because of these studies, there is renewed interest (accompanied by a large amount of controversy) in treating hypothyroid patients who have not had an adequate clinical response to levothyroxine replacement with a combination of levothyroxine and liothyronine, or with desiccated thyroid preparations that contain levothyroxine and liothyronine.

In patients with myxedema coma, 500 to 800 µg of levothyroxine is administered intravenously as a loading dose, followed by 100 µg/day of levothyroxine, hydrocortisone (100 mg IV intravenously three times daily), and intravenous fluids. Steroids should be given before thyroxine in autoimmune conditions. The underlying precipitating event should be corrected. Respiratory assistance and treatment of hypothermia with warming blankets may be required. Although myxedema coma carries a high mortality rate despite appropriate treatment, many patients improve in 1 to 3 days.

Subclinical Hypothyroidism

In subclinical hypothyroidism, T_4 and T_3 levels are normal or low-normal, and TSH is mildly elevated. Some of these patients develop overt hypothyroidism. The decision as to when to treat patients who have a mildly elevated TSH level is controversial. It is frequently recommended that patients should be treated with levothyroxine if they have a TSH level greater than 5 mU/L on two occasions and either positive anti–TPO Ab test results or a goiter. If the patient does not have an appreciable goiter and has negative anti–TPO Ab test results, many experts suggest that levothyroxine should be given only if the TSH level is greater than 10 mU/L on two occasions. Other experts suggest treatment at lower TSH levels depending on the presence of TPO antibody.

GOITER

Enlargement of the thyroid gland is called a *goiter.* Patients with goiters may be euthyroid (simple goiter), hyperthyroid (toxic nodular goiter or Graves' disease), or hypothyroid (nontoxic goiter or Hashimoto's thyroiditis). Thyroid enlargement (often focal) may also be the result of a thyroid adenoma or carcinoma. In nontoxic goiter, inadequate thyroid hormone synthesis leads to TSH stimulation with resultant enlargement of the thyroid gland. Iodine deficiency (endemic goiter) was once the most common cause of nontoxic goiter. Since the widespread availability of iodized salt, endemic goiter is less common in North America.

Goitrogens are agents that can cause a goiter, and iodine and lithium are the two chemicals or drugs that frequently cause a goiter. Natural goitrogens include thioglucosides found in vegetables such as cabbage, broccoli, brussel sprouts, turnips, cauliflower, kale, and other greens. Other foods that are goitrogens include soybeans and soybean products, peanuts, spinach, sweet potatoes, and fruits (e.g., strawberries, pears, and peaches). Thyroid hormone biosynthetic defects can cause goiter associated with hypothyroidism (or, with adequate compensation, euthyroidism).

A careful thyroid examination coupled with thyroid hormone tests can reveal the cause of the goiter. A smooth, symmetrical gland, often with a bruit, and hyperthyroidism are suggestive of Graves' disease. A nodular thyroid gland with hypothyroidism and positive antithyroid antibodies is consistent with Hashimoto's thyroiditis. A diffuse, smooth goiter with hypothyroidism and negative antithyroid antibodies may be indicative of iodine deficiency or a biosynthetic defect. Goiters can become very large, extending substernally and causing dysphagia, respiratory distress, or hoarseness. An ultrasound evaluation or radioactive iodine scan delineates the thyroid gland, and measurement of the TSH level determines the functional activity of the goiter.

Hypothyroid goiters are treated with thyroid hormone at a dose that normalizes TSH. Previously, euthyroid goiters were treated with levothyroxine therapy; however, regression with levothyroxine therapy is unlikely and is no longer recommended. Surgery is indicated for nontoxic goiter only if obstructive symptoms develop or substantial substernal extension is present.

SOLITARY THYROID NODULES

Thyroid nodules are common. They can be detected clinically in about 4% of the population and are found in about 50% of the population at autopsy. Benign thyroid nodules are usually follicular adenomas, colloid nodules, benign cysts, or nodular thyroiditis. Patients may have one prominent nodule on clinical examination, but thyroid ultrasound evaluation may reveal multiple nodules. Although most nodules are benign, a small percentage are malignant. Fortunately, most thyroid cancers are low-grade malignancies. History, physical examination, and laboratory tests can be helpful in differentiating benign from malignant lesions (see Table 63-2). For example, lymph node involvement or hoarseness is strongly suggestive of a malignant tumor.