universally accepted recommendations for the management of subclinical hypothyroidism, but levothyroxine is recommended if the patient is a woman who wishes to conceive or is pregnant, or when TSH levels are above 10 mIU/L. When TSH levels are below 10 mIU/L, treatment should be considered when patients have suggestive symptoms of hypothyroidism, positive TPO antibodies, or any evidence of heart disease. It is important to confirm that any elevation of TSH is sustained over a 3-month period before treatment is given. As long as excessive treatment is avoided, there is no risk in correcting a slightly increased TSH. Treatment is administered by starting with a low dose of levothyroxine (25–50 μg/d) with the goal of normalizing TSH. If levothyroxine is not given, thyroid function should be evaluated annually.

SPECIAL TREATMENT CONSIDERATIONS

Rarely, levothyroxine replacement is associated with pseudotumor cerebri in children. Presentation appears to be idiosyncratic and occurs months after treatment has begun.

Women with a history or high risk of hypothyroidism should ensure that they are euthyroid prior to conception and during early pregnancy because maternal hypothyroidism may adversely affect fetal neural development and cause preterm delivery. The presence of thyroid autoantibodies alone, in a euthyroid patient, is also associated with miscarriage and preterm delivery; it is unclear if levothyroxine therapy improves outcomes. Thyroid function should be evaluated immediately after pregnancy is confirmed and every 4 weeks during the first half of the pregnancy, with less frequent testing after 20 weeks' gestation (every 6–8 weeks depending on whether levothyroxine dose adjustment is ongoing). The levothyroxine dose may need to be increased by up to 50% during pregnancy, with a goal TSH of less than 2.5 mIU/L during the first trimester and less than 3.0 mIU/L during the second and third trimesters. After delivery, thyroxine doses typically return to prepregnancy levels. Pregnant women should be counseled to separate ingestion of prenatal vitamins and iron supplements from levothyroxine by at least 4 h.

Elderly patients may require 20% less thyroxine than younger patients. In the elderly, especially patients with known coronary artery disease, the starting dose of levothyroxine is 12.5–25 μg/d with similar increments every 2–3 months until TSH is normalized. In some patients, it may be impossible to achieve full replacement despite optimal antianginal treatment. *Emergency surgery* is generally safe in patients with untreated hypothyroidism, although routine surgery in a hypothyroid patient should be deferred until euthyroidism is achieved.

Myxedema coma still has a 20–40% mortality rate, despite intensive treatment, and outcomes are independent of the T_4 and TSH levels. Clinical manifestations include reduced level of consciousness, sometimes associated with seizures, as well as the other features of hypothyroidism (Table 405-6). Hypothermia can reach 23°C (74°F). There may be a history of treated hypothyroidism with poor compliance, or the patient may be previously undiagnosed. Myxedema coma almost always occurs in the elderly and is usually precipitated by factors that impair respiration, such as drugs (especially sedatives, anesthetics, and antidepressants), pneumonia, congestive heart failure, myocardial infarction, gastrointestinal bleeding, or cerebrovascular accidents. Sepsis should also be suspected. Exposure to cold may also be a risk factor. Hypoventilation, leading to hypoxia and hypercapnia, plays a major role in pathogenesis; hypoglycemia and dilutional hyponatremia also contribute to the development of myxedema coma.

Levothyroxine can initially be administered as a single IV bolus of 500 μg, which serves as a loading dose. Although further levothyroxine is not strictly necessary for several days, it is usually continued at a dose of 50–100 μg/d. If suitable IV preparation is not available, the same initial dose of levothyroxine can be given by nasogastric tube (although absorption may be impaired in myxedema). An alternative is to give liothyronine (T_3) intravenously or via nasogastric tube, in doses ranging from 10 to 25 μg every 8–12 h. This treatment has been advocated because $T_4 \rightarrow T_3$ conversion is impaired in myxedema coma. However, excess liothyronine has the potential to provoke arrhythmias. Another option is to combine levothyroxine (200 μg) and liothyronine (25 μg) as a single, initial IV bolus followed by daily treatment with levothyroxine (50–100 μg/d) and liothyronine (10 μg every 8 h).

Supportive therapy should be provided to correct any associated metabolic disturbances. External warming is indicated only if the temperature is <30°C, as it can result in cardiovascular collapse **(Chap. 478e)**. Space blankets should be used to prevent further heat loss. Parenteral hydrocortisone (50 mg every 6 h) should be administered, because there is impaired adrenal reserve in profound hypothyroidism. Any precipitating factors should be treated, including the early use of broad-spectrum antibiotics, pending the exclusion of infection. Ventilatory support with regular blood gas analysis is usually needed during the first 48 h. Hypertonic saline or IV glucose may be needed if there is severe hyponatremia or hypoglycemia; hypotonic IV fluids should be avoided because they may exacerbate water retention secondary to reduced renal perfusion and inappropriate vasopressin secretion. The metabolism of most medications is impaired, and sedatives should be avoided if possible or used in reduced doses. Medication blood levels should be monitored, when available, to guide dosage.

THYROTOXICOSIS

Thyrotoxicosis is defined as the state of thyroid hormone excess and is not synonymous with *hyperthyroidism*, which is the result of excessive thyroid function. However, the major etiologies of thyrotoxicosis are hyperthyroidism caused by Graves' disease, toxic MNG, and toxic adenomas. Other causes are listed in **Table 405-7**.

GRAVES' DISEASE

Epidemiology Graves' disease accounts for 60–80% of thyrotoxicosis. The prevalence varies among populations, reflecting genetic factors and iodine intake (high iodine intake is associated with an increased prevalence of Graves' disease). Graves' disease occurs in up to 2% of women but is one-tenth as frequent in men. The disorder rarely begins before adolescence and typically occurs between 20 and 50 years of age; it also occurs in the elderly.

TABLE 405-7 CAUSES OF THYROTOXICOSIS

Primary Hyperthyroidism
Graves' disease
Toxic multinodular goiter
Toxic adenoma
Functioning thyroid carcinoma metastases
Activating mutation of the TSH receptor
Activating mutation of $G_{s\alpha}$ (McCune-Albright syndrome)
Struma ovarii
Drugs: iodine excess (Jod-Basedow phenomenon)
Thyrotoxicosis Without Hyperthyroidism
Subacute thyroiditis
Silent thyroiditis
Other causes of thyroid destruction: amiodarone, radiation, infarction of adenoma
Ingestion of excess thyroid hormone (thyrotoxicosis factitia) or thyroid tissue
Secondary Hyperthyroidism
TSH-secreting pituitary adenoma
Thyroid hormone resistance syndrome: occasional patients may have features of thyrotoxicosis
Chorionic gonadotropin-secreting tumors[a]
Gestational thyrotoxicosis[a]

[a]Circulating TSH levels are low in these forms of secondary hyperthyroidism.

Abbreviations: TSH, thyroid-stimulating hormone.