Part III
Thyroid Underactivity
Introduction

Anthony P. Weetman

Physiology

Thyroid underactivity is commonly classified as either primary, the result of thyroid gland failure, or secondary to pituitary or hypothalamic disease. These two forms can readily be distinguished by measuring the thyroid-stimulating hormone (TSH) levels, which are elevated in primary hypothyroidism and low or inappropriately normal in secondary hypothyroidism; in both cases free thyroxine (FT₄) levels are low. Free triiodothyronine (FT₃) levels, on the other hand, can be normal in a quarter of patients with hypothyroidism. Primary thyroid failure can be further classified into subclinical and clinical or overt hypothyroidism. In the former, the TSH is elevated but FT₄ levels are normal, whereas in the latter TSH is elevated (typically greater than 15 to 20 mU/L) and FT₄ levels are low. There is considerable debate over the clinical importance of subclinical hypothyroidism and whether thyroid hormone replacement has any benefit, although there is a consensus that treatment is warranted if the TSH is above 10 mU/L or if the patient is pregnant [1, 2].

Pathophysiology

The main causes of hypothyroidism are shown in Table III.1. By far the commonest causes in iodine-sufficient areas are autoimmune hypothyroidism and iatrogenic hypothyroidism following radioiodine, external neck irradiation, or surgical treatment of thyrotoxicosis or thyroid cancer [3]. Thyroid autoimmunity is readily diagnosed by measuring thyroperoxidase (TPO) antibodies; in occasional patients thyroglobulin antibodies may be positive in the absence of TPO antibodies. Although thyroid cell destruction in autoimmune hypothyroidism is mainly due to the T-cell infiltrate, some patients also have antibodies that can block the TSH receptor.
Transient episodes of hypothyroidism arise secondary to thyroid destruction caused by viruses, drugs such as amiodarone, or the temporary exacerbation of thyroid autoimmunity that occurs in 5% of women after pregnancy (postpartum thyroiditis). There is often a phase of thyrotoxicosis prior to the appearance of hypothyroidism. Amiodarone may also cause permanent hypothyroidism through the toxic action of the drug on thyroid cells.

**Treatment**

The goal of treatment in primary hypothyroidism is to restore TSH levels to normal. Thyroxine (levothyroxine sodium) at a dose of 1.6 μg/kg/day in complete thyroid failure is the best replacement therapy. There is no clear benefit from the addition of triiodothyronine to thyroxine [4]. Caution is needed in the elderly and those with cardiac disease, in whom thyroxine treatment should be initiated cautiously, with very gradual building up of the full replacement dose. Once TSH levels are normal, annual checks of replacement adequacy are all that is required, although thyroxine treatment in pregnancy requires careful management, as the dosage may need to be increased by 50%.

**References**