Eye symptoms are a common feature of Graves’ disease, where the symptoms have an underlying immunological cause. Several designations have been used: endocrine ophthalmopathy, dysthyroid orbitopathy, dysthyroid ophthalmopathy, orbitopathy, infiltrative ophthalmopathy and thyroid-associated ophthalmopathy (TAO).

TAO has gradually gained favour among thyroidologists internationally. We therefore use this expression for the most part. The advantage of this term is that it indicates a direct association with the thyroid gland. In addition to Graves’ disease, TAO can also be seen in chronic autoimmune thyroiditis, even though this is far less common.

19.1 General Eye Symptoms in Thyrotoxicosis

Clinically observable signs in the eyes are present in 40–50% of all patients with thyrotoxicosis. Retraction of the eyelid is caused by increased activity in the sympathetic nervous system in thyrotoxicosis, and can therefore occur regardless of etiology. The consequence is an increased tone in the levator muscle of the upper eyelid, which can result in a closing defect when the gaze is directed downwards and is called lid lag (lagophthalmus or von Graefe’s sign). Sympathetic activity also contributes to the staring gaze that is often observed. Sometimes, a persistent upper eyelid retraction is a consequence of TAO, clinically most evident if unilateral. Convergence insufficiency (Moebius’ sign) and a higher blinking frequency (Stellwag’s sign) are other typical symptoms. When the hormone levels are normalized these symptoms disappear.

19.2 Eye Symptoms Specific to Graves’ Disease

TAO gives considerable problems in 10–20% of all patients with Graves’ disease. Early stages of TAO often improve when the function of the thyroid has been normalized, but TAO can also have a distinct, prolonged, unpredictable and difficult-to-treat progression. In very severe cases, treatment with high doses of steroid and/or orbital decompression are necessary to avoid compression of the optical nerve.

TAO is normally linked with Graves’ disease, but the same form of ophthalmopathy sometimes occurs in chronic autoimmune thyroiditis. Although less common, the progress of TAO is generally more problematic in males.
19.3 Risk Factors and Pathophysiology

The cause of TAO is not known, but several factors are thought to play a role in the development and progression. In patients who have previously undergone surgery or received radioiodine therapy for Graves’ disease, an activation or reactivation of ophthalmopathy can be observed if they develop hypothyroidism or if the substitution dose of thyroxine is abruptly reduced. Another triggering factor is inadequate control of the disease with fluctuating hormone levels.

The risk for a patient developing or exacerbating TAO is greater after radioiodine therapy compared to surgery or medical therapy (Fig. 19.1). In the study on which this figure is based, the radioiodine-treated patients did not receive thyroxine until they showed signs of hypothyroidism. A recent 3 year randomized study where the radioiodine group was kept euthyroid confirmed the increased risk for TAO by radioiodine treatment. Currently, most institutions give thyroxine a few weeks after radioiodine treatment in an attempt to avoid rapid changes in the hormone balance. Even if hypothyroidism is thereby avoided, this routine does not, however, eliminate the risk of developing TAO after radioiodine treatment. Sometimes development of ophthalmopathy is observed after I-131 treatment of toxic nodular goitre or autonomous nodule.

High/increasing concentrations of TRAb seems to be associated with exacerbation of ophthalmopathy. It can therefore be assumed that TSH receptors in the orbital tissue play a role in the development and progression of TAO.

In TAO, an inflammatory reaction occurs in the eye socket with fibroblast infiltration with effect on the muscles of the eye and on the orbital adipose tissue. Examination with MR, computer tomography or ultrasound reveals an increase in volume in one or more muscles. Occasionally, an increased volume can be seen in the retrobulbar fat. Secondary to the swelling, shortening and stiffness of the muscles can occur resulting in eye muscle dysfunction and diplopia. The increase in the volume of the orbital tissue can result in forward displacement of the eye (proptosis) and disturbance of the venous flow with consequent eyelid oedema. In addition, there is a risk that the optical nerve can be compressed, which can result in optic neuropathy. In severe proptosis, there is an increased risk of a closing defect and corneal lesions.

Fig. 19.1 Probability of developing or worsening TAO in relation to T3 levels and treatment given for Graves’ disease