

## **Chapter 138: Management of Exophthalmos**

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Graves' disease is believed to be an autoimmune illness that usually affects the orbital tissues. The orbital soft tissues undergo a diffuse inflammatory process that results in protrusion of the globe, which often becomes the most distressing component of the disease. Because symptoms may range from slight orbital prominence and mild eye irritation to diffuse orbital swelling causing blindness, the treatment must correspond to the severity of the disease. Patients with vision-threatening or disfiguring exophthalmos can be treated quite satisfactorily by decompression of the orbital contents into the maxillary and ethmoid sinus cavities.

### **Etiology**

The precise mechanism of Graves' ophthalmopathy has never been identified although several theories have been advocated. The pituitary gland has long been suspected of secreting a hormone with exophthalmos-producing activity. Winand and Kohn (1975) demonstrated in animals that a molecular fragment of thyroid-stimulating hormone (TSH) has exophthalmogenic but not thyroid-stimulating properties. The exophthalmogenic fragment, which has a molecular weight of about 20,000, is capable of stimulating adenylate cyclase activity in the retroorbital tissues. The most popular theory regarding the cause of Graves' ophthalmopathy is that it is an autoimmune disease that is separate from, but related to and overlapping with, autoimmune thyroid disease (Jacobson and Gorman, 1984). Specific antibodies against thyroid antigens are found in many patients with Graves' disease, and it has been demonstrated that thyroglobulin and antithyroglobulin immune complexes will bind preparations of human extraocular muscle membranes *in vitro* (Kodama et al, 1982; Konishi et al, 1974). These immune complexes are cytotoxic and presumably incite an inflammatory infiltration and chronic edema that can terminate in fibrosis and impairment of muscle function.

### **Pathology**

Although the pathogenesis of Graves' ophthalmopathy remains elusive, the histologic findings are well documented. Varying degrees of hypertrophy of the orbital muscles and fat are found that are believed to be secondary to a deposition of mucopolysaccharides. Although the precise chemical composition is unknown, fibroblasts have proved to be capable of secreting all the substances implicated in the production of proptosis (Riley, 1972). The extraocular muscles show a twofold to eightfold enlargement, with interstitial edema as well as infiltration with lymphocytes, plasma cells, macrophages, and mast cells. The accumulation of interstitial edema is attributed to the hydropexic properties of the mucopolysaccharides deposited in the muscles and retroorbital fat. Anatomic studies have shown that the medial and inferior recti are more commonly and extensively involved than the other extraocular muscles (Trokel and Hilal, 1979).

Although the optic neuropathy of Graves' disease is well known from a clinical standpoint, histopathologic characterization of optic nerve changes has not been supported (Sergott and

Glazer, 1981). Coronal computed tomographic (CT) scans suggest that the optic neuropathy results from simple compression of the optic nerve at the orbital apex by the massively edematous extraocular muscles (Kennerdell et al, 1981).

The average volume of the orbital cavity is 26 cc; in normal individuals retrobulbar and peribulbar structures occupy 70% of this volume. Because the orbit is a fixed bony cavity, an increase of orbital volume of only 4 cc will result in 6 mm of proptosis (Gorman, 1978). The degree of proptosis does not reliably indicate the severity of the disease or the risk to vision. Variability of the effect on the ocular structures may be related to individual differences such as tightness of the orbital septum and lids, tension of the rectus muscles, and length of the optic nerve.

### **Clinical Features**

Graves' ophthalmopathy presents a wide spectrum of clinical manifestations. The proptosis secondary to the hypertrophy of the retroorbital tissues should be distinguished from the lid lag and stare that occur with hyperthyroidism and that are believed to result from an increased sensitivity of the sympathetic nervous system to catecholamines. About 90% of the patients with progressive proptosis have associated hyperthyroidism; the other 10% have no demonstrable thyroid disease, and their ophthalmopathy is termed *euthyroid Graves' disease*.

The patients with Graves' ophthalmopathy often develop proptosis over a period of several months, although it can occur within a few weeks. As the pressure within the orbit increases, conjunctival chemosis, excessive lacrimation, periorbital edema, and photophobia may develop. Often the patient will complain of orbital pain or at least of the sensation of excessive orbital pressure. Usually both eyes are equally involved; however, in at least 10% of patients, sufficient asymmetry exists so that only one eye appears to be involved. Undoubtedly some degree of extraocular muscle impairment occurs in every patient, although this may not be sufficient to create symptomatic diplopia.

The most troubling feature of Graves' ophthalmopathy is visual loss that may be noted first as a loss of color discrimination. This may result from corneal disease secondary to chronic exposure, with desiccation or impairment of optic nerve function presumably from excessive pressure on the nerve. The elevated intraorbital pressure is believed to produce an ischemic neuropathy or delay of venous return that is usually reversed by decompression of the orbit. High-resolution computed tomography has shown actual optic nerve decompression by the swollen extraocular muscles. Patients with "optic neuritis" will demonstrate a central or paracentral visual field defect that occurs with or without decreased visual acuity. Therefore, measuring visual acuity without measuring the visual field may be inadequate to assess optic nerve function or progression of the disease (DeSanto, 1980).

## **Diagnostic Assessment**

The diagnosis of Graves' ophthalmopathy is clinical and is based on demonstration of the characteristic bilateral eye signs in patients with associated hyperthyroidism. Testing triiodothyronine (T<sub>3</sub>) suppression of the response of thyroid-stimulating hormone (TSH or thyrotropin) to thyrotropin-releasing hormone (TRH) will demonstrate abnormalities in about 30% of patients who do not have overt hyperthyroiditis (Wall et al, 1981). These tests evaluate the pituitary-thyroid axes. The TSH assay is currently believed to be the most sensitive test for the recognition of subtle degrees of hyperthyroidism (Bahn et al, 1988).

Although Graves' ophthalmopathy is the leading cause of adult-onset unilateral exophthalmos, other diseases such as mucocele, lymphoma, intraorbital hemangioma, lymphangioma, and metastatic carcinoma must be excluded. Diseases that may mimic bilateral Graves' ophthalmopathy include Wegener's granulomatosis, inflammatory pseudotumor, and cavernous sinus thrombosis. Perhaps the most difficult disease to differentiate is inflammatory pseudotumor because its clinical course and findings are similar to those of Graves' ophthalmopathy. However, the two diseases usually can be differentiated by computed tomography: an inflammatory pseudotumor will show soft-tissue densities involving the posterior aspect of the globe near the entrance of the optic nerve and choroidal thickening. By contrast, in Graves' disease the CT scan will show characteristic extraocular muscle enlargement.

## **Management**

### **General consideration**

Management of Graves' ophthalmopathy frequently requires the expertise of more than one medical specialist. An important initial objective for the endocrinologist is to achieve euthyroid status whenever the patient is thyrotoxic. Correction of the hyperthyroidism may often improve the stare, lid lag, or lid retraction.

The benefit of thyroid ablation in the prevention of Graves' disease remains controversial. White (1974) reported a large series of patients with thyrotoxic Graves' disease in whom either no ophthalmopathy existed or in whom no progression of existing ophthalmopathy occurred after complete surgical removal of all thyroid tissue. However, Barbosa et al (1972) found no significant difference in the incidence of ophthalmopathy among patients treated with I<sup>131</sup>, thyroidectomy, or antithyroid drugs. Calcaterra and Thompson (1980) also found no relationship between the incidence or severity of ophthalmopathy and the type of therapy selected to treat the hyperthyroidism.

In addition to treating the hyperactive thyroid, a number of nonsurgical measures have been recommended to ameliorate the ophthalmopathy. Mild proptosis without any impairment of vision can be managed conservatively by prescribing the use of methyl cellulose eye drops during the day and eyelid taping or use of a plastic moisture chamber during sleep to prevent corneal drying. Steroids in varying doses have been used to treat active ophthalmopathy for

several years. Steroids in high doses will relieve the congestive eye changes; however, the remission is usually only temporary, or the patient develops serious side effects from the prolonged administration of steroids. Depot injection of steroids into the retrobulbar space has been tried but is considered somewhat risky and does not alter the proptosis significantly. Immunosuppressive drugs have been used with limited success. Several groups have used azathioprine to reduce severe ophthalmopathy. More recently, cyclophosphamide has been used to treat the inflammatory changes of the eyes, although the proptosis usually does not respond (Wall et al, 1981). Although the side effects of cyclophosphamide are potentially severe, they can be predicted, and if they occur, treatment is discontinued. Because of the tendency for eventual spontaneous remission of the ophthalmopathy, judging the efficacy of these drugs is difficult.

Initial attempts to treat Graves' ophthalmopathy by radiation therapy, directing the beam to the pituitary and hypothalamus, were not clinically effective. Predicated on the theory that the ophthalmopathy was an immune reaction involving the sensitizing lymphocytes in the orbit, Donaldson et al (1973) reported on a series of patients undergoing orbital irradiation with a high-energy beam generated by a linear accelerator. The patients receive 2000 rad delivered in 10 fractions over a 2-week period. The treatment field was confined to just behind the lateral canthus to avoid injuring the lens and cornea. Donaldson et al reported that just over half of the 47 patients had good or excellent results, but those with long-term disease or extraocular muscle dysfunction responded poorly. The late effect of low-dose radiation to the orbit is unknown; a troubling possibility is radiation-induced cancer. Theoretically, keeping the dose below 2500 rad should avoid radiation damage to the lens and retina (Brennan et al, 1983).

### **Surgical management**

Dollinger (1911) first described orbital decompression by removing the lateral wall of the bony orbit (Krönlein's operation) to allow the swollen orbital contents to herniate into the temporal fossa. Two decades later Naffziger (1931) published the first account of decompression of the orbital contents into the anterior cranial fossa via a transcranial approach. Sewall (1936), who removed the common wall between the ethmoid sinuses and the orbit to provide a medial decompression, first described the use of the paranasal sinus cavities to decompress the orbit. Hirsch (1950) later reported inferior decompression into the maxillary sinus by removing the orbital floor. Walsh and Ogura (1957) combined the operations of Hirsch and Sewall, removing both the medial and inferior walls of the orbit (Fig. 138-1).

### ***Indications***

The most widely accepted indication for orbital decompression is threatened loss of visual acuity from proptosis that is refractory to medical management. The visual loss may be secondary to exposure keratitis or pressure damage to the optic nerve, and decompression may be necessary on an emergency basis. In recent years the indications for decompression have been expanded to include other symptoms related to excessive orbital pressure and proptosis; among these are chronic eye irritation, excessive tearing, and photophobia.

Orbital decompression has been recommended to precede and facilitate ocular muscle repair for diplopia resulting from proptosis without visual loss; diplopia is also considered an indication for decompression because many of these patients are very disturbed by their appearance.

### *Preoperative evaluation*

Patients should have a preoperative ophthalmologic evaluation that includes evaluation of visual fields and ocular muscle function. A CT scan may be considered if diagnosis of Graves' disease is uncertain. Clinical hyperthyroidism is corrected medically whenever possible. Adequate sinus pneumatization and freedom from significant sinus inflammatory disease are ascertained by sinus radiographs. Patients currently receiving or who have recently received systemic steroids are given corticosteroids parenterally on the evening before and morning of the operation.

### *Technique*

Decompression is carried out with the patient under general endotracheal anesthesia and in a semi-sitting position. The endotracheal tube is taped securely to the chin or wired to a lower premolar tooth. The lower extremities are entirely wrapped with elastic bandages to minimize venous pooling during surgery. The eyes remain uncovered so that they can be observed during the operative procedure. A lubricating solution such as mineral oil is intermittently installed over the globes to prevent corneal dehydration.

A curved sublabial incision is made to approach the maxillary and ethmoid sinuses. A large antrotomy is fashioned in such a way that the portion medial to the infraorbital nerve is carried up to the orbital rim, thereby gaining increased exposure of the anterior ethmoidal cells (Fig. 138-2). The mucous membrane is carefully stripped from the roof and upper medial portion of the maxillary sinus. The ethmoidal cells are then opened with a small curette and exenterated behind the lacrimal crest and superiorly to the ethmoidal roof, which appears as a whitish plate (Fig. 138-3). Multiple fractures of the maxillary roof, including a linear fracture along the maxillary portion of the infraorbital nerve, are made with a 4-mm osteotome. The bone fragments are gently removed from the orbital roof as far laterally as the zygoma with a right-angled nerve hook and delicate periosteal elevator, ensuring the integrity of the orbital rim, infraorbital nerve, and orbital periosteum (Fig. 138-4, A). The lamina papyracea is then fractured medially and removed at the level of the ethmoidal roof (Fig. 138-4, B and C).

The orbital periosteum tends to sag after removal of the bone from the inferior and medial portions of the orbit, allowing recession of up to 3 mm. The position of the eyes should be determined at this point either by using a gas-sterilized exophthalmometer or by sighting the eyes over the forehead to determine the position of the corneal surface in relationship to the supraorbital rim. With experience, the latter method becomes quite reliable. The more proptotic eye is then recessed by carefully placing approximately four radial incisions along the medial periosteum, allowing the fat to herniate through the incision while avoiding any incisional injury to the medial rectus muscle (Fig. 138-5). If the eye is quite proptotic, placing up to five

additional radial incisions along the entire orbital floor periosteum will be necessary until the desired position of the eye is achieved. The less proptotic eye is then approached in a similar manner until both eyes are equal. In no instance is the periosteum cut in a crosshatch fashion, because maintaining some orbital support is necessary to reduce the possibility of aggravated diplopia. Similarly, periorbital fat is not dissected from around the muscles, because the fat ensures their functional integrity. The eyes must never be recessed to a normal position at the conclusion of the operation, because an additional 1 to 2 mm of recession invariably develops within 3 months after surgery.

A conventional nasal antrostomy is created through the inferior meatus of the nose, and the antral cavities are packed gently with antibiotic-impregnated gauze. The entire procedure may be performed on both orbits in about 1 hour. The patient is usually discharged on the second postoperative day when the packing is removed. The patient is cautioned against nose-blowing for at least 2 weeks because this can result in pneumocellulitis of the cheek and orbit.

### **Results**

Up to 8 or 9 mm of recession will occur if the proptosis is severe. The average recession obtained is 4 to 5 mm (Warren et al, 1989). Figs. 138-6 and 138-7 are examples of operative results. If the exophthalmos has been long-standing or if irradiation has been used, the periorbital fat may be gelatinous and resist herniation through the periorbital periosteal incisions. Exposure keratitis is almost always improved by this procedure, and many patients are able to discontinue local medical management. Optic neuropathy, unless long term, usually responds to decompression, and this may be dramatically evident by a substantial improvement of vision within 24 hours of surgery.

In patients without diplopia who are undergoing the operation largely for cosmetic reasons, great care must be exercised in maintaining support of the eye by keeping the inferior orbital periosteum intact while achieving decompression and recession by allowing fat herniation through multiple medial orbital periosteal incisions. In my series (Calcaterra and Thompson, 1980) only one patient who had not had diplopia preoperatively developed it after surgery; however, several patients experienced aggravation of preoperative diplopia.

When ocular muscle surgery is performed after decompression, the patient can usually anticipate fusion of vision. This surgery is usually delayed for at least 6 months until recession of the eye has stabilized. Occasionally, prismatic lenses are sufficient to correct the diplopia. Rarely a patient develops diplopia long after decompression, which results from an exacerbation of the dysthyroid myopathy that produces infiltration and fibrosis.

The normal position of the upper eyelid is 1 to 2 mm below the superior corneoscleral limbus. The lower eyelid normally rests at the inferior limbus. Spasm of the levator palpebral superioris and Müller's muscles creates the stare appearance and these muscles may become fibrotic even without much degree of proptosis (Bahn et al, 1988). In these patients the muscle may be lengthened, followed by decompression, if the patient desires.

Blepharoplasty is sometimes desirable when redundant periorbital skin exists. However, blepharoplasty either before or after decompression in these patients should be extremely conservative, because excessive removal of periorbital skin will aggravate the tendency toward corneal exposure. Similarly, tarsorrhaphy often aggravates the problem of orbital pressure.

### **Complications**

The dreaded complication of optic nerve injury has not been reported to my knowledge. Needless to say, the tenets of ethmoidal surgery must be followed carefully, particularly in the posterior cell complex, and deep incisions in the orbital periosteum near the orbital apex must also be avoided. Fracture of the ethmoidal roof with tearing of the dura mater resulting in cerebrospinal rhinorrhea can also be avoided by systemic exposure of the ethmoidal sinus. Generally, the pearly white ethmoidal roof can be visualized, and the lamina papyracea can be removed to the junction roof. The precise role of decompression on subsequent ocular motility remains uncertain. Motility will be enhanced in some patients (Dixon and Sesser, 1981), but hampered in others (Shorr et al, 1982). If the patient has no preoperative diplopia and the inferior orbital periosteum is largely preserved by placing no more than three or four sagittal incisions, postoperative diplopia will be very unlikely. The surgeon attempts to maximize the decompression in a medial direction, which has less effect on orbital motility dynamics (Smith, 1979). Because most patients do not have symmetric exophthalmos, they must be advised that complete orbital symmetry may not be attainable after surgery (Fig. 138-8). The surgeon must remember that delayed recession will occur in the eye because of the greater amount of orbital bone removal and the larger number of periosteal incisions. Therefore, the more prominent eye before surgery must remain so immediately after decompression to accommodate the anticipated greater recession in that orbit. A slight risk of enophthalmos always exists if excessive bone removal has occurred and too many periosteal incisions have been made, particularly if they were carried out both in the sagittal and coronal directions.

Another potential complication is epiphora, which can result from damage to the lacrimal sac, either within the bony lacrimal fossa or at the orifice below the inferior turbinate if a nasoantral window is positioned too far forward (Osguthorpe and Calcaterra, 1979). Similarly, if the normal ostia of the maxillary sinus fails to function and the nasoantral window undergoes stenosis, the patient may develop chronic maxillary sinusitis. Consequently, a large nasoantral window, preferably with an inferiorly based mucoperiosteal flap, should be designed to ensure long-term patency. This minor surgical adjunct, performed just before closure of the sublabial incision, should minimize the occurrence of chronic maxillary sinusitis.

All patients experience some degree of cheek and upper lip numbness for a variable period of time. The numbness seems to last longer in older patients, although it does not last for more than 6 months; rarely, it may be permanent. Associated potential problems are tooth numbness, ill-fitting dentures, and sore gums.

## Summary

Patients with Graves' ophthalmopathy may have a variety of orbital problems, some of which can be managed conservatively with eye drops, taping of the eyelids at night, or surgical lowering of the upper lid. However, when exposure keratopathy or pressure optic neuropathy threatens vision, more vigorous treatment is indicated. Unfortunately, systemic steroids tend to provide only a temporary remission, and they may cause serious side effects. Irradiation of the orbit is unpredictable and usually does little to relieve the disfiguring proptosis. Moreover, the possible side effects of irradiation, including carcinogenesis, remain disquieting.

Decompression of the swollen orbital contents into the ethmoid and maxillary sinuses has the advantage of using an air-containing space. This technique is more effective than a lateral or superior (cranial) decompression because the soft tissues compromise the space for orbital recession and rarely more than 3 mm of recession can be accomplished by either of the latter two approaches. The antral-ethmoidal decompression permits a great recession, and the degree of recession can be controlled. The cranial approach involves an extensive procedure with a small but significant risk of intracranial complications as well as prolonged postoperative care. In addition, pulsations transmitted to the globe from the intracranial vasculature may be an annoying after effect. The lateral approach requires a facial incision that extends posteriorly from the lateral canthus. None of the decompression operations is capable of correcting diplopia, because irreversible myopathy is usually responsible for the impaired ocular mobility. Indeed, diplopia may become more troublesome after a decompressive procedure if visual acuity is substantially improved. However, planned ocular muscle operation after decompression is facilitated because the eye has been restored to a more normal position and tension on the already damaged muscles has been reduced, thus allowing more precise muscle manipulation.

Indications for orbital decompression have been expanded despite the fact that this procedure alleviates only the pressure-related orbital pathology of Graves' disease. Although this type of surgery was once reserved for patients threatened with blindness, our experience in using antral-ethmoidal decompression indicates that the technique is also effective at less-advanced stages of the diseases and is preferable to long-term, high-dose steroid therapy. In patients who have severe proptosis without visual impairment, antral-ethmoidal decompression is a method that can substantially improve their disfigurement.