THE OCULOROTARY MUSCLES IN GRAVES' DISEASE*

BY *John A. Dyer,* MD

INTRODUCTION

IN A REVIEW, WYBAR[1] IN 1957 NOTED THAT PARRY, IN 1786, HAD DESCRIBED THE association between the enlargement of the thyroid gland and the development of exophthalmos. This observation was published in 1825,[2] and in 1835 Graves[3] redescribed the syndrome, since known as Graves' disease, although von Basedow[4] is credited with publishing a detailed description of the condition in 1840. Wybar said that in spite of the volume of facts that had been presented and the many hypotheses that had evolved during that time, there was still no true understanding of the basic nature of the exophthalmic process.

More sophisticated tests and more accurate pathologic and clinical diagnostic techniques have been devised since then, but the basic causative factors producing this disease, which is often quite crippling to the ocular and general health of many patients, remain a mystery.

PURPOSE

The purpose of this paper is to discuss factors influencing the oculorotary muscles in Graves' disease. The pathophysiology of the orbital and ocular structures and the laboratory and clinical diagnostic aids that are available to implicate the involvement of the extraocular muscles will be reviewed. Research and clinical experiences gained by laboratory studies and surgery in 116 patients with myopathy of Graves' disease are presented. The modes of treatment, primarily surgical, that have proved efficacious in the rehabilitation of the patient suffering from intractable diplopia are discussed.

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PATHOPHYSIOLOGY

In 1955 Werner[5] reported that eye signs of Graves' disease often appear when there is little other evidence of hyperthyroidism. He described 10 patients who had early signs of the disease for 2 to 8 months; 9 were female, 1 was male. The ocular signs were unilateral in five and bilateral in five; three had diplopia. These responded to triiodothyronine (T_3) and thyrotropin, as did patients with overt Graves' disease, and he concluded that they indeed had the disease. He believed that despite the disruption of the normal pituitary-thyroid relationship, euthyroidism can be maintained. T_3 suppression and 24-hour ^{131}I uptake methods were suggested as highly reliable tests of thyroid function.

Brain[6] in 1962 listed five conditions in which endocrine exophthalmos may be associated with ophthalmoplegia: (1) exophthalmic ophthalmoplegia, (2) Graves' disease with myasthenia gravis, (3) exophthalmic ophthalmoplegia with myasthenia gravis, (4) thyrotoxic ocular myopathy, and possibly (5) exophthalmic ophthalmoplegia with thyrotoxic myopathy. Exophthalmic ophthalmoplegia usually was bilateral and often severe in proportion to the ophthalmoplegia; chemosis and lid retraction were often present. Ptosis was unknown. The ophthalmoplegia was often unilateral in mild or early cases or more severe on one side. Elevation and abduction were almost always affected first; adduction and depression were involved in severe cases only. The defect was not made worse by fatigue or improved by administration of neostigmine or edrophonium. On the other hand, patients with Graves' disease and myasthenia gravis had little or only moderate exophthalmos and edema. Ptosis was common, and the ophthalmoplegia did not selectively affect elevation and abduction. Both ptosis and ophthalmoplegia were increased by fatigue and decreased by the use of neostigmine or edrophonium. There usually was evidence elsewhere of myasthenia, particularly in the facial muscles and limbs or trunk.

In 1963 Grob[7] found ocular myopathy to be the commonest myopathy associated with thyroid disease. He reiterated that the eye signs may develop before there is any evidence of hyperthyroidism, and that first a decrease in elevation occurs and then a limitation in abduction. No relationship was found between the degree of ophthalmoplegia and the severity of weakness elsewhere in the body.

In 1969 Werner[8] published an abridged classification of the eye changes of Graves' disease which has gained wide acceptance:

0 No signs or symptoms

1 Only signs, no symptoms (signs = upper lid retraction and stare with or without lid lag and proptosis)
2 Soft tissue involvement (symptoms and signs = lid edema, chemosis, congestion)
3 Proptosis
4 Extraocular muscle involvement
5 Corneal involvement
6 Sight loss (optic nerve involvement)

Although all of the eye signs are of concern in the overall treatment of the patient, my primary interest is in the patient in class 4.

Rundle and Wilson[9] in 1944 reported on 24 patients, 21 of whom had "paralysis" of elevation which was bilateral and symmetrical. As noted by others,[6,7] hypotropia and poor abduction were found most frequently. They thought that "paralysis" of the superior rectus muscles and possibly of the inferior oblique muscles was the primary involvement. Goldstein[10] concurred with these reports.

Some very interesting and illuminating observations were made by Braley[11] in 1953. He reported on a 63-year-old man with lid edema, conjunctival edema, and proptosis of 29 mm in both eyes. The intraocular tension was 80 mm Hg (Schiötz) in one eye and 60 mm Hg in the other when the eyes were in the primary position. On slight down gaze, tension was reduced to 60 and 40 mm Hg, respectively. Papilledema and reduced acuity were present in both eyes. After treatment with thyroid extract, the proptosis was reduced to 19 mm in each eye and the intraocular tension to 19 mm Hg in each eye. He noted that a most consistent finding in patients with malignant exophthalmos was elevated intraocular pressures in up gaze, decreasing on down gaze; in his patients this difference was 10 to 30 mm Hg.

Often we see patients who have a diagnosis of glaucoma and are being treated for it when in fact the proptosed globe and tense ocular muscles of Graves' disease are responsible. Braley noted further, and very astutely, that the histology of the ocular muscles showing round cell and fibrous infiltration indicated that the "palsy" of various muscles as reported by Rundle and Wilson[9] and Woods[12] is in reality an inelasticity of the opposing muscle. This indeed is the case.

Some years later, Miller[13] and Miller and associates[14] reported that, clinically, patients with Graves' disease appear to have involvement of the superior rectus, whereas actually the globe is adherent below; once recognized, this complex problem can be managed by a single muscle procedure—that is, recession of the inferior rectus with lysis of adhesions to the inferior oblique. He stated correctly that forced-duction tests iden-

tify the involved muscle. Further support was added by Smith and Soll,[15] who suggested that when all signs of thyroid disease have ceased and yet a muscle problem persists, surgery that aims for a functional lengthening of the involved muscles rather than an augmentation of their actions should be performed; that is, inability to look up is due to failure of the inferior rectus to relax rather than to a paresis of the elevators.

In 1933 Naffziger[16] described a method of orbital decompression in which the roof of the orbit was removed by the intracranial route. He collected 20 muscle specimens for microscopic studies. In each instance, abnormalities were found in the extraocular muscles, which were increased in size 3 to 8 times. Their color varied from pale to deep red with white fibrous streaks. The muscles felt firm and of a rubbery hardness. In later stages, hyaline changes were found and the muscles were gritty to the knife. Histologic examination of the muscles showed varying degrees of muscle degeneration with fibrosis and cellular infiltration.

Smelser[17] reported a comparative study of experimental and clinical exophthalmos. Histologically, he found edema and wandering cells in the fat and connective tissue of orbits as well as in the ocular muscles of humans and guinea pigs which indicated a general inflammatory reaction throughout. Degeneration of muscle fibers was not striking in his specimens. He[18] later reemphasized these findings and agreed with Naffziger's studies.

Reports, especially those from the connective tissue laboratories of Wegelius and associates,[19] have stressed the accumulation of material with staining characteristics of mucopolysaccharides and changes in the muscles and connective tissue surrounding them. Inclusions were found first within the sarcolemmic sheath of the extraocular muscles; this material reacted as do some mucopolysaccharides. Hypertrophy of the orbital contents in experimental animals with the production of exophthalmos was due largely to increased water content, and this was greatest in the fatty connective tissue. The extraocular muscles also were hypertrophied, and although there was some increase in water content, most of the change was due to hypertrophy of the muscle fibers themselves.

Smelser's evidence[20] suggested that (in the experimental animals) the oxygen consumption of the extraocular muscles is very high when it is correlated with their overall activity and the precision of their movements. These muscles were strikingly independent of thyroid hormone activity. He postulated that because of these factors the extraocular muscles were more vulnerable to any factor that

reduced available oxygen such as decreased circulation from tissue pressure or edema.

The most detailed report of the pathologic changes occurring in the orbital tissues and extraocular muscles of patients with Graves' disease has been that of Kroll and Kuwabara.[21] They noted, as had other authors previously, that the muscles were firm, rubbery, and grossly enlarged 2 to 5 times. The orbital fat was under increased pressure. Histologically, these changes resulted from interstitial edema due to increase in mucopolysaccharides (probably hyaluronic acid), round cell infiltration (lymphocytes, plasma cells, macrophages, and mast cells), the degenerative changes within the muscle cells. Light microscopy showed that (1) the intercellular space between muscle cells was increased, (2) there was infiltration with round cells between muscle cells (freely dispersed or in clumps), (3) fat cells were occasionally present, (4) a number of infiltrating cells were mast cells, and (5) there were no abnormalities of the muscle cells themselves. Electron microscopy showed the following: (1) in intracellular space it confirmed the presence of mononuclear inflammatory cells—lymphocytes, macrophages, and mast cells; also, fibroblasts were plentiful, and bundles of collagen were more widely separated but with usual periodicity; (2) in muscle cells there was no consistent alteration in 9 of 10 patients (18 of 19 dysthyroid biopsies studied); and (3) muscles contained excellent striations. In a later study, Riley[22] did note by electron microscopy some disorganization and loss of striations in the muscles of three patients.

DIAGNOSTIC AIDS

ELECTROMYOGRAPHY

A variety of reports on the use of electromyography of the ocular muscles in the diagnosis of Graves' disease were published in the late 1950's and 1960's. Magora and associates[23] studied 12 patients in whom the electromyographic pattern of the paretic muscles showed myopathy. Schultz and associates[24] stated that, in thyrotoxic ophthalmoplegia, electromyographic studies were consistent with true myopathy; however, in one patient there appeared to be a reduction in motor units in the muscle, with single units being evident in maximal effort at contraction, typical of neurogenic involvement.

Breinin[25] felt strongly that the palsies associated with thyroid exophthalmos, referred to as myopathies by others, in fact showed neurogenic patterns in 11 of 12 patients studied.

Havard and co-workers,[26] in testing skeletal muscles, found that polyphasic and short-duration potentials were seen in early stages of myopathy before wasting had occurred. This type of abnormality is in no way specific for any well-defined group of diseases and is caused by the reduction of the functional complement of the muscle fibers within each motor unit. Such a pattern may, in their opinion, be a normal finding in ocular muscles that have small motor units.

Miller[13] found normal action potentials in all instances, and recruitment continued long after the globe had ceased to elevate. This was interpreted as evidence for a normally functioning superior rectus in which further action was prevented by mechanical limitation of elevation. Their findings never indicated paralysis or dystrophy, and muscles tested were within normal limits.

ULTRASONOGRAPHY

Although electromyographic changes are not specific for Graves' disease, other clinical means have proved to be of diagnostic assistance. These include A-scan and B-scan ultrasonography and the EMI scanner, which in the hands of the expert often provide a very reliable diagnosis.

Coleman and associates[27,28] reported that B-scan ultrasonography often can demonstrate the inflammatory changes that occur in the orbital fat and extraocular muscles in active changes of Graves' disease; this allows differentiation from expanding neoplastic lesions and eliminates the need for orbital biopsy. In the normal orbit, only a small portion of either orbital wall can be seen by B-scan ultrasound. The extraocular muscles are represented acoustically as black spaces between the retrobulbar fat and the occasional low amplitude echoes from the orbital wall—that is, the muscles are "clear" acoustically. In Werner's class 4, a large portion of the orbital wall usually is evident by ultrasound, and occasionally both walls can be demonstrated. The ocular muscles still appear "clear," but the space between the retrobulbar fat and the orbital wall is increased; this increase, which varies from moderate to pronounced, indicates enlargement of the muscle. When the plane of the scan is adjusted to pass through the greatest diameter of the muscle, the increase can be quantified. Although the inferior rectus is the most commonly involved muscle, they noted that it is easier to demonstrate the medial and lateral recti.

In a later report, Werner and co-workers[29] studied 47 patients with Graves' disease who, by ultrasonographic examination, showed consistent involvement of the orbital structures, especially the extraocular muscles. This group included patients without clinical eye changes

as well as those with early changes (Werner's classes 0 and 1). In fact, the eye changes demonstrated on several class 0 patients were identical to those of classes 1 through 4. Since the thickened extraocular muscles resulted in increased acoustic reflections of the muscle orbital wall boundary, they noted that diagnostic ambiguity can result from other causes of myositis. Figure 1 shows the inflammatory reaction in the muscle biopsy; the upper photograph is a low-power (× 100) light-microscopic view and the lower a higher-power (×400) view indicating infiltration of inflammatory cells among the muscle fibers. As demonstrated, the difficulty is resolved by ultrasonic examination of the other eye, since Graves' disease usually causes symmetrical changes. Figure 2 shows the thickened medial recti on B-scan of a patient with bilateral Graves' disease (*arrows*).

Ossoinig[30] preferred the A-mode technique for echo-orbitography. With it orbital lesions can be demonstrated reliably and are seen largely differentiated. The two-dimensional B-scan technique may seem more impressive and easier to interpret, but in his opinion it failed to establish a type-specific diagnosis; its sole advantage was that it showed a better topographic relationship.

McNutt[31] suggested that the signs described by Coleman and associates[27] and Werner and associates[29] in B-scan diagnosis were not specific for Graves' disease and stated that only in severe cases of Graves' orbitopathy are specific patterns produced. He believed that in using the immersion B-scan method one could not align the sound beam perpendicular to an extraocular muscle and thus could not demonstrate its maximal width. Also, the muscle width void varied immensely with the sensitivity setting of the instrument. He listed the following A-scan changes of Graves' disease: (1) no mass lesion, (2) enlarged extraocular muscles, (3) difference in width of corresponding muscles in right and left eyes, (4) widened orbital pattern, (5) higher reflectivity of orbital pattern, and (6) higher spike from bony orbital wall. He regarded A-scan ultrasonography as a useful tool in evaluating patients with Graves' disease by excluding a mass lesion as a cause for exophthalmos and thus confirming the diagnosis of Graves' disease in severe cases.

COMPUTER ASSISTED TOMOGRAPHY (EMI SCAN)

The EMI scan developed by Hounsfield in 1973 at the EMI laboratories in England has proved very useful in the examination of the skull and orbits. Not only can proptosis be noted but so also the characteristics of the lesion producing the abnormality may be visualized.

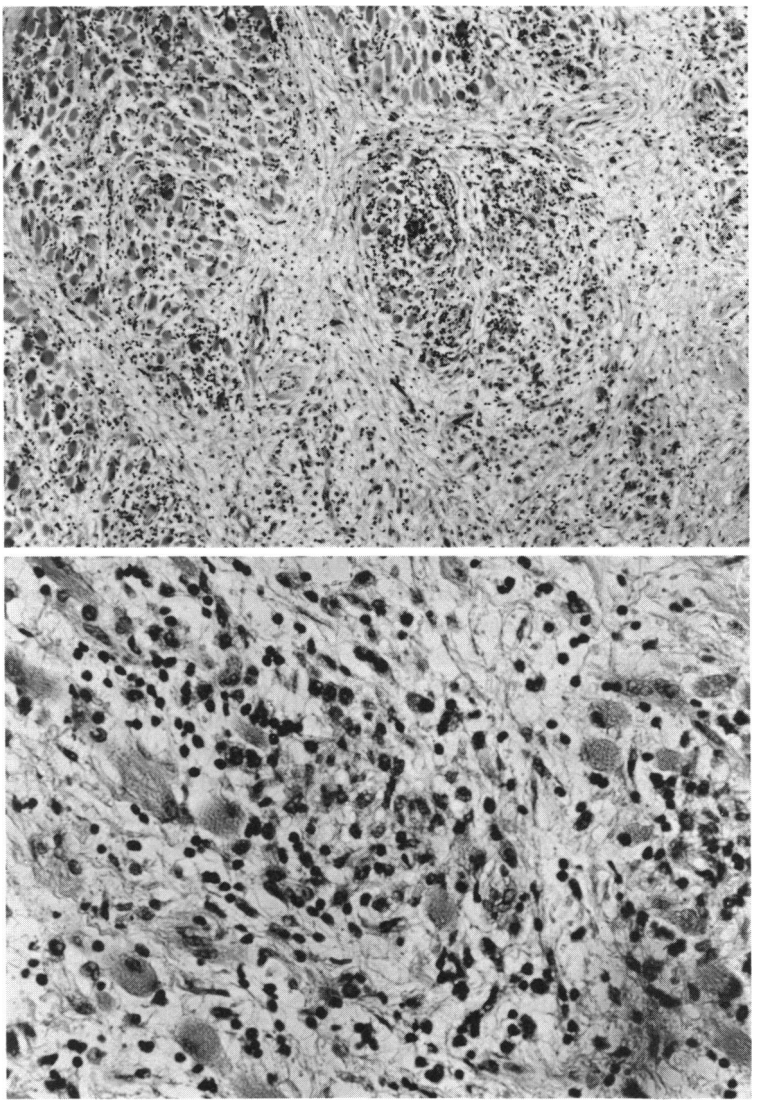

FIGURE 1
Upper photograph is muscle biopsy showing inflammatory cells among muscle fibers (×100); lower photograph shows reaction (×400).

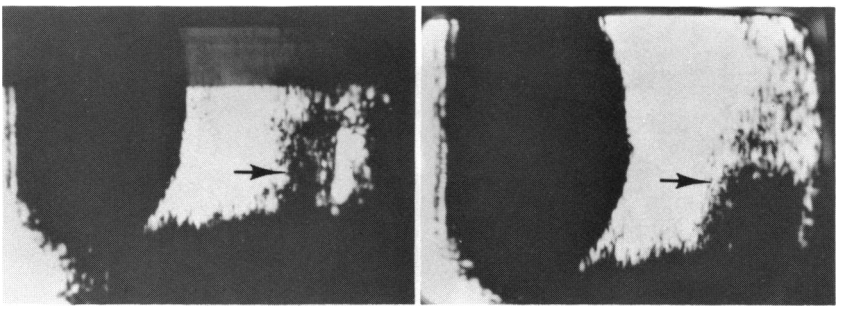

FIGURE 2
B scan ultrasonograph demonstrating thickened medial recti in Graves' ophthalmology.

The prominence of the extraocular muscles is seen to increase in Graves' ophthalmopathy, so that in the absence of a specific mass lesion and the presence of thickened ocular muscles the diagnosis can be made rather accurately.

The recent acquisition of a whole-body EMI scanner (320 matrix) has demonstrated that orbital tomography can be even more accurate (Figure 3). In this scan the globes are proptosed and the medial and lateral recti muscles are thickened—diagnosis, Graves' disease. Precise differentiation of orbital pathologic conditions is facilitated, and this exciting diagnostic method will become even more useful as experience with a variety of orbital problems is acquired.

Cost is a factor to be considered, however; the scan of the skull and orbits now costs about $150. Because of this high cost, the EMI scan may have to be reserved for those patients for whom a precise diagnosis cannot be made by other means.

RESEARCH EXPERIENCE

The use of plastic implants as extensions of, or to, extraocular muscles or as a sleeve to surround them to prevent excessive scarring has been advocated for several years. Bowen and Dyer[32] used a Silastic strip in which Dacron mesh was embedded to act as a substitute tendon for the lateral rectus muscles in dogs. The material became enmeshed in a fibrous sleeve that adhered to the sclera beneath. Beisner[33] used medical grade silicone elastomer and silicone-covered Dacron ribbons sutured under the tendons of rectus muscles in dogs. He

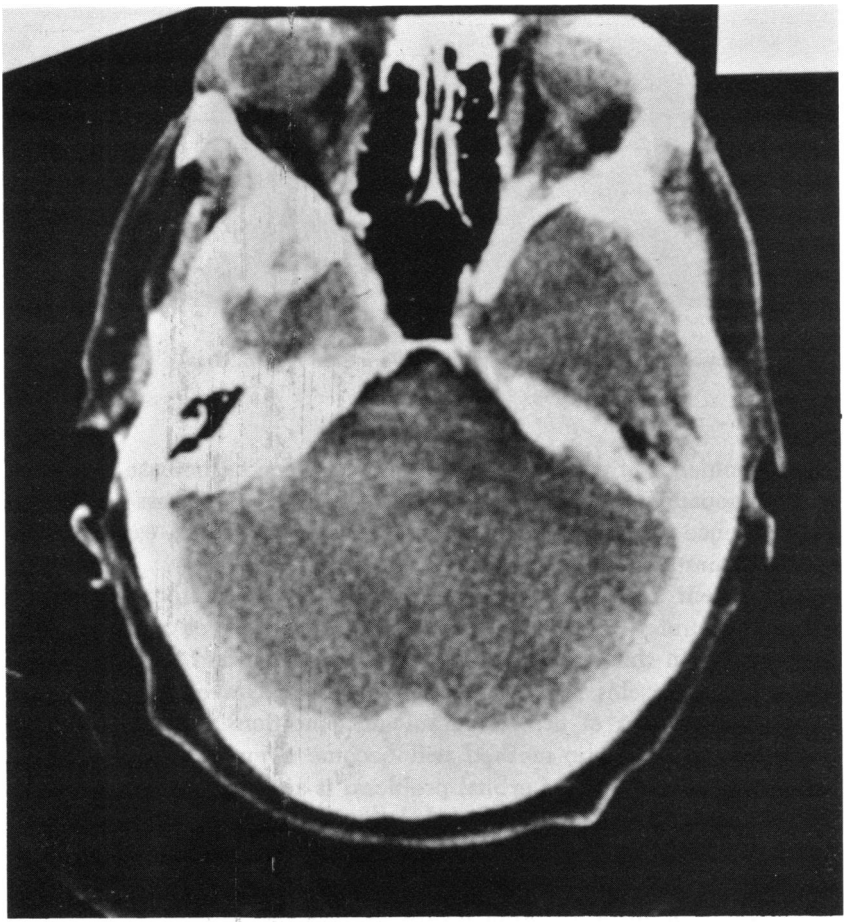

FIGURE 3
EMI scan (whole-body scanner, 320 matrix) demonstrating thickened ocular muscles and proptosis of globes.

concluded that these materials became bound firmly to the sclera by an enveloping fibrous capsule and nullified any theoretical advantage of a tendon prosthesis. Breakdown of the conjunctiva (often delayed) occurred frequently over the anterior edge of the implant regardless of the type of incision or thickness or the type of implants.

On the other hand, Dunlap[34] considered Supramid Extra to be the most inert of the synthetic materials available. The cellular reaction

was minimal at all time intervals in his experiments, and capsules lining the implant sites were consistently thinner. After 8 weeks the cellular reaction around a Supramid sheath was shown to be a thin lining of mature fibroblasts. He concluded that covering the muscle with a Supramid sleeve reduced greatly the postoperative scarring to the sclera or other nearby tissue. Even if a fibrous sheath surrounded the sleeve, it could be separated easily from adjacent structures.

Hiatt[35] used autogenous extraocular muscle to lengthen the action of another muscle and regarded this as a feasible procedure. He used this method in three patients without causing any undue restriction of motion in the direction opposite the action of the muscle receiving the transplant, and there was no unexpected tissue reaction. There was virtually no adherence between the transplanted muscle and the underlying sclera, and the results were deemed satisfactory in each patient. He concluded that for a clinical and experimental procedure this tissue was as good as any synthetic material (such as silicone) used in the past. Since there was no foreign material that was subject to foreign body reaction, no extrusion, external reaction, or other problem occurred in animals or human subjects. He suggested that heterotransplantation of the extraocular muscles could be used where paralyzed muscles exist, or a heterotransplant or homotransplant could be made to a fibrotic site (for example, in thyroidopathy). In large-angle deviations with amblyopia, the resected muscle may also be used to lengthen the recessed muscle or a portion of the inferior oblique to extend the resection of a medial or lateral rectus muscle.

Since synthetic materials produce a greater inflammatory response, and muscle tissue is difficult to manage as a transplant material, the use of the natural tissue—homologous sclera—to serve as a substitute tendon seems quite logical. Accordingly, gamma-irradiated homologous sclera preserved by freezing was used in 13 cats to extend the lateral rectus muscles. In each animal the lateral muscles were exposed, under clean conditions, by incision through conjunctiva and capsule. The lateral rectus muscle of one eye was severed and reattached at the original insertion by a black silk suture. To the lateral rectus muscle of the other eye a piece of homologous sclera 4 to 5 mm long and 3 mm wide was sutured with black silk; a Supramid sleeve was placed over the scleral tendon to cover it and the juncture to the muscle in order to retard or prevent scarring to the recipient's sclera or other tissue. The slip was then sutured to the original insertion with black silk. One cat has continued to be studied as a control for 6 months; the 12 others were killed at 1-week intervals. In no instance

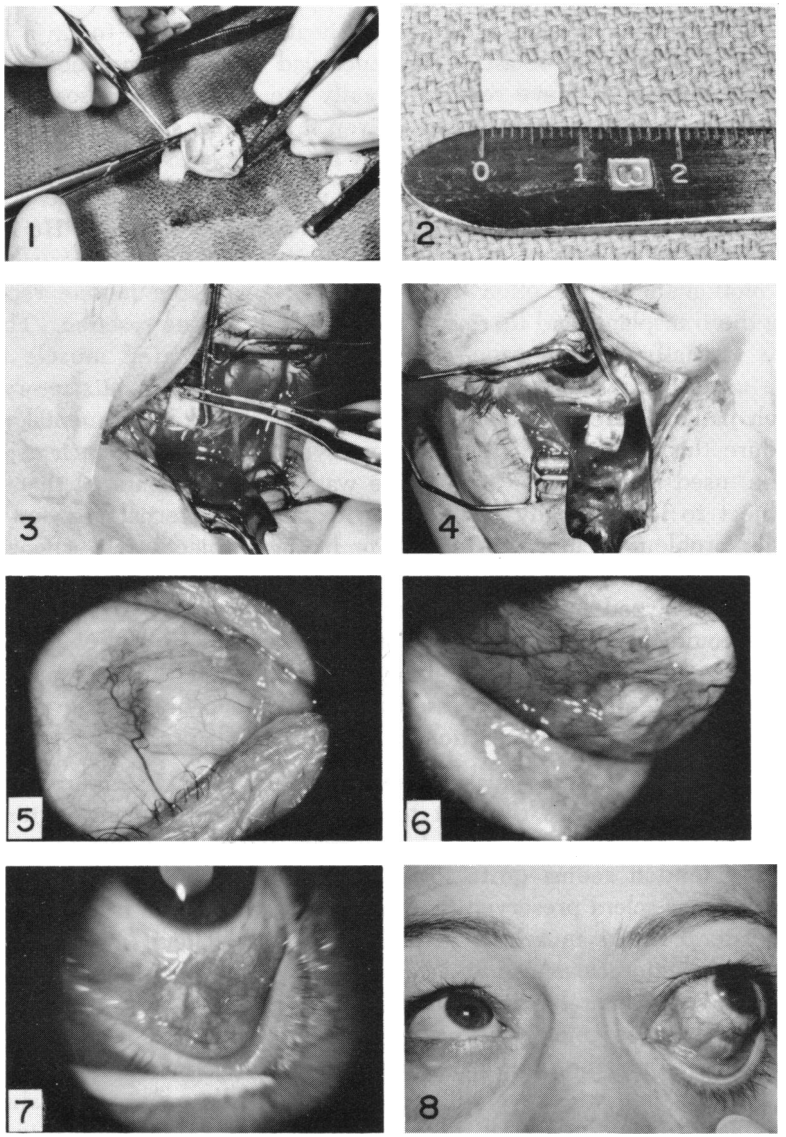

FIGURE 4
Preparation of homologous scleral graft (1, 2), attachment to rectus muscle (3, 4) post-operative appearance (5, 6, 7, 8).

did infection, exposure, or extrusion of the implant occur. No deviation of the eyes resulted. Although there was slight adherence of the sleeve to the surrounding tissue, grossly there was minimal reaction, and the transplanted tissue could be separated with ease. There was little difference in the reaction noted at 1 week and at 12 weeks. The union of scleral transplant to muscle was firm and contiguous.

For clinical trial, homologous cadaver sclera was prepared in a similar manner; that is, the tissue was irradiated and stored in a frozen state. The tissue is thawed just before surgery and is discarded if it is not entirely used. The same material is employed for eyelid grafts. For the purpose of muscle surgery, quarter sections only are prepared and stored. Figure 4 (1) and (2) show the preparation of the graft. The muscle is isolated (3) and the graft is sutured to the muscle near its insertion by a nonabsorbable suture such as 5-0 or 6-0 Mersilene. Detachment of the rectus muscle before this maneuver makes suture placement more difficult. After the graft is attached (4), the muscle is severed from the sclera with a knife, and the distal end of the graft is sutured at the original insertion after a Supramid sleeve of sufficient length to cover the scleral transplant, its junction to the muscle, and a few millimeters of muscle have been placed. Before attachment of the graft it is measured and cut the length of the desired recession of the rectus muscle.

Figure 5 shows these steps diagrammatically from the surgeon's viewpoint. The conjunctiva is incised horizontally in the lower fornix (1). The scleral implant is cut and sutured to the inferior rectus muscle near its insertion (2). With the use of a knife the inferior muscle is disinserted (3) and a Supramid sleeve is placed over the graft and muscle (3a). The graft then is reattached to the original insertion (4) and secured (5) with the sleeve covering the graft and a few millimeters of muscle and the sleeve secured by a suture as the edge (5a). The wound is closed by running or single mattress sutures (6). In recent cases 5-0 Vicryl suture has been used quite successfully and has the advantage of absorption so that unsightly suture remnants are not left visible at the muscle insertion. When the transplants are well covered by Tenon's capsule and conjunctiva, they gradually blend into the normal tissue and, although visible for many months, are not a cosmetic blemish (Fig. 4, 5 to 8).

To date, the transplants have been used for recession procedures only. Two months after the first procedure in this patient an overcorrection was achieved, and a second operation to resect the tissue was necessary. The conjunctiva was incised at the limbus and cleared

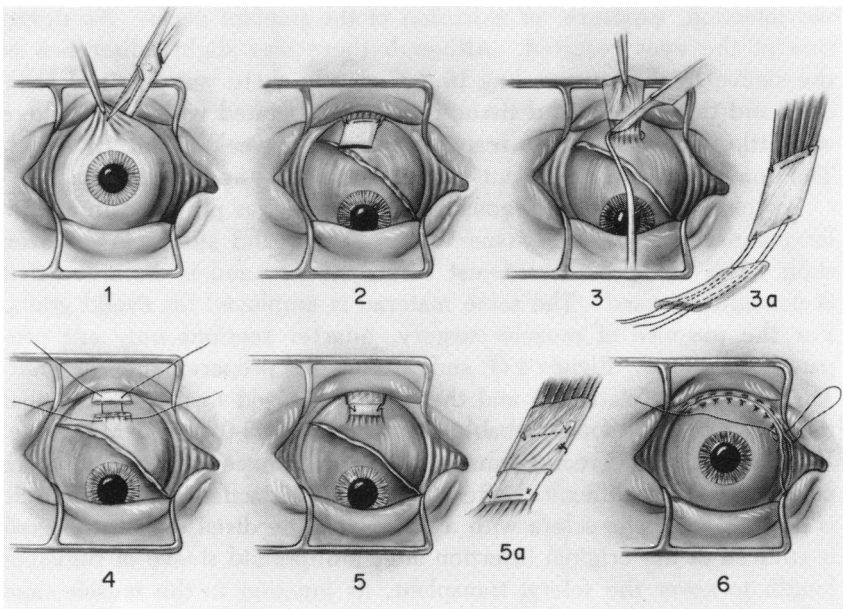

FIGURE 5 (1-6)
Surgical technique for attaching scleral graft to inferior rectus muscle with placement of Supramid sleeve and reattachment of graft to original insertion.

over the inferior rectus muscle. The scleral implant was exposed with relative ease, it being encapsulated by a membranous material similar to that of the normal intermuscular membrane. The union of scleral graft at the original insertion was firm, and the Supramid sleeve could be seen held with forceps. The hook could be slipped beneath the graft and muscle easily. The sleeve was removed, the scleral graft was resected the desired amount, a new sleeve was placed, and the graft was reattached. The graft is now a glistening fibrous cord quite firm and pliable in consistency.

A total of 17 patients have had scleral implants for recession procedures. Exposure of the graft by lysis of the conjunctiva over it is the only complication to date. This occurred in one eye of three patients, one having had two transplants (Fig. 6, 1) and another, one (Fig. 6, 2). In each patient the original conjunctival incision was near or over the muscle insertion, and after closure the tissue was so thin that the more rigid Supramid sleeve eroded through and caused breakdown of

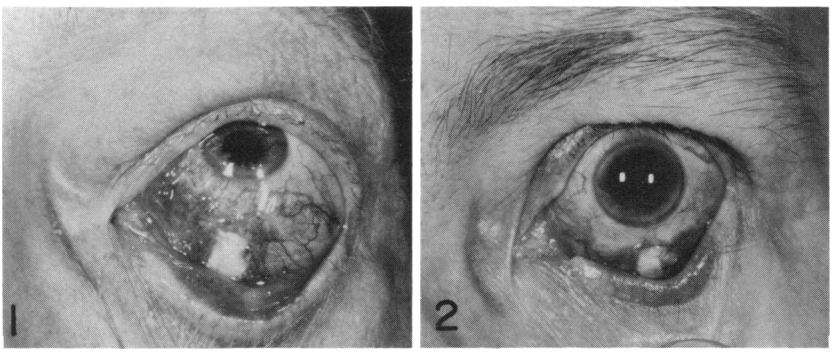

FIGURE 6 (1-2)
Exposed scleral grafts after conjunctiva eroded due to abnormal thickness.

the conjunctiva and exposure of the graft. These patients complained of irritable eyes that were quite injected inferiorly, and there was a profuse mucoid discharge. The exposed scleral implants were whiter in color but maintained good consistency. In one patient (Fig. 6, 1) the conjunctiva was undermined and closed over the graft, and the tissues remained viable. In the other two the scleral slips were removed and the tissue was closed satisfactorily.

In order to prevent this complication, the conjunctiva should be incised at the limbus at the initial operation or in the lower fornix just on the globe side to provide an adequate covering. The fornix incision is my preferred approach to the inferior rectus muscle in patients with Graves' myopathy.

When the muscle is very taut, separation from the insertion is best achieved by using a Bard-Parker knife and cutting on the hook (steel on steel) rather than by using more bulky scissors that may tent up the sclera and result in possible perforation of the globe.

CLINICAL EXPERIENCE

From the middle of 1968 to the middle of 1975, I performed muscle surgery on 116 patients with myopathy of Graves' disease, most of this experience being in the last 3 years (Table I).

Of these 116 patients, 85 (73%) were female and 31 (27%) were male. The youngest was a woman 23 years old, the oldest a man 75 years old. The overall average age was 51 years; the average age for women also was 51 years, and that for men was 48 years. Of the total, 115 were white and 1 was black.

TABLE I: MUSCLE SURGERY IN GRAVES' DISEASE (116 PATIENTS)

Sex		
Female	85 (73%)	
Male	31 (27%)	
Age, yr		
Overall average age	51	
Average female age	51	
Average male age	48	
Race		
White	115	
Black	1	
Orbital decompression		
Total of 68 (59%) before muscle surgery		
Bilateral transantral-ethmoidal		63 (91%)
Transfrontal		3
Transfrontal plus transantral		2
Krönlein (secondary to muscle surgery)		1
Transantral (secondary to muscle surgery)		2
Reoperations		
One procedure only	64 (55%)	
Two procedures	31 (27%)	
Three procedures	3 (<3%)	
Four procedures	2	
Intraocular tension		
Increased on up gaze	27 (23%)	
Muscles operated at first surgery		
Inferior recti only	48 (41%)	
Inferior and medial recti	35 (30%)	
Other combinations	33 (28%)	

Sixty-eight (59%) patients were treated by orbital decompression before muscle surgery. Sixty-three (91%) of these had a bilateral transantral-ethmoidal approach, three a transfrontal (Naffziger), two a transfrontal followed by a transantral-ethmoidal decompression; one had a lateral (Krönlein) after muscle surgery, and two had the transantral-ethmoidal operation secondarily. In patients having decompression, the muscle imbalance was more severe after transantral-ethmoidal decompression but in only one after the transfrontal route.

Sixty-four (55%) of patients had one muscle procedure, 31 (27%) had one reoperation, 16 (14%) had two further operations, three (<3%) had three repeat procedures, and two were operated on four times. At the conclusion of these operations, all results were considered satisfactory since some degree of binocular function was regained. The patients seem in time to adapt well to turning the head for extreme fields of gaze or to suppress these areas effectively. Time is a great ally in their rehabilitation.

FIGURE 7
Preoperative rotations (1-5), postoperative rotations (6-10).

In 27 patients (23%) the intraocular tensions were increased in up gaze and less so in down gaze. In none was there actual evidence of glaucoma.

At first operation, 28 (24%) patients had one inferior rectus recession only; 20 (17%) had both inferior muscles treated; in 35 (30%) both inferior and both medial recti were done; and 11 (9%) had a recession of one medial and resection of the homolateral lateral rectus. Most secondary procedures were further recessions of inferior and medial recti muscles. The average inferior rectus recession was 5+ mm and the average medial rectus recession was 5 mm.

SURGICAL CONSIDERATIONS

It is obviously desirable to accomplish the desired goal of restored binocular vision at one operation. That this is difficult to achieve is attested to by the number of reoperations required. Therefore, a

more generous recession of muscles is necessary in this disease. To recess further those muscles operated on previously is a heroic venture because of the massive postoperative scarring that occurs in most of these patients, but to readvance a muscle that has been recessed too far is even more difficult. Although somewhat more tedious and uncomfortable for the patient, when the operation is performed with the use of topical and local anesthesia plus an intravenous tranquilizer such as Innovar one can have the patient rotate the eyes, and the muscle tension can be adjusted accordingly to give a reliable result. Most patients do not tolerate this well in my experience.

In the presence of a stable thyroid metabolic state, patients with Graves' disease require extraocular muscle surgery when diplopia is a persistent and symptomatic disability. The limitations created by the fibrotic rectus muscles are determined by versions, ductions, and forced-duction tests. In my experience, and in that of others reported earlier in this paper, the inferior rectus muscles are most commonly involved, the medial recti are a close second, and the superior muscles are third; the lateral recti are seldom involved. All the rectus muscles actually are involved in the inflammatory restrictive process, but they affect mobility to varying degrees.

When the eye is restricted in abduction and elevation as determined by versions or ductions, there is little else that can cause this except Graves' disease. The history can exclude trauma to the eye or orbit. Forced-duction tests under topical anesthesia help to confirm the restricted elevation and abduction. Such tests should be performed also at operation before and after the muscle is exposed. Other clinical tests to exclude myasthenia gravis or the presence of the other orbital diseases as previously described are in order.

As a general rule, if only the inferior recti are involved, recess them only, and if only the medial muscles, recess them only; if the superior rectus only is involved, recess the fibrotic muscle *and* resect the antagonist, because it is much more difficult to bring an affected eye down than to permit one to elevate.

Determining the amount of surgery to be performed, and on which muscles, requires a considerable degree of clinical judgment. Usually, too little recession is done. If proptosis is absent or minimal and forced-duction tests reveal a restricted muscle on one side only, recession of 4 to 5 mm of an inferior rectus or a medial rectus is adequate. If restriction is grade 3 to 4 (on the basis of 1 to 4), up to 6 mm or more of recession is required. When proptosis is moderate (more than 20 to 22 mm), one must consider the possibility that release of fibrotic muscles may

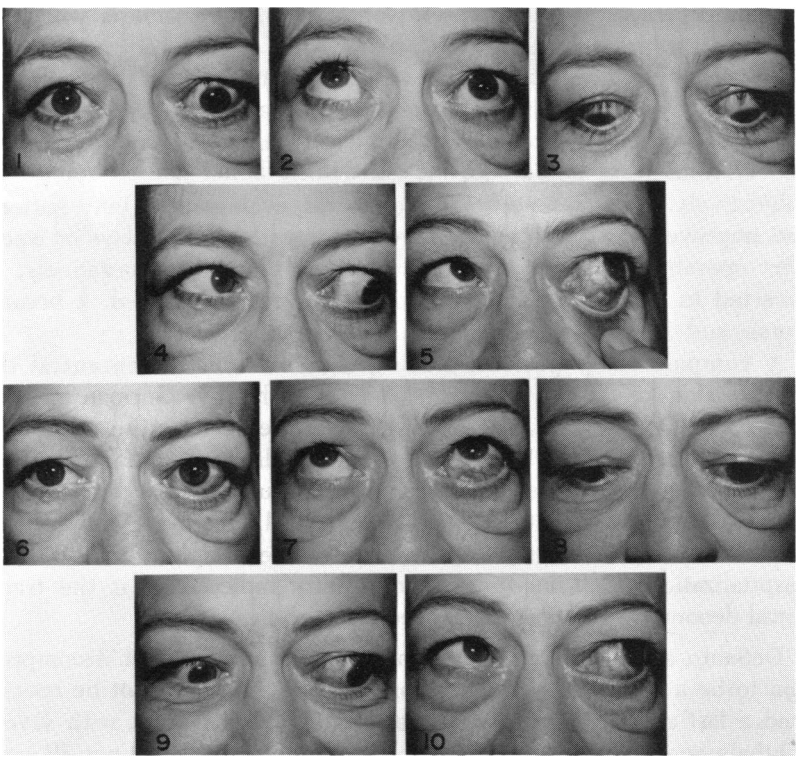

FIGURE 8
Preoperative rotations (1-4), postoperative rotations (5-10).

permit the globe to become more exposed and thereby lead to corneal damage. This is especially true if marked lid retraction is present. In these instances, or if optic neuropathy or exposure from proptosis is threatening the vision, I prefer preliminary transantral-ethmoidal decompression followed in 3 or 4 months by muscle surgery. Decompression usually increases the muscle imbalance, and patients must be apprised of this before operation.

Initially, orbital decompression was reserved for those patients with Graves' disease who experienced visual loss because of optic neuropathy and marked proptosis and those who had evidence of corneal exposure or ulceration not controlled by other means; that is, it was a sight-saving procedure. Increased experience with these procedures has led to the use of bilateral transantral-ethmoidal decompression

preparatory to extraocular muscle surgery and for cosmesis when the globes are so prominent as to be a blemish.

MacCarty and colleagues[36] reviewed 46 patients who had a transfrontal craniotomy and orbital decompression (Naffziger type). The extraocular movements were measured by the Lancaster red-green test, and versions were noted, the muscle defects being graded −1 to −4; subjectively, the presence of diplopia was evaluated. Many patients had improvement of the ocular movements within a few days or weeks after operation. Of 42 with limited ocular rotation preoperatively, 11 reverted to normal, 20 were improved, 3 were unchanged, 1 became worse, and 7 had no measurements postoperatively.

A comparison of patients having transfrontal or transantral decompression for optic neuropathies was published by Gorman and colleagues.[37] Of 10 patients for whom decompression by the transantral route was performed, 3 had postoperative diplopia, whereas in the transfrontal group of 9 patients, no diplopia occurred. The optic neuropathy was relieved by either route equally well, but these authors concluded that the absence of any external visible scar, the much shorter hospitalization, and the reduced morbidity indicated that the transantral decompression was the procedure of choice.

DeSanto and Gorman[38] found the transantral-ethmoidal decompression to be a relatively safe operation and one that need not be considered a last resort. They noted that almost every patient with severe ophthalmopathy has some ocular muscle abnormality, but not all have diplopia. Decompression, in their opinion, will not alter the muscle function in long-standing disease in which the initial muscle inflammatory process has progressed to fibrosis. An earlier operation in stable Graves' disease may decrease the orbital pressure and prevent irreversible muscle changes. The more common use of decompression in patients with myopathy is for the purpose of reducing proptosis before ocular muscle surgery for relief of diplopia. In their series, 34 of 40 patients having decompression had ocular myopathy; 23 of the 34 had symptomatic diplopia. After decompression, 28 of 40 had no change in the extraocular muscle function. In nine, the ocular motility was more restricted; all nine had prior muscle imbalance, but three had no diplopia preoperatively. Three patients had improved muscle function after decompression. The nine had ocular muscle surgery to restore single binocular vision. They concluded that transantral-ethmoidal decompression for significant proptosis in stable ophthalmopathy of Graves' disease before muscle surgery seems quite reasonable. By restoring the eye to a more nearly normal position and relieving the

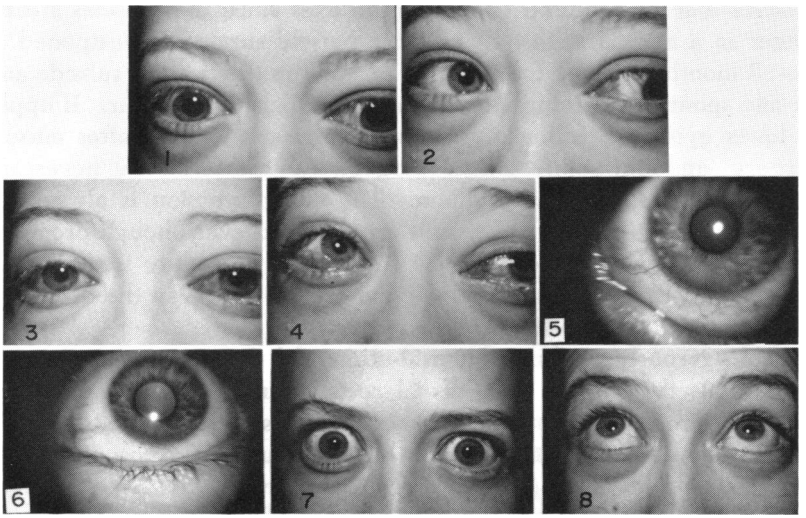

FIGURE 9
Preoperative: (1) Primary position, (2) left hypotropia on levoversion. Postoperative 2 months: (3) primary position, (4) improved elevation in abduction, (5) inferior corneal scar from exposure, (6) healed corneal lesion after use of soft contact lens, (7, 8) two months after decompression, positions excellent.

tension on already damaged muscles, it is thought that more precise muscle manipulation is made possible.

The approach to the problem of Graves' ophthalmopathy with ocular muscle involvement and proptosis has evolved into a team effort. The indications for transantral-ethmoidal decompression have been liberalized to include a cosmetically embarrassing proptosis with or without muscle imbalance; muscle imbalance and moderate or severe proptosis before any consideration of muscle surgery; and, of course, as a sight-saving and protective procedure when optic neuropathy or exposure of the globe is present. This quite safe procedure has been performed by a colleague more than 200 times without adverse effect on the visual system. All patients have a stable thyroid status as determined by the endocrinologist, and the decision to perform the decompression is made by the author and one or two other members of our ophthalmology staff. The patients are advised that from 40% to 50% of patients without an ocular muscle imbalance before decompression may have diplopia after surgery, and those with periodic or constant muscle involvement preoperatively may be worse. They are advised that at least one and probably more operative procedures on the ocular

muscles may be required to realign the eyes since the muscles are no longer in a normal state. Extraocular muscle surgery is postponed at least 3 months in order for all tissue reaction in the orbit to subside and for any spontaneous improvement in muscle balance to occur. If upper or lower eyelid retraction persists or is more pronounced after muscle surgery, an ophthalmic plastic surgeon can perform the necessary operation to relieve this problem. The decompression is always bilateral since both orbits and tissues are involved even though proptosis may be much more severe on one side; if the procedure is unilateral, cosmetic asymmetry results. Reduction of 2 to 10 mm in the degree of protrusion may be expected.

The vigorously performed antral-ethmoidal decompression does in fact permit the inferior and medial rectus muscles and orbital fat to protrude into the antrum and ethmoidal sinuses. This at times actually traps the muscles, creating a more difficult surgical exposure. However, in some instances (see Report of Cases below), release of the taut inferior rectus muscles may permit proptosis to become much more severe, with exposure of the globe. Decompression then may be urgent, and prior muscle surgery creates an inflammatory reaction that reduces its efficacy substantially. For this reason, only those patients who had minimal or no proptosis and diplopia have ocular muscle surgery primarily.

In some patients the eyes appear straight in down gaze but converge excessively on attempted elevation. This results partially from the inability of the taut inferior recti to relax but may also be due to fibrotic medial recti. Forced-duction tests with the muscle hook under the insertion will indicate which muscles are involved and need recession.

In a very informative article, Schimek[39] discussed the surgical management of ocular complications of Graves' disease. He expressed the belief that necessary operations may include maximal recession of a fibrotic inferior rectus to relieve hypotropia from its "leash effect," bilateral inferior rectus recession to relieve restriction of upward gaze, recession of other ocular muscles to correct tropias and diplopia, and orbital decompression to preserve vision and the globe if it is in danger of undue exposure. An inferior muscle recession averages 6 mm in his hands, the amount being determined by the rotatability of the eye. Recession to the equator may be necessary in severe cases. He too emphasized that more recession is needed than for the usual muscle condition and that some patients require more recession on one eye than the other if one muscle is more fibrotic.

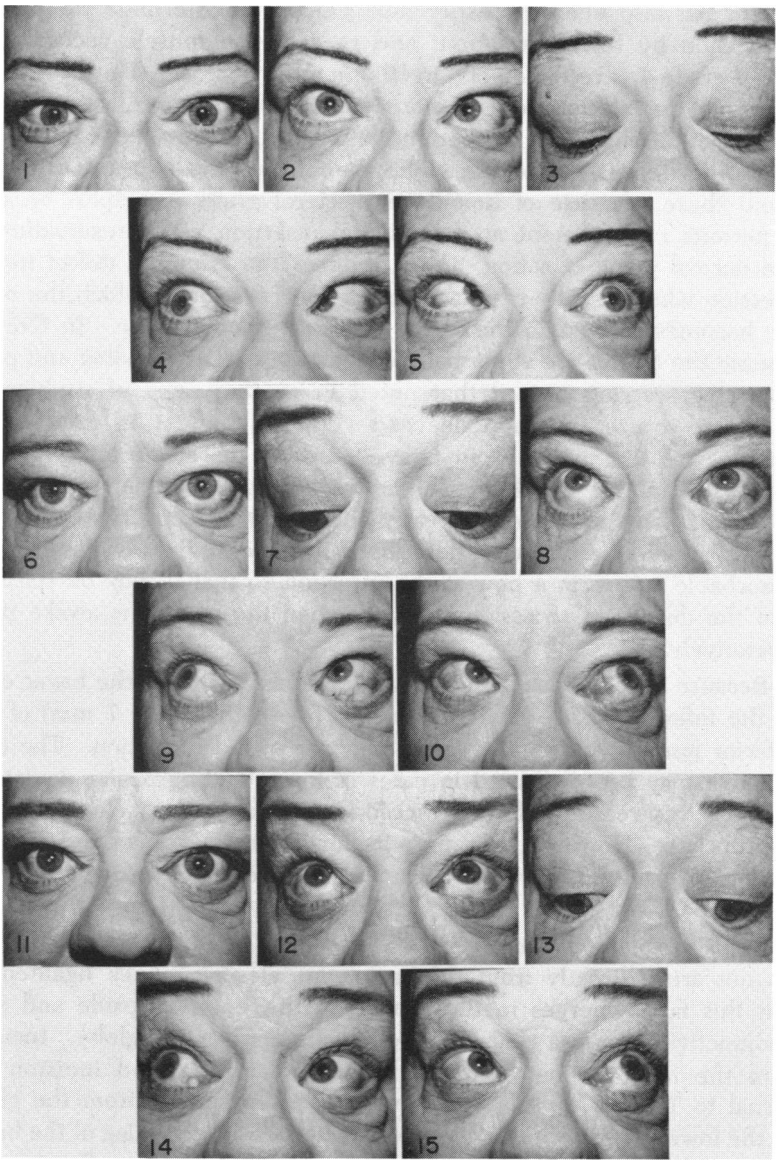

FIGURE 10
Preoperative rotations (1-5), postoperative rotations at 3 months (6-10), postoperative rotations at 7 months (11-15).

This has also been my experience. One can determine the degree of tension by testing traction, and recess each muscle accordingly. If it is grade 4, a recession of 8 to 10 mm must be done. However, a recession of the inferior rectus of more than 5 or 6 mm portends the complications of misalignment of the muscle when it is reattached, poor postoperative depression of the globe, and lower eyelid retraction. To avoid these, the use of homologous scleral grafts is helpful because it permits reattachment at the original insertion with preservation of the normal plane of action, and it reduces the crippling defect in depression which usually results from a large recession in which the muscle becomes scarred to the sclera far down on the globe. In Graves' disease the tissues are abnormally congested, so that bleeding and postoperative scarring exceed that noted in routine cases of strabismus. It is wise to use Supramid sleeves several millimeters in length on all muscles treated surgically in Graves' disease to reduce abnormal adhesions of muscle to sclera. In the event of reoperation, prior use of scleral implants and sleeves greatly enhances the recovery of the muscles. Jampolsky and Scott[40] described a unique method of tying a nonabsorbable suture in a bow at the insertion so that it may be released and the degree of recession adjusted when the patient is awake postoperatively.

Because of the aponeurosis from the inferior rectus to the lower edge of the inferior tarsus, a large recession (more than 6 or 7 mm) of the inferior muscle will usually result in lower eyelid retraction. The conjunctiva may be contracted in cases of long-standing ocular deviation, and for this reason a limbal incision with bare sclera closure seems appropriate. However, this permits further retraction of the muscle, Tenon's capsule, Lockwood's ligament complex, and hence the lower eyelid.

Swan[41] explained that fascial expansions to the lids and orbital wall do not arise directly from the rectus muscles as "check ligaments," but this fascia merges in the fornices with Tenon's capsule and subconjunctiva to form a ring of tissue which encircles the globe. Incision into the fornices may cause adnexal deformities, and incision external to Tenon's capsule may sever fascial expansions from the globe to the lower edge of the tarsal plate, possibly resulting in lag of the lower lid in down gaze and inversion in up gaze. However, Swan[42] suggested that a fornix incision just on the globe side permits exposure directly onto the inferior rectus insertion and allows easy access to the cleaning of tissue from the muscle. This incision, plus stripping away of all tissue external to the inferior muscle and along it as far posteriorly as

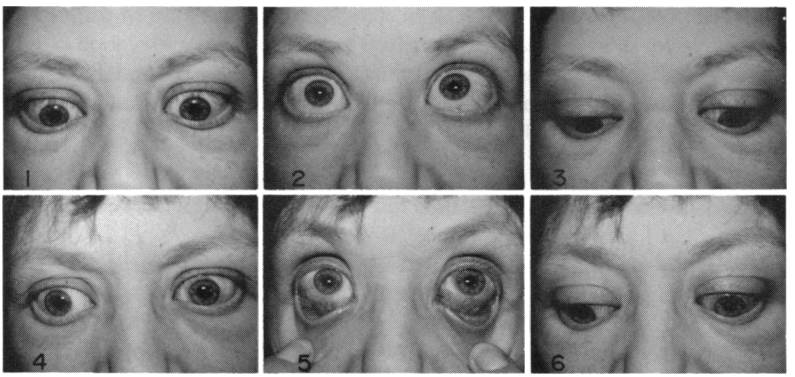

FIGURE 11
Preoperative rotations (1-3), postoperative rotations (4-6).

possible with releasing of the conjoined area with the inferior oblique beneath it, prevents much of the lid retraction previously experienced. A very helpful instrument is a slightly sharpened lid expressor used to separate the tissues away from the inferior rectus, whereas sharp dissection may lead to brisk bleeding.

In cases of severe ophthalmopathy, even release of fibrotic muscles may not permit easy elevation or abduction of the globe, because of diffuse involvement of all orbital contents. As a practical point, if the eyes are straight by light reflex after muscle surgery is completed, they will be so when the patient awakens from anesthesia or after the patches are removed postoperatively.

REPORT OF CASES

The histories of five patients are reviewed in some detail to illustrate a variety of salient points that one can observe in regard to the surgical correction of ocular muscle imbalance in Graves' disease.

CASE 1

White, female, 29 years of age with Graves' disease for 5 years. Now euthyroid. Vertical diplopia for 2 months.

Examination

Vision: 20/20 both eyes, intraocular tension by applanation 16 mm Hg right eye, 14 mm Hg left eye, not increased in elevation.

Krahn exophthalmometer: 17 mm right eye, 21 mm left eye.

Cover test: D:RHt 12 p.d., E4 p.d.
N:O

Versions preoperatively (Fig. 7, 1-5): difficult to elevate eyes to primary position, with upper eyelid retraction increased by effort (1); poor elevation (2), more restricted on the left; depression about normal (3) but excessive on left; restricted elevation (4) in up and right gaze, grade 3; and grade 4 restriction in elevation in abduction looking left (5).

Surgery

Recession left inferior rectus muscle 4.5 mm, resection left superior rectus 4.0 mm, recession right inferior rectus 4.0 mm.

Two months: no diplopia in primary or reading positions.

Versions (Fig. 7, 6-10): eyes straight in primary position with reduction of upper lid retraction (6), down gaze (7) normal, up gaze (8) much improved but still reduced, grade 2 restriction of elevation right eye up and right (9), and similar restriction left eye up and left (10).

Improved elevation of the eyes after release of the fibrotic inferior rectus muscles reduces upper eyelid retraction. Therefore, eyelid surgery should be postponed until muscle surgery is completed. A larger recession (perhaps 6 to 7 mm) of the left inferior rectus may have been preferable to the recess-resect procedure performed. Since proptosis was slight, muscle surgery only was deemed advisable.

CASE 2

White, female, 41 years of age with vertical diplopia for 6 months. Graves' disease known for 1 year. Now euthyroid.

Examination

Vision: 20/20 both eyes; intraocular tension by applanation 18 mm Hg both eyes.

Krahn exophthalmometer base 94: 17 mm right eye, 22 mm left eye.

Cover test: D:RHt 30 p.d.
N:O

Versions (Fig. 8, 1-4): in primary position (1) left eye is depressed, on elevation (2) left eye is restricted, on depression (3) left eye overshoots slightly, on gaze up and left (4) the left eye shows marked limitation.

Surgery

Forced-duction test positive for restricted left inferior rectus muscle. Recession left inferior rectus with 6 mm scleral graft and Supramid sleeve.

Ten months: Cover test: D:O
N:LHt 15 p.d., X8 p.d.

Versions: gaze up and left (5,10) shows good elevation with graft somewhat evident when lid retracted, primary position (6) normal but lower lid retracted, elevation (7) very good, depression (8) showed lag on left as does down and left gaze (9).

No diplopia except in extreme down gaze noted by patient. The larger recession resulted in lower eyelid retraction on the left.

A fornix incision on the globe side has proved more satisfactory so that fascial extensions from the muscle and fascial ring, described by Swan,[41] can be severed to prevent this complication. Also, the scleral graft can be covered more satisfactorily if the conjunctival-Tenon's closure is lower on the globe. Lag on depression may be expected with larger recessions, and the patient should be apprised of possible difficulty in lowering the eye or eyes fully into the reading position, so that higher segments (in bifocals) or a separate pair of reading glasses may be required for the presbyopic patient.

CASE 3

White, female, 23 years of age, with vertical diplopia 3 months. Hyperthyroidism now well controlled.

Examination

Vision: 20/20 both eyes; intraocular tensions normal; exophthalmometer 19 mm both eyes.

Cover test: D:RHt 12 p.d.
N:O

Versions (Fig. 9, 1 and 2): left hypotropia in primary position and marked restriction to elevation in gaze up and left (2).

Surgery

Recession both inferior rectus muscles 3+ mm on right, 4+ mm on left after forced-duction tests were found positive in both eyes at operation.

Two months: eyes are straight in primary position (1) with still some resistance to elevation up and left (2), but eyes injected and a corneal abrasion followed by an ulcer occurred on left as a result of exposure of globe at night when eyelids did not close. Exophthalmos left eye increased by 3 to 4 mm.

Lateral orbital decompression, left, of Krönlein type performed to reduce exophthalmos and protect globe.

Soft contact lens placed on left eye (5) to protect cornea and promote healing; also antibiotic treatment.

Two months after decompression: cornea has healed (6), but faint scar remains; in primary position eyes are straight (7) and elevation (8) is full. Diplopia is absent in all fields of gaze.

After 4 years no change in eye status has occurred. Patient wears soft contact lenses on both eyes for visual purposes.

Although there may be slight exophthalmos, this may be increased by relaxing a taut rectus muscle. If exposure is chronic, and an acute infection ensues, decompression on the involved side by a lateral route may be a useful eye-saving procedure. Other intensive methods of treat-

ment failed here. Soft contact lenses may be a useful adjunct for protection of the cornea and for visual purposes. Medication may be used successfully in conjunction with the lens.

CASE 4

White, female, 47 years old. Antithyroid treatment, but diplopia present and more severe lately. Thyroid state stable.

Examination

Vision: 20/20 both eyes.

Intraocular tension 28 mm Hg right, 23 mm Hg left reducing to 20 both eyes on down gaze.

Krahn exophthalmometer: 29 mm right, 31 mm left.

Surgery

Bilateral transantral-ethmoidal decompression. Exophthalmos reduced to 23 mm right, 27 mm left but ocular muscle imbalance more severe.

Cover test: D:ET 40 p.d., LHt 10 p.d.
N: same

Versions (Fig. 10, 1-5): primary position (1) eyes about straight, up gaze (2) marked esotropia, down gaze (3) normal, up and right (4) restricted elevation, up and left (5) restricted elevation.

Further surgery

Recession left inferior rectus with 7-mm scleral implant and Supramid sleeve, recession right inferior rectus with 6-mm scleral graft, and recession medial recti with 6-mm grafts and sleeves.

Three months postoperatively (Fig. 10, 6-10), a left hypertropia of 4 p.d. developed: primary position (6) shows slight left hypertropia persisting in down and up gaze (7 and 8) and up and right (9) and left (10).

Left inferior rectus with graft isolated with ease, graft resected 3 mm and reattached at original insertion. Minimal scarring encountered.

Seven months: primary position good (11), up and down gaze full (12 and 13) as is gaze up and left (15). Small Tenon's capsule cyst right eye excised later. No diplopia.

Scleral grafts placed both lower eyelids later.

If there is esotropia in up gaze and forced-duction tests are positive for abduction, medial and inferior rectus muscle recessions are in order. The use of scleral implants with Supramid sleeves permits easy recovery of the muscle, and either resection or recession is then performed readily.

CASE 5

White, female, 33 years of age with Graves' disease for 3 years and diplopia past 3 months. Now stable.

Examination

Vision: 20/20 both eyes.

Intraocular tensions: 16 mm Hg both eyes.

Krahn exophthalmometer: 21 mm both eyes.

Corneas show marked keratitis becoming more severe. Lids close poorly in sleep.

Surgery

Bilateral transantral-ethmoidal decompression.

Cover test: D:ET 20 p.d., LHt 4 p.d.
N:LHt 8 p.d.

Versions: more limited motility (Fig. 11, 1-3): cannot elevate to midline easily (1) and poorly with effort (2), depression normal (3).

Further surgery

Recession inferior recti 8 mm right 6 mm left, medial recti 5 mm both eyes with bare sclera closure each muscle.

Six months: poor elevation still persists.

Scleral grafts to both inferior rectus muscles of 5 mm with sleeves. Extensive scarring around muscles from previous surgery.

Two months: no deviation by cover for far or near fixation.

Versions (Fig. 11, 4-6) show eyes straight in primary position (4), good elevation with scleral grafts evident (5) and good depression, somewhat less on the left. No diplopia except on far down gaze.

At reoperation, scleral grafts and Supramid sleeves are useful to re-establish normal muscle alignment and motion and to prevent further restriction from excessive scarring.

SUMMARY

In the presence of ocular muscle imbalance secondary to Graves' disease (Werner, class 4), surgical correction for diplopia is necessary when the thyroid state is stable and no change in the motility is occurring. To exclude other causes of ocular muscle weakness (for example, myasthenia gravis and proptosis if it is present), preliminary tests are necessary—that is, A-mode and B-mode ultrasonography and EMI scan to reveal any evidence of orbital masses and also to demonstrate the thickened extra-ocular muscles so frequently seen in this disease. Impaired versions and

ductions and positive forced-duction tests give a clear-cut clinical impression of fibrotic muscles (which can be confirmed at surgery), which cannot relax and thus lead to the impaired motility. Increased intraocular tension from tense orbital tissues and ocular muscles may simulate glaucoma. The increased intraocular pressure usually decreases on down gaze.

In the absence of proptosis and with minimal eyelid retraction, recession of the taut rectus muscles—usually the inferior and secondly the medial—is in order. The recession should be greater in degree than that required for normal ocular muscles since the fibrosis inhibits normal rotation after, as well as before, surgery.

If proptosis is moderate (20 to 22 mm) and lid retraction is moderate to marked, preliminary bilateral transantral-ethmoidal decompression is advised since relaxation of the ocular muscles first may result in increased proptosis and exposure of the eye, for which emergency decompression to preserve the globe is needed—a more difficult procedure.

When severe proptosis is a cosmetic blemish or exposure of the globes or optic neuropathy is a threat to vision, transantral-ethmoidal decompression also should be performed, followed in 3 to 4 months by ocular muscle surgery. After decompression, the patient without or with occasional preoperative diplopia has a 40% to 50% likelihood of having ocular muscle imbalance and diplopia postoperatively, and virtually all those with an imbalance before decompression will have a more severe imbalance after decompression.

With small degrees of muscle involvement and only slightly positive forced-duction tests, a recession of 5 to 6 mm of a fibrotic muscle may suffice. In severe cases with marked restriction, a recession of 7 to 10 mm is required; possible complications are lower eyelid retraction (especially inferior rectus recession), misalignment of the muscle at reinsertion to the sclera resulting in an abnormal rotary imbalance, and faulty depression or adduction. In these instances, very careful dissection of the tissues away from the muscles is suggested, along with the use of homologous tissue transplants such as donor sclera to lengthen the muscle so that it is reattached at its original insertion in its normal plane of action. Supramid sleeves on all muscles will prevent much of the adherence of operated muscles to surrounding tissue. Reoperation in Graves' disease is very difficult because of the inflammatory reaction already present in the orbital and muscle tissue.

However, reoperation in this condition is common—about 45% in my experience. As a general rule, if the eyes are straight at the conclusion of surgery as determined by the pupillary light reflexes from the operating room light, they will be straight when the patient awakens from anesthesia

or when the patches are removed. All patients should be advised that the preoperative fibrotic state of the ocular muscles will affect mobility after surgery, and the goal is to achieve binocular single vision in the primary and reading positions. Abduction and elevation usually will remain impaired, but the "tincture of time" in the adaptable human body will permit many aggravating symptoms to fade away.

The team approach to the often miserable patient with severe Graves' disease seems workable. When the disease is stable, relieve the proptosis, straighten the eyes, and correct the lid retraction in that order. The patients will be grateful.

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