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Blepharospasm: Past, Present, and Future

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Summary: To investigate causes, associations, and results of treatment with blepharospasm, 1,653 patients were evaluated by extensive questionnaires to study blepharospasm and long-term results of treatment with the full myectomy operation, botulinum-A toxin, drug therapy, and help from the Benign Essential Blepharospasm Research Foundation (BEBRF). The percent of patients improved by the BEBRF was 90%, full myectomy 88%, botulinum-A toxin 86%, and drug therapy 43%. The patient acceptance rate for the BEBRF was 96%, full myectomy 82%, botulinum-A toxin 95%, and drug therapy 57%. Blepharospasm is multifactorial in origin and manifestation. A vicious cycle and defective circuit theory to explain origin and direct treatment rather than a defective specific locus is presented. All four forms of therapy evaluated are useful and must be tailored to the patient's needs. Mattie Lou Koster and the BEBRF have helped blepharospasm sufferers more than any other modality, and all patients should be informed of this support group. The full myectomy is reserved for botulinum-A toxin failures, and the limited myectomy is an excellent adjunct to botulinum-A toxin.
Key Words: Blepharospasm—Myectomy—Botulinum A toxin—Facial dystonia—Benign Essential Blepharospasm Research Foundation.

Evaluating blepharospasm patients for over two decades has provided us with the opportunity to make some important observations and witness great advances in therapy. We present our experience with the full myectomy operation as well as evaluate the efficacy of botulinum-A toxin, oral drugs, and help from the Benign Essential Blepharospasm Research Foundation (BEBRF): the data obtained from 1,653 patients with blepharospasm evaluated with extensive questionnaires will be presented. This study of the largest number of patients with blepharospasm to date was supported by the BEBRF.

We recognize the weaknesses in subjective retrospective studies evaluating patients via extensive questionnaires. However, in blepharospasm, the results are best evaluated subjectively, and this paper provides the most clinically useful information presented on the largest group of patients with blepharospasm studied to date.

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HISTORY

In the sixteenth century, the Flemish artist Brueghel painted a subject with grotesque facial and

FIG. 1. "De Gaper." Painting by Pieter Brueghel from the sixteenth century that is our first record of blepharospasm.

eyelid spasms, and this painting, ''De Gaper'' (Fig. 1), is the first record of blepharospasm and marked lower facial dystonia, which we refer to as ''Brueghel syndrome'' (1). Such patients were institutionalized in insane asylums at that time. Historically, few advances were made in understanding and treating blepharospasm and facial dystonia for many centuries, and until the mid-1900s, most patients were still regarded as being mentally unstable or having voluntary eyelid squeezing.

The first report of blepharospasm in the medical literature was in 1870, when Wood and Talkow (2) described patients with facial and eyelid squeezing disorders. In 1907, Meige (3) described a similar patient, and this dystonia has become known as Meige syndrome (4). It was the twentieth century before any medical treatments for blepharospasm, such as alcohol injection of the facial nerve, neurotomy, neurectomy, and selective facial nerve avulsion, evolved as forms of treatment (5–13). Early treatments were directed at destroying the facial nerve, and patients suffered from a high recurrence rate as well as such side effects as loss of facial expression and facial movement. In addition, the functional and cosmetic deformities associated with blepharospasm, such as brow ptosis, ptosis, dermatochalasis, and eyelid malpositions, were aggravated by facial nerve operations, so that the treatment was nearly as bad as the disease. In 1956, Henderson's (14) classic article on blepharospasm described the disability and treatments to date.

Isolated blepharospasm (spasm limited to the eyelids) is present in only a minority of ''blepharospasm'' patients. The remainder have or develop associated lower facial spasms, or even spasms in other cranial nerve distributions or body distributions. Although blepharospasm is a useful term to describe patients with eyelid and facial spasms, and their greatest disability resulting from eyelid spasms, for diagnostic and treatment purposes we present a clinical division of what collectively is called blepharospasm, as follows: 1) blepharospasm: spasms only in eyelids (Fig. 2); 2) Meige syndrome: spasms in eyelids and midface (Fig. 3); 3) Brueghel's syndrome: spasms in eyelids associated with marked spasms in lower face and neck (Fig. 4); 4) segmental cranial dystonia: eyelid and facial spasms associated with spasms in cranial nerve distributions in addition to the seventh nerve (Fig. 5); and 5) generalized dystonia: eyelid and facial spasms associated with spasms in additional parts of the body.

After personally recording a high recurrence rate and the untoward side effects from neurectomy surgery (Fig. 6), one of the authors (R.L.A.) developed what has been termed the ''full myectomy.'' Earlier authors had described blepharoplasty with removal of the orbicularis muscle as useful in

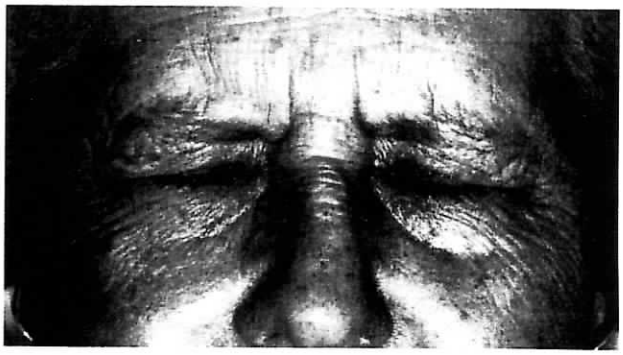


FIG. 2. Blepharospasm. Spasm only in eyelids.

FIG. 3. Meige syndrome. Spasms in eyelids and midface.

blepharospasm, but these cases recurred with time (10,15). In our early operations beginning in 1974, only the upper eyelid orbicularis muscle was removed, similar to what we now call a ''limited myectomy,'' and all of these patients experienced recurrence with time. The operation evolved into a more aggressive procedure, removing virtually all of the orbicularis muscle as well as the corrugator superciliaris and procerus muscles. Since the myectomy operation removes all the orbicularis muscle in the extended lateral raphe and the postorbicular fascia, it also removes the peripheral branches of the facial nerve. Although some have considered this operation to be a neuromyectomy, it is well known that the peripheral nerves will regenerate, whereas the muscle does not. This explains the permanent nature of the full myectomy. We first published the myectomy operation in 1981, and a number of subsequent papers describing the authors' experience as well as that of others have been reported since that time (16–26). The surgical technique of myectomy has been presented and updated many times, and will not be detailed in this paper. However, we would like to emphasize that the myectomy is a difficult and technically demanding operation requiring experience and anatomical and surgical expertise. Results are directly related to the meticulous and complete removal of squeezing muscles. The muscles must be removed en bloc rather than piecemeal to ensure complete removal, to protect normal anatomy and vascular supply, and to decrease blood loss.

In the early 1980s, Scott described botulinum-A toxin treatment for strabismus, and soon after began using it in blepharospasm (27,28). After its approval by the Food and Drug Administration in 1989, we reserved the full myectomy operation for botulinum-A toxin failures or patients who refuse to use botulinum-A toxin. A ''limited myectomy'' is used for patients who are inadequate botulinum-A toxin responders or botulinum-A toxin responders who have cosmetic and functional deformities associated with blepharospasm. Many patients considered botulinum-A toxin ''failures'' are found to have a greatly weakened orbicularis on evaluating their ability to forcibly close the eyelids. Thus, the botulinum-A toxin is working, but is not providing functional relief. In many of these cases, the underlying deformities such as ptosis, dermatochalasis, brow ptosis, entropion, canthal tendon laxity, phimosis, and other eyelid malpositions and rhytids aggravate the blepharospasm, and may be a greater problem than the residual blepharospasm (Fig. 7). Thus, blepharospasm is a vicious cycle between the eyelid spasms and the malpositions caused by blepharospasm. The eyelid malpositions result from the chronic forceful squeezing, and in turn they exacerbate the blepharospasm. Correcting these functional and cosmetic deformities improves the condition and helps break this vicious cycle. Many other patients considered ''failures'' of botulinum-

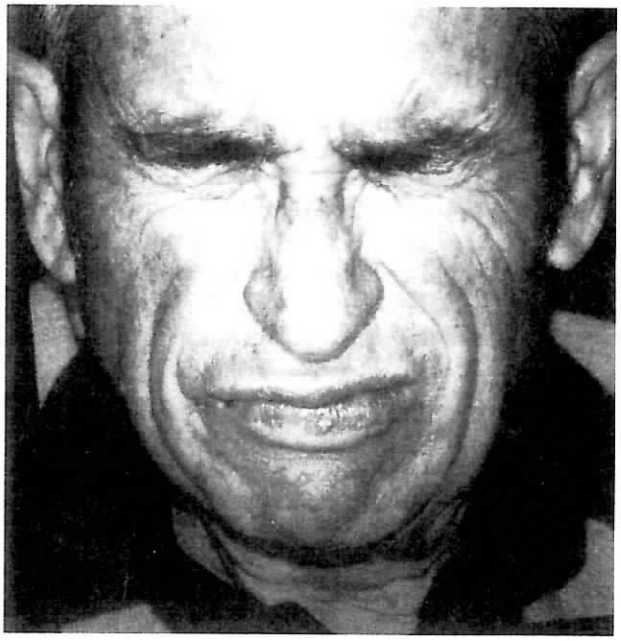


FIG. 4. Brueghel syndrome. Spasms in eyelids associated with marked spasms in lower face and neck.

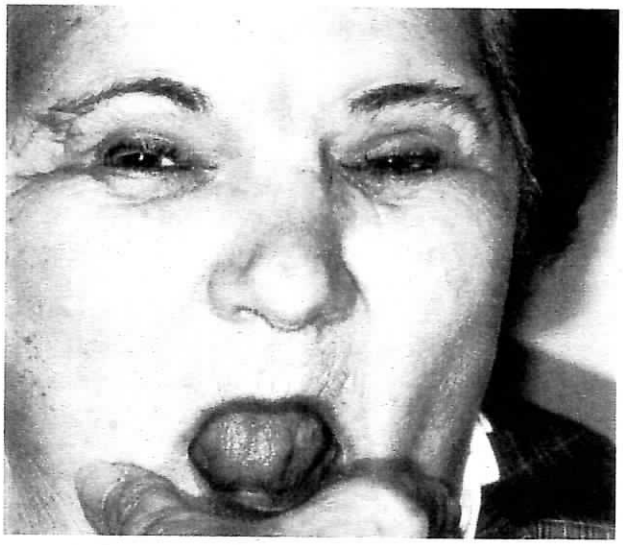


FIG. 5. Segmental cranial dystonia. Eyelid and facial spasms associated with spasms in cranial nerves in addition to the seventh nerve. Note involvement of the tongue and muscles of mastication.

A toxin have associated apraxia of lid opening, which will be discussed later. Apraxia of lid opening is frequently more problematic than blepharospasm (Figs. 8 and 9). A limited myectomy and levator advancement as an adjunct to botulinum-A toxin improves function and cosmesis and converts many botulinum-A toxin "failures" back to good responders (Fig. 10). After limited myectomy, a decreased dosage of botulinum-A toxin is required, and greater portions of the botulinum-A toxin can be directed to the residual spasm areas.

ETIOLOGIC FINDINGS

A specific cause for blepharospasm as well as its central control center remain unidentified. From years of clinical experience, research, and the results of the questionnaires presented in this manuscript, we believe that blepharospasm is multifactorial in origin and manifestation. We view blepharospasm as a defective circuit rather than a defective locus. Although most research has been directed at finding a specific locus, we doubt that a specific locus causes blepharospasm, or that its treatment will cure the disease. Certainly, an as yet unidentifiable central control center exists in the region of the basal ganglia, midbrain, and/or brain stem (29–34). This control center fails to modulate the blinking in blepharospasm, but it is only a part of an overloaded circuit, as we will discuss later (29–34).

Blepharospasm, which literally means eyelid spasm, is a general term for what is frequently a more extensive facial dystonia. If patients with blepharospasm are followed, only approximately 20% remain with isolated eyelid spasm. Most either present with or progress to more extensive facial dystonias, such as Meige syndrome (25). Therefore, blepharospasm is an isolated dystonia related to more generalized dystonias. Recently, genetic abnormalities have been found in some dystonia patients (35–38).

In an attempt to understand blepharospasm as well as the normal blink reflex, we greatly oversimplify this complex and poorly understood area. Normal blinking as well as blepharospasm is a result of the activity and coinhibition of two groups of muscles, the protractors of the eyelids (the orbicularis oculi, corrugator superciliaris, and procerus muscles) and the voluntary retractors of the eyelids (the levator palpebra superioris and the frontalis muscles). Under normal conditions, the protractors and retractors have a coinhibition and function only at separate times. Rarely in patients with blepharospasm, the coinhibition between the protractors and retractors is lost (39–41), as in some cases of apraxia of lid opening. Apraxia of lid opening is a condition where eyelids fail to open even in the absence of squeezing (Figs. 8 and 9).

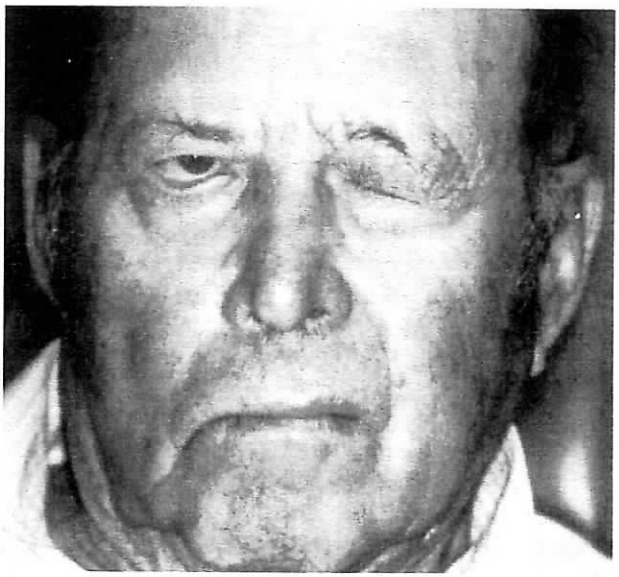


FIG. 6. Patient after selective facial neurectomy surgery. Note recurrence of blepharospasm on left side of face and facial palsy appearance with aggravation of eyelid deformities on "successful" right side of face. The side effects of successful surgery were almost as bad as the disease, and the recurrence rate was high.

FIG. 7. Blepharospasm patient with associated cosmetic and functional deformities. Note brow ptosis, dermatochalasis, ptosis, entropion, and canthal tendon laxity with phimosis and rhytids.

Although more specific neurophysiologic requirements for apraxia of lid opening exist, we find it clinically useful and appropriate to refer to the inability of otherwise normal eyelids to open in the absence of orbicularis spasms as apraxia of lid opening (42,43). We have noted the incidence of apraxia of lid opening to be 7% in a general population of patients with blepharospasm, whereas it is much higher, approaching 50%, in patients who are ''failures'' of botulinum-A toxin therapy (44). These patients are a much more difficult group to treat by any therapeutic method. The only predictable improvement comes from trying to eliminate squeezing in these eyelids and enhancing elevation as much as possible by levator aponeurotic resection and/or enhancement of frontalis function. If botulinum-A toxin is adequately weakening orbicularis function, a full myectomy seldom is more useful than a limited myectomy with aponeurosis advancement in these patients with apraxia of lid opening. Some patients may require frontalis suspension as a last resort.

We simplify the complex circuitry in blepharospasm into a vicious cycle, with an afferent or input limb, a central control center, and an efferent or response limb. The afferent limb of this vicious cycle has multifactorial stimuli, such as light, corneal or eyelid irritation, pain, emotion, stress, psychic issues, and virtually any trigeminal nerve stimulation or outside irritation. These stimuli are transmitted to a central control center, probably in or near the basal ganglia. The efferent pathway is transmitted via the facial nucleus, facial nerve, orbicularis oculi, corrugator, and procerus muscles. In more extensive facial dystonias, virtually all of the muscles supplied by the facial nerve and even other nerves and muscles of the face and body may be involved in the efferent squeezing response. This circuit can become a vicious cycle, where the more input or afferent stimuli, the more efferent or output spasm, and the more spasm, the more stress, irritation of the eyes, and afferent stimulation. The central control center may be defective or weakened from anything from a genetic predisposition to an injury, and it becomes unable to modulate this overloaded circuit. Many patients relate one stressful event, injury, or irritation as the cause of the blepharospasm. We view these events as the ''straw that broke the camel's back.'' Therapy directed at helping to improve any part of this vicious cycle is useful. Prevention is more likely to be found than a cure for this multifactorial disease, as it seems that once the control center is overloaded and the circuit breaks down, it seldom, if ever, spontaneously recovers. Whether or not we are correct with our ''defective circuit'' versus ''defective locus'' theory as the cause of blepharospasm, management should be directed at all parts of the circuit.

THERAPY

There are four major therapies directed at the treatment of blepharospasm. These are the BEBRF with education and support, drugs, botulinum-A toxin, and myectomy surgery. The afferent limb or input limb of this vicious cycle can be improved in all patients. Such treatments as wearing tinted glasses with ultraviolet block to decrease the as yet undefined cause of painful light sensitivity (oculophotodynia) in these patients is recommended. Lid (ocular) hygiene to decrease blepharitis and irritation and artificial tears to relieve the frequent and as yet undetermined relationship between dry eyes and blepharospasm is useful. Support therapy to help manage other irritations, emotional upsets, and especially stress is extremely important. Many patients with blepharospasm have an intense ''Type A'' personality. This personality may be caused by the blepharospasm as part of the vicious cycle, wherein the disease creates stress and intensity, which in turn aggravates the disease. The BEBRF as well as familial and psychological support is very important to help patients and families understand and manage this progressively debilitating disorder. Although the disease is not a psychological illness, it certainly creates stress and psychological problems. When much of our ''normal'' population has received psychological support at

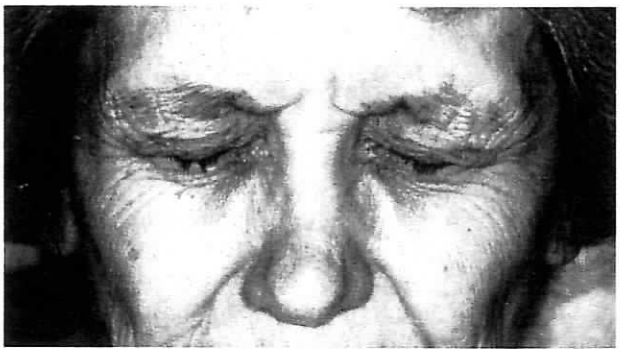


FIG. 8. Blepharospasm patient with associated apraxia of lid opening. In spasm, apraxia of lid opening cannot be diagnosed and is not apparent.

some time, there is no reason why a blepharospasm patient would require less. We recommend that all patients and families be directed to the BEBRF as the first step after diagnosis. The BEBRF has done more to educate, support, and help blepharospasm sufferers than any modality. Patients should not be embarrassed about seeking additional psychological support whenever necessary or feel that blepharospasm is a psychological illness for having such therapy. Since the central control center for blepharospasm is unknown, drug therapy directed at the control center is frequently a "shotgun approach." The drugs directed at the central pathophysiology of blepharospasm and facial dystonias are based on three as yet unproven pharmacologic hypotheses: 1) cholinergic excess, 2) GABA hypofunction, and 3) dopamine excess.

Anticholinergics have been the most common and effective drugs, with GABA-ergic drugs the second most effective general group. Sedative drugs are sometimes helpful, but generally decrease blepharospasm at approximately the same rate that they slow down the patient in general. Unfortunately, the degree of improvement and length of improvement with drugs is limited. At present, drugs are used more as an adjunctive therapy to botulinum-A toxin or myectomy rather than a primary long-term treatment for eyelid spasms. However, drugs may be the most useful treatment in lower facial dystonia and generalized dystonia, where botulinum-A toxin and surgery provide little relief.

The two most effective treatments for eyelid spasms, botulinum-A toxin and myectomy, are directed at normal efferent end organs (eyelid muscles and nerves) to help eliminate the spasm. Botulinum-A toxin temporarily blocks the motor-end plate by blocking the release of acetylcholine. Via motor-end plate sprouting of new nerves and possibly other mechanisms, the effect is overcome in about 3 months (44–46). Some patients become refractory to treatment after multiple injections, perhaps because of excessive sprouting, immunity, or other mechanisms (45–50). Myectomy as well as doxorubicin chemomyectomy is directed at physically destroying the muscle (51). Although nerve removal or nerve blocking agents fail to work with time because of regeneration, muscle removal remains the most permanent form of therapy.

QUESTIONNAIRE

With support from the BEBRF, 1,653 patients treated before 1988 were evaluated with extensive questionnaires regarding their disease and treatment. Patients treated before 1988 were studied, as botulinum-A toxin was approved by the Food and Drug Administration in 1989, and it has become the first line of treatment for blepharospasm. Since then, few patients have been treated initially with drugs or full myectomy, and only the failures of botulinum-A toxin are now treated by other modalities, selecting for a much more difficult group of patients with blepharospasm. Many myectomy operations are now limited myectomy as an adjunct to botulinum-A toxin, and studying patients treated before 1988 provides long-term follow-up, which is important in this disease. Four thousand questionnaires were mailed to patients registered with the BEBRF, and 1,653 (41%) were completed and returned. The following data was obtained.

The age at onset of blepharospasm ranged from 4 to 82 years, with an average of 55.5 years. Seventy-three percent of the patients were women and

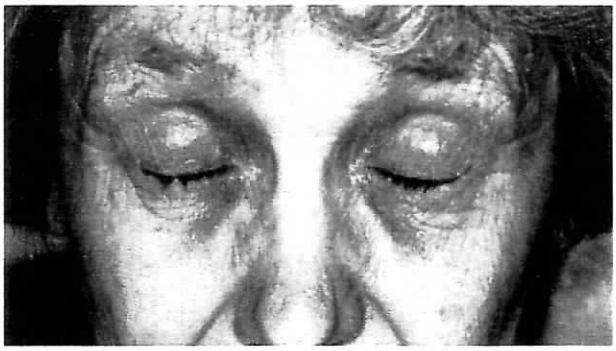


FIG. 9. Blepharospasm patient shown in Figure 8 with associated apraxia of lid opening. After spasms and eyelids not squeezing, the patient still has inability to open the eyelids. Note elevation of brows and appearance of no stimulus to open eyelids.

FIG. 10. Limited myectomy surgery. An upper eyelid crease incision is made and the majority of the orbicularis muscle is removed. The levator aponeurosis is repaired or advanced. An internal brow elevation can be performed via the same incision and excess skin removed. Some patients require a direct brow elevation. The healing is almost as good as with cosmetic surgery, and the patient acceptance rate is even higher. Patients continue to require botulinum-A toxin, but at lesser levels and with more effect after a limited myectomy.

27% were men. Patients saw an average of four doctors before the correct diagnosis was made, with a range of 1 to 75 doctors. The cost of making the correct diagnosis was greater than $1,000 in 59% of patients, and exceeded $50,000 in 1%. This is disappointing when blepharospasm is a visual (literally an Augenblic diagnosis) rather than a laboratory or radiologic diagnosis.

In searching for etiologic agents that may have contributed to the development of blepharospasm, it was found that 32% of patients reported a head injury or whiplash injury and 10% reported exposure to various toxic chemicals. Forty-five percent of patients noted some tobacco use, and 59% reported alcohol consumption.

The initial symptoms of blepharospasm included an increased blink rate in 77% of patients, eyelid spasm in 66%, eye irritation in 55%, midfacial or lower facial spasm in 59%, brow spasm in 24%, and an eyelid tic in 22%. The lower facial problems associated with blepharospasm included involuntary jaw movement in 25%, neck spasms in 24%, difficulty speaking in 23%, difficulty swallowing in 21%, and difficulty breathing in 20%. Extrafacial involvement included poor equilibrium in 40% of patients with blepharospasm, leg or arm spasms in 17%, writer's cramp in 12%, and abdominal spasms in 10%. The progression of symptoms to debilitating involvement occurred over weeks in 11%, months in 37%, and years in 52%. The conditions aggravating blepharospasm included bright lights in 79%, stress in 78%, fatigue in 63%, driving in 45%, television in 45%, and reading in 43%. The conditions relieving blepharospasm included sleep in 75%, relaxation in 55%, inferior gaze in 27%, artificial tears in 24%, traction on the eyelids in 22%, talking in 22%, singing in 20%, and humming in 19%.

Additional diagnoses in patients with blepharospasm included dry eyes in 49%, psychological illness requiring professional support in 33%, and other neurological disease in 8%. Forty-seven percent of patients believed people thought they were malingering, and 16% had been told by a physician that they were malingering.

The disability caused by blepharospasm may be severe. Fifty-eight percent of the patients responding to our questionnaire were unable to drive, 46% unable to read, 41% unable to watch television, 29% unable to work, and 18% unable to leave home. Of those patients still working, 16% indicated they were unable to perform 5% to 25% of their duties, 24% were unable to perform 30% to 50% of their duties, 10% were unable to perform 55% to 75% of their duties, and 10% were unable to perform 80% to 95% of their duties. Forty percent of the blepharospasm patient population were retired either because of age or disability from blepharospasm. Only 14% of patients indicated they had no significant disability from their blepharospasm.

The type of health care provider first seen by patients with blepharospasm was an ophthalmologist in 30%, family physician in 24%, optometrist in 13%, neurologist in 10%, internist in 8%, and all others in 15%. The health care provider first making the correct diagnosis was an ophthalmologist in 56%, neurologist in 27%, neurosurgeon in 5%, optometrist in 4%, family physician in 3%, self-diagnosis in 2%, and all other health care providers in 3%.

RESULTS

After many years of trying to evaluate therapy in patients with blepharospasm, we have found that it is impossible to evaluate objectively a patient's treatment response and improvement rate. A patient's subjective improvement rate remains the best indicator of treatment efficacy. The patient acceptance rate of therapy combines treatment im-

TABLE 1. *Drug therapy*

Drug	Percent of patients improved	No. patients treated
Lorazepam	67	88
Orphenadrine	58	59
Clonazepam	42	264
Artane	41	260
Sinemet	28	53
Diazepam	23	191
Lioresal	21	112
Carbamazepine	14	58
Amitriptyline	13	83
Haloperidol	9	135

provement with desirability of treatment (i.e., after undergoing treatment, whether they would recommend this therapy to another patient). The patient acceptance rate includes all variables, such as side effects, pain, morbidity, cost, length of recovery, psychological aspects of therapy, etc., and is the best overall estimate of patient satisfaction with each treatment.

Benign Essential Blepharospasm Research Foundation

Mattie Lou Koster and the Benign Essential Blepharospasm Research Foundation (BEBRF), which she founded in 1981, has provided the greatest support and relief for blepharospasm sufferers worldwide. The year 1981 was a good year for blepharospasm, as Mattie Lou Koster founded the BEBRF, Scott reported the clinical use of botulinum-A toxin, and Anderson published the myectomy for blepharospasm (16,27). In 1982, Mattie Lou Koster succeeded in getting an editorial on blepharospasm published on the front page of the most widely read "medical journal," *The Wall Street Journal* (52). We were impressed with the power of the press and Mattie Lou Koster; three sentences referring to the Anderson myectomy provided more exposure for this operation than all the scientific papers and book chapters we have written on this subject. Mattie Lou Koster, her daughter, Mary Lou Thompson, and the BEBRF have demanded awareness of this disease, organized support groups for patients and families, and funded research to help find the cause and better treatments for this disease. Most of the improvements in diagnosis, therapy, and understanding of blepharospasm in the last 15 years can be attributed directly or indirectly to Mattie Lou Koster and the BEBRF. She brought this disabling disease out of the closet and to the attention of patients, physicians, and the public. All newly diagnosed patients with blepharospasm should be placed in touch with the BEBRF to provide education, support, and treatment. Forty-three percent of patients were informed about the BEBRF by their doctor. Thirty percent had read about the BEBRF in a newspaper. Eighteen percent had heard from a friend, and 5% had learned via television. Ninety percent of patients felt that the BEBRF had provided them with significant help and relief, or a 90% improvement rate. The patient acceptance rate for the BEBRF was 96%.

Drug Therapy

Of the 1,653 patients with blepharospasm responding to our questionnaire, 1,162 (70%) had tried oral therapy. Forty-three percent of the patients trying drug therapy noted improvement. Of those noting improvement, 52% noted less than 50% improvement, 22% noted 50% to 75% improvement, 14% noted 75% to 90% improvement, and 12% noted more than a 90% improvement with one or more drugs. The improvement was usually of limited duration. Of the patients who tried drugs, the patient acceptance rate was 57%. The 57% acceptance rate is higher than the 43% improvement rate because of the simplicity of drug therapy and the logical desire of patients to take a pill to cure a disease. Obviously, patients would prefer pills to shots or surgery if efficacy were similar.

Table 1 presents the percent of patients improved by various drugs and the number who tried each drug. There is a poor correlation between the efficacy of a drug and the number of times it was prescribed. Hopefully, Table 1 will provide physicians with patient feedback regarding drug therapy.

Botulinum-A Toxin Therapy

One-thousand eighty-three patients (66%) had undergone botulinum-A toxin treatment. Eighty-six percent of these patients stated they were improved by botulinum-A toxin treatment. Of the 86% who were improved, the effect lasted less than 2 weeks in 8%, 2 to 4 weeks in 5%, 1 to 2 months in 22%, 3 to 4 months in 44%, and more than 4 months in 22%. In the botulinum-A toxin responders, 24% noticed less than 50% improvement. Thirty-two percent noted 50% to 75% improvement, and 44% noted 75% to 90% improvement. It is surprising that no patient in this study reported over 90% functional improvement in eyelid squeezing with botulinum-A toxin. Although 86% of patients im-

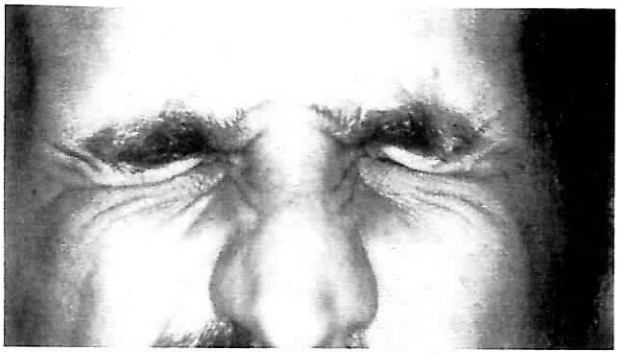


FIG. 11. Preoperative full myectomy patient with severe blepharospasm and mild Meige syndrome.

proved by using botulinum-A toxin, the patient acceptance rate was 95%. This demonstrates the simplicity and high level of patient satisfaction with botulinum-A toxin.

Myectomy Surgery

Three hundred thirty patients (20%) underwent full upper myectomy surgery. Fifty percent of these patients (165) also had lower myectomy surgery. Limited myectomy patients were excluded from this study. Even though we had hoped to evaluate patients who were primarily treated by myectomy, 34% of patients undergoing full myectomy surgery had failed botulinum-A toxin, and 64% had failed drug therapy. This selects for a more difficult group of patients. Failure of other modes of therapy selects for a higher incidence of patients with apraxia of lid opening as well as more extensive facial squeezing disorders. At present, virtually all of our patients presenting for full myectomy have "failed" botulinum-A toxin and drugs.

Of the patients undergoing a full myectomy operation, 88% noted improvement. Twenty-seven percent noted less than 50% improvement, 21% noted 50% to 75% improvement, 29% noted 75% to 90% improvement, and 23% noted more than 90% improvement. Eighteen percent of patients required an additional touch-up surgery or a revision after myectomy operations. Thirty-eight percent of patients required botulinum-A toxin after the full myectomy operation. Considering that 50% of myectomy patients had not had lower myectomy surgery, it is likely that many of the myectomy patients requiring botulinum-A toxin were in this group. It is also likely that results in the myectomy group would be improved if all patients had undergone lower myectomy.

The patient acceptance rate was 82% with full myectomy surgery, which is less than the 88% improvement rate. This is presumably the result of the negative side effects and complications of surgery as well as the psychology of surgery and the extended recovery and healing time compared to drugs or botulinum-A toxin. It usually requires months for complete healing after a full myectomy. Patients continue to improve in functional disability as well as cosmesis for 6 months to 1 year after full myectomy surgery.

The disability caused by blepharospasm and the effect of treatment is an important consideration. Of the 29% of patients who were no longer able to work, 69% were able to return to work after myectomy surgery, 61% after botulinum-A toxin therapy, and 48% after drug therapy.

There are several negative side effects of myectomy. They are predictable and occur to some degree in all patients. The one causing the most concern is lymphedema, which may be present for days, months, or, rarely, even years in some patients. Lymphedema is much worse when an upper and lower myectomy is performed at the same setting (Figs. 11 and 12). At present we do not perform full upper and lower myectomy operations at the same surgical setting. Should lower eyelid surgery be required, we wait at least 6 months.

Another negative side effect of full myectomy is supraorbital anesthesia or hypesthesia. It is nearly impossible to remove adequately the corrugator and procerus muscles without damage to the supraorbital nerve. Supraorbital anesthesia improves with time in most patients.

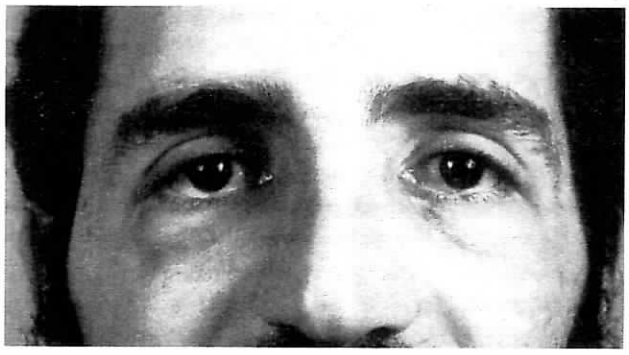
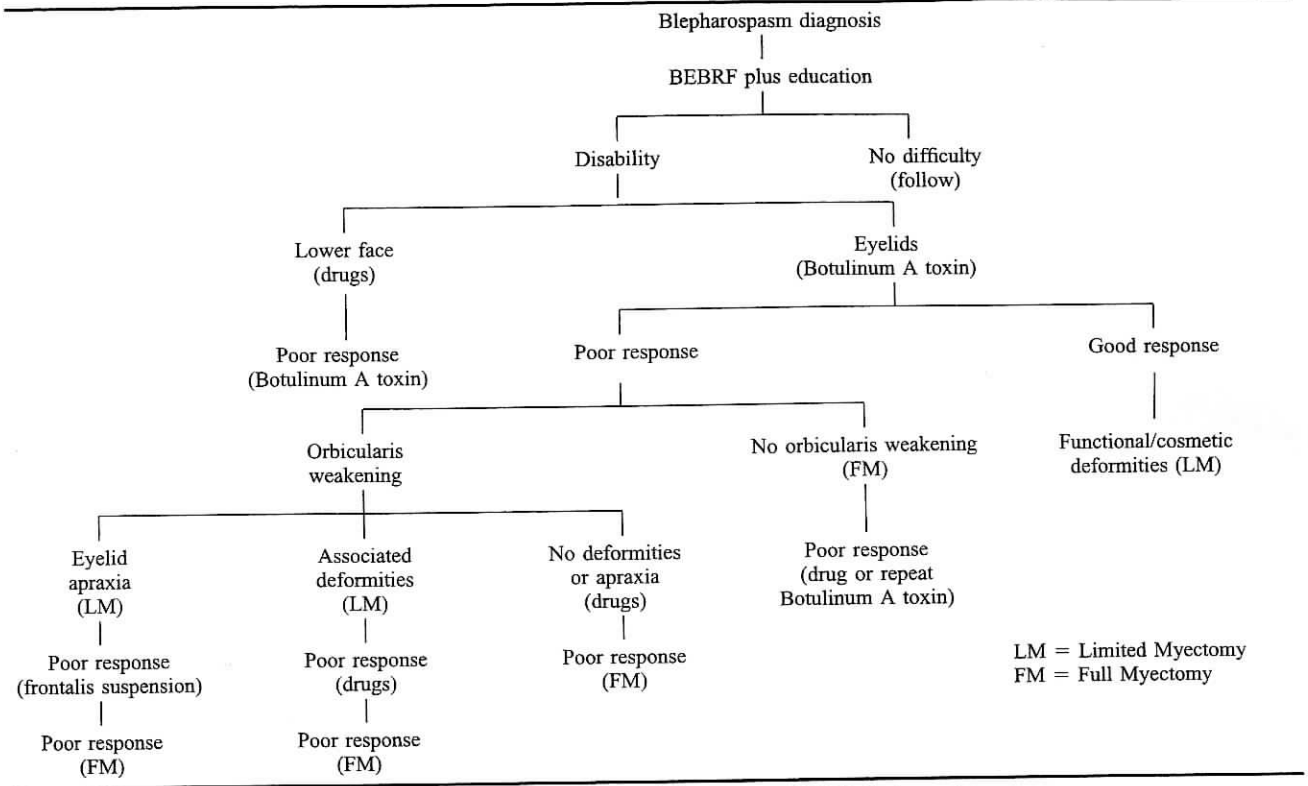


FIG. 12. Same patient as in Figure 11, 6 months after full myectomy surgery, with both upper and lower myectomy performed at the same setting. Note good position of brows and upper eyelids and acceptable scars. Note persistent lymphedema in eyelids (especially the lower eyelids) and mild lower lid retraction. To decrease these complications and negative side-effects, the lower eyelids are now operated at least 6 months after the upper eyelids.

TABLE 2. *Outline for the treatment of blepharospasm*



BEBRF, Benign Essential Blepharospasm Research Foundation; FM, full myectomy; LM, limited myectomy.

Decreased orbicularis function and closure is a necessary negative side effect, but may result in corneal exposure and increased dry eyes, necessitating more lubricants. This is temporarily the case in most patients. It is surprising that a permanent increase in dry eyes and exposure does not always occur with myectomy and botulinum-A toxin. The eyelids may act as better ''windshield wipers'' or resurfacing agents for the cornea after relieving the spasms, and may open and close in a more physiologic fashion after healing. The lacrimal pump is weakened, which maintains more tears around the eyes and may help dry eyes. Punctal occlusion is very useful in those experiencing dry-eye blepharospasm.

A predictable side effect is loss of volume and wrinkles of the eyelid tissues. After complete healing, this is usually a positive benefit in comparison with the preoperative state (Figs. 11 and 12). In most cases, cosmesis is improved because of the absence of wrinkles and excess tissues as well as correction of drooping in the eyelids and brows. The limited myectomy gives a more predictable cosmetic improvement. However, it only provides adequate relief in patients who are also responding to botulinum-A toxin.

The complications experienced in over 500 myectomy operations by one of the authors (R.L.A.) include: infection, hematoma or hemorrhage, brow hair loss, skin loss requiring skin graft, ptosis, upper lid retraction, lower lid retraction, trichiasis, and canthal deformity. Fortunately, except for some permanent cosmetic disfigurement, most of these complications were minor or correctable with additional surgery. There was no occurrence of permanent visual loss, and despite the extensive nature of a full myectomy operation in an older patient population, there was no occurrence of death or permanent disability from surgery.

It is obvious from this study and our experience that many patients require all four forms of therapy to obtain maximum relief. It is unfortunate that some patients are forced by physicians into a single treatment longer than it is providing adequate relief because of a lack of expertise or information regarding other treatments. Although patients and physicians would prefer not to have surgery, in fact, myectomy provided a higher improvement

rate than botulinum-A toxin, and should not be considered a last resort. There are many patients with lower facial involvement where drug therapy may provide relief in addition to other treatments. If a physician is not comfortable with drug therapy, the patient should be referred to a neurologist who is willing to try different drugs. Therapy must be tailored to the patient's needs. We recommend the BEBRF and botulinum-A toxin as the first treatment for patients with blepharospasm. If a patient fails botulinum-A toxin therapy, then it is important to differentiate whether the "failure" is the result of inadequate orbicularis weakening or associated problems and deformities. This can be evaluated by having the patient return for evaluation 2 or 3 weeks after injection when the botulinum-A toxin should be maximally effective. The patient is instructed to squeeze the eyelids shut as tight as possible, and the amount of orbicularis function is evaluated by forcibly prying the eyelids open. If near normal orbicularis force is generated, then the botulinum-A toxin is ineffective, and a full myectomy is recommended. If the eyelids can be pried open easily, the botulinum-A toxin is providing relief of spasm, and the other associated conditions must be evaluated and treated in addition to a full myectomy. When several months are allowed for the botulinum-A toxin to wear off completely, many patients who feel they are botulinum-A toxin "failures" realize that botulinum-A toxin was helping spasms to some degree. The baseline of most patients' blepharospasm worsens with time. This works against any mode of therapy, as the patient feels that the therapy is no longer working as well, whereas in fact the disease has progressed.

Many patients with blepharospasm have cosmetic and functional deformities of the eyelids, such as brow ptosis, ptosis, dermatochalasis, canthal tendon laxity, and eyelid malpositions, which can be as much of a functional problem as the blepharospasm (Fig. 7). Years of forceful squeezing result in these functional and cosmetic deformities, and botulinum-A toxin may aggravate these deformities. Such patients benefit from a limited myectomy operation. The orbicularis muscle is removed from an upper eyelid incision along with the excess skin, and the levator aponeurosis is tightened (Fig. 10). If brow elevation is required, the available orbital orbicularis muscle is also removed. Patients who respond to botulinum-A toxin and undergo a "limited myectomy" for associated deformities are the most satisfied group. The results are almost as good as with cosmetic surgery, with only weeks rather than months for complete healing. Although limited myectomy patients were not evaluated in this questionnaire, we have found the patient acceptance rate for limited myectomy to be even higher than for cosmetic surgery. These patients have greater functional and cosmetic deformities than most cosmetic patients, and are grateful for the functional as well as cosmetic improvement.

Our present outline for the treatment of patients with blepharospasm is shown in Table 2. All newly diagnosed patients should be registered with the BEBRF for education regarding their disease and support. If blepharospasm is the main problem, then botulinum-A toxin is the primary treatment. If lower facial, neck, or body spasm is the main problem and eyelid spasm is a minor or secondary component, then drugs should be tried first. If a patient has both eyelid and lower facial components, then botulinum-A toxin as well as drugs may be required. If a patient with blepharospasm is a nonresponder to botulinum-A toxin, then we recommend the full myectomy operation. Many patients with blepharospasm who are botulinum-A toxin nonresponders will require an upper as well as lower myectomy, but at least 6 months between operations is advised. Some patients who are considered botulinum-A toxin nonresponders may be converted to botulinum-A toxin responders in their lower eyelids after an upper full myectomy. If a patient is a "failure" of botulinum-A toxin or is obtaining inadequate relief, but the toxin is providing orbicularis weakening, then the patient usually has associated functional and cosmetic deformities, apraxia of lid opening, or both, and a limited myectomy is recommended.

CONCLUSIONS

In summary, the information gathered from studying the largest group of patients with blepharospasm to date and the personal experience of one of the authors (R.L.A.) has presented many important findings.

1. Blepharospasm remains a frequently missed diagnosis.
2. Blepharospasm is a localized dystonia frequently associated with more extensive facial or even generalized dystonias.
3. The specific cause and control center for blepharospasm is unknown (probably the basal ganglia region), but the disease is multifactorial in its origin and manifestation.

4. A defective circuit theory of blepharospasm origin and management rather than a defective locus theory is presented.
5. Blepharospasm is a vicious cycle, with an afferent limb, central control center, and efferent limb, and therapy should be directed at all parts of the cycle to obtain maximum relief.
6. Apraxia of lid opening is the most difficult disorder associated with blepharospasm to manage, and there is a high incidence in botulinum-A toxin failure.
7. There are four useful treatments for blepharospasm. The BEBRF has a 90% patient improvement rate and 96% patient acceptance rate. All patients should be registered with this support group. Botulinum-A toxin has become the first line blepharospasm therapy, with an 86% patient improvement rate and 95% patient acceptance rate. Full myectomy is the best surgical treatment and most permanent form of therapy, with an 88% patient improvement rate and 82% patient acceptance rate. Drugs are seldom a primary treatment for blepharospasm, but are a primary form of therapy in lower facial squeezing, with a 43% improvement rate and a 57% patient acceptance rate. All treatments must be tailored to a patient's needs, and some patients require all four to obtain maximum relief.
8. Although blepharospasm at present is not curable, it is treatable with well-proven therapies. In incurable, variably progressive, stressful diseases, many superstitions or even charlatan treatments arise. Patients and physicians should strive for new and better treatment modalities, but demand scientific testing to confirm safety and efficacy. Considering the progressive, multifactorial, degenerative, and dystonic nature of blepharospasm, it is unlikely that a "cure" will be found, but better prevention and causes and treatments will be identified.
9. The full myectomy is a complete removal of the protractors (squeezing muscles) around the eyelids, and is the best surgical and most permanent treatment for patients with blepharospasm who do not respond to botulinum-A toxin. The limited myectomy is an excellent adjunct to botulinum-A toxin and corrects the functional and cosmetic deformities, which may be as much of a problem as the blepharospasm.
10. Mattie Lou Koster and the BEBRF, which she founded, have helped more patients than any other organization.

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