
Special Topics

Blepharospasm and Its Treatment, with Emphasis on the Use of Botulinum Toxin

Gary E. Borodic, M.D., and David Cozzolino

Boston, Mass.

CLINICAL ASPECTS OF THE PROBLEM

Blepharospasm is defined as involuntary eyelid closure resulting in significant visual disability. When blepharospasm is encountered in ophthalmologic practice, the usual cause is an irritating eye disease such as iritis, corneal ulceration, keratitis, or other form of ocular surface disease. When ophthalmologic examination fails to reveal a cause for the blepharospasm, the involuntary closure of the eyelids is described as *neurologic blepharospasm*, i.e., a primary disorder of the blink reflex mechanism which controls frequency and intensity of orbicularis oculi muscle contraction. Symptoms of neurologic blepharospasm can be so debilitating that routine daily activities such as driving can prove to be stressful in early stages and progress to actively preventing independent ambulation without the assistance of a cane or another individual in advanced stages. The symptoms of involuntary eyelid closure may be very sporadic so that at times the spasmodic contractions of the orbicularis oculi force the eyelid closed (Fig. 1), while at other times no apparent abnormality is present. Because of the intermittent nature of this disorder and the absence of clearly objective findings on ocular examination, the condition is often misdiagnosed as dry-eye syndrome, ocular allergy, or chronic blepharitis.

From a historic perspective, most cases of primary involuntary eyelid closure were initially thought to be psychosomatic in nature, without an organic basis.¹ Although most cases of facial dyskinesia and blepharospasm are not psychosomatic in origin, there is a definite subset of patients in which blepharospasm may represent a psychologic conversion reaction to emotional stress.² Since computerized axial tomograms are

usually normal and magnetic resonance imaging has failed to demonstrate any consistent structural brain abnormalities, the diagnosis must be made on a clinical basis. Many younger patients with blepharospasm have had a traumatic situation just prior to the onset of blepharospasm or have had a prior history of conversion hysteria. The typical patient with neurologic blepharospasm, however, demonstrates clinical characteristics quite distinct and different from a patient with a psychiatric disorder. Neurologic blepharospasm usually begins in patients in early or late middle age (greater than 50 years old) without a prior psychiatric history and without a clear preceding emotional event. The condition is chronic in nature, progressing over a period of months to years. Very often there are associated involuntary movements in facial muscles other than the orbicularis oculi (e.g., frontalis muscle, orbicularis ori) as well as in the muscles of the head

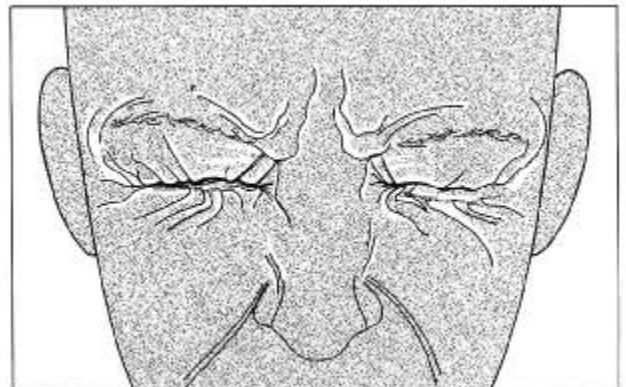


FIG. 1. Bilateral involuntary contractions of the orbicularis oculi muscles impair vision. The periocular contractions are not necessarily limited to muscles of the upper face but may involve other muscles of the head and neck region.

and neck.³⁻⁵ Occasionally, changes in the quality of the voice (20 percent) can be associated with involuntary blepharospasm.⁶ Blepharospasm has been associated with other more typical diseases of the basal ganglia such as Parkinson's disease,⁷ hereditary basal ganglia disease,⁸ tardive dyskinesia,⁹ and rarely, lesions of the rostral brain stem.¹⁰ There has been a loose hereditary component to this disorder; the authors have observed neurologic blepharospasm in both identical twins. When neurologic blepharospasm is associated with involuntary movements of other areas of the face, head, or neck, the term *cranial-cervical dystonia* may be used, which is equivalent to the eponyms Meige's syndrome, Wood's syndrome, and Brueghel's syndrome.⁴⁻⁶ The involuntary movements characteristic of cranial-cervical dystonia may begin in the lower facial musculature and in the muscles of the neck and progress to involve the orbicularis oculi and produce visual symptoms. In the rare patient with cranial-cervical dystonia, the involuntary contractions in the neck can be so forceful that the upper airway may be compromised, requiring a tracheostomy.

Hemifacial spasm is a distinct form of involuntary facial movement disorder which is limited to the muscles innervated by one facial nerve. The involuntary contractions are very characteristic in that all the facial muscles supplied by the motor portion of one facial nerve contract synchronously. Because the stapedius muscle also receives its innervation from the motor portion of the seventh cranial nerve, these patients may complain of low-pitched auditory hallucinations from the ear on the side of the involuntary facial spasms. As with various forms of bilateral facial spasms, hemifacial spasm is intermittent in intensity of symptoms and may progressively worsen over a number of years. Constant twitching of one side of the face is more prominent in some patients, while an intermittent tonic contraction of hemifacial muscles represents the major finding in other patients (Fig. 2). When the eyelid closes, the nasolabial folds retract superiorly, giving a typical distortion of facial contour (Fig. 2). Occasionally, contraction of the mentalis muscle produces an intermittent lip ectropion. These patients frequently have subtle evidence of hemifacial weakness when the strength of the muscles is assessed between spasms. The etiology of hemifacial spasm has not yet been clearly elucidated, but most evidence suggests that an area of demyelination or damage is created on the intra-

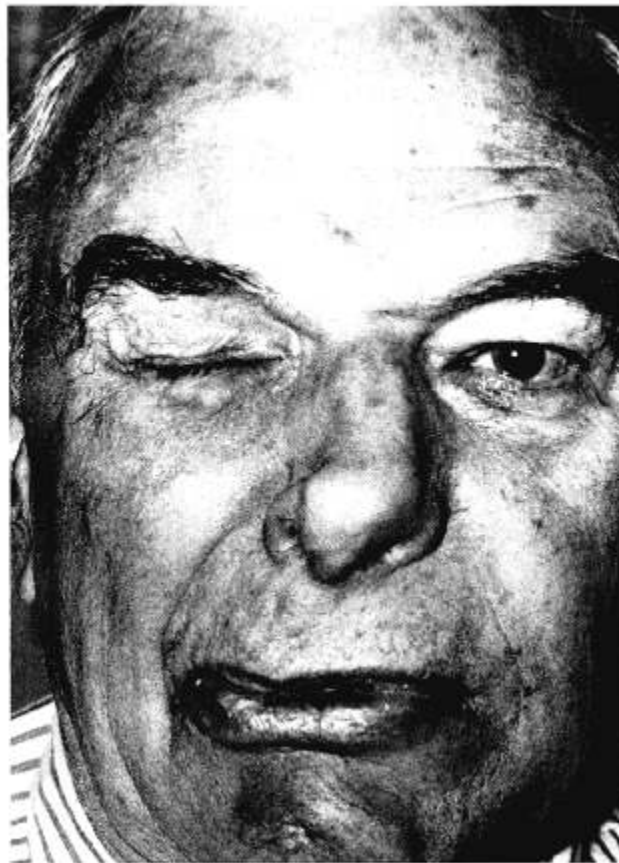


FIG. 2. Fifteen-year history of hemifacial spasm. Synchronous contractions of all muscles supplied by one facial nerve lead to this deformity. Characteristic disfigurements include closed eyelid, elevated nasolabial fold, and lower lip ectropion.

cranial portion of the seventh nerve which leads to the foci of ectopic excitation.^{11,12} Electromyographic analysis of the facial muscles in these patients demonstrates denervation, which accounts for the weakness observed on physical examination.¹² The results of electromyography also have suggested that the ephaptic transmission (side to side) may account for the synchronous nature of the contractions.¹² The defect within the intracranial portion of the seventh nerve has been postulated to be caused by an aberrant or tortuous blood vessel.¹¹ Occasionally, hemifacial spasm has been associated with a space-occupying lesion within the posterior fossa in close apposition to the intracranial portion of the facial nerve. Aneurysm,¹³ arteriovenous malformation,¹⁴ and cerebral pontine angle tumors have been described.¹⁵ The actual incidence of space-occupying lesions within the posterior fossa is very small (less than 1 percent) in the absence of other cranial nerve dysfunction.¹⁶

Hemifacial spasm should be distinguished from two conditions: aberrant regeneration of the facial nerve and orbicularis myokymia. Aberrant regeneration of the facial nerve occurs after Bell's palsy, facial nerve dysfunction following removal of acoustic neuroma, and facial nerve trauma. The involuntary blepharospasm represents abnormal synkinesis, i.e., an involuntary movement that occurs when a voluntary movement is initiated. When these patients smile or chew using their lower facial muscles, there is involuntary closure of the eyelid on the side of the facial nerve pathology (inverse Marcus-Gunn phenomenon). These patients also frequently demonstrate aberrant regeneration within the autonomic nerves. When eating and while salivating, the eye on the side of the nerve injury develops epiphora (tearing). Although there is involuntary movement in the orbicularis muscle, this involuntary movement occurs only in association with movements initiated within the lower face. The involuntary contractions of hemifacial spasm are spontaneous and not associated with or initiated by other facial movements. Myokymia of the orbicularis muscle results from spontaneous fibrillations and undulations of the muscle not generating enough force to actually close the eyelid. Orbicularis myokymia is very common, remains well localized, and has no pathologic significance.

ANATOMIC CHANGES WITHIN EYELID CAUSED BY BLEPHAROSPASM

Constant involuntary contraction of the orbicularis oculi muscle often has adverse consequences on eyelid anatomy. With bilateral blepharospasm (Meige's syndrome), the constant contractions lead to hypertrophy of the orbicularis oculi. Probably because of the partial denervation, hypertrophy of the orbicularis oculi muscle is not a feature of hemifacial spasm. The antagonists to the orbicularis oculi are the levator palpebral superioris muscle and Mueller's muscle for the upper lid and the inferior lid retractors for the lower lid. Because of the constant squeezing of the eyelids, the tendons of the lid retractors tend to disinsert at the tarsal plate (Fig. 3). The clinical consequences of this anatomic change are different for the upper and lower eyelids. For the upper eyelid, disinsertion of the levator aponeurosis results in involuntal ptosis (Fig. 4). Ptosis of the eyelid may further impair vision in a patient with preexisting blepharospasm. Involuntal ptosis is associated with other

deformities of the eyelid, such as superior sulcus deepening from retraction of the preaponeurotic fat pad within the superior orbit and retraction of the superior lid folds resulting from disinsertion of the levator aponeurosis. In the lower eyelid, disinsertion of the lid retractor tendon (capsulopalpebral fascia) from the tarsal plate can be associated with involuntal entropion. The spasms of the orbicularis oculi muscle against a disinserted lower eyelid retractor can invert the lower lid margin, with the lashes directed toward the cornea (Fig. 5). The involuntary blepharospasm is further aggravated by corneal erosion from the inverted lid margin. Chronic corneal erosion may lead to secondary infection with ulceration and serious loss of vision (Fig. 5).

THERAPY FOR BLEPHAROSPASM

Principle for Initiating Treatment

Prior to recommending any medical or surgical therapy for blepharospasm, the patient should be questioned as to the chronicity of the blepharospasm, the extent to which the blepharospasm impairs routine activities such as driving and independently walking, the presence of preexisting ocular disease, and prior history of psychiatric illness or recent emotional trauma. All patients should have a complete ocular examination to rule out a primary ocular disease causing secondary blepharospasm. If the involuntary movements are of recent onset (several weeks to several months), it may be better to wait and establish a clear, consistent objective finding prior to initiating therapy. Conversion hysteria will frequently resolve spontaneously in several weeks, whereas true neurologic blepharospasm persists and occasionally worsens over several months. Younger patients (young adults and children) with bilateral blepharospasm are particularly suspect for an emotional basis for blepharospasm. The degree of impairment needs to be assessed. Major surgery or botulinum toxin may not be appropriate if the blepharospasm causes only minor impairment.

An accurate diagnosis should be made, and the decision to pursue neurologic evaluation should be based on other neurologic signs or symptoms. Table I outlines the most common differential diagnoses.

Medical Therapy

Various neuroleptic medications used to treat other forms of movement disorders have been

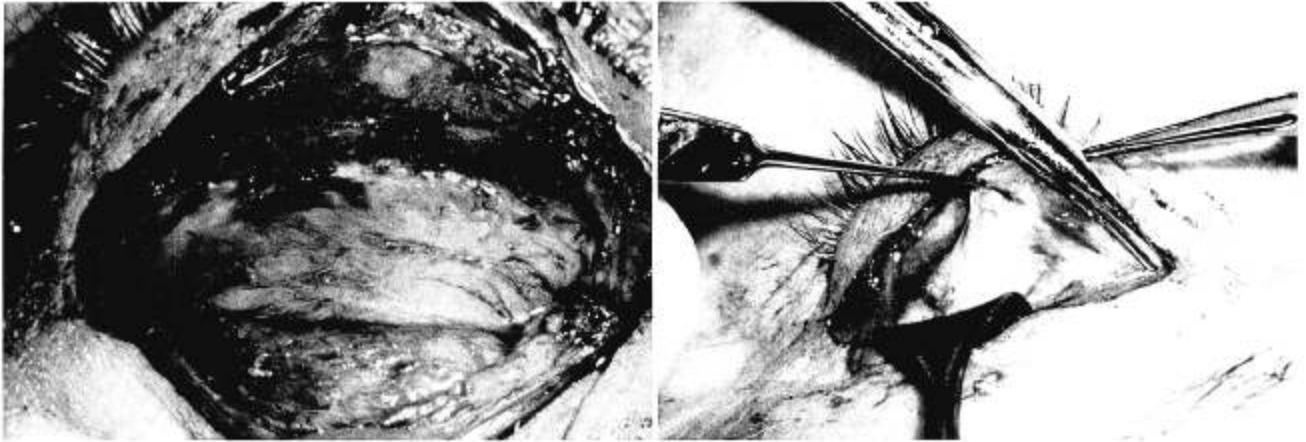


FIG. 3. Disinsertion of the levator aponeurosis in a blepharospasm patient. The leading edge of the levator aponeurosis (arrows) has separated from its usual insertion at the tarsal plate (arrowhead). The band of muscle between the levator aponeurosis and tarsal plate is Mueller's muscle.



FIG. 4. A patient with involutorial ptosis resulting from blepharospasm. Note the elevation of the lid fold in the left eye and the deepened left superior sulcus. The distance between the corneal reflex and lid margin is substantially reduced in the left eye, indicating significant ptosis.

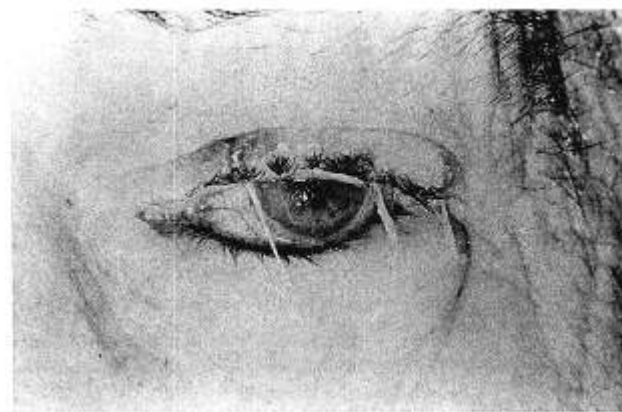


FIG. 5. This patient's blepharospasm was severe and associated with other involuntary movements of the lower face. Because of disinsertion of the lower eyelid retractors, the patient developed an entropion which resulted in corneal ulceration and infection.

TABLE I
Differential Diagnoses for Blepharospasm

Secondary to irritating ocular disease
Essential blepharospasm (bilateral movement)
Meige's syndrome (cranial-cervical dystonia)
Hemifacial spasm (unilateral facial contraction)
Aberrant regeneration of the facial nerve
Facial myokymia
Conversion reaction (emotional)

tried. The results of this therapy are usually less than satisfactory. Jankovic and Ford,¹⁷ in reviewing multiple forms of neuroleptic drugs, have found that Clonopin and Artane, the medications with the best results, produced a long-term beneficial response at a rate of 25 percent. For hemifacial spasm, neuroleptic medications have had a poor result. In addition to their lack of efficacy, the long-term use of these medications may lead to systemic toxicity (e.g., hepatic necrosis with Tegretol and urinary retention with Artane).

Surgical Therapy

When blepharospasm becomes visually significant and routine activities are impaired, surgical therapy can be considered. Various procedures have been tried to attempt to relieve the blepharospasm without creating substantial disfigurements to other areas of the face. Facial neurectomy was the earliest procedure used to treat this disorder.¹⁸⁻²⁰ Because the facial neurectomy produced paralysis on both sides of the facial region, such disfigurements as mouth drop, paralytic ectropion, lagophthalmos, masklike face (facial diplegia), and brow ptosis are not

uncommon. Furthermore, the facial nerve tended to reinnervate facial muscles; hence the necessity for multiple procedures is common. In order to attempt to limit the paralytic facial deformity caused by complete neurectomy, attempts to preform a partial facial neurectomy were made. Cutting the temporal branch of the facial nerve (differential neurectomy) or stripping the lateral portion of the orbicularis oculi muscle was preformed.^{21,22} Despite the problem with reinnervation from subsequent nerve growth, many of the partial facial neurectomies were probably ineffective because of the nature of the innervation to the orbicularis oculi. The work of Fugita,²⁵ which consisted of careful dissections of the superficial portions of the facial nerve, suggested that the orbicularis oculi muscle receives facial nerve innervation not only from the temporal branch but also from multiple ramifications of the zygomatic and buccal branches. Motor point testing²⁶ of the facial nerve demonstrates that motor nerve fascicles enter the muscle superolaterally as well as inferonasally. If these anatomic and physiologic findings are correct, then in order to effectively denervate the orbicularis oculi muscle, temporal, buccal, and zygomatic branches would need to be cut, and some facial deformity would almost certainly accompany any facial neurectomy extensive enough to be effective for a prolonged period.

Another surgical approach to blepharospasm that has been advocated by Gillum and Anderson²⁷ involves surgical intervention on the protractor and retractor muscles of the eyelid. A blepharoplasty type of incision is made between the upper lid fold and the brow. Surgical dissection is taken down to the anterior tarsal surface. The orbicularis muscle is stripped in the pretarsal, preseptal, and preorbital regions (Fig. 6). Surgical dissection is then taken down through the orbital septum to the preaponeurotic fat pad. The levator aponeurosis is identified, and if it is disinserted, it is advanced and resutured to the tarsal surface. Tucking of the levator aponeurosis can further tighten the upper lid retractors. A lateral block of the orbicularis oculi muscle is removed down to the periosteal covering of the lateral orbital rim. A direct brow lift incision is made to further facilitate orbicularis stripping and to accomplish a maximal degree of brow lift and facilitate stripping of the orbicularis muscle under the brow (Fig. 7). The blepharoplasty incision is closed with skin sutures taken through the levator aponeurosis, creating a lid fold and



FIG. 6. Pretarsal orbicularis muscle is excised in a myectomy procedure.



FIG. 7. Direct brow lift incision is made to facilitate orbicularis stripping and elevate the brow region above the superior orbital rim.

further reinforcing the insertion of the upper eyelid retractor. The procedure may be extended to involve stripping of the orbicularis oculi of the lower eyelid with reinforcement of the attachment of the capsulopalpebral fascia to the inferior border of the tarsal plate.

The procedure described by Gillum and Anderson²⁷ has been noted to be effective in 85 percent in the short term. Complications include numbness in the region supplied by the supraorbital nerve, lagophthalmos, and corneal exposure. The most common adverse effect is persistent symptoms despite the effort to weaken the orbicularis muscle and tighten the retractors. Occasionally, the procedure needs to be repeated.

A modification of this procedure has been advocated by McCord et al.²⁸ The direct brow lift is replaced by a corneal flap, and the orbicularis, procerus, and glabella muscles are stripped

from the underside of the corneal flap. In addition, a coronal scalp resection can give a substantial degree of brow lift prior to closing the wound with surgical staples.

The surgical treatment of hemifacial spasm has been advocated by Janetta et al.¹¹ The procedure involves approaching the brain stem by means of a posterior craniotomy. Surgical exposure of the seventh cranial nerve is accomplished with an operating microscope, and vessels in close proximity to the facial nerve are identified and isolated from contact with the nerve trunk. This neurosurgical procedure has been described as 80 to 90 percent effective in competent hands. The disadvantages of this form of therapy are evident in that a craniotomy is required with attendant surgical complications. The risk-benefit ratio for hemifacial spasm and craniotomy may be less than favorable.

BOTULINUM TOXIN AND FACIAL SPASTIC DISEASE

Botulinum toxin was introduced to clinical medicine by Dr. Alan Scott in 1978 for the initial purpose of treating childhood strabismus.²⁹ The application to facial dyskinesias came several years later.³⁰ The toxin acts essentially to weaken striated muscle, decrease muscle tone, and relieve spasms. Because the muscle is only partially weakened, enough strength remains so that a treated muscle may still be able to perform its primary action. Figure 8 compares striated muscle from a section of orbicularis from a patient treated with four cycles of botulinum toxin to that of a section of orbicularis from a routine

ptosis patient. Note the decrease in the diameter of the muscle fibers and the increase in fibrous tissue between various fiber bundles.

Botulinum toxin has been shown to exist as multiple immunotypes.²⁹ Type A is the form of the toxin that has been used in clinical research to date.

Several unique pharmacologic properties have made botulinum toxin particularly effective in the treatment of facial movement disorders. Unlike conventional surgical procedures, in which motor nerves are severed, tendons tightened, or muscle layers removed, the degree of weakening from denervation muscular atrophy can be titrated directly according to dose and injection intervals of the toxin. Furthermore, unlike surgical procedures, the effects of botulinum toxin are reversible. The drug is unique among the category of myoneural blocking agents in that it has an activity duration of 3 to 6 months.³¹ The amount given can be modulated according to the intensity of the involuntary movements, the diagnosis, and individual patient responses.

Botulinum toxin acts as a myoneural blocking agent which prevents the release of acetylcholine from presynaptic vesicles coupled with nerve impulse.³² The drug is a protein with a molecular weight equal to 150,000, having a light and heavy chain.³³ The light chain is thought to contain the binding site, whereas the heavy chain is thought to be internalized within the cellular membrane. Because acetylcholine release is blocked, the force of muscular contractions is reduced. Furthermore, denervation-related effects begin to take place, such as narrowing in

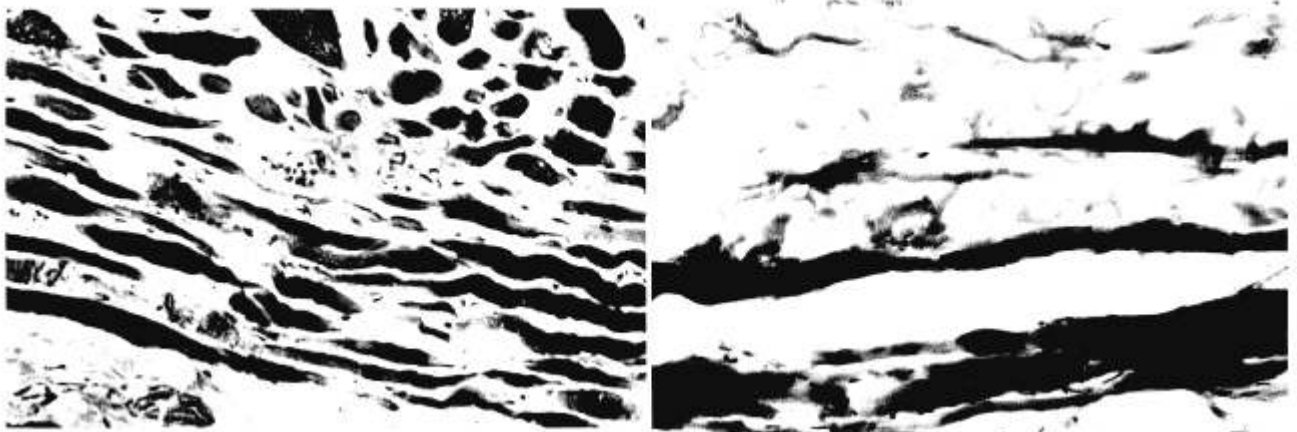


FIG. 8. (Left) Section of orbicularis muscle in tissue removed from routine repair of involutional ptosis. Note the normal fiber size and connective-tissue configuration. (Right) Orbicularis muscle specimen in a blepharospasm patient who has received four cycles of botulinum toxin therapy. Note the decreased fiber size and the increased fibrous tissue in the connective-tissue matrix.

muscle fiber diameter and muscle fibrosis. Whether the myoneural blockade has any further role with respect to interference with stretch-receptor feedback loops into the central nervous system remains to be determined.

The toxin is quantified against a biologic standard. One international unit (I.U.) is equivalent to the LD₅₀ for a white mouse.²⁹ It is stored at a temperature of 4°C in a freeze-dried form and is reconstituted with saline just prior to injection.

Method of Injection for Blepharospasm

Scott et al.³⁰ have determined the conventional sites of injection for blepharospasm based on experience. Generally, a starting dose of 10 to 20 I.U. is injected along four to six sites as shown in Figure 9.^{34,35} Booster injections are sometimes necessary to achieve sufficient results. Injections above the brow are given only if significant involuntary movements are recurring in this region. For lid injections, it is important to stay as close to the lash line as possible and away from the midline of the lid. If the toxin is injected too close to the upper lid fold, diffusion through the orbital septum can weaken the levator palpebrae superioris muscle and cause ptosis. If the toxin is injected too medially in the lower lid, the nasolacrimal pumping mechanism can be excessively weakened, resulting in epiphora. Also, the origin of the inferior oblique muscle lies very close to the anterior orbital rim of this region, and toxin diffusion can temporarily impair extraocular muscle function and result in diplopia. Based on the experiences of Borodic and Townsend³¹ with 94 patients, a list of local ocular complications is given in Table II. All complications have been transient to date. There have been no systemic complications in the dose range used to treat facial dyskinesias. Anaphylaxis has not been re-

TABLE II
Complications

Complication	No. of Patients
Ptosis	13 (severe 2)
Conjunctivitis	2
Epiphora	4
Aggravation of dry eye/exposure keratitis	2
Ectropion	1

Based on Borodic and Townsend, Analysis of 94 Patients with Neurologic Blepharospasm.³¹

ported, probably because of the small amount of protein needed to produce a therapeutic response; 2.5 I.U. is approximately equal to 1×10^{-9} gm—a lethal dose of botulinum toxin is of the order of 2×10^{-6} gm.²⁹

RESULTS

Generally favorable results are found by most investigators.^{30,31,34} Based on 94 patients followed an average of 11 months, Borodic and Townsend³¹ found only 5 dropouts, 2 from aggravation of dry-eye syndrome, 2 for lack of effectiveness, and 1 for no apparent cause. No

TABLE III
Duration of Action

Dose	BEB/Meige/Facial Dystonia	Hemifacial Spasm
First injection	2.7 months; $n = 35$; $s = 1.3$	5.3 months; $n = 14$; $s = 1.3$
Second injection	2.9 months; $n = 35$; $s = 1.1$	
Third injection	3.4 months; $n = 12$; $s = 1.3$	
Fourth injection	3.4 months; $n = 6$; $s = 1.0$	

Note: Based on Borodic and Townsend's 94 patients.³¹ n = number of subjects; s = standard deviation.

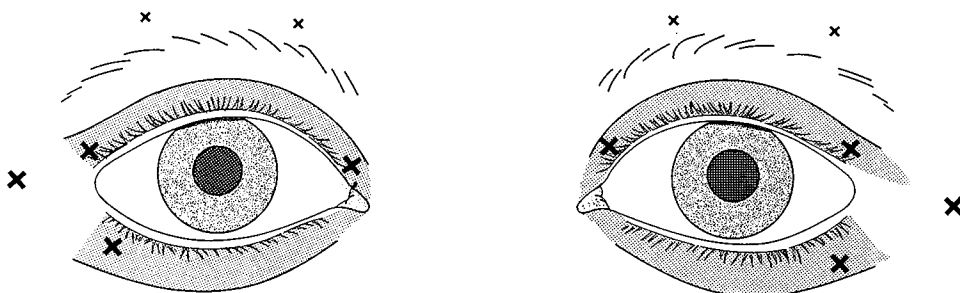


FIG. 9. Usual injection configuration for a patient with bilateral blepharospasm. Injections should be given away from the midline of the lid and close to the lash bases of the upper lid.

TABLE IV
Dose Requirements

Dose	BEB/Meige/Facial Dystonia	Hemifacial Spasm
First injection	25.51 I.U.; n = 61; s = 7	15.0 I.U.; n = 23; s = 4.8
Second injection	38.9 I.U.	19.0 I.U.; n = 9; s = 8.3
Third injection	48.5 I.U.; n = 17; s = 13.8	31.7 I.U.; n = 3
Fourth injection	61.9 I.U.; n = 8; s = 19	

Note: Based on Borodic and Townsend's 94 patients.³¹

patient with hemifacial spasm has dropped out. For benign essential blepharospasm and Meige's syndrome, the average duration of effect was 3.5 months (Table III), and for hemifacial spasm, the average duration of action was longer than 5 months. When symptoms of blepharospasm or involuntary facial movements recur, repeated injections are necessary. With repeated injections, the doses required to achieve the initial level of effectiveness appear to increase over the first several cycles (Tables IV and V) and eventually level off. Whether the early increase in dose requirement represents resistance locally in muscle, immunologic resistance, or a learning curve for the clinician is unknown. Antibodies to the toxin have been demonstrated when larger doses of the toxin have been given to patients.³⁶

Clearly, botulinum toxin has offered a promising method by which these patients can be effectively managed without surgical intervention or an adjunct to surgical intervention. The long-term effectiveness of the drug and the detection of any latent side effects still remain to be established.

Gary E. Borodic, M.D.
100 Charles River Plaza
Boston, Mass. 02114

TABLE V
Procedure: Starting Doses

Essential blepharospasm:	20 to 30 I.U. injected into pretarsal orbicularis
Meige's syndrome:	25 to 30 I.U. injected into pretarsal orbicularis, preorbital orbicularis, and lower facial muscles
Hemifacial spasm:	10 to 15 I.U. injected into pretarsal orbicularis and lower facial muscles

Note: If after 10 days therapy is not effective, injections are repeated at 25 percent higher dose.

REFERENCES

- Walsh, F. B., and Hoyt, W. F. *Textbook of Clinical Neuro-Ophthalmology*, 3d Ed. Baltimore: Williams & Wilkins, 1969.
- Trobe, J. D., Diamond, E. L., and Belar, C. D. Psychologic abnormalities in blepharospasm. *Adv. Ophthalmol.* 4: 137, 1985.
- Tolosa, E. S. Clinical features of Meige's disease (idiopathic orofacial dystonia: A report of 17 cases. *Arch. Neurol.* 38: 147, 1981.
- Marsden, C. D. Blepharospasm-romandibular dystonia (Brueghel's syndrome). *J. Neurol. Neurosurg. Psychiatry* 39: 1204, 1976.
- Meige, H. Les convulsions de la face, una forme clinique de la convulsions faciale, bilaterale et midiane. *Rev. Neurol. (Paris)* 70: 437, 1910.
- Jankovic, J. Etiology and differential diagnosis of blepharospasm and oromandibular dystonia. *Adv. Neurol.* 49: 103, 1988.
- Jankovic, J. Blepharospasm with basal ganglion lesions. *Arch. Neurol.* 43: 866, 1986.
- Jankovic, J., Kirkpatrick, J. B., Blomquist, K. A., et al. Late onset Hallervorden-Spatz disease presenting as familial parkinsonism. *Neurology* 35: 227, 1985.
- Jankovic, J. Drug-induced and other orofacial-cervical dyskinesias. *Ann. Intern. Med.* 94: 788, 1981.
- Jankovic, J., and Patel, S. Blepharospasm associated with brain stem lesions. *Neurology* 33: 1237, 1983.
- Janetta, P. J., Abbasy, M., Maroon, J. C., Ramos, F. M., and Albin, M. S. Etiology and differential microsurgical treatment of hemifacial spasm. *J. Neurosurg.* 47: 321, 1977.
- Nielson, V. K. Electrophysiology of the facial nerve in hemifacial spasm: Ectopic/ephaptic excitation. *Muscle Nerve* 8: 545, 1985.
- Katf, N. Y., and Tatlow, W. F. T. Two cases of vertebral-basilar aneurysm. *Can. Med. Assoc. J.* 92: 471, 1965.
- Dujonvy, M., Osgood, C. P., Faille, R., Bennet, M. H., and Kerber, C. Posterior fossa AVM producing hemifacial spasm. *Angiology*, 30: 425, 1979.
- Davis, W. E., Luteran, B. F., Pulliam, M. W., and Templer, J. W. Hemifacial spasm caused by cholesteatoma. *Am. J. Otol.* 2: 272, 1981.
- Wirtshaffer, J. Incidence of intracranial lesions in patients with hemifacial spasm. Presented at the American Academy of Ophthalmology, 1987.
- Jankovic, J., and Ford, J. Blepharospasm and orofacial dystonia: Pharmacological findings in 100 patients. *Ann. Neurol.* 36: 635, 1979.
- Rochen-Durigneaud, and Weill, A. Blepharospasm. *Rev. Neurol.* 15: 1296, 1907.
- Gurdjian, E. S., and Williams, H. W. The surgical treatment of intractable cases of blepharospasm. *J.A.M.A.* 91: 2053, 1928.
- Coleman, C. C. Surgical treatment of facial spasms. *Ann. Surg.* 105: 647, 1937.
- Frueh, B. R., Callahan, A., Dortzbach, R. R., et al. The effects of differential section of the VIIth nerve on patients with intractable blepharospasm. *Trans. Am. Acad. Ophthalmol. Otolaryngol.* 81: 595, 1976.
- Reynolds, D. H., Smith, J. L., and Walsh, T. J. Differential section of the facial nerve for

- blepharospasm. *Trans. Am. Acad. Ophthalmol. Otolaryngol.* 71: 656, 1967.
23. Callahan, A. Blepharospasm with resection of part of orbicularis nerve supply. *Arch. Ophthalmol.* 70: 508, 1963.
 24. Callahan, A. Surgical correction of intractable blepharospasm: Technical improvement. *Am. J. Ophthalmol.* 60: 788, 1965.
 25. Fugita, T. Über die Ausbreitung des N. faciales beim Menschen, Gegenbaws. *Mioph. Jahrb.* 73: 578, 1934.
 26. Borodic, G., Weiner, A., and Young, R. Motor point determination of the orbicularis oculi muscle. Presented at the Sixth International Meeting of the Benign Essential Blepharospasm Research Foundation, Cambridge, Mass., 1988.
 27. Gillum, W. N., and Anderson, R. L. Blepharospasm surgery: An anatomic approach. *Arch. Ophthalmol.* 99: 1056, 1981.
 28. McCord, C. D., Shore, J., and Putnam, J. R. Treatment of essential blepharospasm. II. A modification of exposure of a muscle-stripping technique. *Arch. Ophthalmol.* 102: 269, 1984.
 29. Scott, A. B. Botulinum toxin injections of eye muscles to correct strabismus. *Trans. Am. Ophthalmol. Soc.* 79: 734, 1981.
 30. Scott, A. B., Kennedy, R. A., and Stubbs, H. A. Botulinum: A toxin injection as a treatment for blepharospasm. *Arch. Ophthalmol.* 103: 374, 1985.
 31. Borodic, G., and Townsend, D. Dose-response relationships in botulinum toxin therapy. *Assoc. Res. Vision. Ophthalmol.* (Abstract) 1986.
 32. Kao, I., Drachman, D., and Price, D. L. Botulinum toxin: Mechanism of presynaptic blockade. *Science* 193: 1256, 1976.
 33. Simpson, L. L. The binding fragment from tetanus toxin antagonizes the neuromuscular blocking actions of botulinum toxin. *J. Pharmacol. Exp. Ther.* 229: 182, 1984.
 34. Elston, J. S., and Russell, R. W. Effect of treatment with botulinum toxin on neurogenic blepharospasm. *Br. Med. J.* 290: 1857, 1985.
 35. Townsend, D., and Borodic, G. Botulinum Toxin for Facial Spastic Disease. In A. Hornblass (Ed.), *Textbook of Oculoplastic Surgery*. Baltimore: Williams & Wilkins, 1988. Chap. 44.
 36. Brin, M. Personal communication, 1988.