EXCESSIVE OR ANOMALOUS EYELID CLOSURE

Unlike insufficient eyelid closure, which can be caused by neurologic, neuromuscular, or myopathic causes, excessive or inappropriate eyelid closure usually is neurologic in origin.

Essential Blepharospasm and the Blepharospasm-Oromandibular Dystonia Syndrome (Meige Syndrome; Brueghel Syndrome)

Blepharospasm is an involuntary closure of the eyelids evoked by contraction of the orbicularis oculi. When blepharospasm occurs in isolation without other evidence of neurologic or ocular disease, the condition is called essential blepharospasm (Fig. 24.55). When these focal dystonic eyelid movements spread to other cranial muscles, the syndrome is called blepharospasm-oromandibular dystonia or Meige syndrome (336–342). The disorder occurs most frequently in women over 50 years of age. Initially, there is an increased frequency of blinking, particularly in response to sunlight, wind, noise, movement, or stress. This blinking progresses to involuntary spasms, initially on one side, but inevitably on both. Certain maneuvers like touching the eyelid, coughing, vocalizing, or chewing gum may alleviate the spasms, which increase in frequency and severity as the disease progresses.

Patients with Meige syndrome may experience involuntary chewing movements, lip pursing, trismus, wide opening of the mouth, spasmodic deviations of the jaw, abnormal tongue movements (protrusion, retraction, and writhing), spasmodic dysphonia, and, rarely, difficulty swallowing (343–345). In addition to orofacial spasms, such patients may have oculogyric crises, platysmal contractions, torticollis, retrocollis, or other forms of focal dystonia. Generalized dystonia is rare, however.

Many patients with essential blepharospasm and Meige syndrome stop reading, watching television, and driving; some become depressed, occupationally disabled and, in some cases, functionally blind. The disorder may plateau at any point along its progression. Remissions are rare but occur in about 11% of patients, almost always within 5 years of the onset of symptoms (340,343,346,347).

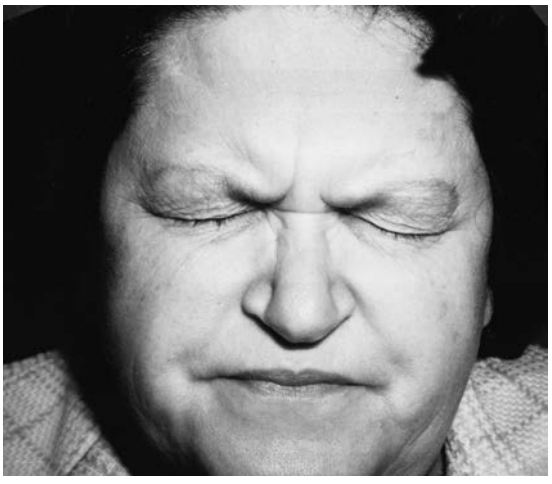

Figure 24.55. Essential blepharospasm. The patient first noted intermittent spasms of lid closure several years earlier. By the time she was examined, she was experiencing almost continuous, bilateral symmetric spasms of the orbicularis oculi muscles.

Most cases of essential blepharospasm and Meige syndrome are sporadic, although there are familial occurrences (348). In addition, patients with essential blepharospasm and Meige syndrome often have a family history of other movement disorders (e.g., essential tremor, Parkinson disease, oromandibular dystonia, blepharospasm, habit tics) (339, 342,347,349,350), or they may give a past history of tics or excessive blinking, sometimes dating back to childhood (341,352). Thus, familial blepharospasm and craniocervical dystonia may be phenotypically heterogeneous and autosomal-dominantly inherited with incomplete penetrance (349).

Many patients with blepharospasm, whether of the essential variety or part of Meige syndrome, complain of dryness, grittiness, irritation, or photophobia. Such patients typically have evidence of dry eyes or ocular surface disease by slit-lamp biomicroscopy or Schirmer testing (343,347,351,353). Indeed, disturbances of the ocular surface may be a precondition for blepharospasm in certain cases. On the other hand, some patients with blepharospasm have severe photophobia with no evidence of dry eyes or ocular inflammation or with dry eyes out of proportion to their complaints. In such patients, a supranuclear neuropathic mechanism may be responsible.

Although there are scattered reports of an association between blepharospasm and certain autoimmune disorders (e.g., systemic lupus erythematosus, myasthenia gravis, rheumatoid arthritis, thyroid disease) (354–357), there is no convincing evidence that autoimmunity is the underlying mechanism of idiopathic blepharospasm.

EMG studies of the orbicularis oculi in patients with blepharospasm show a variety of patterns. The most common is repetitive bursts that last 100–200 msec, with variable interburst intervals ranging from 200–800 msec. Some patients exhibit tonic spasms lasting 3–4 seconds (358,359) or combinations of tonic and repetitive bursts. The characteristic lowering of the brow (Charcot sign) may be absent among a subgroup of patients with blepharospasm in whom contractions are confined to the pretarsal portion of the orbicularis oculi (42).

The cause of essential blepharospasm and Meige syndrome is uncertain. Although psychologic factors are an important component of this disorder in some patients (342,360–362), there is abundant clinical and neurophysiologic evidence that essential blepharospasm and Meige syndrome are **focal dystonias** caused by dysfunction of the basal ganglia or brainstem (336,363). For example, blepharospasm can be a component of an assortment of extrapyramidal and brainstem disorders, and imaging studies show that focal lesions of the rostral brainstem, diencephalon, and basal ganglia may be associated with blepharospasm (364). In addition, there is clear evidence of brainstem dysfunction in many patients with essential blepharospasm. About 30% of patients with essential blepharospasm exhibit abnormalities of the brainstem auditory-evoked response that localize to

the mid to upper brainstem (365). The reciprocal relationship between the orbicularis oculi and levator may be altered in such patients, and there may be inappropriate episodes of levator inhibition or co-contraction (42,359). Although the latency of the blink and corneal reflexes are normal in patients with essential blepharospasm, both amplitude and duration are abnormally increased (358,363). Patients with essential blepharospasm and patients with oromandibular dystonia have a more rapid R2 recovery cycle than normal control subjects, indicating that the brainstem interneurons that mediate the blink reflex are abnormally excitable (358, 366–368). Similar findings can be documented in many patients with other cranial dystonias, even in those without blepharospasm (363,366,367,370–373). The basal ganglia, which play a central role in the genesis of these movement disorders, are probably responsible for this facilitatory effect on brainstem interneurons.

Blepharospasm may be associated with a variety of eye movement disturbances that also occur in other extrapyramidal disorders. Motion-picture or video analysis of eyelid movements in patients with essential blepharospasm reveals impersistence of gaze, eyelid retraction, head tilt, and head jerk (374,375). In addition, some patients experience episodes of prolonged involuntary conjugate spasmodic upward deviations lasting 1–10 seconds (33). These episodes are similar to those seen in patients with oculogyric crises. Abnormalities in saccadic eye movements also occur in patients with essential blepharospasm. They are nonspecific (376,377) but consistent with extrapyramidal dysfunction (378).

The histopathologic findings in patients with essential blepharospasm are variable, although the basal ganglia are often abnormal. Some cases show microscopic abnormalities that consist of neuronal cell loss and severe gliosis in a unique pattern that produces a ''mosaic appearance'' in the dorsal halves of the caudate and putamen (379). In others, there is mild- to- moderate cell loss in the pars compacta of the substantia nigra, the locus ceruleus, and several other areas in the brainstem (380,381). Some cases show no abnormalities or unrelated changes (382,383); however, the lack of morphologic changes does not necessarily imply normal function. For example, neurochemical analysis of the brain from a patient with Meige syndrome who had no significant neuropathologic findings at autopsy nevertheless demonstrated substantial increases in norepinephrine and dopamine in the red nucleus and substantia nigra (384).

Botulinum toxin type A is the primary form of therapy for patients with blepharospasm. Its effects generally last 2–4 months. Other drugs can also be used to treat essential blepharospasm and Meige syndrome, but they are less efficacious. For example, in some patients with mild essential blepharospasm, tranquilizers may be of short-term benefit. For patients with more severe disease, drugs that inhibit catecholamine synthesis (α-methyl-1-tyrosine), block dopamine receptors (phenothiazine, butyrophenones), deplete brain monoamines (reserpine, tetrabenazine), or increase central cholinergic effects (physostigmine, choline, lecithin) may suppress the abnormal movements (340,385–389). Tetrabenazine, clonazepam, trihexyphenidyl, lithium carbonate, and baclofen are of particular benefit in selected patients (340,342,390,391). In addition, selective inhibitors of serotonin re-uptake, such as fluoxetine (Prozac), may reduce facial and eyelid spasms in patients with severe blepharospasm, Meige syndrome, or both (392). L-dopa occasionally is useful in patients with blepharospasm related to parkinsonism, particularly that form induced by MPTP (393), but this drug is of little or no benefit in the treatment of essential blepharospasm.

Essential blepharospasm can be treated surgically by removing all or part of the orbicularis oculi muscle (394–398) or by avulsing or otherwise destroying branches of the facial nerve (399–403). Complications, variable effectiveness, and frequent recurrence are major limitations of both procedures (403,404); however, comparisons of the two approaches (403,405) indicate that myectomy is preferable because it results in a more prolonged relief of symptoms, fewer recurrences requiring additional surgery, greater patient acceptance, and fewer complications than selective facial nerve avulsion. Nevertheless, complete healing may take 6 months or more after myectomy and may be associated with considerable facial swelling from lymphedema. In addition, subsequent injections of botulinum toxin are associated with increased discomfort in the region of surgery. With facial nerve avulsion, there is a fourfold increase in the need for secondary procedures in addition to the complications associated with facial paresis and particularly insufficient eyelid closure (405,406–408). We believe that surgery should be reserved for patients with disabling blepharospasm that does not respond to botulinum toxin, oral medications, or a combination of these treatments, or for patients who cannot tolerate these treatments.

Patients with essential blepharospasm often have associated dermatochalasis, ptosis, or both. These can be treated with blepharoplasty and ptosis surgery, both of which often reduce the severity of the blepharospasm to some extent. However, these procedures are merely adjuncts to the treatment of blepharospasm and should not be considered as primary treatments for the condition.

Blepharospasm Associated with Lesions of the Brainstem and Basal Ganglia

Blepharospasm may be caused by a variety of lesions and disorders of the basal ganglia and mesodiencephalic region. These include strokes, demyelinating diseases (364,409,410), progressive supranuclear palsy (31,135,136), Parkinson disease (29), MPTP-induced parkinsonism (393), Huntington disease, Wilson disease, Lytico-Bodig syndrome (38), Hallervorden-Spatz syndrome (411,412), olivopontocerebellar atrophy (413), communicating hydrocephalus (249,414), and encephalitis lethargica (415). Calcification of the basal ganglia associated with blepharospasm occurs in some patients with Meige syndrome (416), pseudohypoparathyroidism (417), and ill-defined neurodegenerative disorders of unknown etiology (418).

The blepharospasm that follows a cerebrovascular accident frequently begins months to years after the stroke and is associated with other localizing signs, such as hemiplegia,

midbrain ocular motor dysfunction, and extrapyramidal signs (361,409,419–423). The causative lesion may be unilateral or bilateral, but the blepharospasm usually is bilateral and symmetric. Delayed blepharospasm after stroke also may be associated with palatal or oculopalatal myoclonus (27,424,425).

There are several possible explanations for the delay in onset of blepharospasm in patients with lesions of the brainstem and basal ganglia: (*a*) denervation supersensitivity of the facial nuclear complex; (*b*) disinhibition of facial nuclear and brainstem reflexes; and (*c*) delayed-onset dystonia caused by sprouting of surviving axons (409). If one assumes that the basal ganglia facilitate the development of blepharospasm, this delay is not surprising because eyelid spasms would not develop until there was an adaptive increase in blink excitability from chronic trigeminal stimulation.

Blepharoclonus and Reflex Blepharospasm

Typical blepharospasm is characterized by repetitive episodes of tonic contractions of the orbicularis oculi, and EMG studies show that the orbicularis contractions in many such patients consist of rhythmic phasic bursts at a rate of 3–6 Hz. When such contractions result in visible repetitive upward jerks of the eyelids, the term **blepharoclonus** is used (426,427).

Blepharoclonus occurs in patients with brainstem syndromes caused by stroke or trauma (428), hydrocephalus from aqueductal stenosis in the setting of parkinsonism (429), and MS (426). In one case, blepharoclonus was precipitated by eccentric gaze and was not present when the patient looked straight ahead (426).

Reflex blepharospasm is a condition in which eyelid spasms are induced by voluntary lid closure or attempts to manually open the eyelids. It is a well-documented finding in patients with recent, nondominant temporoparietal strokes, in which case it is associated with hemiplegia (430). The lid spasms usually are confined to the nonparalyzed side and are evoked when the examiner attempts to hold the eyelids apart. Some patients with spontaneous blepharospasm from extrapyramidal or brainstem lesions also have reflex blepharospasm during attempts by the examiner to open the eyelids (364,403,419). Likewise, gentle lid closure in some patients with Parkinson disease will evoke a ''lid tremor'' that EMG reveals is a result of reciprocal contractions of the levator and orbicularis oculi muscles (253). Rarely, reflex blepharospasm is hereditary, with onset in early childhood (431).

Blepharoclonus and reflex blepharospasm probably are different manifestations of similar pathophysiologic processes. Although the origin of the primary stimulus may vary (e.g., extrapyramidal dysfunction, hemisphere or brainstem lesions, or stretching of the orbicularis), the final pathway is an increase in blink excitability. Suprasegmental disinhibition or adaptive responses to peripheral lesions enhance the neuronal activity of the blink pathways.

Although blepharoclonus and reflex blepharospasm usually occur in patients with cortical, extrapyramidal, brainstem, and trigeminal disturbances, some patients with these conditions have no evidence of neurologic disease (432).

Ocular Blepharospasm

Blepharospasm occasionally is caused by irritative or painful ocular disease. Photophobia and lacrimation are also present in patients with this form of blepharospasm, often called **ocular blepharospasm**. The most common causes of ocular blepharospasm are disturbances of the eyelids (e.g., blepharitis, trichiasis, entropion), disturbances of the corneal epithelium, severe dry eyes, iritis, scleritis, and angle-closure glaucoma. Although less common, patients with ocular albinism, congenital achromatopsia, aniridia, or posterior subcapsular cataracts may experience blepharospasm and photophobia in response to bright light (433). Chemotherapeutic agents such as cyclophosphamide, doxorubicin, fluorouracil, tegafur (furanyl-5-fluorouracil), and mitomycin-C (434–436) may produce ocular irritation and severe blepharospasm, as may a variety of topical medications (437.)

Rarely, patients with strabismus develop what appears to be a unilateral tonic blepharospasm to avoid diplopia. This is particularly common in patients with acquired paralytic strabismus and in patients with intermittent exotropia. It is most obvious in bright light.

In our experience, patients with essential blepharospasm often have ocular surface abnormalities that may contribute to the spasms, but true ocular blepharospasm is rare. Nevertheless, ocular causes of blepharospasm should always be excluded before a search for a neurologic cause of blepharospasm is undertaken or a diagnosis of essential blepharospasm is made.

Blepharospasm Associated with Drug-Induced Tardive Dyskinesia

Patients with tardive dyskinesia have blepharospasm and facial tics similar to those seen in patients with Meige syndrome (see above); however, patients with tardive dyskinesia have choreic movements of the extremities as opposed to the more sustained, dystonic movements observed in patients with Meige syndrome (438–440). The most important distinguishing feature of tardive dyskinesia, however, is that it is always drug-induced, usually developing 1–2 years after starting the medication. In most instances, the responsible agents are antipsychotic or neuroleptic drugs, such as dopamine-blocking or dopamine-stimulating agents (439,441–443). Drug-induced dyskinesia can also occur after the use of antiemetics, anorectics, or nasal decongestants that contain sympathomimetic agents and antihistamines (444–447). Orofacial dyskinesia developed in one patient following an overdose of carbamazepine (448).

From 15–30% of patients on continuous neuroleptic therapy eventually develop tardive dyskinesia (449–452). The risk of acquiring this complication increases with higher doses and prolonged use of the drug, and with increasing age of the patient. Women are more frequently affected than men.

The blepharospasm and facial tics of tardive dyskinesia may improve if the drug responsible is identified and discon-

tinued. If the symptoms persist, or if the drug cannot be stopped for medical reasons, botulinum toxin can be used to control the spasms.

In contrast to tardive dyskinesia, which occurs 1–2 years after initiating drug therapy, some patients develop an acute dystonic reaction after 2–5 days on neuroleptics. The reaction usually consists of abnormal posturing and intermittent or sustained muscle spasms, but some patients develop blepharospasm or oculogyric crises. This reaction is more likely to occur among young patients on high doses of medication (452).

Facial Tics and Tourette Syndrome

In contrast to the sustained, dystonic movements typical of blepharospasm, facial tics are usually brief, clonic, and jerk-like. They tend to be stereotyped and repetitive. They can vary in frequency, increasing when the patient is bored, tired, or anxious. Eye-winking tics are most commonly observed in childhood, tend to be unilateral, and affect boys more often than girls. They resolve spontaneously after months or years (352).

When facial tics begin between 2 and 15 years of age, last more than 1 year, fluctuate in severity, and are associated with tics in multiple other bodily locations, vocalizations (e.g., grunting, sniffing, barking, throat-clearing, utterance of obscenities), obscene gestures, and other aberrancies of behavior, Tourette syndrome (also called Gilles de la Tourette syndrome) is the likely diagnosis (400,453–456). Ocular manifestations are common in this condition and include increased blinking, blepharospasm, forced staring, and involuntary gaze deviation (456,457).

Patients with Tourette syndrome have enhanced recovery cycles (372). In addition, tics and blepharospasm may coexist in the same patient and among other family members. These findings suggest that many of these disorders share common underlying mechanisms.

Nonorganic Blepharospasm

Nonorganic blepharospasm generally has a sudden onset and usually is preceded by an emotionally traumatic event (458,459). Although quite rare, it is more common among children and young adults with serious psychologic problems. The blepharospasm is frequently bilateral and may last for hours, weeks, or even months, at which point it may resolve spontaneously. The eyelids are sometimes gently, sometimes forcibly, closed. In some patients, psychotherapy, behavior therapy, hypnosis, or biofeedback are of benefit (460–462). In others, a single injection of botulinum toxin is sufficient to eliminate the spasms permanently.

Focal Seizures

Several eyelid phenomena are associated with seizures. An adversive (jacksonian) seizure from an irritative focus in the frontal eye fields can evoke contralateral spasmodic eyelid closure, twitching of the face, and ''spastic'' lateral gaze. Blinking or fluttering of the eyelids also may be observed in psychomotor or absence seizures (463–465). Blinking is usually bilateral and symmetric, although unilateral blinking ipsilateral to the seizure focus has been described (466).

A form of **photomyoclonic epilepsy** consists of the combination of eyelid ''myoclonia'' and absence spells. Upon closure of the eyelids, patients with this condition experience marked eyelid spasms, upward deviation of the eyes, and brief periods during which they seem unaware of their surroundings (i.e., absence spells) and electroencephalography shows bilateral 3–5 Hz spike-and-wave discharges (465,467). These seizures are triggered by the elimination of central fixation (i.e., they are fixation-off sensitive) (468). The marked jerking of the lids during eyelid closure and the upward gaze deviation that occur in photomyoclonic epilepsy usually are sufficient to distinguish this condition from the slight flutter of the eyelids unassociated with ocular gaze deviation that is seen in patients with pure absence seizures.

Seizures induced by eyelid closure or blinking represent a rare form of stimulus-sensitive epilepsy (usually absences or myoclonic attacks). The stimulus responsible for inducing the seizure in some cases is presumed to be proprioceptive. In other cases, a loss of central fixation brought on by eyelid closure precipitates the seizure. In addition, a decrease in retinal illumination alone, or with eyelid closure, is sufficient to induce a ''scotosensitive'' seizure (469–476).

Lid-Triggered Synkinesias

Eyelid closure occasionally triggers movements of muscles that are not innervated by the facial nerve, presumably from a central or supranuclear disturbance (477). In one patient with a progressive neurodegenerative condition of unknown etiology, eyelid closure was associated with mouth opening and fanning of the fingers (478). In another case, eyelid closure was associated with closing of the hand.

In some patients with such eyelid-triggered dyskinesias, firm external stimulation of the cornea elicits a brisk anterolateral jaw movement to the side opposite the stimulus associated with eyelid closure: the **corneomandibular reflex**. In other patients, an acquired **palpebromandibular synkinesia** is present that is similar to the corneomandibular reflex except that the jaw movements that regularly accompany spontaneous eye blinks can occur without an external corneal stimulus (479). The palpebromandibular reflex usually is associated with bihemispheric or upper brainstem pathology.

Facial Myokymia (with and without Spastic Paretic Facial Contracture)

The term facial myokymia refers to involuntary, fine, continuous, undulating contractions that spread across facial muscles. The contractions are usually unilateral. Electrophysiologically, affected muscles show brief tetanic bursts of motor-unit potentials that recur in a rhythmic or semirhythmic fashion several times a second as singlets, doublets, or groups (480–482). These bursts recur at a rate of 3–8 Hz.

The most common type of facial myokymia occurs in otherwise normal persons and affects only the orbicularis

oculi of the lower (or, occasionally, the upper) eyelid on one side. This **eyelid myokymia** often begins at times of excessive fatigue or stress. It usually lasts for several days, but it may persist for a few weeks and even for several months. During this time, it is usually intermittent, lasting for several hours at a time. Patients with this condition may become alarmed, particularly because they can feel the eyelid fasciculations. They often believe that their eye is ''jumping,'' and some patients actually experience oscillopsia from the effects of the myokymic eyelid against the globe (483); however, this type of transient eyelid myokymia is almost always benign.

Eyelid myokymia that persists continuously for several months or even years may be an isolated phenomenon of no systemic or neurologic significance; however, it also may be the first sign of MS or an intrinsic lesion near the facial nerve nucleus in the dorsal pons. Thus, we believe that patients in whom isolated eyelid myokymia persists for more than 3 months should undergo MR imaging, as should patients with eyelid myokymia who have or develop other neurologic manifestations.

Many disorders characterized by involuntary movements of the facial muscles can begin with eyelid myokymia, including essential blepharospasm, Meige syndrome, hemifacial spasm, and **spastic-paretic facial contracture**. This last disorder is characterized by myokymia that first begins in the orbicularis oculi muscle and gradually spreads to most of the muscles on one side of the face. At the same time, associated tonic contracture of the affected muscles becomes evident. Over a period of weeks or months, the nasolabial groove slowly deepens, the corner of the mouth is drawn laterally, the palpebral fissure narrows, and all the facial muscles become weak. As the contracture becomes more pronounced, voluntary facial movements on the affected side diminish (Fig. 24.56). Spastic-paretic facial contracture is a sign of pontine dysfunction in the region of the facial nerve nucleus. Disorders that may produce it include MS (484,485), intrinsic brainstem neoplasms (particularly gliomas but also metastatic tumors) (486–489), extra-axial neoplasms compressing the brainstem (e.g., chordomas) (489,490), syringobulbia (491), brainstem vascular lesions (493), GBS (482), obstructive hydrocephalus (493), subarachnoid hemorrhage (494), basilar invagination (495), Machado-Joseph disease (496), brainstem tuberculoma (497), cysticercosis (398), and autosomal-dominant striatonigral degeneration (483). In most instances, the phenomenon and the pathology that causes it are unilateral, but bilateral facial myokymia from bilateral pontine disease may occur in patients with GBS (482,500,501), following cardiopulmonary arrest (502), during the course of a lymphocytic meningoradiculitis (503), and following exposure to a variety of toxins (492,504).

The pathophysiology of transient facial myokymia is unknown. MR imaging in patients with MS who have continuous facial myokymia often shows changes consistent with demyelination in the postgenu portion of the fascicle of the facial nerve in the dorsolateral pontine tegmentum (485). In all autopsy cases in which a brainstem tumor is responsible for the condition, the tumor infiltrates the pontine tegmentum, basis pontis, or both, sparing the facial nerve nucleus and its neurons (486,488,489,505). It has therefore been suggested that the lack of direct damage to the ipsilateral facial nerve nucleus in the presence of more rostrally placed lesions produces a functional deafferentation, possibly of local circuit neurons. This, in turn, results in hyperexcitability of facial nerve neurons, thus causing myokymia or spastic-paretic facial contracture (487,489). When the facial nerve nucleus itself is damaged by the pathologic process, the facial spasm resolves, leaving only facial paralysis and contracture (492,497). This hypothesis explains the phenomenon of facial myokymia and spastic-paretic facial contracture in patients with brainstem lesions but not in patients with peripheral neuropathies (discussion following).

Facial Myokymia with Peripheral Neuropathy

The development of facial myokymia in patients with GBS, poliomyelitis, parotid gland tumor, and some other disorders of the peripheral facial nerve (506–508) indicates that damage to the peripheral facial nerve alone can produce hyperactivity of facial muscles. Other evidence that peripheral nerve injury can produce facial hyperactivity includes EMG studies that reveal that myokymia is common in patients with Bell's palsy (509), and the observation that timber rattlesnake evenomation causes facial myokymia from damage to the peripheral portion of the facial nerve (510). Thus, the occurrence of facial myokymia in a patient with apparent peripheral facial nerve dysfunction does not necessarily indicate an underlying central process (501). Myokymic discharges of peripheral nerve origin are usually attributed to spontaneous ectopic excitation arising in demyelinated fibers.

Hemifacial Spasm

Hemifacial spasm (HFS) is characterized by involuntary paroxysmal bursts of painless, unilateral, tonic or clonic contractions of muscles innervated by the facial nerve (Fig. 24.57). It occurs most commonly in middle-aged adults, but it may develop at any age, including infancy and childhood (511–515). The condition is almost always sporadic, but there are familial cases (516–518). Bilateral cases occur but are exceptionally rare (511,519), and some reported cases may actually be examples of blepharospasm with Meige syndrome.

HFS usually first appears as spasms of the orbicularis oculi and then spreads slowly to the lower facial muscles over months to years. The spasms may occur spontaneously or be triggered by voluntary facial movements or changes in position (520), and they may worsen with fatigue, stress, or anxiety. Long-standing HFS almost always is associated with ipsilateral lower facial weakness (521,522), although this may be hard to detect, either because it usually is fairly mild or because of the constant spasms. In any event, facial movements between spasms usually appear normal. Most patients with HFS have clinical evidence, EMG evidence, or both, of synkinesis between the orbicularis oculi and orbicularis oris muscles (523).

There is considerable evidence, based primarily on direct

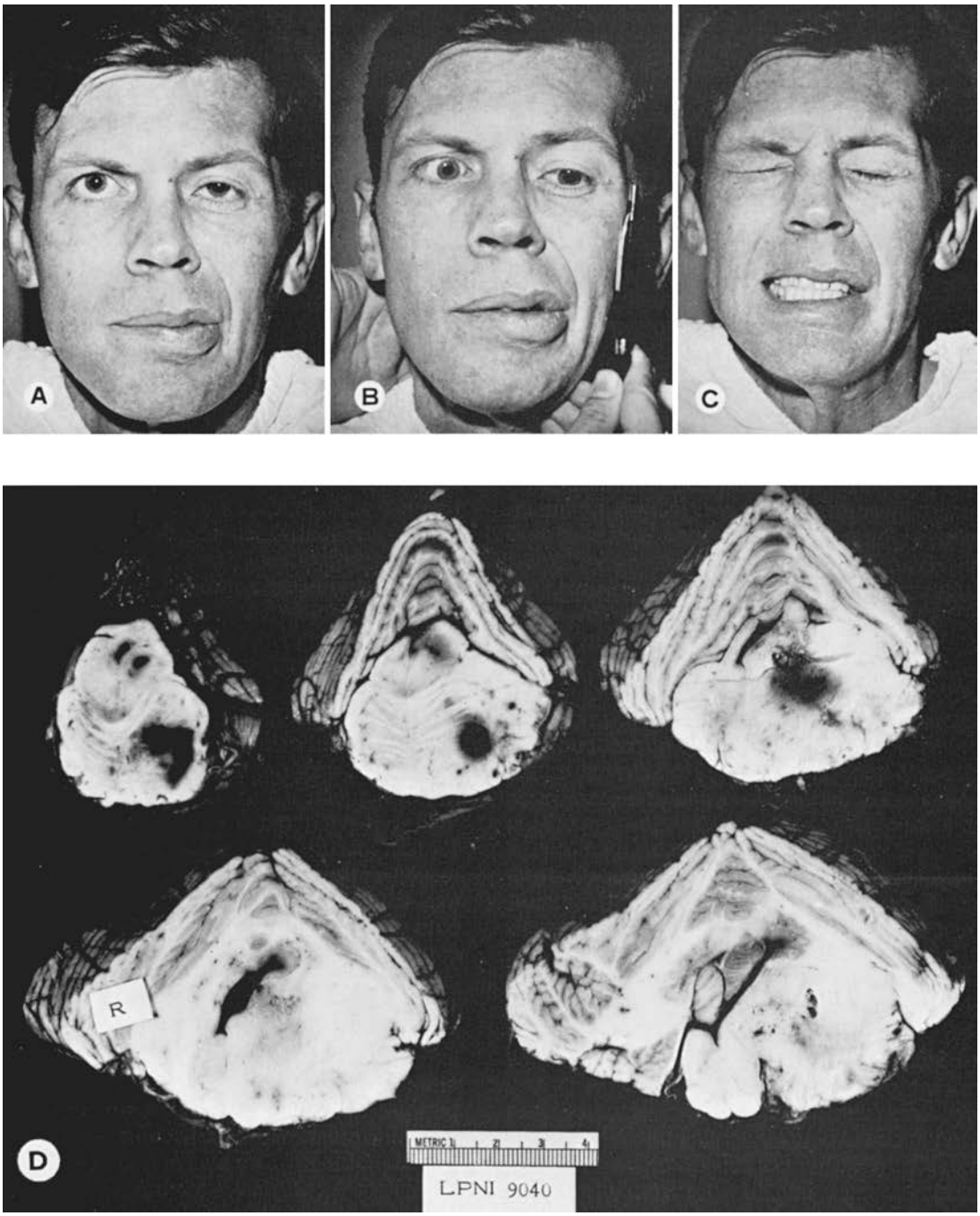

Figure 24.56. Spastic paretic facial contracture associated with a pontine astrocystoma. *A*, The patient's face is at rest. Note deepened nasolabial groove and narrowed palpebral fissure on the left. *B*, On attempted left gaze, the patient shows a horizontal gaze palsy. *C*, Voluntary forced eyelid closure exposes the paresis of the left orbicularis oculi and the left side of the face. The patient subsequently died and an autopsy was performed. *D*, Serial sections through the brainstem of the patient show a left-sided astrocytoma. (From Sogg RL, Hoyt WF, Boldrey E. Spastic paretic facial contracture: A rare sign of brain stem tumor. Neurology 1963;13:607–612.)

observations at surgery, that most cases of HFS are caused by pulsatile compression of the proximal region of the facial nerve at the root entry zone (the transitional zone between central and peripheral myelin) by normal vessels in an aberrant location (524–530) or by dolichoectatic vessels (528,531). The blood vessels most commonly responsible for the compression are the anterior inferior cerebellar artery, the posterior inferior cerebellar artery, and the vertebral ar-

Figure 24.57. Left hemifacial spasm. Photograph is a composite of multiple frames of a video that shows the development of the hemifacial spasm. Note that between spasms, the patient's face appears normal; however, when the spasms occur, the left side of the mouth draws up, the midfacial muscles contract, and the left eyelid closes. (From Garibaldi DC, Miller NR. Tortuous basilar artery as etiology of hemifacial spasm. Arch Neurol 2003;60:626–627.)

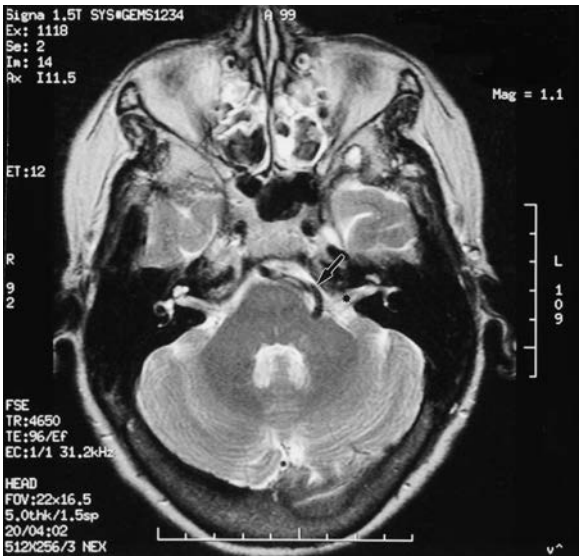

Figure 24.58. Neuroimaging showing vascular compression of the left facial nerve in a the patient with ipsilateral hemifacial spasm shown in Figure 24.57. Proton-density magnetic resonance image, axial view, shows compression of the left facial nerve (*) by a tortuous basilar artery (*arrow*). The patient was treated successfully with botulinum toxin A. (From Garibaldi DC, Miller NR. Tortuous basilar artery as etiology of hemifacial spasm. Arch Neurol 2003;60:626–627.)

tery. Less commonly, one or more veins accompanying these vessels appear to be responsible. A variety of imaging techniques, including CT scanning, MR imaging, MR angiography, and CT angiography may show ipsilateral displacement, tortuosity, or enlargement of the basilar or vertebral arteries in patients with HFS (532–537) (Fig. 24.58).

Although HFS appears to be caused by vascular compression from otherwise normal arteries or veins in over 99% of cases, vascular structures other than normal vessels also can compress the facial nerve at the root entry zone, producing HFS. These lesions include aneurysms (524, 531,538–540), AVMs (524,540), infratemporal hemangiomas (541), and arterial dissections (542) (Fig. 24.59). Extraaxial tumors located in the CPA can produce HFS. These include epidermoids, vestibular schwannomas (acoustic neuromas), meningiomas, cholesteatomas, and lipomas (543–545). Occasionally, HSF is produced by intraparenchymal brainstem lesions, including tumors and granulomas (546,547). Other rare causes include arachnoid cysts (548,549), MS (546), pontine infarction (550), hemosiderosis (551), arachnoiditis (552), and lesions or structural abnormalities of the bone of the skull base (553–557). HFS may occur as a false localizing sign in patients with tumors located in the contralateral CPA (558,559) and in patients with pseudotumor cerebri (560). It may also occur after injury to the peripheral facial nerve (512,561–563). In some cases, HFS is associated with evidence of hyperactivity of other cranial nerves. The most common association is with trigeminal neuralgia (564–566).

Although there is general agreement regarding the importance of facial nerve decompression in the treatment of HFS (discussion following), the underlying neurophysiologic mechanism that produces the condition remains controversial (523,567–569). One theory is that HFS is the result of ephaptic transmission or crosstalk between branches of the facial nerve at the root entry zone; for example, in an area of demyelination (523,526,570–574). Another theory, however, is that the facial motor nucleus changes in response to

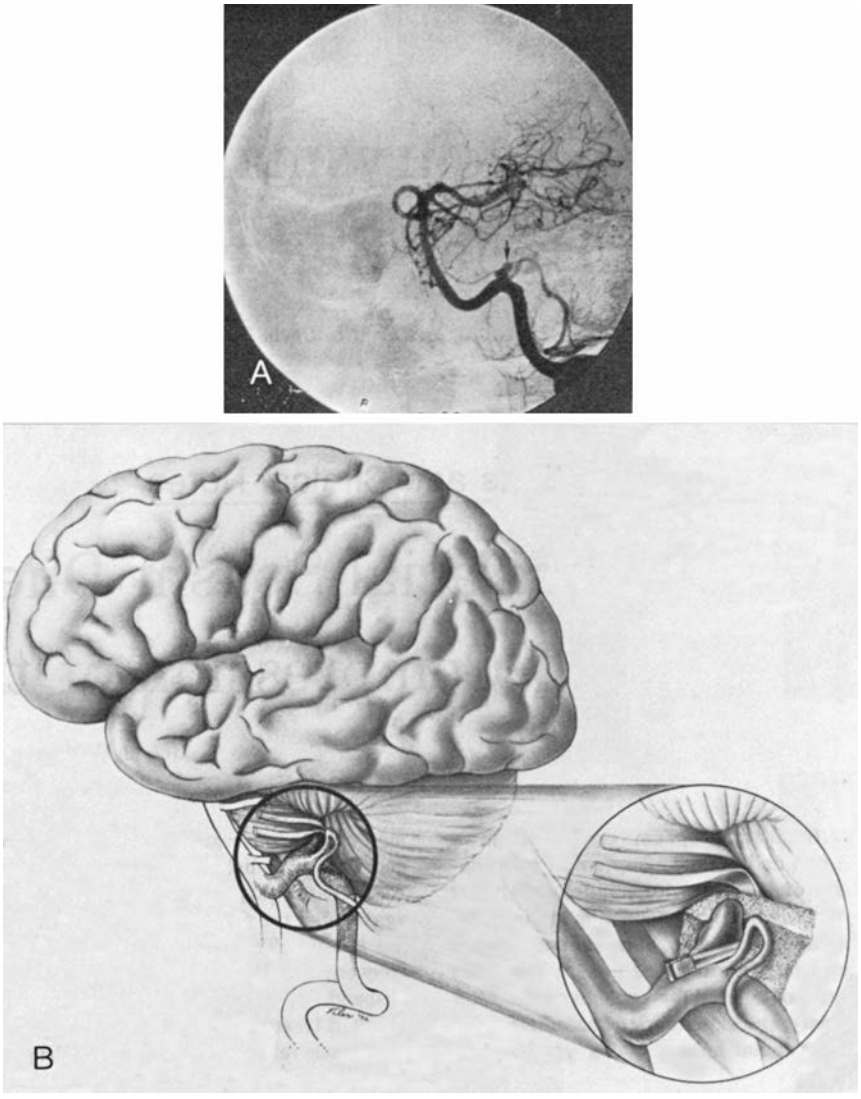

Figure 24.59. Hemifacial spasm caused by an intracranial aneurysm. *A*, In a patient with left-sided hemifacial spasm, a vertebral artery angiogram (oblique projection) shows an aneurysm at the origin of the posterior inferior cerebellar artery (*arrow*). *B*, Schematic representation of the aneurysmal compression of the left facial nerve before and after clipping and mobilization of the aneurysm. (From Maroon JC, Lunsford LD, Deeb ZL. Hemifacial spasm due to aneurysmal compression of the facial nerve. Arch Neurol 1978;35:545–546.)

peripheral nerve injury (546,547,575–579). Central anatomic change in response to peripheral nerve injury is a well-established phenomenon that could theoretically unmask synkinetic facial movements (561). It has also been suggested that chronic pulsatile arterial antidromic stimulation of the facial nerve increases the excitability of facial motor neurons through a phenomenon called ''kindling'' (577–580).

There appears to be a subgroup of patients with HFS who have no obvious vascular compression yet improve after surgery. The improvement in such patients may be consequent to mild operative trauma and manipulation of the nerve since the nerve was not decompressed (581–583). In addition, the severity of vascular compression observed in patients with HFS is extremely variable, ranging from obvious displacement and grooving of the facial nerve, to displacement without grooving, and to touching without either displacement or grooving. That veins and, in some cases, venules, can cause HFS by apparent compression of the facial nerve is also problematic.

The only way to cure HFS is posterior fossa microvascular decompression (524–525,527–529,538,581,584–587). Although this procedure has potential mortality and a well-defined morbidity (discussion following), the results are generally excellent. When performed by an experienced surgeon, the overall cure rate is 85–90%. In most patients who are cured, the HFS disappears within 3–10 days after surgery, although in a smaller group, resolution can take weeks to months. Among patients whose HFS persists or recurs after apparently successful surgery (i.e., the vessel compressing the nerve is identified and moved), 5–10% are cured after a second operation (587).

The complication rate of posterior fossa microvascular decompression for HFS, like the success rate, varies according to the experience of the surgeon performing the operation. In some series, the complication rate is reported to be as high as 25%; in others, it is 1–2% (523,586,587). The most common persistent complications are ipsilateral hearing loss (1–13%) and facial paralysis (1–6%). The mortality with this procedure is exceptionally low; however, death or disabling stroke from brainstem or cerebellar infarction can occur.

The results of medical therapy for HFS are generally disappointing. The most commonly used drugs are carbamazepine (Tegretol) (588,589), diphenylhydantoin (Dilantin), and dimethylaminoethanol (Deanol) (590). Gabapentin (Neurontin) has also been reported to be of value in selected patients.

Surgical procedures other than microvascular decompression, including intracanalicular facial nerve neurotomy (591) and partial avulsion, section, longitudinal splitting, or radiofrequency destruction of the extracranial portion of the facial nerve (592–594), generally produce disappointing results. In some instances, after section of the facial nerve, a hypoglossal-facial anastomosis is performed to relieve the resultant facial paralysis (595). None of these procedures is without complication, and the recurrence rate is considerable.

Intramuscular injections of botulinum toxin can be used to control, but not cure, HFS (596,597). In our opinion, this mode of therapy is the best alternative for patients who are unwilling or unable to undergo posterior fossa microvascular decompression of the facial nerve (see above). Other injectable drugs, particularly doxorubicin (Adriamycin) continue to be investigated (598,599).

Excessive Eyelid Closure of Neuromuscular Origin

Neuromuscular hyperexcitability of the orbicularis oculi usually is part of a generalized disorder. The excitability may be latent, spasmodic, or constant. In hypoparathyroidism or during hyperventilation, a tap over the lateral orbital margin produces contraction of the ipsilateral orbicularis muscles and the surrounding facial muscles (latent hyperexcitability). Strychnine poisoning causes spasmodic hyperexcitability and tetanus causes a constant or sustained neuromuscular hyperexcitability manifested in the facial muscles as **risus sardonicus** (600–602) (Fig. 24.60).

Excessive Eyelid Closure of Myopathic Origin

Myotonia of the orbicularis oculi may occur in association with a number of disorders. For example, patients can develop eyelid myotonia in association with primary hypothyroidism (603,604). The myotonia typically disappears after such patients are treated with replacement thyroid medication (Fig. 24.61).

Patients with both the congenital and adult forms of myotonic dystrophy may show myotonia of the orbicularis oculi.

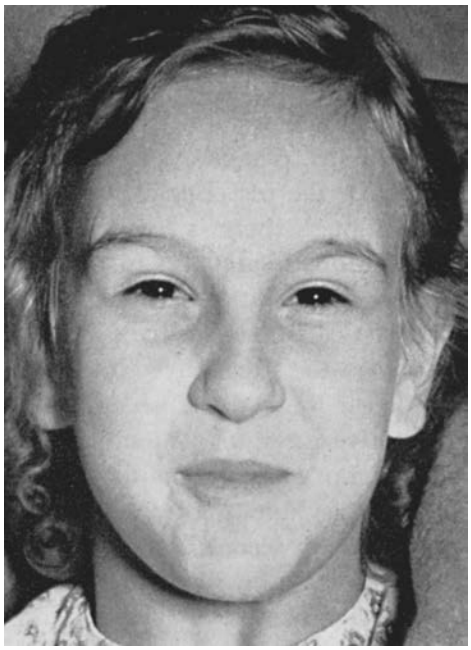

Figure 24.60. Risus sardonicus in a child with tetanus. Increased tone of all facial muscles is evident. Note that the child appears to be smiling. Her apparent bilateral ptosis is caused by myotonia of the orbicularis oculi muscles. (From Ford FR. Diseases of the Nervous System in Infancy, Childhood and Adolescence, 5th Ed 5. Springfield, IL: CC Thomas, 1966:621.)

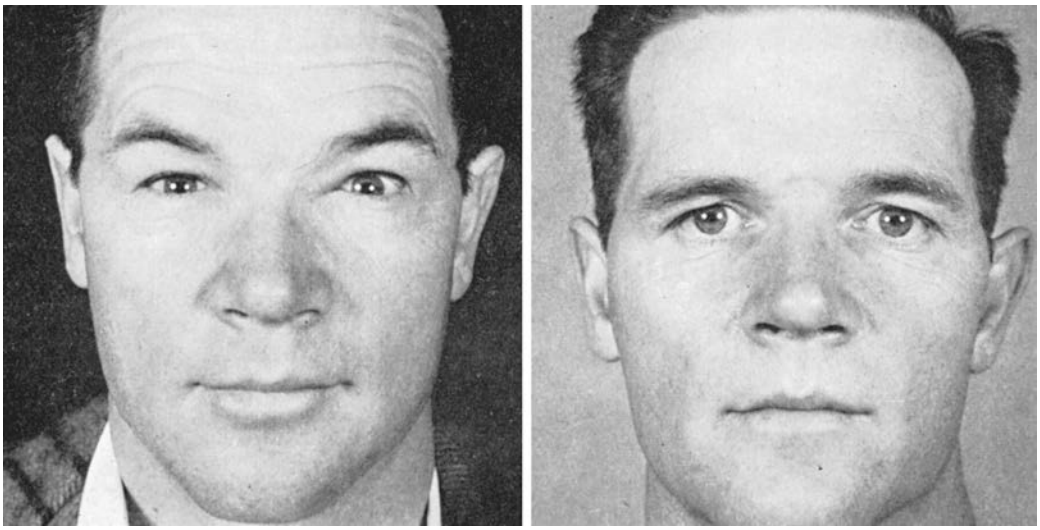

Figure 24.61. Myotonia of the orbicularis oculi in a patient with hypothyroidism. Both photographs were taken 2 seconds after forceful closure of the patient's eyelids. *A*, The patient has difficulty opening the eyes due to myotonia of the orbicularis oculi muscles. *B,* After thyroid hormone therapy was instituted, the patient's myotonia disappeared. (From Sisson JC, Beierwaltes WH, Koepke GH, et al. ''Myotonia'' of the orbicularis oculi with myxedema. Arch Intern Med 1962;110:323–327.)

One infant with congenital myotonic dystrophy exhibited a startle response to a loud noise or a bright light that produced tight eye closure followed by slow opening over many seconds (605). In adults with myotonic dystrophy, EMG studies demonstrate evidence of prolonged contraction in the orbicularis oculi following a blink (606) (see Chapter 22).

Myotonia of the orbicularis oculi may occur in patients with hyperkalemic familial periodic paralysis. Slowness of eyelid opening or temporary narrowing of the palpebral fissure may occur following sustained eyelid closure, application of ice to the lids, or administration of potassium salts (235). Eyelid myotonia can also occur in patients with chondrodystrophic myotonia (Schwartz-Jampel syndrome) (607) (see Chapter 22).

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