Abstract: This article is structured around a literature review that was carried out using Ovid and Medline with the key words “botulinum,” “toxin,” and “ENT.” Botulinum toxin has been used safely in humans for more than 20 years. The effects are transient, such that treatments are required to be repeated at intervals. Its application to ENT provides a useful tool to treat dystonia, autonomic dysfunction, facial nerve paresis, and hyperfunctional lines. It may also be of benefit in laryngeal rebalancing and the treatment of headaches. Further research is being carried out and new indications for treatment with botulinum toxin may include sialorrhea and rhinorrhea. © 2005 Wiley Periodicals, Inc. Head Neck 27: 525–535, 2005

Keywords: Botulinum; toxin; ENT

A HISTORY OF BOTULINUM TOXIN

The use of botulinum toxin for aesthetic purposes has become one of the most common cosmetic procedures performed today, and its use is a commonly discussed topic in the media. It was first developed as therapeutic agent for the treatment of disorders characterized by localized muscle hyperactivity, especially around the eyes. Botulinum toxin is now widely used to treat many conditions including most types of focal dystonias.

Its use in facial dystonias improves the disfigurement and the discomfort and disability associated with the condition.

The word “botulism,” which is the clinical syndrome of botulinum toxin poisoning, comes from the Greek word for sausage, botulus, because for a long time it was used to refer to a particular illness caused by the ingestion of spoiled sausages. Clostridium botulinum was first identified as a causative agent in food poisoning in 1895 by Professor Emile Pierre van Ermengem. He was asked to investigate an episode of lethal food poisoning that arose because of the consumption of uncooked ham at a wake. The symptoms demonstrated were of autonomous dysfunction (dryness of the mouth, nausea, paralytic ileus, postural hypotension) and flaccid paralysis, all in the absence of fever. van Ermengem examined autopsy specimens, the spoiled meat, and its effect when fed to a series of animals.

It was discovered in 1919 by Professor Burke of Stanford University that there were different strains of the bacterium and that they produced serologically different types of botulinum toxin. He proposed an alphabetical classification and identified two serotypes, types A and B, in his experiments. Further studies demonstrated another
five serotypes so that, to date, seven serotypes of botulinum neurotoxin have been identified and named A to G.²

A crude form of botulinum toxin type A was isolated in the 1920s, and later the first attempts at purification were made.⁵,⁷ During World War II, the US government assigned a number of scientists at Fort Detrick in Maryland to develop protection against such agents. It was isolated by this group in crystalline form in 1946, and initial insights into the mechanism of action came when it was shown to block the release of acetylcholine from motor nerve endings.⁸,⁹

Botulinum toxin was first tested in animals in the 1960s and 1970s by Dr. Alan Scott, who was an ophthalmologist seeking an alternative or adjunct to surgery for strabismus. He had come into contact with Dr. Edward Schantz, a toxicologist who had participated in the work at Fort Detrick. Its safety was shown in humans in 1980, when the selective weakening of specific extraocular muscles with intramuscular injections of botulinum toxin type A could correct gaze misalignment in strabismus.¹⁰,¹¹

Botulinum toxin type B is now commercially available, with research into the other subtypes awaited.

PHARMACOLOGY AND MECHANISM OF ACTION

Botulinum neurotoxins are primarily inactive, polypeptide di chains of 150 kDa that are released during bacterial lysis and are cleaved by tissue proteases into heavy (100 kDa) and light (50 kDa) chains with different roles in nerve cell intoxication. After lysis, this generates an active di-chain neurotoxin composed of a heavy chain and a light chain bridged by an interchain disulfide bond.¹² They are bound with nontoxic proteins to form a complex giving a total molecular weight of approximately 900 kDa for type A and 700 kDa for type B.¹³

The intoxication occurs in four distinct steps (which are shown in Figure 1): cell binding, internalization by means of endocytosis, membrane translocation, and catalyzation of the hydrolysis of peptides.

In types A and B, the heavy chain is responsible for selective binding of the neurotoxin to receptors on the surface of the presynaptic membrane of cholinergic nerve cells. This is followed by internalization inside vesicles by means of endocytosis and membrane translocation of the light chain into the nerve cell cytoplasm. The translocation is triggered by acidification of the vesicle lumen by a proton pumping ATPase, which leads to conformational change of the toxin. In its acid conformation, the toxin inserts into the lipid bilayer, and translocation of the light chain is promoted. The light chain is set free by reduction of the interchain disulfide bond and acts as a zinc-dependent metalloproteinase inside the cell to prevent the release of vesicle-bound acetylcholine.¹²,¹⁴ The neurotoxins are able to prevent release by disrupting peptides necessary for docking and ultimately exocytosis of the acetylcholine-containing vesicle. In type A, the light chain cleaves SNAP-25, a 25-kDa synaptosomal-associated protein, whereas the light chain of type B cleaves vesicle-associated membrane protein (VAMP).¹⁵,¹⁶

Little is known of the intracellular events after type B use. However, the clinical effects of type A subside because of collateral sprouting of new nerve terminals occurring with time. With time, the original functional endplate is re-established, and the sprouts regress.¹⁷

These differences in mechanism of action may explain variations in clinical performance. Type B
studies have shown that doses many times greater than that of type A are required to treat those with the same indications. There are also differences in the complication profile.18–23

**BOTULINUM TOXIN PRODUCTS**

Botulinum toxin type A is commercially available as either Botox or Dysport, both of which are sold in a lyophilized form that must be reconstituted with physiologic saline. Botox, which is manufactured by Allergan Inc. (Irvine, CA), is available internationally in 100 U per vial. It is shipped on dry ice and should be stored in a freezer at \(-5^\circ\text{C}\). Dysport is manufactured by Ipsen Limited (Berkshire, UK) and is primarily used in Europe, because it is not licensed in the United States. It is distributed in 500-U vials and needs to be stored at 2 to 8 \(^\circ\text{C}\). Type B toxin is sold as Neurobloc (or Myobloc in the United States), which is a premanufactured aqueous solution. It is distributed in 2500, 5000, or 10,000 U and is licensed in the United States and several European countries in the treatment of cervical dystonia.

For all the preceding products, doses are determined by in vitro mouse assays in units of biologic activity (U). One unit is defined as the amount of neurotoxin complex protein that is lethal in 50% of female, Swiss-Webster mice after an intraperitoneal injection (mouse LD\(_{50}\)). However, differences in serotype, formulation, and the way lethality tests are performed between manufacturers means results in units that vary greatly in their potency between the products. This leads to marked differences in dosing. Doses of Dysport can therefore be three to six times higher than the doses of Botox typically used to treat the same condition.24,25

**ADMINISTERING BOTULINUM TOXIN**

When administering the toxin, the physician should evaluate the patient with a thorough history and examination. A discussion of the nature of the problem and the expected effect should take place with informed consent obtained. If a cosmetic change is anticipated, photographs of the patient’s face at rest and activity should be taken. The skin should be prepared and marked at the site for injection, which should be recorded on a diagram in the patient’s medical records. A topical anesthetic such as eutectic mixture of local anesthetics (EMLA) cream may be used to decrease the discomfort of the procedure. The toxin is drawn up in syringe and injected with a 30-gauge needle at an angle of 30 degrees. Anatomy is essential in choosing the site for injection, although some clinicians favor the use of the electromyographic (EMG) needle. This is connected to the EMG machine and ground and reference leads placed on the face or supraclavicular area. If the needle is in the active part of the muscle and the patient now accentuates the specific facial expression that produces the unwanted line, a burst of activity will be heard on the speaker of the EMG. A distant signal (ie, one in which there is a low frequency, dull sound) should provoke the needle being moved until the signal is maximal and the toxin then injected. After the injections, the patient should be asked not to massage the injected area for several hours to avoid diffusion to adjacent muscles.26

The clinical effect of botulinum toxin is dose related. This allows treatment to be modified according to the requirements of individual patients. The dose required to produce a given degree of denervation is related to the mass of the targeted muscle. There is no way to determine in advance the dose of botulinum toxin required for therapeutic effect in a patient never treated before. The dose used also obviously is determined by the particular clinical application it is used for. The range of effective doses between patients for a given disorder may differ by several orders of magnitude.27

Improvement in symptoms usually occurs within 3 to 5 days, with clinical efficacy generally seen within the first 7 to 10 days. The effect of botulinum toxin begins to wear off 10 to 12 weeks after injection.28

**COMPLICATIONS AND ADVERSE REACTIONS**

Contraindications to the use of botulinum toxin include pregnancy or active breastfeeding, and it is relative contraindicated in pre-existing neuromuscular conditions. Some medications, such as aminoglycosides, penicillamine, quinine, and calcium channel blockers, can potentiate their effect by interfering with neuromuscular transmission and should not be used concomitantly with the treatment.29

The therapeutic use of botulinum toxin generally has been safe and well tolerated. Formation of antibodies may occur if the neurotoxins elicit an immune response. Although this is not a safety concern, it may lead to a nonresponse of subse-
quent botulinum toxin injection by blocking the therapeutic effects. Neutralizing antibodies developed against one serotype have not been reported to block the biologic activity of another serotype.\textsuperscript{30} Prevalence of resistance is <5%\textsuperscript{31} and is associated with dose and frequency of treatments. To minimize the chance of resistance, the smallest effective dose is used, and the interval between treatments is extended for as long as possible to minimize exposure.\textsuperscript{32} This research, however, was based on old preparations that had an increased protein load compared with the newer toxin, which has reportedly less antigenicity.

Botulinum toxin may diffuse to nearby or adjacent muscle, leading to adverse effects such as ptosis or drooling after facial injections.\textsuperscript{33} It may also affect muscles distant from the site of injection; a recent report documented three cases of generalized muscular weakness associated with its use.\textsuperscript{34} Long-term use of botulinum toxin causes reversible denervation atrophy in the muscles injected.\textsuperscript{35} Further research has demonstrated diminished size of type IIB fibers in muscles distant from the injection site\textsuperscript{36} and abnormalities on EMG.\textsuperscript{37,38}

Generalized reactions that have idiosyncratically occurred include nausea, fatigue, malaise, flu-like symptoms, and rashes at sites distant from the injection. Single-fiber electromyographic weakness and changes in neuromuscular transmission have been found in muscles distant to the injection site. This is possibly due to a small amount of toxin diffusing into the circulation.\textsuperscript{39,40}

Untoward sequelae that may occur at any injection site include pain, edema, erythema, ecchymosis, headache, and short-term hyperesthesia.\textsuperscript{41}

In the 23 years that botulinum toxin has been used in humans, there have been no reported deaths from an overdose. The estimated lethal dose for a 70-kg human, based on primates, is approximately 2800 U (40 U/kg).\textsuperscript{42}

**Clinical Uses for Botulinum Toxin in Otorhinolaryngology**

In otorhinolaryngology, the use of botulinum toxin is rapidly expanding. This includes the treatment of autonomic dysfunction; spasmodic dysphonia, vocal tics, stuttering and voice tremor, oromandibular and cervical dystonia, and blepharospasm; hemifacial spasm and facial nerve paresis; cricopharyngeal dysfunction, laryngeal rebalancing, and tension headache, as well as use in cosmetic applications.

**Autonomic Dysfunction.** Frey’s syndrome and hyperhidrosis (gustatory sweating and flushing on the cheek) is a well-described complication of parotid gland surgery. It was first reported in 1757 by Duphenix in a case secondary to trauma but is most commonly seen after parotid gland surgery. It has also been described after radical neck dissection\textsuperscript{43} or submaxillary gland surgery and may also occur after infection. The incidence of Frey’s syndrome after parotidectomy has been reported to be as high as 100% when a Minor’s starch test was used for diagnosis.\textsuperscript{44} However, many of these are asymptomatic, with only 30% being severely embarrassed by sweating after parotidectomy.\textsuperscript{43}

The cause of the syndrome is thought to be misdirected regeneration of damaged axons.\textsuperscript{45} When the skin is raised during parotidectomy, the postganglionic sympathetic fibers to the sweat glands in the flap are severed. Postganglionic parasympathetic fibers from the auriculotemporal branch of the mandibular nerve supplying the parotid gland are also severed when the salivary gland is removed. This allows cross-innervation of the sweat glands by branches of the auriculotemporal nerve and consequently gustatory stimulation.\textsuperscript{46}

Botulinum toxin, in addition to acting on muscle, has an effect on cholinergic autonomic nerve terminals.\textsuperscript{47} Both the parasympathetic nerves stimulating salivary gland secretion and the sympathetic fibers that cause sweating are cholinergic autonomic fibers. Hence, the regeneration of axons may be misdirected, and botulinum toxin inhibits both salivation and sweating.

Drobik and Laskawi\textsuperscript{48} first proposed treatment of Frey’s syndrome with botulinum toxin injection in 1994 and presented a case with 12 months’ follow-up in the following year. The methods described include identification of the area for injection using Minor’s starch test. This involves the application of a solution containing iodine, ricine oil, and alcohol painted onto the affected cheek.\textsuperscript{49} The identified area is then marked and divided into small squares of approximately 4 cm\textsuperscript{2}. In each square, 2.5 U of botulinum toxin type A (Botox) are injected intracutaneously. Patient self-assessment and a repeated Minor’s test after treatment demonstrate excellent results.\textsuperscript{50} Indeed, intracutaneous injections in the area of sweating seem to have the potential to be curative in the treatment of Frey’s syndrome, perhaps through sweat gland atrophy from chronic denervation. Some patients may re-
quire more than one treatment, but the extent of sweating decreases with each successive set of injections until it is no longer troublesome. Experience with intracutaneous injection in cases of Frey’s syndrome among some clinicians suggest it is a technically difficult procedure that may be unnecessary. Furthermore, its proposed immediate subcutaneous injection may allow a greater diffusion of drug and has lasting clinical effects in treating gustatory sweating.

Spasmodic Dysphonia and Voice Tremor. “Spasmodic dysphonia” and “laryngeal dystonia” are clinical terms used to describe an action-induced, laryngeal motion disorder. Patients with dystonia may have primary (idiopathic) or secondary (eg, neurologic) disease. Dystonia may be generalized, multifocal, or focal. Spasmodic dysphonia is a form of focal dystonia in which the action is that of speaking. It was first described in 1871 by Traube using the term “spastic dysphonia” when describing a patient with nervous hoarseness. In 1899, Gowers described functional laryngeal spasm in which the vocal cords were brought together too forcibly in speech. Aronson formally distinguished between two types of spasmodic dysphonia: an adductor type caused by irregular hyperabduction of the vocal cords and an abductor type caused by intermittent abduction of the vocal cords. Some patients display a combination of mixed adductor and abductor dysphonia. The first injection of botulinum toxin into the human larynx took place in 1984, with significant relief of symptoms.

Patients with the adductor type exhibit a choked, strained strangled voice quality with abrupt initiation and termination of voice, resulting in short breaks in phonation. The voice is generally reduced in loudness and is monotone. Voice tremor is frequently observed, as are a slow speech rate and decreased smoothness of speech, which reduces intelligibility.

Patients with the abductor type have a breathy, effortful voice quality, with abrupt termination of voicing resulting in aphonie, whispered segments of speech. The voice is reduced in loudness, and vocal tremor related to intermittent spasm or hypertonia of the posterior cricoarytenoid muscles is frequently observed.

Vocal tremor is a common feature of neurologic disorders and is a sign of neurologic disturbance. Some disorders may demonstrate voice tremor in combination with dysarthric speech (eg, Parkinson’s disease). It is present in 25% to 65% of patients with spasmodic dysphonia. Its treatment is essentially the same with injection of botulinum toxin into thyroarytenoid muscles and in some cases into the cricothyroid or thyrohyoid muscles.

In a series of patients with primary laryngeal involvement, 16% had spread of dystonia to another part of the body.

All patients considered for treatment should have a full history and head and neck examination. Fiberoptic laryngoscopy is performed in all patients to observe glottal function with particular reference to disruptions, spasms, breathy breaks, and tremor while the patient speaks with connected speech segments. Diagnosis may be aided by video recording and analyzing with slow speed and stop action. Additional speciality examinations include acoustic and aerodynamic measurements to evaluate for tremor, fundamental frequency, pitch and amplitude perturbation, harshness, fluency breaks, breathiness during sustained phonation and speech, and percutaneous EMG to evaluate tremor and areas of hyperactivity.

For the treatment of adductor dystonia, the injection of botulinum toxin into the thyroarytenoid complex is achieved with an EMG needle. The patient is placed in the supine position with a pillow underneath the upper back and the neck extended. The thyroid and cricoid cartilages are palpated, and the midline of the cricothyroid membrane is identified. The needle is placed into the thyroarytenoid vocalis complex by impaling the muscle through the cricothyroid membrane. The needle is advanced at an approximately 30-degree angle up and 30-degree angle laterally. The laryngologist listens for the muscle interference pattern on the EMG. Patients are instructed not to cough or swallow while the needle is in the airway. If there is difficulty tolerating the procedure, 0.3 cm$^3$ of 1% lidocaine may be injected into the airway through the cricothyroid membrane. The needle is advanced at an approximately 30-degree angle up and 30-degree angle laterally. The laryngologist listens for the muscle interference pattern on the EMG. Patients are instructed not to cough or swallow while the needle is in the airway. If there is difficulty tolerating the procedure, 0.3 cm$^3$ of 1% lidocaine may be injected into the airway through the cricothyroid membrane. In the treatment of abductor dystonia, the same preparation is used, although in this case, the needle is placed posterior to the posterior edge of the thyroid lamina. The needle is advanced through the inferior constrictor muscle to the cricoid cartilage and then moved under EMG guidance to the optimum position. The patient is asked to sniff to yield maximum abduction; 2.5 U/0.1 cm$^3$ is used per thyroarytenoid muscle in each case, and repeated treatments are usually required. One side at a time is injected, and further doses may be into the same muscle or contralat-
eral muscle, depending on response. Side effects of this treatment include breathy hypophonia and clinically insignificant aspiration. In the abductor patient, treatment is associated with greater risk, including mild to severe stridor caused by paralysis of the posterior cricoarytenoid muscle. There have been anecdotal reports requiring tracheostomies. Results of treatment of adductor spasmodic dysphonia with botulinum toxin injection are excellent, with an average benefit of 90% of normal function achieved. Treatment of the abductor type leads to an average benefit of 66.7% of normal voice.61

Vocal Tics and Stuttering. The success of botulinum toxin in the treatment of spasmodic dysphonia has led to its use in other conditions in which there is inappropriate or excessive muscular contraction in the larynx. Stuttering blocks, similar to dystonic spasms, are action-induced, task-specific movement abnormalities. They may involve respiratory, phonatory, and/or articulatory mechanisms of speech. When the glottis is affected, treatment with botulinum toxin may result in an increased fluency by both subjective and objective measures.62 The effectiveness of behavioral therapy has meant it is not used as a long-term treatment.

Botulinum toxin has been used successfully in controlling vocal tics of Gilles de la Tourette syndrome, including coprolalia.63–65 Its success in this context suggests an effect on the central nervous system, possible mediated through afferent pathways.

Oromandibular Dystonia. Oromandibular dystonia is classified according to the clinical effects of the predominant muscular forces. It may, therefore, be jaw opening, jaw closing, jaw deviation, or tongue protrusion dystonia or a combination of these. Some of these will be less amenable to treatment because of difficulties in compromising function during treatment. For example, tongue muscle treatment may lead to dysarthria and dysphagia.66 Injection of the digastric muscles in jaw opening may cause swallowing to be affected by diffusion of toxin to intrinsic tongue muscles, and it may be necessary to manage this complication with the insertion of a nasogastric tube. These problems have led to a limitation of what may be achieved intraorally with this treatment. The types of oromandibular dystonia treated most successfully are limited to involvement of the masseter, temporalis, and external pterygoid muscles.

Its use in this condition has led to its application in the treatment of temporomandibular disorders. These are described as a group of conditions affecting the temporomandibular joint, masticatory muscles, and associated structures. It often is seen as pain and dysfunction specific to the jaw.67,68

Botulinum toxin has also been used in the treatment of the tensor veli palatine muscle to relieve the clicking tinnitus of palatal myoclonus.69,70 Localizing the muscle may be difficult, because mouth opening may suppress the myoclonus. EMG is particularly useful in placing the injection.71

Cervical Dystonia. Cervical dystonia or torticollis is a common form of focal dystonia.72 The use of botulinum toxin was first described by Tsui in 1986, and since that time, its injection into the various neck muscles has become the first-line therapeutic approach.73

The treatment of cervical dystonia, as in other cases, relies on a thorough knowledge of anatomy. This may include the sternocleidomastoid, the trapezius, semispinalis capitis, the splenius capitis, the levator scapulae, and all of the lesser paraspinal muscles. Botulinum toxin type A (Botox) is injected into the affected muscles using total doses of 100 U per neck.73 It must be remembered that weakening one muscle will lead to the unopposed pull of its antagonist, and this may lead to a change in direction of the neck deviation.

Most patients report subjective improvement in the pain caused by muscle spasm. The most common adverse events are dysphagia, neck muscle weakness, and voice changes.74

Blepharospasm. Blepharospasm is the involuntary eye closure produced by spasmodic contractions of the orbicularis oculi.75 It is termed “essential blepharospasm” when only the orbital and periorbital muscles are involved. However in most patients with blepharospasm, other facial, pharyngeal, laryngeal, oromandibular, and cervical muscles are affected. Idiopathic cervicocranial dystonia characterized by blepharospasm and by oromandibular involuntary movements is referred to as Meige’s syndrome.

In blepharospasm, the lateral and medial parts of the eyelid are injected subcutaneously.
with botulinum toxin. One study describes the use of botulinum A toxin with an initial dosage of 12.5 U per eyelid in two separate injections, a total of four injections or 25 U per eye. Published reports document that in approximately two thirds of patients, the condition was improved, with many regaining nearly normal function. In addition to the reduction of spasms, patients also report a decrease in associated sensory complaints such as foreign body sensations in the eyes and photophobia.

Treatment is directed to minimize the chance of ptosis, diplopia, midface weakness, and epiphora. This is achieved by injecting no closer to the eye than the orbital margin to minimize intraorbital diffusion, avoiding the medial lower lid to spare the lacrimal pumping apparatus, and injecting no lower than the malar eminence to prevent midface effects.

Hemifacial Spasm. Hemifacial spasm is characterized by initially progressive, involuntary, irregular, clonic or tonic movements of muscles innervated by the seventh cranial nerve unilaterally. It often initially affects the orbicularis oculi muscle, followed by gradual spread to other parts of the face.

This disorder arises when the nerve is compressed at the root exit zone by an ectopic anatomic or pathologic structure, resulting in emphatic transmission. The most common cause of hemifacial spasm is compression by an atherosclerotic aberrant or intracranial artery as first described by Cambell and Keedy in 1974. Microvascular decompression of the facial nerve root through a retrosigmoid craniotomy has proven to be very successful in controlling this disorder, so that botulinum toxin remains a nonsurgical alternative. The facial muscles for injection are identified with a thorough knowledge of anatomy and the aid of EMG. These may include orbicularis oculi, orbicularis oris, the zygomatic muscles, frontalis, corrugator, paranasal region, mentalis, submental area, and platysma. Doses of botulinum toxin type A (Botox) used vary, but one publication gives an average of approximately 30 U per muscle in this application. The treatment gives excellent results, with 95% of patients having a marked to moderate improvement, and it may be used to manage the condition in the long term by repeated injection. Temporary facial weakness is the most common side effect, followed by lid weakness and ptosis.

The principal disadvantages of this method are the necessity for chronic treatment, the potential for ophthalmic complications similar to those of blepharospasm, and facial asymmetry secondary to muscle weakening.

Facial Nerve Paresis. During the acute phase of facial nerve paresis, botulinum toxin may be used to effect a therapeutic ptosis for corneal protection. In the recovery phase, facial nerve paresis may be accompanied by synkinesis. When this is troublesome, as in the case of involuntary eyelid closure, botulinum toxin may be useful.

Botulinum toxin has also been used to improve the facial symmetry of patients with facial paralysis by decreasing the excessive pull of the contralateral facial muscles during emotional expression. Injections of 2.5 to 5 U into each of the contralateral zygomaticus major, levators labii superiors, and anguli oris or risorius muscles leads to increased symmetry of the smile of moderate or marked benefit in most cases.

Cricopharyngeal Dysfunction. The cricopharyngeus muscle is the major component of the upper esophageal sphincter. The ring-shaped structure maintains a constant basal tone and luminal occlusion at rest but allows rapid relaxation and contraction on swallowing. Dysfunction of this muscle is a well-known cause of dysphagia that is most effectively treated in persistent cases by cricopharyngeal myotomy. In unclear cases or where there are temporary problems, botulinum toxin may be used.

The cricopharyngeus, as stated, is activated at rest, which permits the use of EMG guidance in percutaneous injection. An alternative is by directly injecting the muscle at endoscopy with the patient under general anesthesia. Patients demonstrate a 70% to 100% improvement when undertaking this treatment. Some cricopharyngeal spasm is caused or aggravated by reflux of gastric acid, which must be treated before relaxing the sphincter. Heartburn has been reported as a complication of this procedure.

Cricopharyngeal spasm may rarely prevent the successful use of tracheoesophageal speech after laryngectomy, and botulinum toxin has been used in its treatment.

Laryngeal Rebalancing. Rontal and Rontal coined the term “laryngeal rebalancing” to refer...
to the chemodenervation of the interarytenoid muscle and the ipsilateral thyroarytenoid and lateral cricoarytenoid muscle in the treatment of anteromedial cricoarytenoid dislocation. This term may be appropriately applied to an array of uses. Botulinum toxin has been used to weaken adductors as an adjunct to the treatment of vocal fold granuloma, posterior glottic synechiae, and dysphonia plicae ventriculares. The underlying principle is manipulation of the neural input to the larynx to improve healing or resolution of existing disease. It has been proposed that botulinum toxin be used to lateralize the vocal folds to maintain the airway in cases of bilateral paralysis, but, as yet, it has only been reported in an animal model.

**Tension Headache.** Binder first noted that patients receiving botulinum toxin for cosmetic reasons reported an improvement or cessation of migraine symptoms. This was confirmed in a double-blind, controlled trial. This treatment has also been promising in the treatment of chronic treatment of chronic tension headache.

**Cosmetic Applications.** Hyperfunctional facial lines that run perpendicular to underling muscle forces are caused by skin pleating with muscle contraction. Weakening the underlying muscle with botulinum toxin reduces or eliminates these lines, which has been shown in a placebo-controlled, double-blind study. It is effective in improvement of lines of the forehead, glabella, lateral orbits, and the nasolabial region. Botulinum toxin has also been used to reduce platysmal bands and adjust brow position.

With glabellar hyperkinetic lines as an example of technique, 10 U of botulinum toxin type A (Botox) may be injected into each corrugator muscle either with or without EMG guidance. This treatment gives excellent results, and 75% of patients are satisfied with the improvement in their appearance.

**Future Research Areas.** Further research in the use of botulinum toxin in the treatment of sialorrhea is awaited; however, there are no current documented studies of its use in humans at present. There is also potential for the treatment of rhinorrhea, with work currently underway on a suitable delivery vehicle for the toxin.

**CONCLUSION**

Botulinum toxin has been used safely in humans for more than 20 years. The effects are transient, such that treatments are required to be repeated at intervals. Its application to ENT provides a useful tool to treat dystonia, autonomic dysfunction, facial nerve paresis, and hyperfunctional lines. It may also be of benefit in laryngeal rebalancing and the treatment of headaches. Further research is being carried out, and new indications for treatment with botulinum toxin may include sialorrhea and rhinorrhea.

**REFERENCES**


104. Kendall KA, Leonard RD. Treatment of ventricular


