The Cosmetic Use of Botulinum Toxin

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Learning Objectives: After studying this article, the participant should be able to: 1. Discuss the basic science behind chemodenervation. 2. Describe examples of injection techniques for various facial areas. 3. Discuss potential side effects and their avoidance.

The approach to facial rejuvenation continues to evolve. For decades, the primary focus on rejuvenation has centered on modalities such as skin care, skin resurfacing, soft-tissue augmentation, and surgical intervention. A better understanding of the physiologic changes that occur with facial aging lends itself to new approaches and techniques that are mindful of the causes. As animation has shown to be a significant contributor to both the appearance of facial lines and soft-tissue malposition, there has been recent interest in chemodenervating agents and their applications in the field of facial rejuvenation. These agents, by and large, efface rhytides by selective and precise focal paralysis of the underlying facial musculature and, therefore, reduce or eliminate the prominence of the overlying rhytides. In addition, chemodenervation can serve as an adjunct for facial rejuvenation because of its influence on facial soft-tissue position and shape. Botulinum toxin, derived from Clostridium botulinum, is the most widely used agent; therefore, this new modality, its applications in cosmetic plastic surgery, and its applications to other areas will be discussed. (Plast. Reconstr. Surg. 112 [Suppl.]: 177S, 2003.)

Botulinum toxin is derived from the bacterium Clostridium botulinum, which is an obligate anaerobe. There are eight different subtypes of botulinum toxin (A, B, C1, C2, D, E, F, and G),1 although only two (types A and B) are currently manufactured for commercial use. All eight subtypes effect muscular paralysis by preventing the release of acetylcholine from the presynaptic neuron at the neuromuscular junction, but they do so at different target sites and with variable effectiveness.2,3 Botulinum toxin A is the most potent of all the subtypes and, therefore, is the one clinically used most frequently. Its effects are both dose dependent and reversible.4 Muscle weakness can be appreciated as soon as 6 hours after exposure. However, full paralysis and obvious clinical effects usually manifest by 7 days5 (though sometimes even longer), and last between 3 and 6 months. Physiologic and clinical effects dissipate as new neuromuscular junctions develop and axonal sprouting takes place.6

The first described use of botulinum toxin as an injectable local paralytic agent was by Scott in 1980, when he used the toxin to manage strabismus caused by ocular muscle spasticity.7 Subsequently, botulinum toxin has been applied in the management of various disorders, including but not limited to various dystonias, facial and generalized muscle spasms and other spastic muscle disorders, autonomic disorders, migraine headaches, and involuntary movement disorders.8–39

The first described use of the toxin in aesthetic circumstances was by Clark and Berris in 1989,40 when it was used to help correct facial asymmetry caused by facial nerve paralysis after rhytidectomy. In 1992, Carruthers and Carruthers41 reported positive effects of the toxin on the appearance of deep glabellar furrows in patients treated in the periorbital region for benign essential blepharospasm. Its uses in fa-
cial rejuvenation have blossomed since that time, although all of these applications were considered “off-label” uses. On April 15, 2002, the U.S. Food and Drug Administration approved the use of botulinum toxin type A to ameliorate moderate to severe glabellar rhytides. Other common cosmetic uses, such as the treatment of crow’s feet, perioral rhytides, and platysmal bands, still remain off-label.

THE PRODUCT

There are currently three botulinum toxin formulations available, two of the A subtype and one of the B. The two sources of commercially available type A subtypes are Botox (Allergan, Irvine, Calif.) and Dysport (Speywood Pharmaceuticals, Maidenhead, England; Inamed, Santa Barbara, Calif.). Botox is used most often in the United States. Botox is two to four times as effective in similar-unit doses as Dysport, which is why it is available in smaller vials (100-U vials for Botox versus 500-U vials for Dysport). Myobloc (Elan Pharmaceuticals, South San Francisco, Calif.) is derived from the botulinum toxin B subtype, and is far less potent per unit dose, in general, than the A subtype (though the bioequivalency formulation has yet to be established). Although all agents have comparable effects, they vary in several ways, including local discomfort with injection, onset of action, and duration of effects.

All forms of commercially available botulinum toxin are fragile and should be reconstituted and administered in a specific way to optimize drug potency. The manufacturer of Botox (Allergan) distributes the vials containing 100 U of freeze-dried crystalline toxin, 0.9 mg of sodium chloride, and 0.5 mg of human albumin in an environment of −5°C. Reconstitution of the dehydrated toxin should be performed with care. We prefer to use nonbacteriostatic saline; however, some prefer preserved saline solution with 0.9% benzyl alcohol to decrease potential contamination during storage of the reconstituted vial. When reconstituting the toxin, great care must be taken to avoid turbulence and agitation when adding the saline or when shaking the bottle; both actions can lead to foaming, which can lead to possible denaturation and subsequent clinical ineffectiveness. Using a larger-gauge needle (such as an 18-gauge needle) for reconstitution, or even breaking the vacuum seal by removing the rubber stopper, can help to limit turbulence. Alcohol, used either on the vial cap or on the patient’s skin, should be allowed to evaporate completely before use of the toxin, because it can inactivate the toxin, as well.

Although the vial can be reconstituted to a dilution of 8 ml/100 U, we prefer a dilution with 4 cc of saline to yield a concentration of 2.5 U/0.1 ml. The reduced volume may limit the potential for possible unwanted diffusion of the toxin to surrounding areas. However, precise application is the most important parameter to reduce side effects.

The reconstituted toxin must be stored in the refrigerator. Although the manufacturer recommends use within 4 hours, some have reported effectiveness up to 30 days after reconstitution. Others have shown a significant loss of efficacy after 3 to 7 days. Bacterial colonization of the solution must be taken into account with long storage times, especially if nonbacteriostatic saline is used as the reconstituting agent. Freezing the reconstituted toxin should be avoided, because this substantially decreases the efficacy of the toxin.

TECHNIQUE OF ADMINISTRATION

As with any medical procedure, informed consent should be obtained by the physician. The patient should avoid all medications that can predispose to bleeding or coagulation problems for 10 to 14 days before treatment, because this will lead to more ecchymosis after injection. Ice (before or after) and/or topical anesthetic agents are used to lessen patient discomfort. Furthermore, the use of small-gauge needles (30 gauge) not only helps make the treatment more tolerable but also reduces the potential for ecchymosis, especially in the lateral canthal area.

Accurate injection of small volumes of properly concentrated solution is preferred, as has been discussed. It is important to isolate the muscle to be treated (by voluntary muscle contraction and nondominant-hand palpation), to avoid inadvertent injection and undesired paralysis. Electromyographic guidance has been used for those muscles that cannot be readily appreciated by visualization or palpation, but it is generally not necessary in clinical practice. An electromyogram can also be used to analyze the muscle function in those patients who have been treated but who have not shown the desired or expected effect. This may help eliminate one of the variables that could be liable for treatment failure. Electromyographic
studies have shown that the toxin can spread by diffusion to an area up to 3 cm or more from the injection site, so accurate intramuscular injection, preferably into the muscle belly itself, is recommended in most cases (Fig. 1). Deep massage may affect the treated area, and could result in unwanted spread of toxin.

**Clinical Applications**

Although botulinum toxin has many clinical applications, this article will specifically address its cosmetic uses in facial rejuvenation, including its effects on the effacement of rhytides and its role in cosmetic facial reshaping. Both uses require an inherent knowledge base of the underlying muscles of facial expression.

**Upper Third of the Face**

Four muscles are primarily responsible for the primary dynamic rhytides of the upper third of the face: the frontalis, the procerus, the corrugator supercilii, and the orbicularis oculi muscles. The procerus, corrugator, and orbicularis all serve to depress the eyebrow at different regions along its length, whereas the frontalis acts to elevate the brow. Each of these muscles has different effects, either alone or in combination, to produce overlying rhytides (Table I).

Although exact amounts of toxin to be used per area can vary, the underlying principle is that the more mass the target muscle has, the higher the dose required to obtain the desired effect. Therefore, in general, the more bulky corrugator muscle requires more toxin than the thinner orbicularis. Furthermore, the dose is also dependent on sex (males generally require more secondary to increased muscle mass), prior exposure, and time interval since the last injection.

**Forehead.** Effacement of forehead rhytides can be accomplished by first marking the rhytides with a marker during active contraction and subsequently injecting along the demarcated line every 1 or 1.5 cm, for a total of 10 to 20 U (Fig. 2). Alternatively, patients can be asked to raise their forehead and eyebrows while injection is given to these areas without the need for marking. However, in men with thicker frontalis and corrugator muscles and more prominent rhytides, an additional 10 to 15 U may be required. Most clinicians avoid injection within 1 cm superior to the eyebrow to reduce the chance for migration and diffusion of the toxin that may affect the upper eyelid elevators. We prefer more superficial injections in this area, because deeper injections (near the periosteum) can lead to brow ptosis.

Occasionally, chemodenervation of the frontalis muscle may unmask previously undiagnosed upper eyelid ptosis that had been compensated for by the frontalis. Therefore, evaluation of this potential situation should be performed before treatment (having the patient look forward in repose and removing the frontalis contribution), and its possibility should be discussed with the patient. Furthermore, overly aggressive injection into the frontalis can also lead to unopposed brow depressor function with resultant brow ptosis, which can be highly unaesthetic. Treatment of such a complication may involve chemodenervating the opposing procerus and lateral orbital orbicularis oculi muscles.

**Procerus and corrugator.** The procerus, corrugators, and medial orbital orbicularis oculi muscles are all, to varying degrees, responsible for the vertical glabellar rhytides and the hor-

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**TABLE I**

Muscles of the Upper Third of the Face Primarily Responsible for Rhytides

<table>
<thead>
<tr>
<th>Muscle</th>
<th>Function</th>
<th>Corresponding Rhytides</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frontalis</td>
<td>Brow elevator</td>
<td>Horizontal forehead lines</td>
</tr>
<tr>
<td>Procerus</td>
<td>Medial brow depressor</td>
<td>Transverse glabellar lines</td>
</tr>
<tr>
<td>Corrugator supercilii</td>
<td>Brow depressor</td>
<td>Vertical glabellar lines</td>
</tr>
<tr>
<td>Orbicularis oculi</td>
<td>Brow depressor</td>
<td>Crow’s feet (lateral canthal)</td>
</tr>
</tbody>
</table>

Fig. 1. Botulinum toxin can spread to an area up to 3 cm from the injection site.
Horizontal rhytides at the bridge of the nose. The procerus is prominent between the medial margins of each eyebrow, whereas the corrugators lie more laterally. To chemodenervate this area, several injection sites are used.

Some plastic surgeons prefer the hourglass technique shown in Figure 2, left, and Figure 3. In this technique, the waist, or narrowest portion of the hourglass, is a single point just inferior to a line joining the medial brow margins. This point receives 2 or 3 U of toxin. The inferior (wider) aspect of the hourglass consists of two points just lateral to the dorsal aesthetic lines along a plane just inferior to the medial canthi. These points receive approximately 2 U per site and are used to chemodenervate the proximal nasalis muscle to prevent the “bunny” look. The superior portion of the hourglass is formed by points just above the medial brow (in line with the medial canthus) that course along the superior orbital rim. Here, 4 or 5 U of toxin is injected on each side. Of course, these doses can be adjusted depending on the prominence of the rhytides and the mass of the underlying muscles.

Orbicularis oculi. The orbicularis oculi has three parts: the outer orbital part, the inner palpebral portion, and the medial lacrimal part. The medial aspect serves as a brow depressor and can be addressed as above. Hyperfunctional movement and resultant hypertrophy of the lateral fibers are primarily responsible for rhytides that radiate axially away from the lateral canthus, forming what is known as crow’s feet. Because this muscle is the underlying etiology for the rhytides, chemodenervation is the optimal treatment rather than other modalities such as excisional techniques, resurfacing, or soft-tissue augmentation. However, because the orbicularis function is necessary to close the ocular aperture, complete paralysis of this muscle is unreasonable. Rather, weakness of the muscle is the objective.²²

It is important to identify and locate the areas of orbicularis to be treated. This is done by having the patient actively squint (Fig. 4). The toxin is then injected in three or four areas.²⁶,²⁷ It is important to use a high concentration (low volume) of Botox⁶⁸,⁷¹ and inject slowly⁶⁹ to prevent potential diffusion to un-
wanted areas. The areas of injection extend from just inferior to the lateral edge of the eyebrow, down the lateral aspect of the lateral orbital rim, to a point lateral to the infraorbital rim. Two or three units of toxin are injected at each point. To avoid complications, it is important to restrict injection to these areas. If the injection site is too medial, diffusion of the toxin can affect the medial orbital portion of the orbicularis oculi muscle, resulting in lower lid ptosis (retraction and/or ectropion), strabismus, epiphora, and diplopia, as well as the possibility of potentiating dry eye symptoms. Injecting more inferiorly can result in unwanted paralysis of the zygomaticus major, resulting in lip ptosis and an asymmetric smile. Injecting more superiorly can result in paralysis of the inferior fibers of the frontalis muscle, resulting in eyebrow ptosis. Furthermore, many practitioners inject the periocular area in a subcutaneous rather than intramuscular plane to allow for treatment of a larger area with fewer injection sites. The thinner orbicularis seems to respond adequately to this more superficial injection. Because there is a rich vascular plexus in this area, more injection sites can result in more unwanted ecchymosis.

Eyebrow. Mild to moderate brow ptosis can be managed in selected patients with chemodenervation of the brow depressors. This technique can also be used as a treatment for inadvertent paralysis of the inferior frontalis fibers, as previously described. The result is, in effect, a "chemical brow lift," although it usually only results in approximately 1 or 2 mm of elevation. More significant ptosis is reserved for surgical treatment.
The brow contour can also be reshaped using chemodenervation, which can result in an apparent improvement of the brow position. For instance, the medial frontalis muscle can be chemodenervated with concurrent treatment to the lateral brow depressor. This combination can give the illusion of a chemical brow lift by affecting the relative positions of the medial and lateral aspects of the brow, despite minimal absolute changes.

### Middle Third of the Face

In general, it is important to distinguish between dynamic rhytides caused by underlying muscle hyperkinetics and static rhytides resulting from the natural process of aging (collagen loss and photodamage). This difference should be explained to the patient to reduce the incidence of patient dissatisfaction, because chemodenervation will not ameliorate static rhytides. Because static rhytides are more common in the midface, accurate diagnosis and proper counseling are imperative for a successful outcome. Furthermore, chemodenervation of the mimetic muscles causing dynamic rhytides in this region of the face is done with great caution, because functional deficits in this region are common.

**Nose.** In patients with severe nasal flaring resulting in increased columellar show, the alar portion of the nasalis muscle has been chemodenervated to reduce the flaring. Approximately 5 U of toxin is injected per side where the nasalis is visible on active nostril flaring. The nostril geometry itself is not altered with this treatment, because its configuration is based more on the lateral crus than on the nasalis.

**Nasolabial fold.** In 1992, Pessa and Brown performed a cadaver study to determine the relative influences various mimetic muscles had on the nasolabial fold. They found that the levator labii superioris alaeque nasi had the most prominent effect on the medial nasolabial fold, whereas the levator labii superioris had the greatest influence on the middle of the fold. On the basis of this information, Kane tried chemodenervation of the levator labii superioris alaeque nasi to efface the medial nasolabial fold. He found that the greatest improvement (and satisfaction) was in those people with “canine” smiles (according to Rubin’s classification) with high central lip elevations and large resultant incisor show. Still, some patients felt that the tradeoff of alterations in their smile mechanics was not worth the aesthetic improvement, even in this subgroup. Others have tried chemodenervation of these mimetic muscles and have also found lengthening of the upper lip and decreased tooth show. The alteration of smile mechanics can be especially dramatic in the instance of zygomatic major muscle chemodenervation, because this muscle is responsible for the predominant smile morphology in population studies. As a result, rejuvenation of this area is best accomplished by other modalities, such as rhytidectomy and collagen or fat injection.

### Lower Third of the Face

**Mouth and lips.** The main muscles of this region are the orbicularis oris, depressor anguli oris, and mentalis. As with the other regions of the face, it is imperative to distinguish between dynamic rhytides resulting from functional underlying muscle hyperkinetics and static rhytides resulting from the natural process of aging and atrophy. The small, vertically oriented rhytides of the upper lip can, in some instances, be treated by chemodenervation of the orbicularis oris. To differentiate functional rhytides from senescent changes, have the patient actively purse the lips. This maneuver will exacerbate the rhytides if they are functional in nature. To treat this area, the most prominent rhytides are

![Fig. 5. Perioral rhytides in repose and with active contraction (pursing of the lips). The dots indicate areas of anticipated injection sites.](image-url)
marked, and toxin is injected in a subcutaneous plane on both sides of the rhytides (Fig. 5). Each site should receive approximately 0.5 to 1 U of toxin. Again, overly aggressive injection, either in depth or amount, can result in flaccid paralysis of the orbicularis with resultant oral incompetence and lip asymmetry.

If the oral commissures are persistently downward sloping from an overactive depressor anguli oris muscle, or if the patient has prominent marionette lines or labiomental creases, chemodenervation may help. The muscles are located by having the patient actively frown. The depressors are marked and subsequently injected with 2 or 3 U of toxin. The location of the intramuscular injection should be approximately 1 cm lateral and 1 cm inferior to the angle of the mouth. Orbicularis incompetence can result if these margins are violated. A reduced amount of lower tooth show will be variably induced with the treatment of the lip depressors. The preoperative assessment will determine the individual appropriateness of this approach.

**Mentalis.** Occasionally, topographic chin irregularities (such as cobblestoning) can be seen as a result of a hyperkinetic mentalis muscle. To successfully chemodenervate this area, a total of 10 U of toxin is subcutaneously injected (in several aliquots) into the affected area, making sure to stay at least 1 cm inferior to the mental sulcus. This technique will help avoid oral incompetence due to inadvertent orbicularis oris paralysis from toxin migration.

**The Neck**

The aesthetic appearance of the neck is significantly affected by age and by a hyperkinetic underlying platysma. Although lipodystrophy and static rhytides are not amenable to treatment with botulinum toxin, vertical muscle banding and horizontal neck rhytides can be ameliorated by chemodenervation. These changes are thought to be secondary to a hyperkinetic platysma with concomitant loss of tone.\(^{81,82}\)

Chemodenervation of the neck can be performed rapidly, safely, and repeatedly, with predictable results. In general, the neck requires larger doses than the face, and the onset of action of toxin is relatively faster. Matarasso et al. have developed a modified classification system for age-related neck degeneration (Table II).\(^{59,83}\) This system, in turn, is helpful in determining the dosage of botulinum toxin required to chemodenervate the platysma (Table III).\(^{59}\) It is also helpful in estimating the pretreatment prediction of positive outcome, with the best results found in category II and III necks (98.5 percent good to excellent results).\(^{59}\) The effect usually lasts for 3 to 6 months. If suboptimal results are obtained after the first treatment, reinjection can be performed after 14 days.

The technique of treatment is as follows: obtain informed consent; cleanse skin with alcohol; in seated position, have patient forcefully grimace (Fig. 6); identify and isolate the platysmal bands with the nondominant hand (Fig. 7); inject 2.5 to 5 U of toxin into the muscle belly at 1-cm to 1.5-cm intervals along the band, including down to where the muscle meets the clavicle, when present.

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**TABLE II**

Classification of Age-Related Neck Degeneration*

<table>
<thead>
<tr>
<th>Category</th>
<th>Horizontal Neck Rhytides</th>
<th>Platysmal Bands</th>
<th>Skin Laxity</th>
<th>Subcutaneous/Submuscular Fat</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Minimal</td>
<td>Detectable with minimal neck contracture</td>
<td>Minimal</td>
<td>Variable</td>
</tr>
<tr>
<td>II</td>
<td>Mild</td>
<td>Thin, mild flaccidity</td>
<td>Mild</td>
<td>Variable</td>
</tr>
<tr>
<td>III</td>
<td>Moderate</td>
<td>Thick, moderate flaccidity</td>
<td>Moderate</td>
<td>Variable</td>
</tr>
<tr>
<td>IV</td>
<td>Deep</td>
<td>Heavy, severe flaccidity and hypertrophy at rest</td>
<td>Severe</td>
<td>Variable</td>
</tr>
</tbody>
</table>


**TABLE III**

Correlation of Category of Aging Neck Deformity with Suggested Dose of Botulinum A Exotoxin

<table>
<thead>
<tr>
<th>Category of Neck Degeneration</th>
<th>Dose Range*</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>30–50 U</td>
</tr>
<tr>
<td>II</td>
<td>30–75 U</td>
</tr>
<tr>
<td>III</td>
<td>50–100 U</td>
</tr>
<tr>
<td>IV</td>
<td>50–250 U</td>
</tr>
</tbody>
</table>

It is important to confine the injection of toxin to the superficial platysma, rather than the deeper musculature, because weakness of the neck flexors and dysphagia have been reported with injection into the muscles of deglutition. Meticulous attention should be directed to the thinner necks of women to avoid this potential complication.

**Complications**

Although botulinum toxin is relatively safe if used properly, it must be remembered that it is one of the deadliest toxins known to humans. Contraindications to treatment are pregnancy, lactation, allergic reaction to human albumin, history of neuromuscular disorders (myasthenia gravis, Eaton-Lambert syndrome, amyotrophic lateral sclerosis), concomitant use of certain medications known to potentiate the effects of botulinum toxin (penicillamine, quinine, calcium channel blockers, and aminoglycosides), and psychological instability.

Complications can be subdivided into three categories: local, regional, and systemic. The most common local side effect is pain at the injection site. Other local effects can include erythema, rash, ecchymosis, edema, hyperesthesia, and hematoma. These can be minimized by slow injection rates, topical anesthetics, ice, and avoidance of treatment in patients currently taking nonsteroidal anti-inflammatory drugs.

Regional complications, such as unwanted weakness or paralysis of muscles adjacent to the point of injection, have been previously described. Upper lid ptosis from levator paralysis, brow ptosis from frontalis dysfunction, lip asymmetry from zygomaticus major paralysis, and dysphagia from deep neck muscle weakness all result from migration and diffusion of toxin. To minimize these unwanted results, landmarks and boundaries to injection sites and the depth of injection must be adhered to. Mild to moderate upper eyelid ptosis can be effectively treated until the lid ptosis resolves with the use of topical antihistamine or decongestant agents (eye drops) that have the adrenergic side effect of contracting the Müller muscle (Naphcon A eye drops; Alcon, Inc., Fort Worth, Texas).

In rare instances, systemic reaction has been
described. As mentioned previously, those with allergies to human albumin should avoid this product altogether, because human albumin is an ingredient. Reactions such as fatigue, malaise, distant rashes, and nausea can occur, but are rare. There are two cases reports of severe systemic reactions. One report describes lower limb anaphylaxis after injection for foot dystonias, and the other details a case of respiratory arrest after treatment for muscle spasticity. It should also be mentioned that occasionally antitoxin antibodies can develop, rendering the toxin inactive. This effect is more likely to occur if higher-than-recommended doses are given or when treatments are performed more frequently than suggested.

OTHER APPLICATIONS

Other medical conditions have been successfully managed by harnessing the effects of botulinum toxin. The following conditions have demonstrated improvement with chemodenervation: benign essential blepharospasm, cervical dystonias (including torticollis), general spasticity, strabismus, vaginismus, posthrytidectomy synkinesis after partial facial nerve palsy, cranial nerve disorders (including hemifacial spasm), Frey’s syndrome (gustatory sweating), excessive perspiration, migraine headaches, stress headaches, Hirschsprung disease, anal fissures, and esophageal motility disorders.

SUMMARY

The chemodenervating effect of botulinum toxin has been successfully harvested and applied to the field of cosmetic plastic surgery. Treatment is safe, effective, predictable, minimally invasive, and repeatable. Its temporary effect on the hyperkinetic muscles of the face and neck, with subsequent ameliorating effects of the overlying rhytides, makes botulinum toxin a useful adjunctive therapy in aesthetic rejuvenation. If performed by qualified individuals on carefully selected patients, this treatment modality may offer a viable nonsurgical choice for rejuvenation of the aging face.

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Self-Assessment Examination follows on the next page.
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1. REGARDING THE DOSE AND DURATION OF ACTION, CHEMODENERVATION BY BOTULINUM TOXIN IS:
   A) Dose independent and permanent
   B) Dose independent and temporary
   C) Dose dependent and permanent
   D) Dose dependent and temporary
   E) None of the above

2. WHICH OF THE FOLLOWING IS RECOMMENDED FOR THE SAFE HANDLING OF BOTULINUM TOXIN TYPE A?
   A) Keep vial frozen before reconstitution
   B) Use sterile water for reconstitution
   C) Shake vial well after reconstitution
   D) Keep reconstituted solution at room temperature
   E) Discard unused solution after 30 days

3. IN ORDER TO MINIMIZE ADVERSE OR UNTOWARD SIDE EFFECTS WHEN USING BOTULINUM TOXIN TYPE A:
   A) Use the most dilute concentration possible
   B) Use large-bore needles
   C) Use nonsteroidal anti-inflammatory drugs preoperatively to reduce inflammation
   D) Massage area after injection
   E) Apply ice to area after injection

4. STATIC RHYTIDES CAN BE TREATED WITH THE SAME EFFECTIVENESS AS DYNAMIC RHYTIDES:
   A) True
   B) False

5. OF THE FOLLOWING, WHICH IS THE MOST SIGNIFICANT POSSIBLE COMPLICATION OF BOTULINUM TOXIN TYPE A USED IN THE SUPRAORBITAL REGION?
   A) Pain on injection
   B) Ecchymosis
   C) Hematoma
   D) Blepharoptosis
   E) Brow ptosis

To complete the examination for CME credit, turn to page 192S for instructions and the response form.