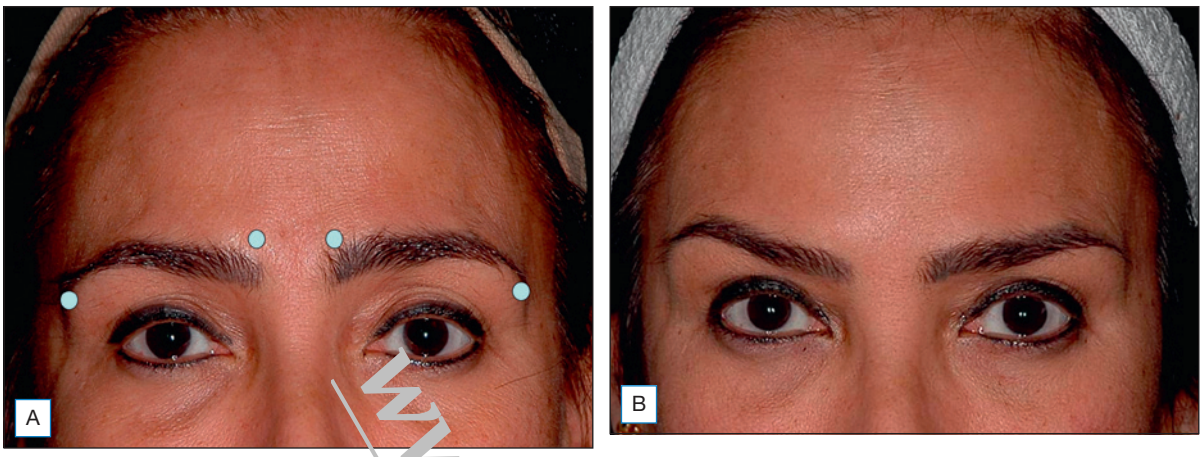

Figure 5.4 The chemical brow lift: **A,** Injection sites for a chemical brow lift if performed alone are shown (5 to 10 s.U or 3 to 5 OnaBoNT units per injection site). This patient had a male pattern eyebrow without perceptible arching. She received AboBoNT treatment to the lateral tail of each eyebrow (10 s.U per side) and into the corrugator bodies (total 20 s.U) *(blue dots)*, and to the frontalis (20 s.U). **B,** Posttreatment photo at 33 days reveals an elevated and laterally arched feminine brow.

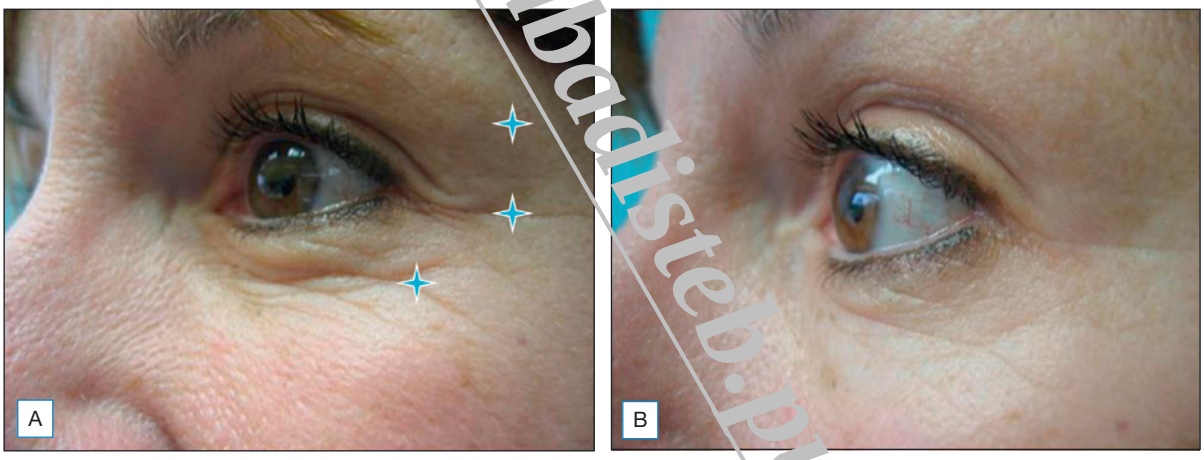

Figure 5.5 Crow's feet injection: the standard three-point crow's feet injection is depicted (**A**). The patient received 5 OnaBoNT units at each point and had an excellent response (**B**).

into each corrugator body. In combination with medial and central frontalis denervation, which tends to lower the medial brow, a pleasingly arched female pattern eyebrow can be shaped (see Fig. 5.4B).

Crow's feet

Lateral periorbital wrinkling is effectively treated with neurotoxin. Crow's feet are typically treated with three equal injections of 10 to 15 s.U evenly spaced along an arc at the external orbital rim (Fig. 5.5A and B). The middle injection is placed in line with the lateral canthus. Injections flanking this point at 8 to 10 mm are then placed, but their exact positioning depends on the width of the individual's canthal lines.

An additional injection of 2 s.U microinjections can be judiciously placed in the lower lid at the midpupillary line 2 mm below the tarsal plate (Fig. 5.6). This will flatten the bulging muscle and create an image of an "open eye." However, overaggressive treatment may create an unwanted ectropion.

Treatment of the lower face

Treatment of the lower face should be performed with more precaution because overdosage leads to significant dysfunction of the orbicularis oris, creating an asymmetric smile and oral aperture. Dosage recommendations in the lower face are shown in Table 5.2. As with OnaBoNT treatment, the physician must have a thorough understanding

Figure 6.4 The total-face approach: injection sites to treat the glabellar region **(A)**, eyebrows **(B)**, mephisto **(C)**, lateral canthal lines **(D)**, forehead **(E)**, lower eyelid **(F)**, open eye **(G)**, bunny lines **(H)**, gummy smile **(I)**, upper and lower lip **(J)**, marionette lines **(K)**, mentalis **(L)**, and platysma **(M)**. *Courtesy of Merz Pharmaceuticals.*

Figure 8.1 Neuronox® is marketed under different brand names, such as Botulift®, Siax®, Cunox®, and Meditoxin®.

Figure 8.2 Innotox® is a new innovative botulinum toxin type A (BoNT-A) product that was approved in South Korea in 2013 and is both the first liquid and non-animal substance-based BoNT-A.

0.9 mg of sodium chloride and 0.5 mg of human serum albumin. The package insert for Neuronox® recommends reconstitution with nonpreserved 0.9% sodium chloride solution.

Three double-blind, randomized, comparative studies of Neuronox® and Botox® concluded there were no significant differences between both treatment groups in treating essential blepharospasm, spasticity in children with cerebral palsy, and glabellar lines, at a 1 : 1 dose ratio.

Innotox®: novel liquid botulinum toxin type A product

Innotox® (MT10109L, Medytox Inc., South Korea) is the first liquid injectable form of BoNT-A, approved by the Ministry of Food and Drug Safety in South Korea in 2013. Innotox® is produced by the same strain of C. *botulinum* as Neuronox® and Botox®. The molecular weight of Innotox® analyzed using size exclusion SE-HPLC is approximately 900 kDa, which is highly comparable to those of Neuronox® and Botox®, and its diffusion capacity is similar to that of Botox®.

Innotox® is provided as a ready-to-use sterile liquid with 4 U/0.1 mL concentration. Therefore no risk of contamination or inaccurate dosing due to human errors during reconstitution exists, which ultimately enhances the treatment safety and efficacy. Furthermore, its storage and reuse are more convenient, and Innotox® has a long stability with an expiration of 36 months under 2°C to 8°C storage conditions.

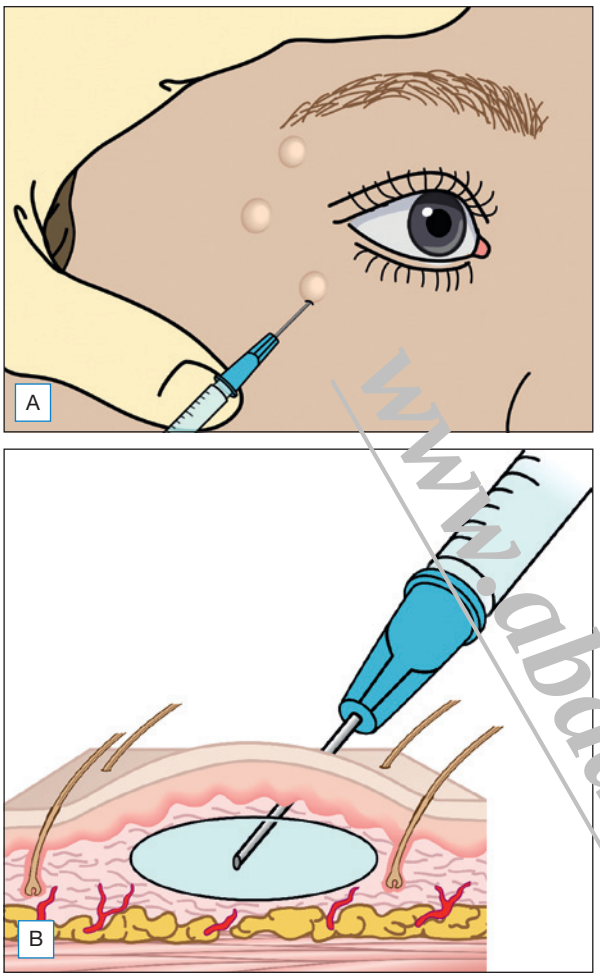

Figure 18.4 (A) Injection wheals illustrating the superficial injection technique of botulinum toxin around the periocular region. **(B)** Placement of botulinum toxin into the dermis rather than the underlying muscle or at the level of periosteum.

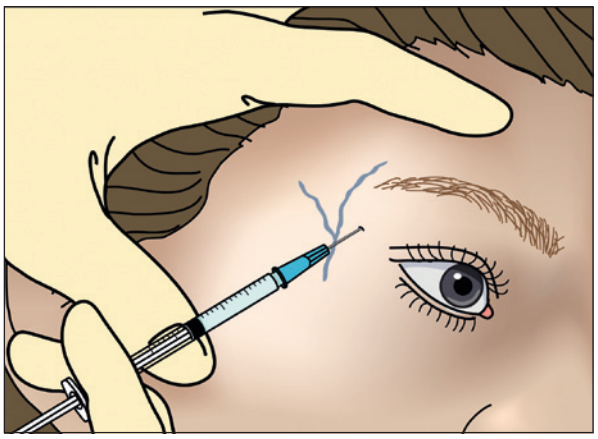

Figure 18.5 Stretching of the skin and side lighting can aid in identifying and then avoiding blood vessels during botulinum toxin injection.

in 0.05 mL). The more concentrated side had a slightly greater effect of reducing wrinkling; however, there was no statistically significant difference observed in between the two sides. Currently, the standard of care allows for use of botulinum toxin more than 24 hours after reconstitution and to use on more than one patient per vial. The most recent consensus statement from a task force of experts suggests that botulinum toxin can be refrigerated for at least 4 weeks before injection without significant risk for contamination or decreased effectiveness and also it can be used to treat multiple patients.

For standard treatment of periorbital rhytides, injections are commonly placed 1.5 cm from the lateral canthus or 1 cm lateral to the bony orbital rim. Some injectors place the injection on or even inside the orbital rim with equal effect and no increase in side effects. The injected dose and pattern are adjusted to account for individual patient preference, as well as the strength and size of the orbicularis oculi muscle.

The early studies suggested that 6 to 18 U of onabotulinumtoxinA (Botox®) be injected per side as three to four injections along a 90- to 180-degree arc, spaced at 1 to 1.5 cm intervals. However, based on the phase II study comparing 12 to 24 U, subjects responded better to 24 U. The efficacy and safety of onabotulinumtoxinA treatment of moderate-to-severe CFLs were evaluated in two randomized, controlled phase III studies consisting of 1362 patients. The 24 U dose was used, and two injection patterns were used, with three injection sites per side in the lateral orbicularis oculi muscle (Fig. 18.6). The injections were made with the needle bevel tip pointed up and oriented away from the eye. Each injection was 0.1 mL in volume and contained 4 U onabotulinumtoxinA, for a total dose of 24 U. The CFL responder rates were significantly greater with onabotulinumtoxinA compared with placebo at day 30 ($p < 0.001$). Of note, eyelid edema was the only adverse event reported in greater than 1% of patients receiving onabotulinumtoxinA, and it occurred more frequently with onabotulinumtoxinA than with placebo.

With regard to abobotulinumtoxinA (Dysport®), Ascher et al. evaluated the efficacy and safety of 15, 30, and 45 U injections per side in the treatment of crow's feet. At week 4, response rates at maximum smile were 42% in the 15 U group, 60% in the 30 U group, and 57% in the 45 U group, with response defined as an improvement in crow's feet severity of at least one grade from baseline on both sides. This improvement in rhytides was maintained for up to 8 weeks in the 15 U group and for up to 12 weeks in the 30 and 45 U groups. Although a statistically significant difference in efficacy was not appreciated when comparing the 30 and 45 U groups, one patient in the 45 U group did develop eyelid ptosis, which resolved by day 31. Beyond this, no difference in the safety profile between

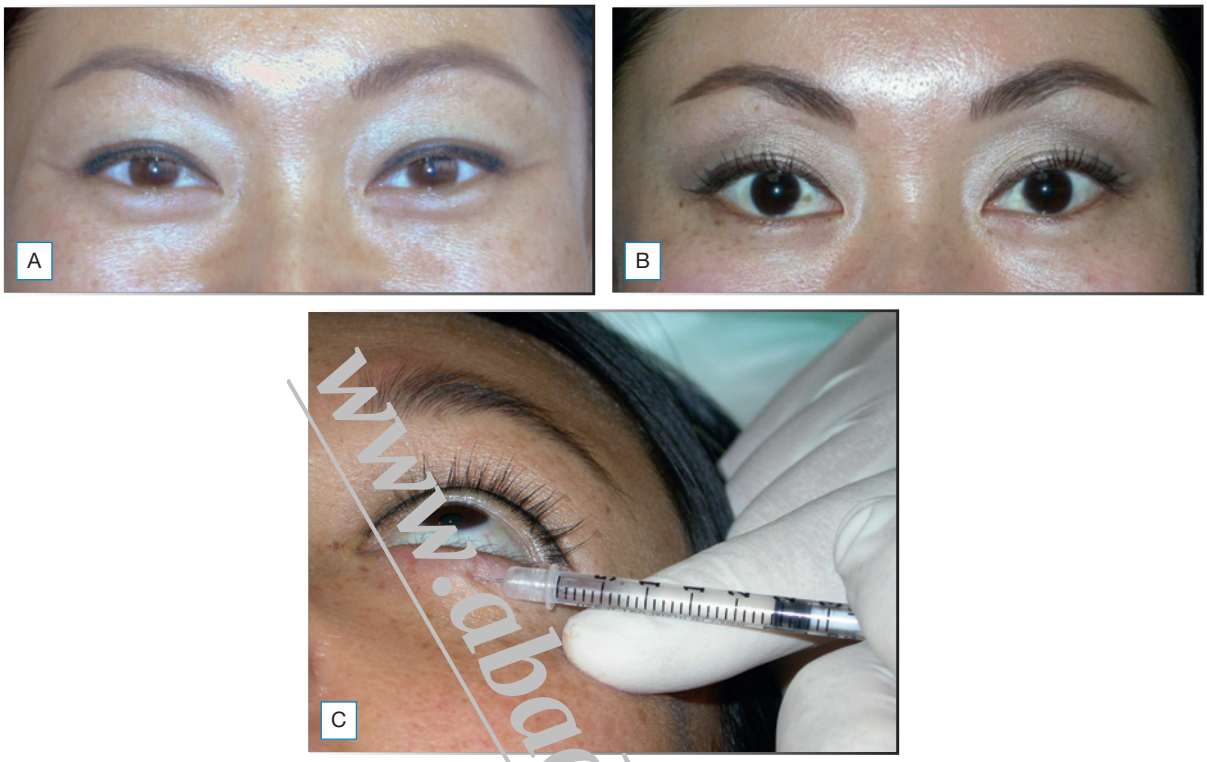

Figure 19.2 Flattening of hypertrophic orbicularis oculi and widening of palpebral aperture following 2 U BoNT-A midpupillary line 3 mm inferior to lash margin: **(A)** before, **(B)** after, and **(C)** injection technique.

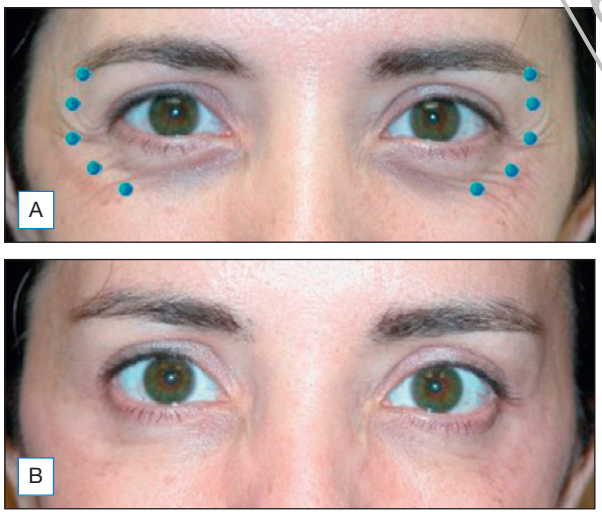

Figure 19.3 Improvement of rhytides and widening of palpebral aperture: **(A)** before and **(B)** after 2 U BoNT (Botox®) under the eye and 12 U in the lateral canthal rhytides.

enhance the size of the palpebral aperture. The authors therefore recommend a conservative approach with the smallest dose (1 to 2 U at two sites) in the lower lid, with retreatment after 2 to 4 weeks if necessary.

CASE STUDY 1 (see Fig. 19.2)

A healthy 32-year-old Filipino-Canadian woman presented complaining of a "jelly roll" underneath her eyes when she smiled. She requested a more Western wide-eyed look and reduction of the jelly roll. Fig. 19.2A demonstrates a hypertrophic orbicularis oculi. A "snap-test" demonstrated excellent elasticity, which, in conjunction with the youthful tone and texture of the skin, indicated that the patient was a suitable candidate for intradermal BoNT-A treatment. To achieve a wider aperture and flattening of hypertrophic orbicularis oculi (see Fig. 19.2B) 2 U of BoNT-A was injected in the midpupillary line 4 mm below the lid margin bilaterally. Fig. 19.2C demonstrates the injection site and technique.

Lid ptosis, malposition, and asymmetry

BoNT is an effective treatment for the temporary management of mild-to-moderate upper lid ptosis, malposition, and eyelid–fissure asymmetry. Research by Fagien indicates that correct placement, dosing, and careful patient selection will determine predictability of response. Eyelid malposition of any etiology has typically been treated by surgical correction of the underlying cause, with nonsurgical options for upper lid ptosis limited to adrenergic topical ophthalmic drops. Low-dose subdermal injection of BoNT