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## Introduction

**B**OTULINUM TOXIN IS A MINIMALLY invasive technique that has revolutionized the cosmetic approach to rejuvenation of the aging face. The interest in and the usage of botulinum toxin A over the past several years for cosmetic indications by physicians have increased almost exponentially. This has been a truly amazing process to behold. Naturally, there are a number of reasons for this phenomenal explosion of interest. Facial wrinkles are frequently caused by repeated muscle contraction. Botulinum A exotoxin can produce weakness or paralysis of these muscles and offers a novel approach for the treatment of certain facial rhytides and improved cosmetic appearance. This cosmetic use is not FDA approved and is thus considered off-label. The disappearance of wrinkles through the paralysis of these muscles, although temporary, is extremely popular with both patients and physicians. There is a low incidence of side effects and it is a relatively easy technique to perform. For these reasons, botulinum toxin A has gained rapid and enthusiastic acceptance. BOTOX (Allergan, Inc, Irvine, CA) is now a well-established method for the treatment of facial rhytides. Its major cosmetic indications in the facial area are glabellar frown lines, crow's feet, horizontal lines of the forehead, and reshaping of the brow. Some of the intermediate applications are the lines on nasal scrunch along the side of the nose, opening the eye, chin dimpling, and neck rejuvenation. Minor applications are in the lip lines and the corners of the mouth.

Nevertheless, the road from the isolation in 1895 of the microbe (*Clostridium botulinum*) responsible for the deadly neurotoxin that causes botulism poison to the present cosmetic and noncosmetic applications of this self-same toxin could certainly be considered a journey of serendipity. Attempts at purification of the toxin began in 1920 by Dr Herman Sommer. However, it was not until 1946 that type A toxin was purified in crystalline form. This work was performed by Dr Edward J. Schantz at Camp Detrick in Maryland.

One of the most pivotal individuals in the history of the medicinal use of botulinum toxin is Dr Alan Scott whose search for a nonsurgical treatment for strabismus brought him into contact with Dr Schantz and his purified toxin. It was his union with Schantz and Schantz's purified type A toxin that would ultimately make nonsurgical treatment of strabismus possible. Thus, the age of botulinum toxin began. In November of 1979, Dr Schantz prepared a batch of crystalline botulinum toxin type A that, until recently in

1997, was the only batch to receive FDA approval and was the source of all BOTOX dispensed until the new batch was approved in 1997.

The Carruthers became aware of the cosmetic possibilities of botulinum toxin type A in 1987 when a patient with blepharospasm pointed out the smooth, relaxed appearance she had after treatment of the glabellar area. Jean Carruthers was making regular visits to Dr Scott's laboratory and clinic and observed the effect of Botox on the vertical glabellar creases in patients treated for blepharospasm. At the instigation of Dr Theodore Tromovich, the Carruthers began by treating the glabella and shortly afterwards the crow's feet area with Botox. Although an abstract was published early in 1990, the first presentation occurred in 1991, which was published early in 1992. These articles set the stage for the appearance enhancement applications of BOTOX that have virtually been revolutionary.

Experience since the worldwide approval of the first therapeutic botulinum-neurotoxin based product in 1989, BOTOX, has shown that this therapeutic agent is safe and effective for numerous indications, including movement disorders. Subsequently, another botulinum toxin type A complex, DYSPORT (Ipsen Limited, Berkshire, England), was approved in the United Kingdom in 1991, but is not currently available in the United States. Recently, the FDA has approved a type B complex preparation, MYOBLOC (Elan Pharmaceuticals, South San Francisco, CA), for use in cervical dystonia patients.

The most common adverse effects are either excessive weakness of the treated muscle or the local diffusion of the neurotoxin from the injection site causing unwanted weakness in adjacent muscles. All of these muscle-weakness adverse effects with BOTOX are generally mild and of limited duration.

In addition to its previously noted off-label cosmetic indications, BOTOX in all likelihood will be shown to be safe and effective in placebo-controlled studies for a wide range of medical conditions including achalasia, dysphonia, cervical dystonia, cerebral palsy, chronic anal fissures, migraines and, of course, hyperhidrosis.

Botulinum toxin therapy has been reported to alleviate pain associated with various conditions with or without concomitant excess muscle contractions. Tension-associated headaches have been reported to be alleviated with BOTOX therapy. Therefore, the treatment of primary pain continues to mature with a sufficient number of successes that warrant further investigations.

What does the future hold? First, the current uses will expand. The cosmetic use for glabellar frown lines, crow's feet, and horizontal forehead lines is widespread but will become more so, such that this is as common as the use of injectable collagen is today. Newer uses, such as for hyperhidrosis, its adjunctive use with laser resurfacing and perhaps its use for platysma, will be better appreciated and more widely used. The use of Botox in smaller doses to produce more subtle facial alterations will expand and increase. Finally, the hope is that BOTOX itself will change. Agents that have both longer and shorter durations could be extremely useful. Prolonging the time between injections would be valuable and reduce the cost to patients.

BOTOX has proven to be a dramatically successful new form of cosmetic therapy and I am delighted to have been a part of its development and success as an agent for the aesthetic rejuvenation of the aging face. I look forward to participating in its continued successful future.

We feel that this special issue of *Seminars in Cutaneous Medicine and Surgery* on the use of botulinum toxin comprises a comprehensive look at the subject and that all of us, the novice user and the highly experienced, can increase our knowledge from reading these articles.

This issue of *Seminars* was not sponsored or underwritten in any way by the manufacturers of the botulinum toxin products discussed, and this issue does not in any way constitute an endorsement of these products by the publisher. The articles are included because of the interest shown by readers in learning more about these special uses.

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