

BOTULINUM TOXIN: MOVING BEYOND WRINKLES

Emmanuelle Bassmann discusses the uses of, and developments in neuromodulators, the number one aesthetic procedure in most markets worldwide



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PRAISED BY MANY AS THE ULTIMATE ELIXIR OF YOUTH, BOTULINUM toxin has been gracing the foreheads of Hollywood royalty, models and more for many years. First pioneered by aesthetic physicians in North America over 25 years ago, the rising affordability of the treatment, paired with improved techniques, has resulted in women from the boardroom to the locker room visiting clinics to wipe away the years.

At its inception, the toxin was mainly known for treating serious motor conditions, such as cerebral palsy in the lower limbs or partially blind patients suffering from severe blepharospasm. Now, neurotoxins are the number one aesthetic procedure in the United States, remaining the gold standard in the quest for eternal youth.

The toxin, which is used to treat the upper as well as lower face, is also regarded as a multi-faceted weapon to improve the appearance of scars and skin conditions, including acne and rosacea. And if that wasn't enough, new studies suggest it could also be a successful treatment for mild depression in some.

The discovery of the toxin

Botulinum toxin, a purified protein derived from the bacterium *Clostridium botulinum*, was first identified in 1895. There are different variations of *C. botulinum* (A, B, C, D, E, F and G). OnabotulinumtoxinA (BOTOX; Allergan, Irvine, California, USA) contains tiny amounts of highly purified botulinum toxin protein refined from the bacterium.

Oculinum was first approved by the US Food and Drug Administration (FDA) in 1989 to treat strabismus and blepharospasm in those aged 12 years and older. In 1998, botulinum toxin A (BoNTA) was approved for lower limb spasticity in cerebral palsy, followed by approval for severe primary axillary hyperhidrosis in 2001. In fact, it was only in 2002 that the toxin was approved for cosmetic use to improve the appearance of moderate to severe glabellar frown lines in people aged 18-65 years. However, that doesn't mean that aesthetic physicians waited until 2002 to use the toxin in practice. The panel of experts interviewed for this article, who are among the leading neurotoxin pioneers for cosmetic indications, have been using it as early as 1987.

Dr Jean Carruthers hasn't frowned since 1987 when she started to use neurotoxins on herself. This was, at the time, the only way to persuade her patients that it was safe to use on the face. 'Look what it does to me,' she would tell her patients. And they liked what they saw.

The fact that the toxin was approved for patients up to 65 years of age does not relate to how physicians are using it today, however. Ageing baby boomers nearing their 70s are now living longer and want to stay youthful-looking until the end of their lives. ▷

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▷ BoNTA is being used in highly successful practices in women in their 80s and even their 90s, according to the doctors interviewed for this article. It is being used differently, often in higher doses, and in synergy with other injectables.

A more recent approval for the toxin in 2010 is for patients suffering from chronic headaches at least 15 days per month, of which at least 8 days are migraines. BoNTA is still one of the most researched drugs: over \$300 million in R&D investment, more than 2500 peer-reviewed articles, and approximately 65 clinical trials involving 15 000 patients. Over the past 20 years BOTOX has been approved in 80 countries for 21 different indications, and only one for cosmetics at this point. BOTOX has been joined by other neurotoxins, such as Dysport/Azzalure (Q-Med, A Galderma Division, Uppsala, Sweden) and Xeomin/Bocouture (Merz Aesthetics, Frankfurt, Germany), and it is expected that more will arrive on the market over the next year.

Beautiful, untroubled expression

Over the past 20 years, the perception of BoNTA treatment has changed a great deal. From a simple forehead line relaxer, it is now seen as a pick-me-up, with many patients reporting increased happiness, relaxation, and even greater professional success. By preventing the ability to frown, patients believe they are sending a better message, giving them a sense of

positivity—a valuable tool in today's challenging workplace.

The toxin is now being studied as a potential tool to treat mild depression. A new generation of physicians believes that the neurotoxin might be a safe and potentially effective way to help millions of people who are not responding well to pharmacological and psychotherapy treatments. In the recently published *The Face of Emotion: How Botox Affects Our Moods and Relationship*¹, author Eric Finzi suggests that up to half of all wrinkle-busting procedures can dramatically improve mood, as well as our relationships with others. His study, with Dr Erika Wasserman, evaluated 10 clinically depressed patients who had never received any BOTOX injections. Two months after receiving treatment with BOTOX, patients reported a dramatic decrease in their feelings of depression. Although based on a reduced sample group, this study is showing promise for the manifold applications of the toxin. Extended and larger clinical trials should be carried out to verify the therapeutic effects of neurotoxins in fighting depression, as more physicians report a feel-good effect in patients following injection.

Main target: glabellar lines

There is no doubt that BoNTA is the most successful treatment to relax forehead wrinkles. Women are encouraged to start young, as early as their late 20s, with tiny

amounts as a preventive measure to stop smaller wrinkles forming. As we know, the toxin is not only about smoothing out wrinkles, but is also effective to lift the eyebrows. The depression of the eyebrow and the loss of its curvy shape are what many patients are aiming to correct. Even though it remains the most popular use, this is not an easy procedure—particularly in women aged 50 years and over, when the skin loses its underlying support. Loss of volume needs to be addressed and it becomes a more complex treatment: it is about the art of combining toxins and dermal fillers for a 3-dimensional finish.

Targeting the lower face

Experts have been using neurotoxins to correct the jawline and lift the neck for 20 years, with doctors interviewed for this article reporting that up to 75% of their patients also treat the lower face with BoNTA. When the jawline begins to lose its definition, excess skin may obscure and efface the distinction between the face and the neck. Enter the masseter muscle, fast becoming one of the key targets for BoNTA injections. Even though the amount of the toxin required to lift the neck and reshape the jawline is smaller than that used on the upper face, its effects last longer: a striking paradox for practitioners. Unfortunately, it's only a successful treatment in the hands of highly skilled physicians: if a doctor gets it wrong, resulting in facial asymmetry, it could take 6 months for the toxin to be cleared away.

Lines around the mouth also respond well to treatment with neurotoxin. Patients report strong satisfaction after the injection of small units around the mouth to lift sagging at the corners. Again, there is a small chance of getting it wrong, with some patients reporting the inability to talk without pulling their lips down.

Another soft spot for botulinum toxins—especially in a wrinkly face—is the centre of the chin. Injecting the mentalis muscle can bring beautiful results, but it's not easy and highly recommended to inject only tiny doses.

It has also been observed that in women with stressful jobs and prone to bruxism, a small application of neurotoxin to relax their masseter muscle can be life-changing. The muscle may be so tight in some patients that they end up grinding their teeth excessively and not being able to eat an apple. ▷



“By stopping the face from frowning, patients believe they are sending a better message, giving them a sense of positivity—a valuable tool in today's challenging workplace.”

▷ **BoNTA and dermal fillers: the ultimate treatment**

According to Dr Fredric Brandt, fillers and neurotoxins work in tandem to lengthen the muscles. Using the toxin alone does not ensure perfect results, however, and especially in women aged 55 years and over, and even when injecting higher doses: the patient may no longer frown but lines remain visible.

Older patients with wrinkles, ageing-related volume loss and years of photodamage benefit the most from a two-pronged approach using BoNTA and a measured amount of dermal fillers. These help achieve a line-free forehead, a lifted eyebrow, and nicely shaped jawline. A small dose of dermal fillers either in the forehead or along the brow line will help achieve the desired outcome. In the lower face, the injection of fillers in specific places such as low along the jawline, in the masseter muscle, and in the vertical neck muscles, might also be necessary.

Botox: some just can't get enough

Women with extreme addiction to their youthful new look are, however, being warned by doctors as some just cannot get enough of neurotoxin treatments and are returning to physicians even when there is only a slight movement in the forehead, failing to respect the 3-4-month interval between sessions. In some cases, injecting more than the usual dose at shorter intervals might make it harder to keep the eyebrows from drooping. The problem can be addressed by educating the patient, explaining the consequences of over-use.

Using botulinum toxin regularly does not mean that the proportion of patients becoming immune to the

toxin will rise, as reported in the press. Doctors interviewed for this article are reporting only a handful of cases in more than two decades of application. This issue is typically solved by switching to a different toxin. Dr Nicholas Lowe believes that neurotoxin type B might play a role when patients become resistant to type A, and has published a comparison study of toxin types A and B in the lower face, using the standard dosage, which shows that type B has only a slightly shorter duration of 10-12 weeks, compared with 16 weeks for type A².

Caucasian versus Asian

The use of toxins among different ethnicities is also the subject of more recent studies, addressing varying responses to treatment between Asian and Caucasian faces based on shape and movement. Doctors explain that while an Asian face will not need much toxin in the forehead, as culturally, they do not frown so much, they might require more fillers in the mid-face, and a little in their upper face. Owing to a typically more 'flat' facial shape, patients usually look for volumising treatments. Doctors also use neurotoxins in the lower face to target a slightly more square, masculine jaw.

According to Dr Michael Kane, author of *Classification of crow's feet patterns among Caucasian women*³, his clinic sees a lot of first-time, young female patients of Asian descent seeking botulinum toxin treatments for crow's feet.

Unique applications **Healing scars**

The use of botulinum toxin to improve the appearance of scar tissue, and for scar revision, has been used for more than 10 years by some experts. Injecting a small dose into the scar following skin excision in the forehead, upper lip and around the neck, improves the quality of the tissue. In a highly mobile forehead, it is advised to inject the toxin 1 week prior to excision. It has also been reported that not only thinner scars, but less inflamed and less itchy scars on the chest can be achieved with some toxin injection.

Acne and rosacea

Botulinum toxin might also be effective to clear acne, with many

physicians strongly believing that the toxin plays a role when injected intradermally to treat large pores, reduce oil production, and diminish acne breakouts. However, more work needs to be done to prove the effect of the toxin on sebaceous glands. Dr Kane stopped using the toxin for this purpose in 1996, even though it decreases acne, as it dries the skin and can make it appear shiny in his experience.

For rosacea and facial erythema, even though it makes sense to believe the toxin might reduce vessel dilation, a great deal of further studies need to be carried out. However, it is expected that with the arrival of topical botulinum toxin in a few years, the impact of neurotoxins on these conditions will be studied further.

“**Botulinum toxin remains the gold standard treatment when targeting wrinkles and fine lines, but only in the hands of highly skilled physicians.**”

Conclusions

Botulinum toxin remains the gold standard treatment when targeting wrinkles and fine lines, but only in the hands of highly skilled physicians. The variety of applications, not only aesthetically, but also to target other skin problems as well as mental health, will ensure that botulinum toxin remains at the forefront of aesthetic medicine for years to come.

▶ **The author would like to thank the professionals who agreed to be interviewed for this article:**

- ▶ Dr Jean Carruthers, Vancouver
- ▶ Dr Fredric Brandt, New York and Florida
- ▶ Dr Nicholas J. Lowe, London & Los Angeles
- ▶ Dr Michael Kane, New York
- ▶ Dr Michael Prager, London

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