

## **An Introduction to Botulinum Toxin and Dermal Fillers for Dentists: Part 1**

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### **Abstract**

Non-surgical facial rejuvenation using chemicals like botulinum toxin and hyaluronic acid is gaining an increasing popularity in the middle east and in different parts of the world over the last 10 years. These three papers aim at filling the gap in the dental literature with regards to this new and fast developing field of treatment and at giving an overview on such chemicals used currently in enhancing facial aesthetics and their potential use in dental practices.

**Clinical Relevance:** Facial rejuvenation substances have an important role to play in enhancing the appearance of our dental patients, particularly in “Gummy Smile” cases and cases with masseter hypertrophy or mild facial asymmetry/disharmony. Their medical uses are well established but some of their aesthetic benefits and dentally-related uses have just been approved in the recent years. This article will generally introduce botulinum toxin and hyaluronic acid to our dental fellow colleagues and provide them with the basic knowledge that will support them throughout their facial rejuvenation journey.

**Keywords:** *Botulinum Toxin; Hyaluronic Acid; Facial Rejuvenation; Dermal Fillers*

### **Introduction**

Increased demands to achieve superior dental aesthetics have played an important role over the recent years in improving the quality of the available dental materials and dental techniques. This enhanced the research to achieving superior dental materials and encouraged dentists to obtain higher degrees in this expanding cosmetic field and to introduce high-tech equipments to their dental practices in order to fulfil their patients’ needs. (Non-surgical) facial aesthetics, on the other hand, did not have so much attention from the dental profession until recently when chemicals such as hyaluronic acid fillers and botulinum toxin started to be demanded by patients and dental manufactures started to make them more available and incorporated these materials in their catalogues and advertisements.

Increasing number of basic and advanced accredited hands-on training courses in the use of such materials have been advertised in most of the currently available dental journals and periodicals. Dentists were kind of hesitant, at first, to introduce such new techniques to their daily practice as there was and still no formal acceptance from the competent authorities for such materials to be used by dentists in most areas of the head and neck for cosmetic or dentally related treatments. That was perhaps; on the other hand, one of the reasons why medical malpractice insurances were limited and insurance companies demanded heavy fees and placed a large number of strict guidelines for such procedures.

These three papers will not discuss the current legal issues in relation to the use of such materials by dentists, as this topic is controversial in some countries and its regulations are changing very rapidly. It seems to be heading towards revised and modified solutions based on the USA experience and aiming at obtaining special privileges/licenses and memberships following a number of recognised and supervised training courses.

In general, the competent authorities opinion is that “registrants choosing to offer botox or other non-surgical cosmetic procedures should note that the health authority expects the same high standards of them, whatever the type of treatment they are carrying out”. In particular, they are advised to work within their knowledge and professional competence and be prepared to back up the decisions they make”. Careful thought also needs to be given to maintaining professional standards in relation to advertising these services and to the need to be indemnified’.

Dental practitioners, however, have a responsibility to explain that these medicines are currently licensed or not for cosmetic use and ensuring that the patient understands this. Current regulations in the UK, for example, advise that botulinum toxin treatments should not be advertised and mixed with dentistry to the general public and that any advertisements related to brand names such as Botox®, Vistabel®, Azzalure® or Dysport® should be reported to the medicines and healthcare products regulatory agency (MHRA) and could lead to persecution. Other VAT related issues might need to be explored if the total facial rejuvenation income exceeded 70 - 80K a year.

The first article in this series will discuss in some depth the general and medical use of botulinum toxin as well as its use for enhancing facial aesthetics. Additionally, this article will give some practical advice for the new starters in this field regarding choosing the right patient for such treatments, obtaining informed consent, relevant medical history, brief treatment manual, post-operative instructions and finally how to correct mistakes and deal with side effects.

The second paper, on the other hand, will concentrate on the use of botulinum toxin in the temporary reduction of the excessive gingival display (the gummy smiles) as a non-invasive and considerably cheap alternative to surgery.

Special emphasis will be laid upon incorporating the use of botulinum toxin in the routine management of the temporomandibular joint disorders.

Additionally, a brief explanation will be given to the benefit of using Botulinum Toxin in a number of dental fields such as in orthodontics and dental implant fields and will propose some ideas to develop further research in other related areas.

Dermal fillers and how to use them on their own or with combination with other techniques (Such as botulinum toxin) in order to achieve the best facial balance and harmony for the dental patients, will be discussed in the third paper.

### **Botulinum toxin (Botox®)**

#### **Historical overview**

Although botulinum toxin was discovered over a100 years ago, it was not until late 1980s when it was approved in the USA by the FDA (Food and drug administration) for its medical use for selective cases such as strabismus, VII nerve disorders and blepharo-spasm (an involuntary spasm of the eyelids).

Since then, *Clostridium* botulinum toxin type A neurotoxin complex, (one of seven main serotypes) which was originally developed to treat muscle spasms associated with diseases such as multiple sclerosis, quickly gained acceptance for other ophthalmological disorders (including nystagmus) and other neurological disorders (including spasmodic neck muscles, writer’s cramp, tremors, tics, multiple sclerosis, cerebral palsy, post stroke states, spinal cord injuries, nerve palsies, cervical dystonia, parkinson’s disease and facial spasms). Recent studies even initially approved botulinum toxin type A to be useful in treating bladder neck hypertrophy [1], many gynaecological

applications, period cramps and even for the treatment of prostate enlargement, voice disorders, migraines and Oro-motor dystonias (i.e. uncontrollable muscle spasms that occur in the TMJ muscles that move the jaw. Depending upon which muscle is involved, the jaw moves in a different position) [2].

Just by a pure chance in 1988, Drs Alistair and Jean Carruthers. Dr J. Carruthers (a Vancouver Ophthalmologist) discovered that botulinum toxin type A could also be used to soften the skin and to treat wrinkles when she noticed significant improvement in both forehead frown lines and crow's feet when she treated her patients with botulinum toxin type A in order to stop their eyelid spasms. No significant side effects were noted then beyond the expected injection discomfort. The length of effective improvement for the forehead frown lines was approximately 17 weeks [3,4]. Since then, botulinum toxin type A, increased in popularity in treating wrinkles and in enhancing facial aesthetics and become a well-known anti-aging substance.

Different brand names are currently available for botulinum toxin type A such as BOTOX® in the USA (by Allergan), Xeomin® in Germany (by Merz), and in the UK, Neurobloc® and Dysport®. It has to be noted that currently in the UK only Vistabel® and Azzalure® is licensed to be used cosmetically and only for the Glabella area (the vertical lines between the eyebrows).

### Mechanism of action

Botulinum toxin type A prevents nerves from functioning normally (a neurotoxin) by preventing them from releasing a chemical called acetylcholine, which is essential for the nerves to communicate with muscle cells. This toxin therefore prevents muscles from receiving nerve stimulation and forcing them to become paralyzed temporarily until such time as the nerve develops new endings to communicate with the muscles again [5-8].

In order botulinum toxin exerts its "poisoning" effect, the toxin must proceed through a complex sequence of events that involves (1) binding, (2) productive internalization and (3) intra-cellular expression of catalytic activity. Botulinum toxin does not cause cellular death but the muscles will be blocked from movements and paralyzed. Usually, muscle activity returns gradually over a period of months through either "axonal sprouting" mechanism or through a recovery of the affected neuromuscular junction [5-8].

The toxin is also useful for preventing excessive sweating, as it prevents nerve signals from reaching the sweat (sebum) glands in the same manner. For this purpose, the toxin is injected into the skin in the (axilla) armpit for the treatment of hyperhidrosis. Botulinum toxin should only be used when other available treatments (i.e. aluminum salts) have failed [9].

Electrochemical messages are usually transmitted from the nerves ends to the targeted muscles by an important substance called acetylcholine. Increasing release of acetylcholine will lead to unpleasant symptoms such as muscular hyper-activity or even to spasms or tens-ups (Figure 1). Blocking releasing acetylcholine via substances like botulinum toxin will reduce or even stop the muscular responses and provide temporary relief from such symptoms (Figure 2).

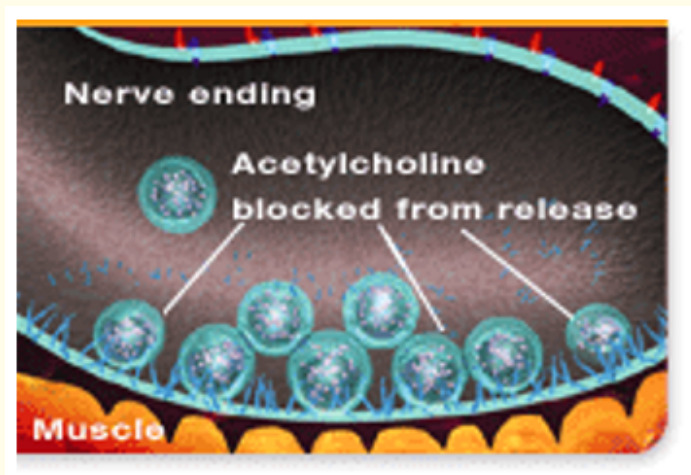
### Facial anatomy knowledge is very essential

Since botulinum toxin effects are mainly by inactivating muscle contraction via reducing or stopping the release of acetylcholine, it is very essential for the dental practitioner to be familiar with the facial muscle anatomy and their interactions in order to avoid unnecessary complications and to obtain optimal and specific results.

Facial muscle anatomy is very complex and requires a thorough understanding of both agonist and antagonist muscles (i.e. elevators and depressors), whose relationship to one another must be appreciated prior to administering botulinum toxin. The dental practitioner should update his knowledge and regularly review the relevant anatomy of the forehead, brow, and peri-ocular region as well as the other muscles of the face and neck that are commonly treated with botulinum toxin [10-12] such as:



**Figure 1:** Normal acetylcholine release.



**Figure 2:** Botulinum toxin effect on blocking the acetylcholine release. Figure 1 and 2 reused with permission from K-T Training.

- In the upper face: The frontalis, corrugator/depressor supercilli complex, procerus, orbicularis oculi, and nasalis muscles.
- In the middle face: A number of muscles that include the levator labii superioris alaeque nasi (LLSAN) and levator labii superioris (LLS) and the zygomaticus minor (Zm) muscles.
- In the lower face: The perioral region may be treated by injecting small doses of botulinum toxin into the orbicularis oris at multiple sites and the depressor anguli oris.

- The neck, on the other hand, may be treated by injecting the platysma muscle (superficially).

**Patient assessment**

Thorough patient assessment covering all patient past and current medical history, allergies and medications is very essential [13]. Listening to and understanding the patient requirements is a very important step in obtaining successful and acceptable results by patients. Patients of unreasonable expectations should not be treated and should always be reminded that this is a non-surgical treatment and that it has its limitations.

All agreed points should be carefully recorded in the notes and an informed consent form should be signed after the patient careful reading of the information sheets and after having enough time to discuss all aspects of the treatment with the dentist and all his/her questions were satisfactory answered.

Dentists should be aware of the possible adverse side effects, interactions and complications of botulinum toxin [14-16]. Table 1 summaries some of the main conditions where the use of botulinum toxin should be avoided.

- Pregnancy or Breastfeeding
- Known allergy to any of the ingredients of the Botulinum Toxin.
- Generalized skin diseases.
- Infection at the proposed injection site.
- Chronic disease affecting the skin or the muscles (i.e. Eaton Lambert Syndrome).
- Abnormal muscle weakness (i.e. Myasthenia Gravis).
- Better not to be used in patients with uncontrolled diabetes.
- Better not to be used in patients with severe auto-immune disease.

**Table 1:** Botulinum toxin not to be used in.

A number of common medications might have some undesirable effects if co-administrated with botulinum toxin. Table 2 summaries some of the main ones.

- Aminoglycosides (or any other agents interfering with neuromuscular transmission (i.e. Curare-like compounds).
- Alzheimer’s disease medications
- Medications to treat heart rhythm complications
- Some Antibiotics (i.e. Polymyxins, Tetracyclines, Lincomycins etc.)
- Spectinomycins.
- Muscle relaxants (i.e. those used in general anaesthesia).
- Some over the counter medications (i.e. Vitamin E, Multivitamins, St. John’s Wort, and a number of the anti-inflammatory agents such as Aspirin).

**Table 2:** Cautions/interactions of botulinum toxin.

*N.B. Patients should inform their GPs/Anaesthetists that they had some Botulinum Toxin recently as during the surgery there might be a need to check some muscle-reaction (especially on the face) to known stimulation in order to adjust the amount of anaesthesia given to the patient.*

It is worth to be noted that manufacturers advised that although the botulinum toxin products contain albumin (a derivative usually of human blood), and based on effective donor screening and product manufacturing process, it carries an extremely remote risk of transmission of viral diseases such as Creutzfeldt-Jakob disease (CJD).

Antibody formation for botulinum toxin was a problem in the past but reducing the protein load and the new manufacturing and production techniques have played a very important role in decreasing that negative reaction.

### Application of botulinum toxin

The product usually contains a sterile, vacuum-dried purified botulinum toxin type A, produced from fermentation of Hall strain *Clostridium* purified neurotoxin complex. This complex is then dissolved in sterile sodium chloride solution containing albumin and is sterile filtered (to 0.2 microns) prior to filling and vacuum-drying.

It is advised by the manufacturers that botulinum toxin should mainly be diluted with 0.9% non-preserved sodium chloride. Other diluents, including lidocaine or marcaine should not be used for reconstitution. The solution should be mixed by gently rotating the vial (not shaking it). The reconstituted solution should be clear, colourless and free of particulate matter. The reconstituted solution should be used within 4 hours and during that time it should be kept refrigerated (2 to 8°) if possible. Date, time and the concentration of the dilution should be recorded on the special space on the label provided and in the patient notes, in addition to the LOT. Number and the expiry date.

The USA trials protocols dilution approved by the FDA was 2.5 cc while the most commonly used nowadays in the UK is 2.0 cc (i.e. adding 2.0 ml of 0.9% NPSC to a 100U vial of Botulinum Toxin). Other brand names might have different dilution protocols (such as Azzalure, for example, where it is advised to mix 0.63 ml of NaCl 0.9% solution to its 125 speywood unites).

Very small amounts of botulinum toxin are then injected carefully using a very fine 30 Gauge needle into the target muscles while the patient is seated up. The most common locations of its cosmetic application (world-wide) are the “frown lines,” forehead wrinkles, and “crow’s feet lines” and for axillary’s excessive sweating (to eliminate the need for antiperspirants). Emla® topical anaesthetic cream or ice is sometimes used before and after the procedure to minimize discomfort, which is minimal and lasts only a few seconds (Figure 3-6). The ice pack use will have the advantage of reducing any potential bruising after the procedure.



**Figure 3:** Clean the skin with alcohol wipes.



**Figure 4:** Apply emla cream and ice bag to the area.



**Figure 5:** Inject botox intramuscularly.



**Figure 6:** Keep away from the critical anatomical areas and the eyes.

The effect of the botulinum toxin is generally not visible until the next week (ranging between 3 - 14 days) (Figure 7-10). Results normally last on average between 4 - 6 months although the results can last longer with repeated treatments. Botulinum toxin may be less effective for people aged 60 and over because the muscles underlying the skin are not as firm. Results in hyperhidrosis cases may last for more than 10 months (Figure 11-16).



**Figure 7:** Horizontal wrinkles on the forehead.

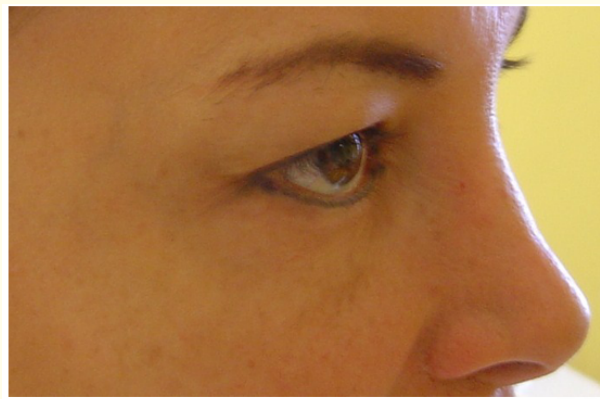


**Figure 8:** Total elimination of the dynamic wrinkles on the forehead 2 weeks after botox application.





**Figure 9:** Crow's feet wrinkles.



**Figure 10:** Total elimination of the crow's feet wrinkles 2 weeks after the botox application.



**Figure 11:** Armpit hair should be removed.



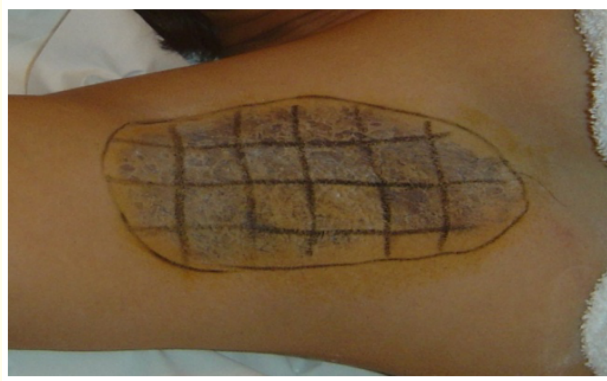
**Figure 12:** Iodine is applied to the area.



**Figure 13:** Cornflower is applied to the area.



**Figure 14:** Sweat glands will be then easily identified.



**Figure 15:** Careful and accurate marking to the treated area is essential.



**Figure 16:** Superficial injection of botox in equal amounts to reduce or even stop the excessive sweating for months.

The safe and effective use of botulinum toxin depends mainly upon proper patient selection, proper storage of the product, and selection of the proper dose, proper reconstitution, proper administration techniques and the proper knowledge of the anatomy of the treated area.

As a general rule, the practitioner should aim at carefully targeting the elevator muscles in the region with a sufficient amount of botulinum toxin if the final results wished to be achieved are to depress the treated area and vice-versa. The neighboring musculature and their interaction should always be kept in mind as they always play compensatory roles when the main muscles are blocked from movement.

By careful use of botulinum toxin practitioners could even be able to reduce the “Gummy-Smile” by targeting a group of deeply-placed small muscles such as the levator labii superioris [17,18], treating facial asymmetry, treating trismus and masseter hypertrophy [19]

reducing nasal scrunch and nasal flare, reducing “poppy” chin, platysmal bands and chemical (non-surgical) eyebrow lifting, and even use it in a number of condition such as migraines [20] bruxism and temporomandibular joint disorders [21].

**Side effects of treatment**

In general, there are no generalized side effects to botulinum toxin. It is remarkable for both its effectiveness and safety. On the other hand, medicines and their possible side effects can affect individual people in different ways. It is very hard to predict exactly how botulinum toxin injections will affect your patients’ muscles. You may therefore find that the results are not what you intended. Very occasionally patients who receive botulinum toxin injections in the forehead experience a drooping of the eyelids or eyebrows, although this is temporary and will resolve itself when the effects of botulinum toxin wear off these superficial nerve endings affected (within 1 - 6 weeks).

Table 3 summarizes some of the side effects that are known to be occasionally associated with botulinum toxin treatment. Because a side effect is stated here, it does not mean that all people using this medicine will experience that or any of the mentioned side effects.

- Pain, soreness or bruising at the injection site.
- Rash or itching (severe allergy is very rare).
- Nearby muscles might get affected and excessive doses may even paralyze muscles that are not near the injection site (very rare side-effect).
- The soft eyelid tissues bruise easily. In order to reduce this, applying gentle pressure after giving the injection, is highly advisable.
- Drooping of the upper eyelid and possible limited range of motion.
- Sensitivity of the eyes to light.
- Eye irritation and double vision.
- Dry eyes.
- Watering eyes.
- Facial swelling.
- Difficulty closing the eyelid.
- Inflammation of the front of the eye (cornea).
- Increased sweating from areas not treated (mainly for Hyperhidrosis treatment).
- Hot flushes.
- Fever (pyrexia).
- Flu-like symptoms.
- Difficulty or pain when swallowing (dysphagia) - mainly associated with neck treatments.

**Table 3:** Some side effects of botulinum botox treatment.

The side effects listed above may not include all of the side effects reported by the drug’s manufacturer. In general, most side effects last between 1 - 2 weeks and if severe between 3 - 5 weeks.

Although most people continue to respond well to BOTOX® injections, some people have experienced a diminished response over time. There may be several explanations for this, as mentioned in the manufacturer’s instructions:

1. Changes in the condition: If the pattern of the muscle activity changes, the healthcare provider (dental practitioner) may need to inject new muscles and/or change your dose. Identifying and injecting the affected muscle can be difficult, complicated by the changing pattern of muscle involvement and progression of the disorder.

2. Setting appropriate expectations: Patients may believe that their first BOTOX® injections were more helpful than subsequent injections. That is usually because their conditions were perhaps quite severe when they had their first injections. Subsequent injections are usually given before their conditions become that severe again. Therefore, the relief they experienced with subsequent injections may not have been as dramatic as the first time.
3. Antibody formation: Very rarely, when foreign proteins, like botulinum toxins, enter the body, antibodies may form. If antibodies to Botulinum Toxin develop, patients may no longer respond to treatment.

**Potential problems of botulinum toxin treatments**

No negative long-term effects have been observed with botulinum toxin. Very few short-term problems, however, have been reported. If botulinum toxin, for example, is injected too deep or too close to the upper eyelids, or too lateral in the forehead region, temporary upper eyelid droop may result (Figure 17). This can take few weeks to improve. Eye drops such as lodipine or vasocon-a, could be used as common antidotes to help lift the eyelids slightly. Similar problems might happen when injecting too much of botulinum toxin in the lower face or too deep in the cheek area. “Spooky” over lifted eyebrows as well are as common (Figure 18) and treating this problem is so easy by injecting little botulinum toxin very superficially like 1 cm above the affected area.



*Figure 17: Temporary upper right eyelid drooping after botulinum toxin use.*



*Figure 18: Over lifted (spooky) eyebrows after botulinum toxin application.*

### Some medical/dental uses of botulinum toxin

Despite its popularity, most people are only aware of the cosmetic applications of botulinum toxin such as in removing crows' feet and frown-lines from aged faces.

Very few people know about the other medical uses for botulinum toxin such as in multiple sclerosis cases, many ophthalmological disorders (including nystagmus) and other neurological disorders (including spasmodic neck muscles, writer's cramp, tremors, tics, multiple sclerosis, cerebral palsy, post stroke states, spinal cord injuries, nerve palsies, cervical dystonia, parkinson's disease and facial spasms). Botulinum toxin type A could be useful as well, in treating bladder neck hypertrophy [1], migraines, period cramps and even for the treatment of prostate enlargement, voice disorders and many gynaecological applications.

In the oral environment and other dentally related fields, botulinum toxin has promising results in many cases such as: myofascial pain, TTH (tension-type headaches, bruxism (grinding and clenching of teeth), masseteric hypertrophy, recurrent dislocation of the TMJ, oro-motor dystonias (i.e. uncontrollable muscle spasms that occur in the TMJ muscles that move the jaw. Depending upon which muscle is involved, the jaw moves in a different position) [2].

Other examples could include rhytides, gummy or asymmetric smiles, migraine headaches, reduction of frenal tension near dental implants, multiple trigger points and complicated endodontic treatments, oral and maxillofacial surgery (i.e. Zygomatic fracture fixation surgeries), cerebral palsy related drooling and angular cheilitis problems, frey's syndrome social complications, hemifacial spasms, sialorrhoea (excessive saliva production), limited mouth opening, lip tonicity problems, frenum attachments and problems associated with tongue thrusts, tolerance problems of orthotics including provisional temporaries, functional retainers and apnea appliances, and accepting sudden changes in vertical dimension prior or post full mouth rehabilitation approaches, trigeminal neuralgia, bell's palsy and many others.

Some of those uses would be covered and discussed to some extent in the second article of this series while the third one will cover the use of hyaluronic acid based dermal fillers in the oral and dental environment such as in building up dental papillae, gummy smile cases and in dental implantology among other maxillofacial applications.

### Conclusion

In addition to the increasing number of medical uses of botulinum toxin, non-surgical facial rejuvenation techniques have an important role to play in enhancing the appearance and achieving the facial balance and harmony of our dental patients, particularly in "gummy smile" cases and cases with Masseter hypertrophy or mild facial disharmony.

It is very essential that the performer dental practitioner is fully equipped with the necessary anatomical and pharmacological knowledge and the practical skills and techniques before starting to offer these enhancing techniques at the dental practice. Following the competent authorities and the insurance companies' guidelines is very important as well as keeping up-to-date in using such substances through attending approved courses and workshops.

In the following articles, more emphases would be laid on the technical aspects of using botulinum toxin in isolation or in conjunction with dermal fillers in a number of oral and dentally related fields.

Finally, it should be noted how interesting it is to know that botulinum toxin had that strange and unique place in the public eye. Even more interesting, on the other hand, are the remarkable potential medical and cosmetic uses for this "deadly neurotoxin" in almost all parts of the human body!

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