

TIME

Depression.
Heart trouble.
Migraines.
Erectile dysfunction.
Back pain.
Sweaty palms.
Drooling.
And 793 other problems.

**How Botox
Became the
Drug That's
Treating
Everything.**

By Alexandra Sifferlin

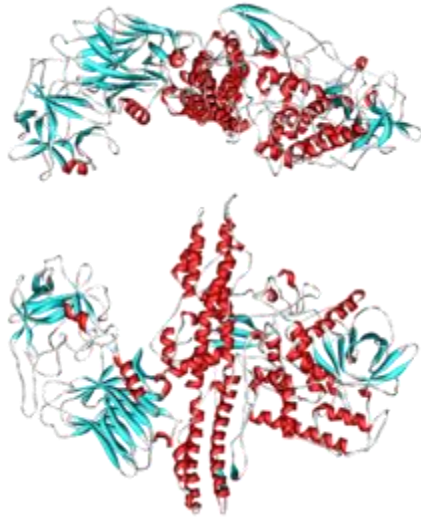


THE BOTOX STORY

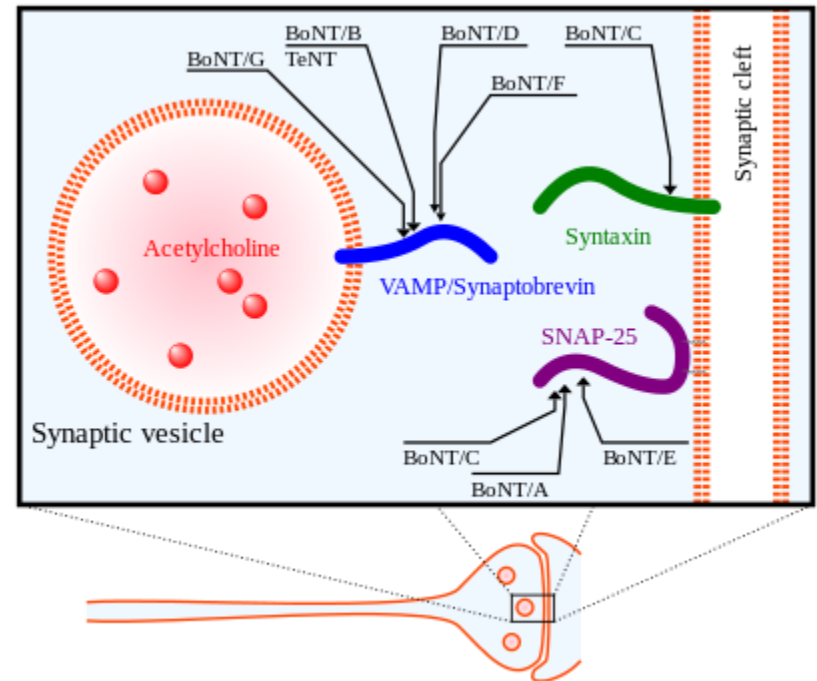
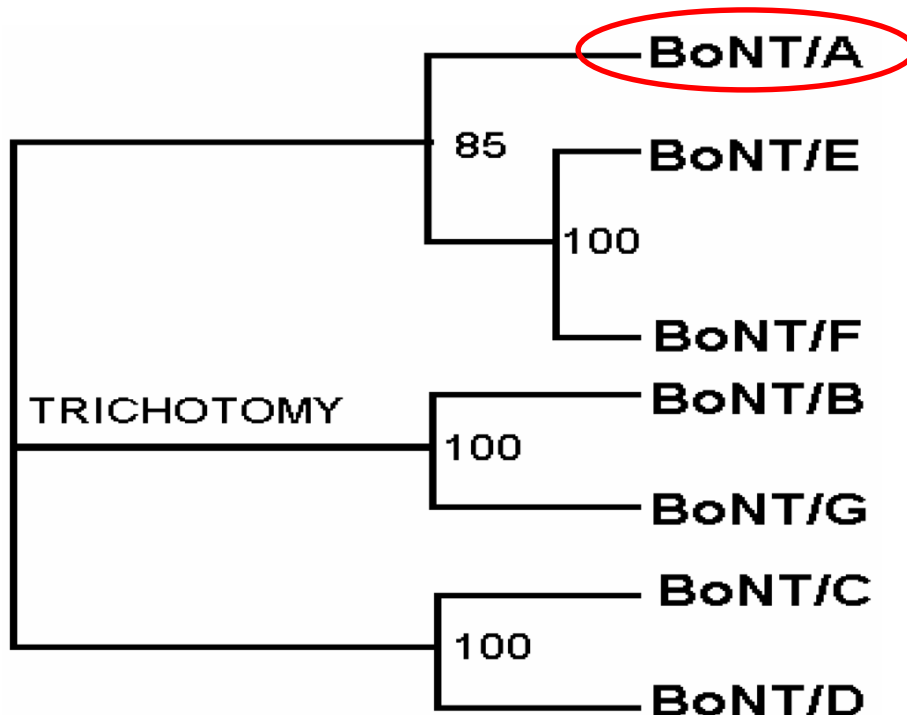
Disclaimer

- All information shared in this presentation is in the public domain.
 - Hence, no trade secret related to drug formulation, manufacturing process, commercial practice, etc.
- The views expressed in this presentation, as well as comments during any discussion, are solely those of the presenter's and do not reflect the position of any company or other individuals.

What Exactly is Botox?



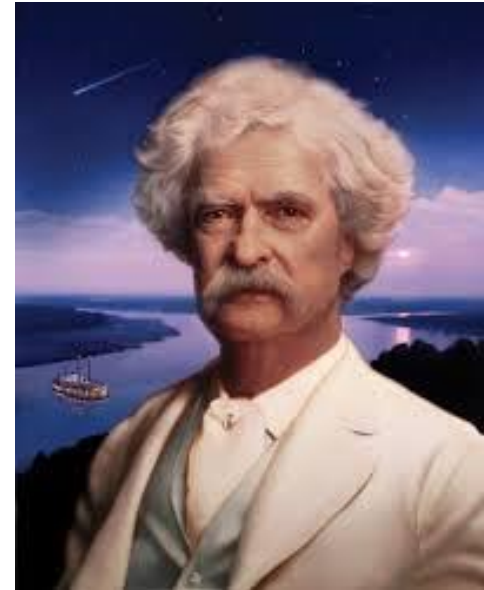
Botulinum neurotoxin serotype A
150kD pure toxin + 750kD accessory proteins



<https://youtu.be/M4PdZUhzaT8>

**“Name the greatest of all inventors.
Accident.”**

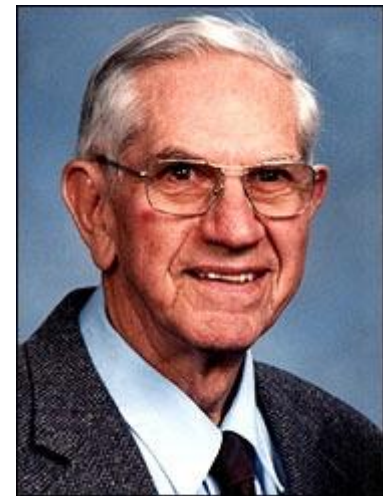
Botox was an accident.



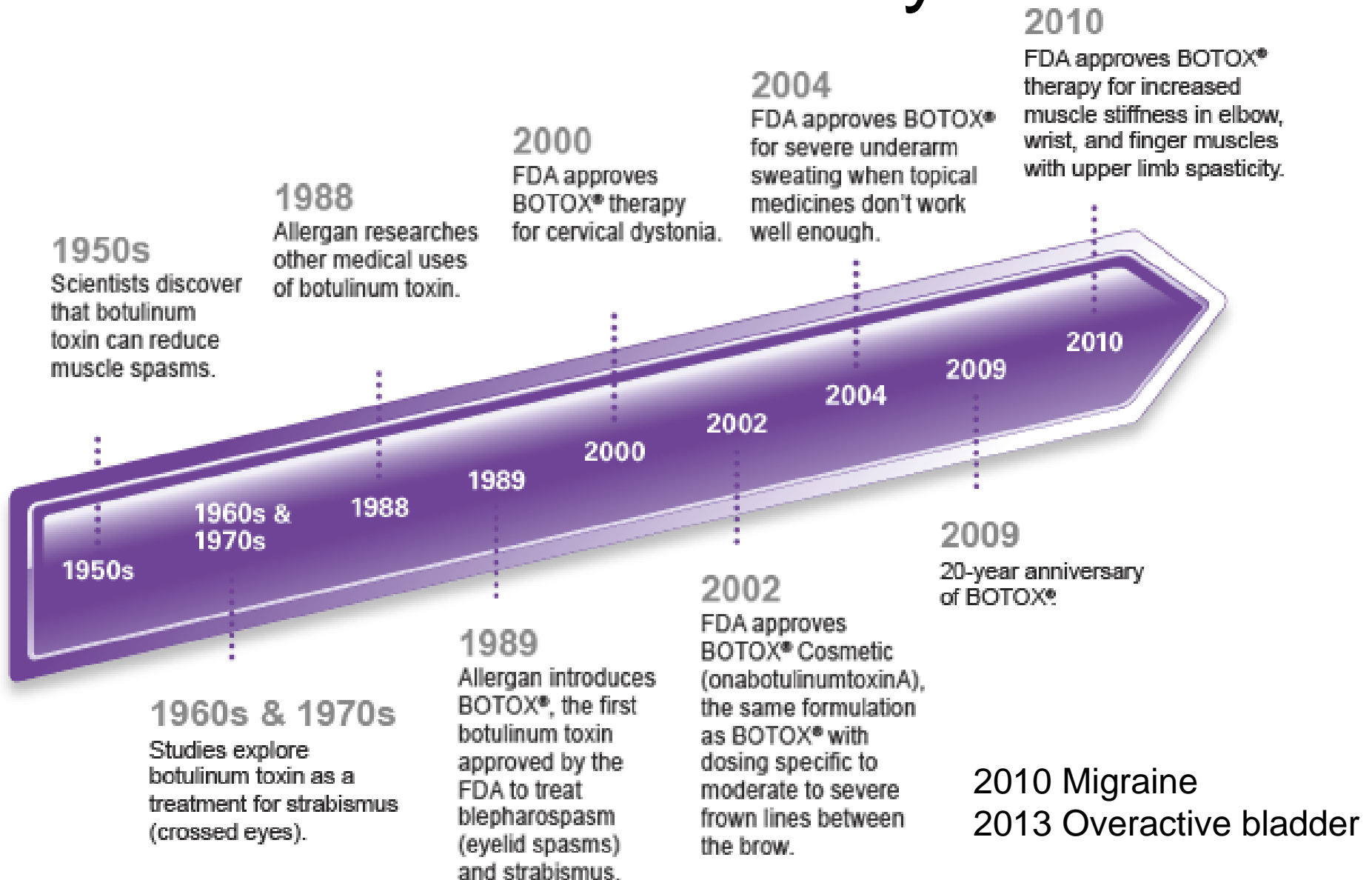
Dr. Alan B. Scott

In the late 1960's, Dr. Alan B. Scott, tested a sample on monkeys in a bid to find a nonsurgical cure for crossed eyes, by relaxing the eye muscles.

In 1978, he received FDA approval to initiate first therapeutic testing in humans with Oculinum (botulinum toxin type A). Results revealed that it was a safe and effective treatment for crossed eyes.



Botox History



So in how many ways can Botox
make you look young and
beautiful?

It can remove forehead lines



It can remove these wrinkles

Before



After (at day 7)



It can erase your frown lines





Lip lines - gone



Not an approved indication

Neck lines - gone



Botox® Cosmetic Neck Lift

Not an approved indication

It can fix your sad smile



Before

After


—Cosmetic

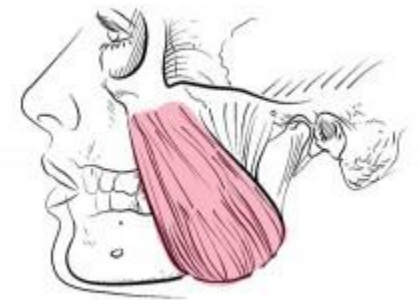
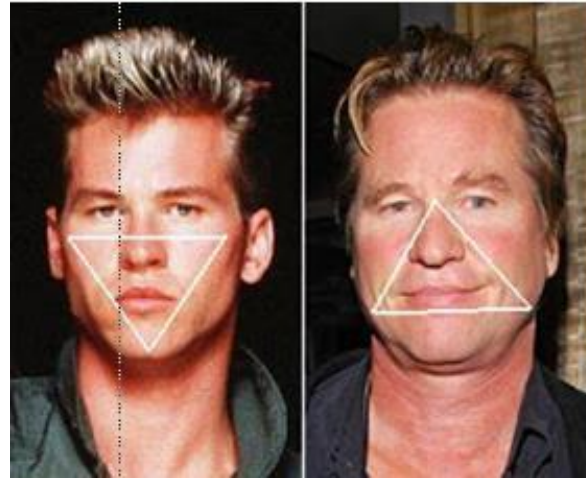
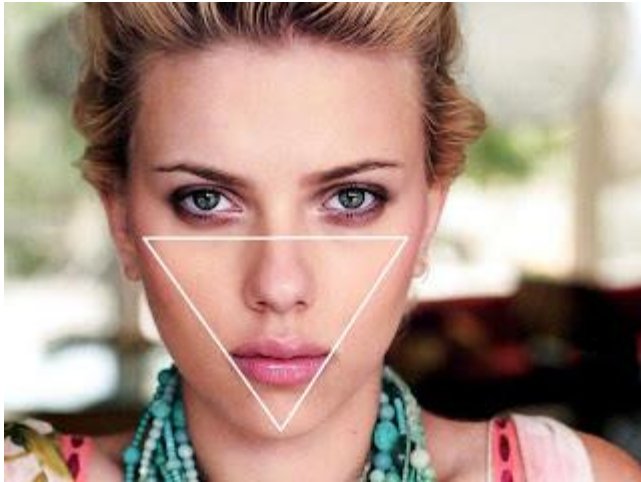

Cosmetic
Dermatology
DUBLIN, IRELAND

Not an approved indication

It can fix your gummy smile



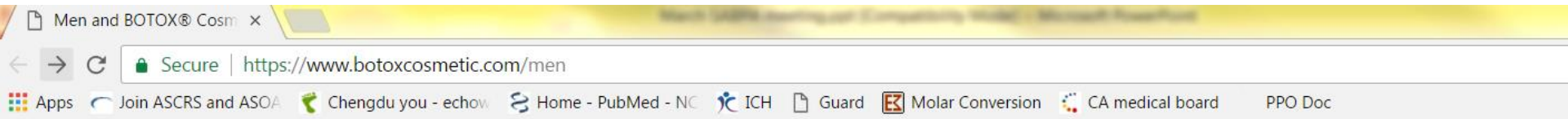
It can narrow your face!



Not an approved indication

咬肌

You think it's only for women?



[Product Information including Medication Guide](#)

[For Healthcare Professionals](#)

[For Women](#)



[ADDRESSING MYTHS](#)

[BEFORE & AFTER PHOTOS](#)

[FACTS ABOUT
BOTOX® COSMETIC](#)

[CHOOSING A SPECI...](#)

SOFTEN YOUR LINES,
NOT YOUR EDGE

[SEE JIM'S RESULTS](#)

BOTOX® Cosmetic—the **only** FDA-approved product that temporarily improves **both** moderate to severe crow's feet AND frown lines between the brows in adults.



Actual patient after treatment.
Results may vary.

Men and BOTOX® Cosmetic



Approximately 1 in 10 BOTOX® Cosmetic patients (n = 2013) are men

Gender-specific Anatomical Differences

- Craniofacial size
 - More square/angular
- Soft tissue displacement
 - Muscle movement more expansive
- Brow position
 - Lower, flatter arch
- Cheek prominence
- Jawline/chin prominence
 - Wider



Botox Sales: Cosmetic vs. Therapeutic



Year	Total
2001	\$0.3 B
2006	\$1 B
2010	\$1.4 B
2013	\$2 B
2018 (projected)	\$3 B

At least since 2006, BOTOX sale has been split even between cosmetic and therapeutic usage

What's in the BOTOX Product Label?

Approvals for cosmetic use:

- Glabellar lines (frown lines between the eyebrows)
- Crows feet (lines on the side of the eyes)
- Forehead lines

Approvals for therapeutic use:

- Strabismus (crossed eye)
- Blepharospasm (sustained, forced, involuntary closing of the eyelids)
- Cervical dystonia (neck muscles contracting involuntarily)
- Upper limb spasticity
- Lower limb spasticity
- Hyperhidrosis (excessive sweating)
- Chronic migraine
- Overactive bladder and urine incontinence due to neurological disease

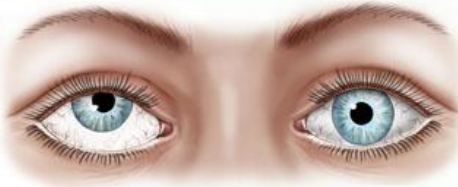
Strabismus



Normal



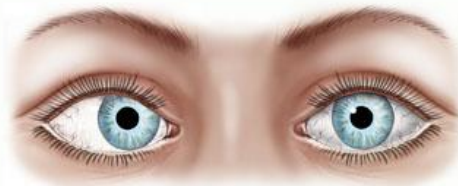
Hypotropia (eye turns down)



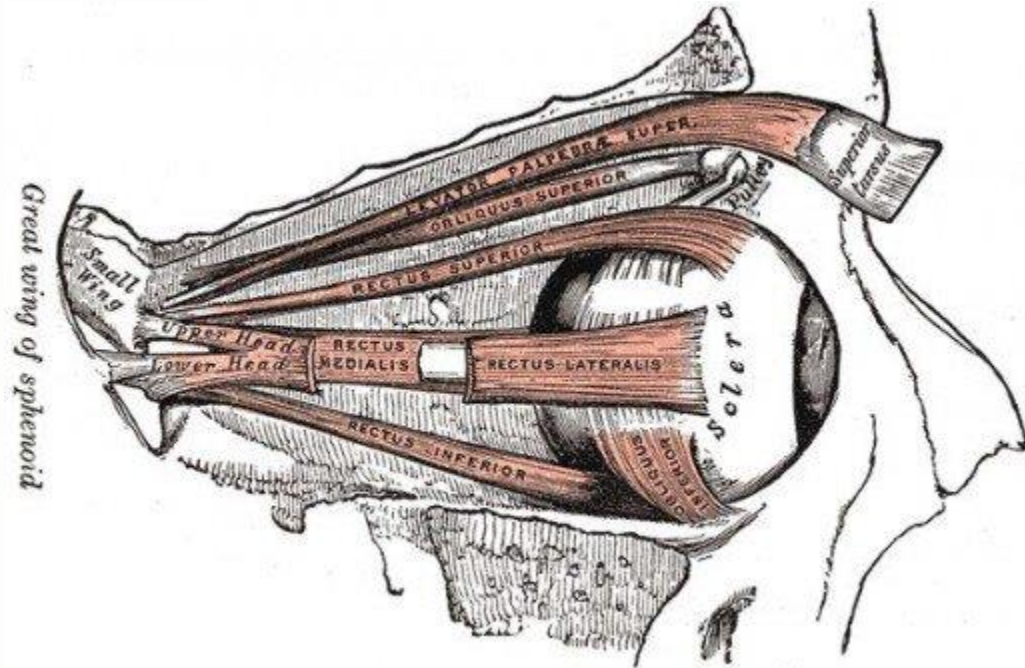
Hypertropia (eye turns up)



Exotropia (eye turns out)



Esotropia (eye turns in)



Label provides recommendation on dose level based on degree of deviation.

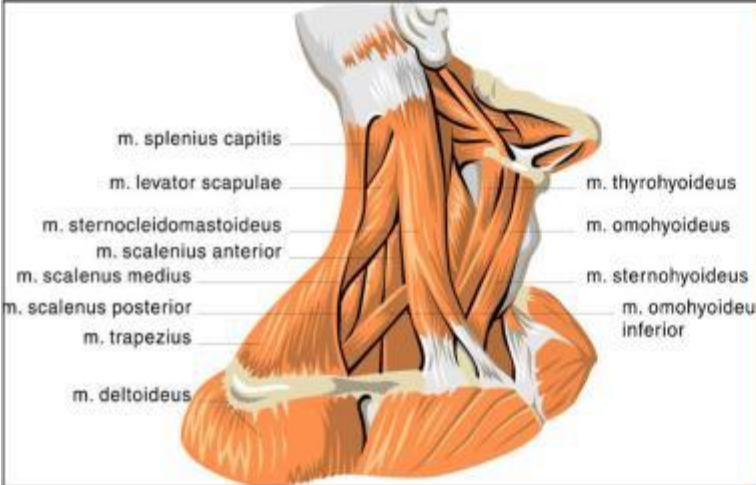
The maximum recommended dose as a single injection for any one muscle is 25 Units.

Blepharospasm



The initial recommended dose is 1.25 Units-2.5 Units (0.05 mL to 0.1 mL volume at each site) injected into the medial and lateral pre-tarsal orbicularis oculi of the upper lid and into the lateral pre-tarsal orbicularis oculi of the lower lid.

Cervical Dystonia



m. splenius capitis
m. levator scapulae
m. sternocleidomastoideus
m. scalenius anterior
m. scalenus medius
m. scalenus posterior
m. trapezius
m. deltoideus
m. thyrohyoideus
m. omohyoideus
m. sternohyoideus
m. omohyoideus inferior

Cervical Dystonia

Neck pain **Head turn**

Swallowing difficulties

Head twisting **Tremor**

Awkward postures

Muscle spasms **Cramps**

www.australiandystoniasupportgroup.wordpress.com



Injection Guide

- Dosing in initial and sequential treatment sessions should be tailored to the individual patient based on the patient's head and neck position, localization of pain, muscle hypertrophy, patient response, and adverse event history.
- The initial dose for a patient without prior use of BOTOX should be at a lower dose, with subsequent dosing adjusted based on individual response.
- In general, no more than 50 Units per site should be administered.

Upper Limb Spasticity



Bent wrist

Wrist is bent with the fingers pointing down and back toward the forearm.



Closed fist

Fingers are tightly clasped into the palm of the hand.

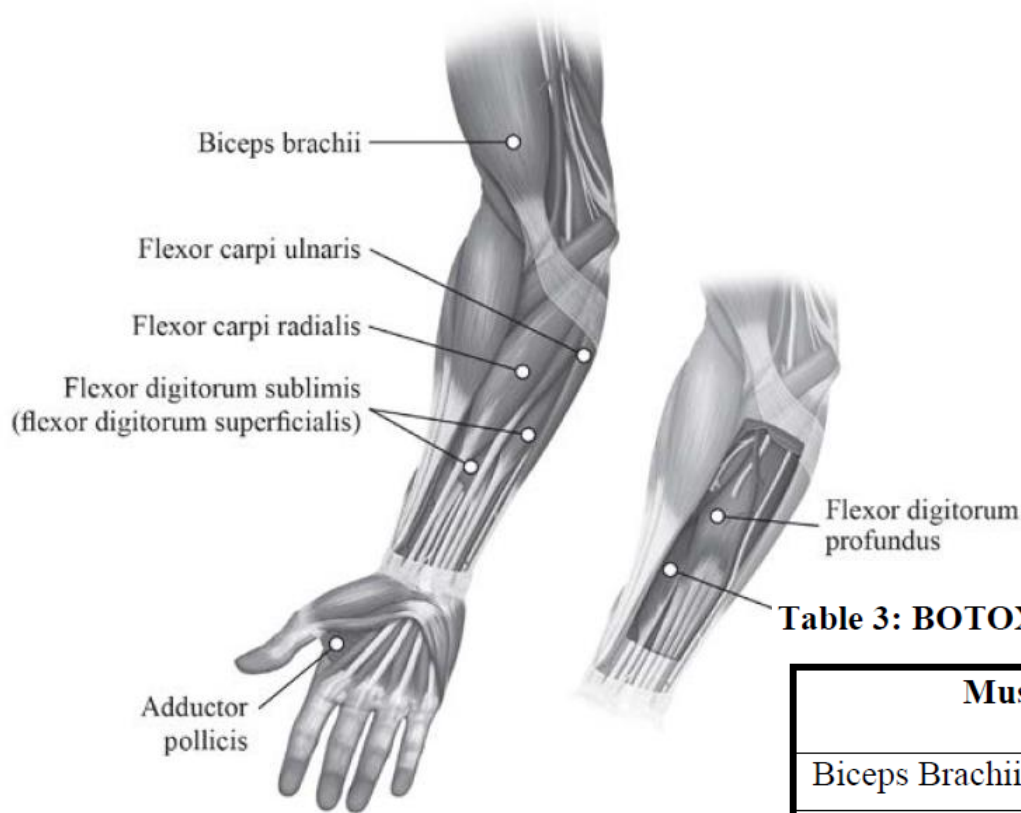


Flexed elbow

Elbow is bent with the hand at the shoulder.

Injection Guide

Figure 2: Injection Sites for Upper Limb Spasticity



In clinical trials, doses ranging from 75 Units to 400 Units were divided among selected muscles (see Table 3 and Figure 2) at a given treatment session.

Table 3: BOTOX Dosing by Muscle for Upper Limb Spasticity

Muscle	Recommended Dose Total Dosage (Number of Sites)
Biceps Brachii	100 Units-200 Units divided in 4 sites
Flexor Carpi Radialis	12.5 Units-50 Units in 1 site
Flexor Carpi Ulnaris	12.5 Units-50 Units in 1 site
Flexor Digitorum Profundus	30 Units-50 Units in 1 site
Flexor Digitorum Sublimis	30 Units-50 Units in 1 site
Adductor Pollicis	20 Units in 1 site
Flexor Pollicis Longus	20 Units in 1 site

Lower Limb Spasticity

Presentation of focal lower limb spasticity



Flexed ankle (gastrocnemius, soleus, tibialis posterior)



Injection Guide

Figure 3: Injection Sites for Lower Limb Spasticity

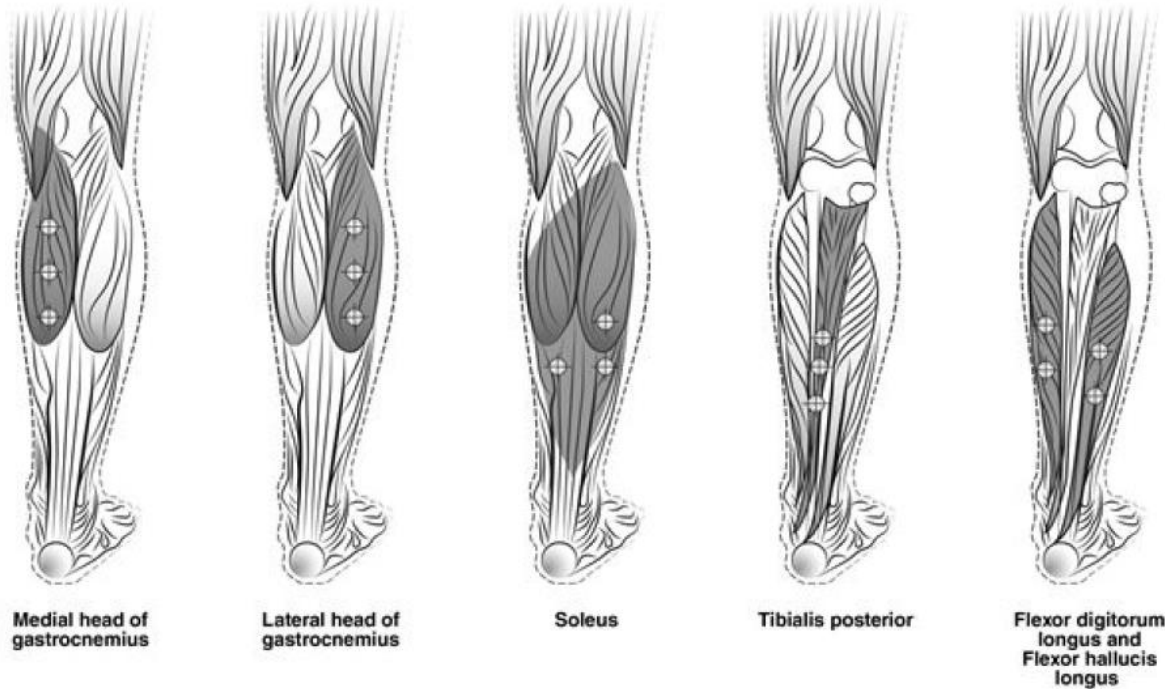
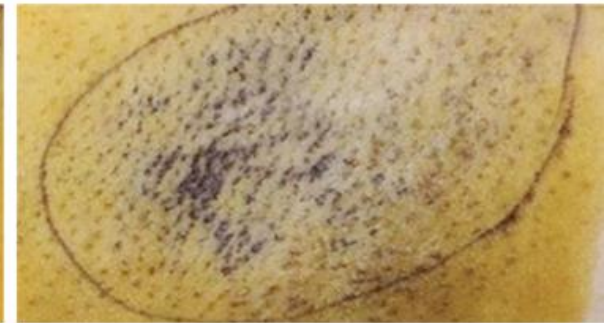


Table 4: BOTOX Dosing by Muscle for Lower Limb Spasticity

Muscle	Recommended Dose Total Dosage (Number of Sites)
Gastrocnemius medial head	75 Units divided in 3 sites
Gastrocnemius lateral head	75 Units divided in 3 sites
Soleus	75 Units divided in 3 sites
Tibialis Posterior	75 Units divided in 3 sites
Flexor hallucis longus	50 Units divided in 2 sites
Flexor digitorum longus	50 Units divided in 2 sites

The recommended dose for treating lower limb spasticity is 300 Units to 400 Units divided among 5 muscles

Hyperhidrosis



stop the
SWEATING



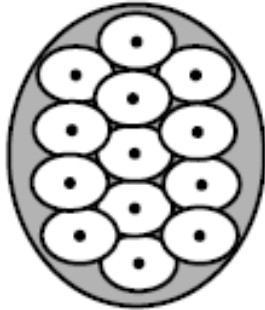
Hyperhidrosis

Excessive Sweating
Hands, Feet, Underarms



Injection Guide

Figure 4: Injection Pattern for Primary Axillary Hyperhidrosis



The recommended dose is 50 Units per axilla.

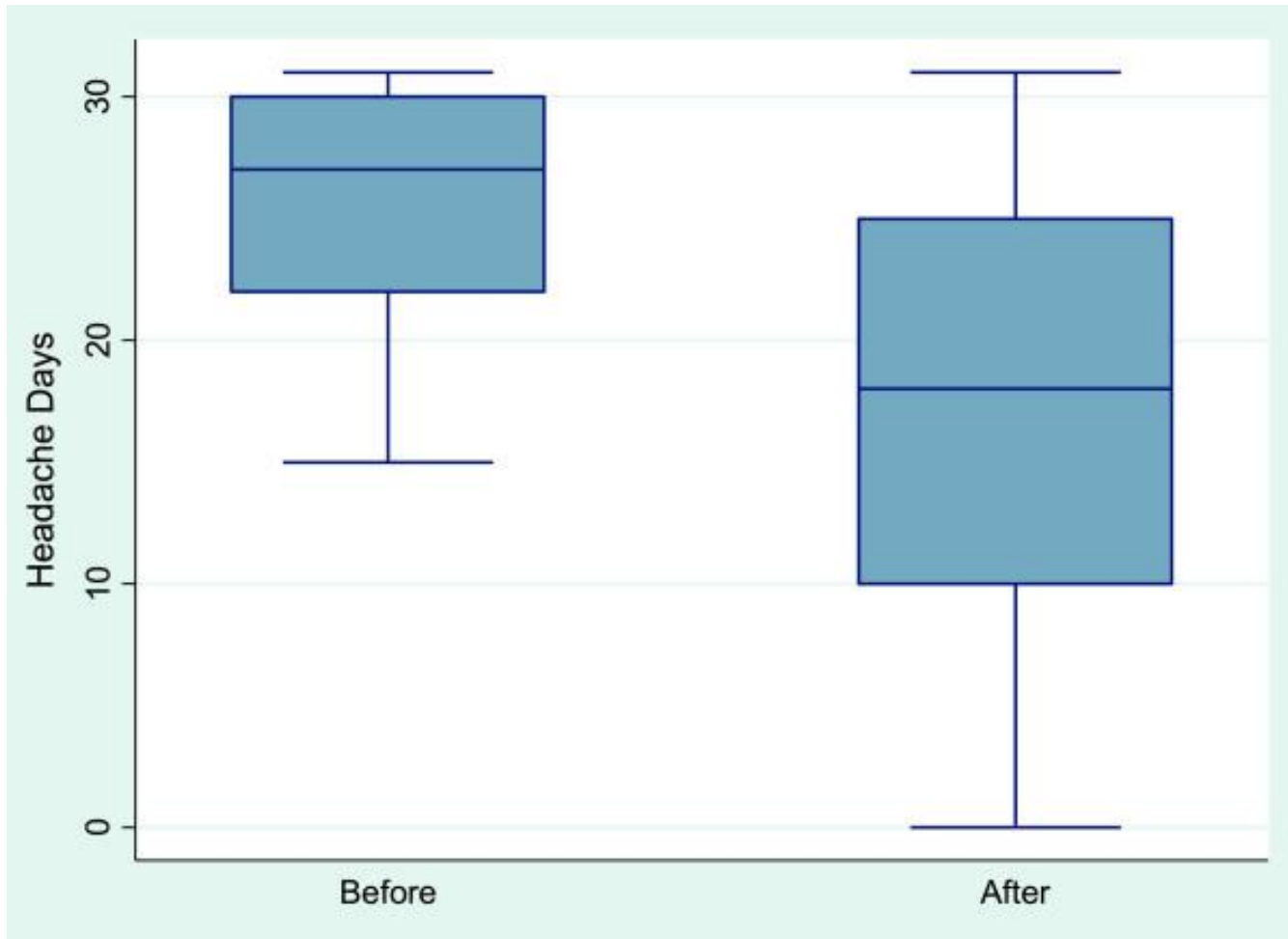
Frances' Story

I had seriously [sweaty armpits](#). I could never wear cute tank tops or fun colors. I always wore bulky black clothes and jackets. I had super [clammy hands](#) and totally [sweaty feet](#), too - I'm talking dripping sweat.

By the time I was 13, I gave up drawing because I was always smearing the paper. At 15, I cried because I couldn't go to a sleepover party because then people would find out about my problem. I stopped hanging out with my friends.

I'd just go to school, come home, do my homework, and go to bed. I didn't want to, but I didn't see any other way. I finally got my mom to listen to me and take me to [talk to a dermatologist](#). Now I get [Botox for my underarms](#). I want to help other kids like me, who are going through the same thing. I hope that people will be more aware of hyperhidrosis and know that they are not the only person who has it, that it's OK, and that you can get treated. I went through so much, but I'm a stronger person because of it. If you suffer from hyperhidrosis, have confidence, feel good about yourself, and keep your head up high. I feel like I can do almost anything now.

Chronic Migraine

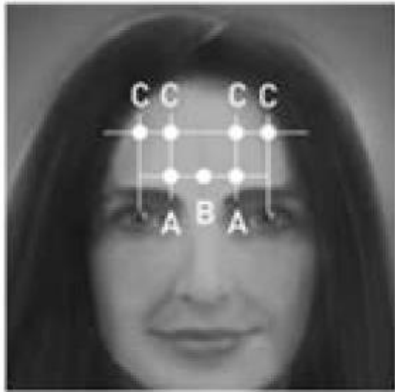


Prospective analysis of the use of OnabotulinumtoxinA (BOTOX) in the treatment of chronic migraine; real-life data in 254 patients

Injection Guide

Diagrams 1-4: Recommended Injection Sites (A through G) for Chronic Migraine

1

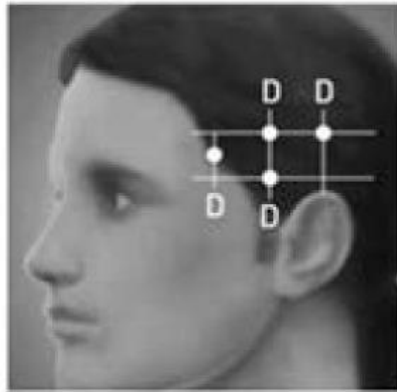


A. Corrugator: 5 U each side

B. Procerus: 5 U [one site]

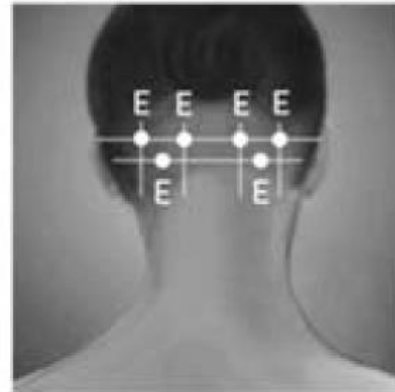
C. Frontalis: 10 U each side

2



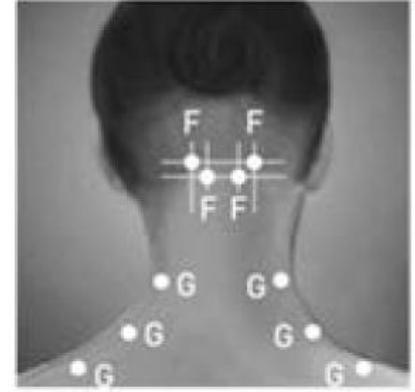
D. Temporalis: 20 U each side

3



E. Occipitalis: 15 U each side

4

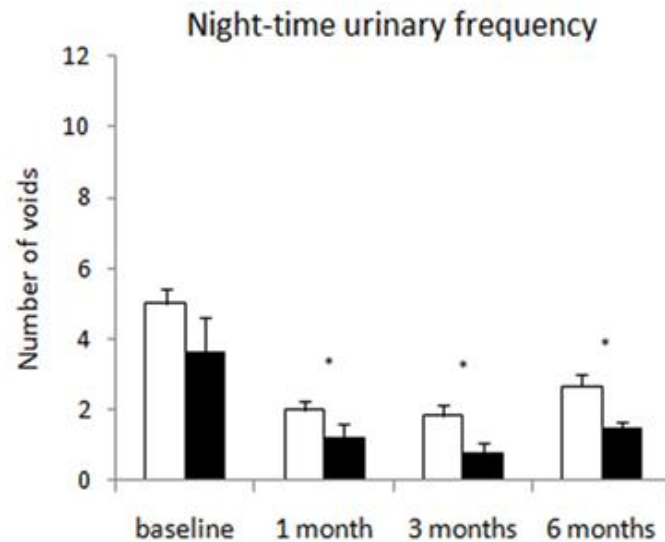
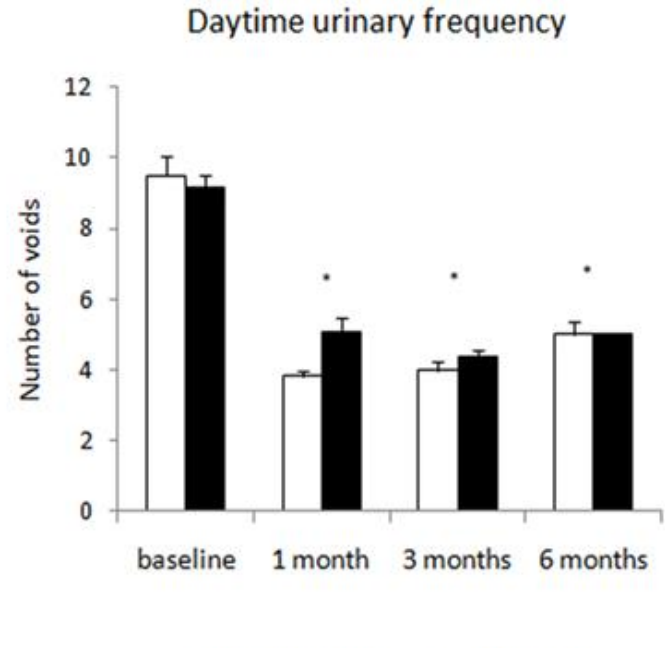
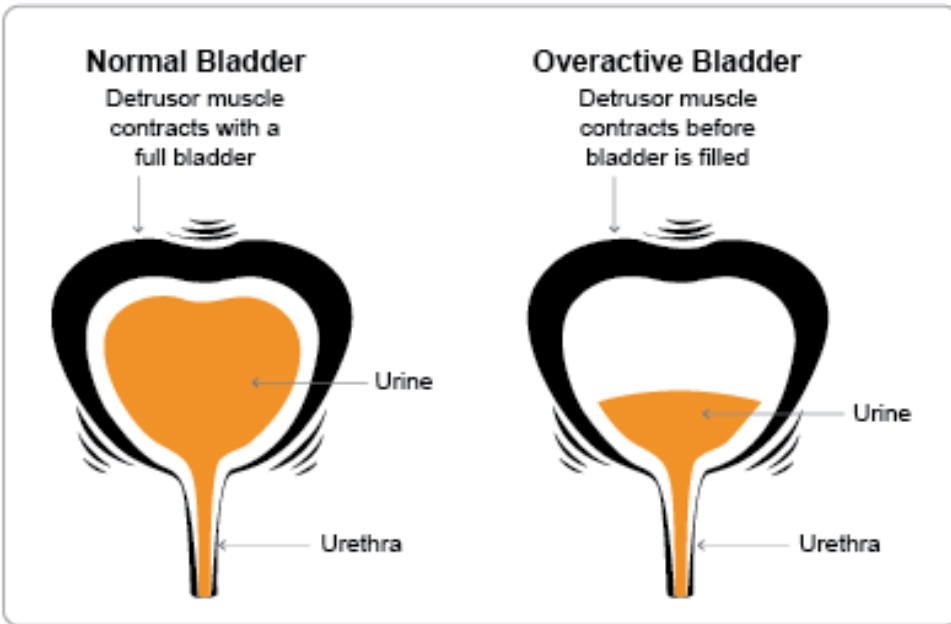


F. Cervical paraspinal:
10 U each side

G. Trapezius:
15 U each side

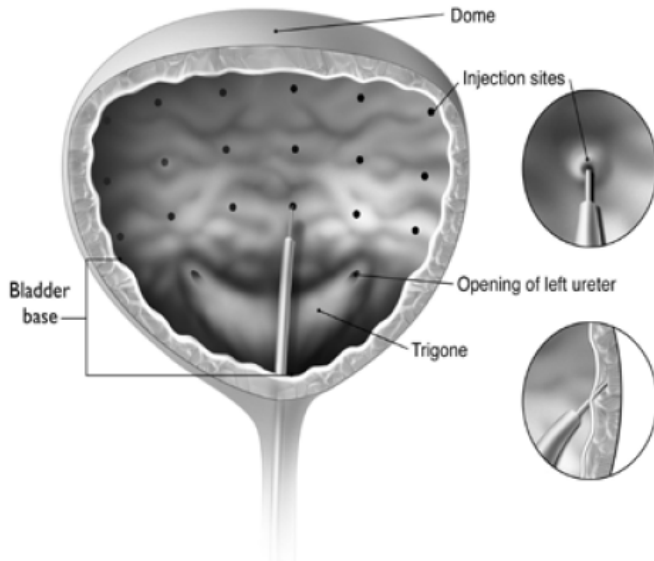
The recommended dose for treating chronic migraine is 155 Units administered intramuscularly using a sterile 30-gauge, 0.5 inch needle as 0.1 mL (5 Units) injections per each site. The recommended re-treatment schedule is every 12 weeks.

Overactive Bladder

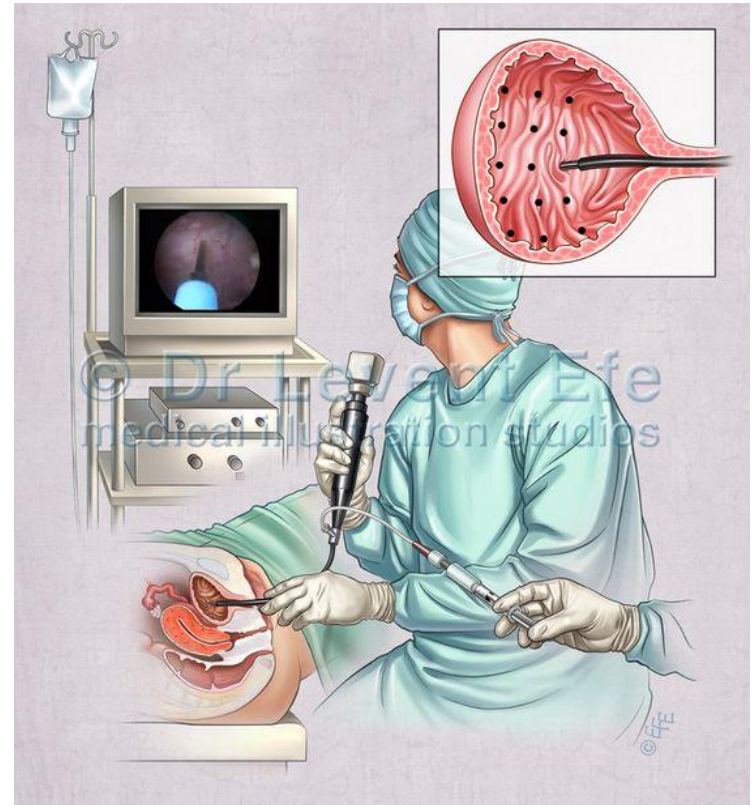


Injection Guide

Figure 1: Injection Pattern for Intradetrusor Injections for Treatment of Overactive Bladder and Detrusor Overactivity associated with a Neurologic Condition



The recommended dose is 100-200 Units via 20-30 injections spaced approximately 1 cm apart



The

drug

that's

treating

everything

FORGET WRINKLES. BOTOX IS NOW BEING USED TO TREAT MIGRAINES, DEPRESSION, TWITCHING EYES, OVERACTIVE BLADDERS, SWEATY PALMS AND MORE. SOME CALL IT A MARVEL OF MEDICINE; OTHERS CAUTION THE RISKS ARE STILL UNKNOWN. INSIDE THE EXPLODING BUSINESS AND STRANGE SCIENCE OF BOTOX

BY ALEXANDRA SIFFERLIN

PHOTO-ILLUSTRATION BY TIME

What are the other indications under investigation?

ClinicalTrials.gov

A service of the U.S. National Institutes of Health

[Try our beta test site](#)

Example: "Heart attack" AND "Los Angeles"

Search for studies:

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671 studies found for: botox

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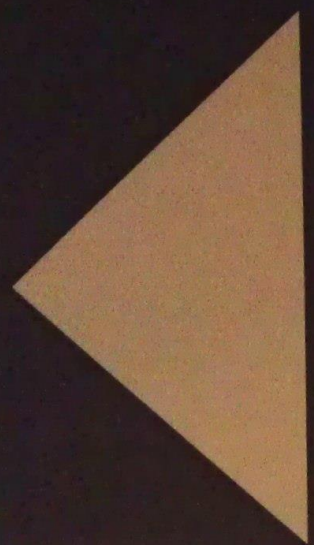
- Depression
- Atrial fibrillation
- Borderline personality disorder
- Psoriasis vulgaris
- Itch relieving
- Scar prevention/reduction
- Premature ejaculation
- Rosacea
- Anal fissure
- Painful sex
- Severely cold hands
- Parkinson's disease symptoms
- Drooling
- Teeth grinding

Competition – it's a crowded field

- US and EU:
 - Dysport
 - Xeomin
- China
 - Prosigne (by Lanzhou Institute of Biological Products)
- Korea
 - Neuronox, Siax, Botulift, Cunox, Meditoxin, Nabota, Evolus, Botulax

Other Serotypes May Play a Role

- A and B: currently approved for human use
- Serotypes with short term effects
 - C and E are being developed for new uses
 - E shows faster onset of action and shorter duration of effect
 - F was tested in human as an alternative to A, in case of resistance



**the
story
continues...**