Botulinum toxin: Getting started with cosmetic treatment
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I have no financial disclosures.

Learning Objectives
- To understand facial aging changes
- To review anatomy of facial muscles of expression
- To understand the history and uses of botulinum toxin
- To review product reconstitution and injection technique
- To review the newest products on the market

The Aging Face
- Prominent facial lines can be misinterpreted as
  - anger
  - anxiety
  - fatigue
  - sadness

The Aging Face
- Causative factors
  - Chronic gravitational pull
  - Volumetric loss of fat
  - Actinic damage
  - Hyperfunctional lines

The Aging Face
- Hyperfunctional lines are the result of underlying muscle contraction
  - Glabellar lines
  - Forehead “furrows”
The Aging Face

- Treat the underlying pathophysiology
- For hyperfunctional lines, treat the muscles

What is Botulinum toxin?

- Produced by anaerobic gram negative rod bacterium
  *Clostridium botulinum*
- Most toxic poison known to man
- Exotoxin liberated from bacteria in culture
  - Purified, freeze-dried
- Eight sub-types
  - A, B, C1, C2, D, E, F, G

What is Botulinum toxin?

- Mechanism of action
  - Binds to receptor in pre-synaptic neuromuscular endplate
  - Enters nerve via endocytosis
  - Prevents release of acetylcholine
  - Results in TEMPORARY PARALYSIS
  - Resolves as nerve regenerates new endplates

History of Botulinum toxin

- Early 1970’s
  - Dr. A. Scott (ophthalmologist) - first clinical use of botulinum toxin - in strabismus
- Mid 1980’s
  - Dr. Caruthers - “father” of cosmetic Botox
  - Observes wrinkle-free glabella after blepharospasm treatment

History of Botulinum toxin

- 1989
  - FDA approval for strabismus, blepharospasm, hemifacial spasm
- 1990
  - NIH consensus recommendation for use in dystonias
- 2002
FDA approval for glabellar lines

13 Uses of Botulinum toxin

- Spastic disorders
  - BEB, HFS, Parkinson’s, MS, CP, traumatic brain injury, post-CVA, dysphonia
- Dystonic disorders
  - Cervical dystonia, torticollis, etc
- Strabismus
- Hyperhidrosis
  - Axilla, palms

14 Uses of Botulinum toxin

- Cosmetic
  - Forehead furrows, glabellar folds, crows feet, mentalis, lips, nasal flare, platysmal bands
- Miscellaneous uses
  - Headache, TMJ, constipation, low back pain

15 Dilution and Storage

- “Botox” produced by Allergan in US
- Each Botox (botulinum toxin A) vial contains
  - Approx. 100 Units freeze-dried toxin
  - 0.5 mg human albumin
  - 0.9 mg sodium chloride
- Kept refrigerated until reconstituted

16 Dilution and Storage

- 1 Unit toxin = LD (50) for a group of female Swiss Webster mice
  - LD (50) is the estimated lethal dose for 50% of individuals
  - For humans, LD (50) = 40 U/kg or 2500-3000 U for a 70-kg man

18 Dilution and Storage

- Diluent
  - Manufacturer recommends NON-preserved saline
  - Concern that preservative deactivates toxin
  - Many physicians use preserved saline
  - 0.9% benzyl alcohol
Better buffered, so less pain on injection
Safer to use at a later time

Dilution and Storage
Botulinum toxin is FRAGILE
Add diluent SLOWLY to bottle
SWIRL vial to mix, don’t shake
Alcohol swabbed onto cap should evaporate prior to needle insertion

Dilution and Storage
What is the best dilution?
Manufacturer provides table up to 8 mL
Most physicians use 2 to 4 mL per vial
Example of calculation
100 Unit vial/2 mL saline = 5 U/0.1 mL

Dilution and Storage
High concentration (low volume)
Precise placement of toxin
Less diffusion into surrounding tissues
Greater duration of effect
Lower concentration (high volume)
Encourages toxin spread
Desirable in some areas
Shorter duration of effect

Dilution and Storage
Once reconstituted, Botox must be refrigerated
Package insert recommends use within 4 hours
Actual effectiveness is longer
CONTROVERSIAL

Dilution and Storage
Longevity studies with variable results
44% loss of activity in 12 hours
No loss of activity in 24 hours
No loss of potency at 30 days!!
Potential problems arise with sterility
Must consider using preserved saline

Many practitioners limit use to 24 hours

24 **Contraindications**
- Neuromuscular junction disease
  - Myasthenia gravis, Eaton-Lambert
- Hypersensitivity to human albumin
- Pregnancy
  - Category C drug
    - "not established whether harmful"
- Breast feeding
  - Not known whether excreted

25 **Relative Contraindications**
- Recent use (2 weeks) aminoglycosides, penicillamine, quinine, Ca channel blocker
- Can potentiate effects of toxin
- Anticoagulation
  - Ecchymosis and hematoma at injection sites

26 **Candidate Selection**
- Hyperfunctional lines
  - Due to action of underlying muscles
- "Spread test”
  - The ability to efface the lines by manually spreading surrounding skin
  - Predictive of favorable response to Botox

27 **Candidate Selection**
- Avoid patients with wrinkles in thick, sebaceous skin areas
  - Suggests dermal fibrosis to underlying muscles
  - Predictive of unfavorable response to Botox

28 **Muscular Anatomy**
- Frontalis
  - Origin: galea aponeurosis
  - Insertion: frontal bone & fibers of procerus, corrugator
  - Elevates brow
  - Horizontal forehead wrinkles
- Overtreatment: brow droop or ptosis

29  **Muscular anatomy**
- Corrugator supercilii
  - On frontal bone of upper medial orbit
  - Origin: frontal bone medial to brow
  - Insertion: dermis above middle third of brow
  - Brow adductor (down and medial)
  - Causes vertical glabellar crease

30  **Muscular anatomy**
- Procerus
  - Origin: lower nasal bone
  - Insertion: skin overlying nasal bridge
  - Causes “snout” contraction with horizontal nasal wrinkles

31  **Muscular anatomy**
- Orbicularis oculi
  - Origin: anterior aspect orbital rims
  - Insertion: medial and lateral canthal tendons
  - Closes eyes and depresses brow
  - Causes “crows feet” laterally

32  **Injection technique**
- Obtain written consent
- Cleanse areas with alcohol
- Ask patient to make facial expression to accentuate problem areas
- +/- marking pen
- Use 1/2 inch 30 gauge needle

33  **Injection technique**
- Inject into muscle, NOT the crease
  - Opposite of filler techniques
- Record injection sites and doses
- Photograph pre-injection & follow-up
- Err on side of injecting too little the first time
  - At 2 week exam, may reinject if needed

34  **Injection technique**
- Dosing
  - Individual thresholds and longevity of effect are highly
Individual thresholds and longevity of effect are highly variable.

- **Approximate dosages**
  - Frontalis: 5 to 25 U
  - Glabella: 5 to 20 U
  - Crows feet: 5 to 15 U

35 **Injection technique**
- Applying pressure immediately after injection may decrease ecchymosis
- Will spread area of toxin effect
- May or may not be desirable
- Effects reported as early as 24 to 48 hours
- May take up to 7 days
- Effects last approx. 3 to 6 months

36 **Injection technique**
- Glabella
  - Inject into corrugator (deep)
  - May insert needle to bone and pull back
  - Into procerus if horizontal line

37 **Injection technique**
- Forehead
  - Stay at least 2 cm above brow
  - Caution lateral to pupils
  - Avoid brow ptosis
  - Inject intramuscularly in alternating pattern above and below crease

38 **Injection technique**
- Crows feet
  - Ask patient to squint to localize lines
  - Alternate along lines
  - Stay lateral to orbital rim
  - Inject into orbicularis
  - Just deep to skin
  - About 10 U each side

39 **Botox as adjuvant therapy**
- Endoscopic brow lift PLUS Botox
- Decrease corrugator and procerus action
- Allows healing to new position more securely
- Laser-resurfacing PLUS Botox
  - Prevents reappearance of lines if underlying muscles are paralyzed during healing
- Filler injection PLUS Botox
  - Implanted material not compressed by muscle contraction

**Complications**
- FDA reports 16 deaths from botulinum toxin, 4 in kids <18 YO
  - In cervical dystonia injections
    - Respiratory muscle paralysis
    - Aspiration pneumonia
- Localized reactions (common)
  - Pain, bruising, hematoma, edema, erythema
  - May pretreat with EMLA or ice

**Complications**
- Inadvertent spread of toxin
  - Temporary weakness of adjacent muscles
  - Lid or brow ptosis, ectropion, corneal exposure, lagophthalmos, diplopia, epiphora
- Ways to avoid
  - Don’t massage, inject low volumes, avoid injection near orbital rim

**Complications**
- Mild ptosis may be treated with alpha-adrenergic agonist eyedrop
  - Apraclonidine 0.5% (Iopidine)
  - Causes Muller’s muscle contraction
  - Gives 1-2 mm upper lid lift

**Antibodies to Botox**
- Botulinum toxin is an antigenic protein
- Patients receiving repetitive, high-dose injections may develop antibodies
- These IgG’s block/neutralize Botox
  - Causes resistance to treatment effect
  - Do NOT cause hypersensitivity reactions
Botulinum Products Available
- Botox (type A) – Allergan, USA
- Dysport (type A) – made in Ireland, FDA approved in USA
- Botulinum toxin type A from Lanzhou Inst. in China
- Neuronox (type A) by Medy Tox in South Korea began in 2009

Another Botulinum toxin product available
- Xeomin
  - Manufactured by Merz in Greensboro, NC
  - FDA approved in 2010
  - cervical dystonia and blepharospasm
  - An isolate of active toxin
  - Without non-toxic accessory proteins
  - “low protein load”

Botulinum toxin Type B
- Myobloc
  - FDA approved 2000 for cervical dystonia
- Unique immunologic profile
  - Effective for patients with antibodies to typeA
- Treatment effective for 12 to 14 weeks
- More diffusion of toxin to adjacent tissues
  - High rate of undesired regional effects

Before and After