NEUROTOXINS: CAN A MEDICATION BE THE FOUNTAIN OF YOUTH?

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OBJECTIVES

• Describe mechanism of action of botulinum toxin type A for cosmetic applications
• Identify appropriate botulinum toxin type A treatment areas
• Identify the uses of botulinum toxin type A
• Identify effects of botulinum toxin type A treatment
SKIN ANATOMY AND FUNCTION
Epidermal appendages

- Sebaceous glands
- Hair
- Sweat glands
- Nails

Skin Anatomy
FUNCTIONS OF THE SKIN

- Highly specialized structure
- Prevents invasion of microorganisms
- Regulates fluid loss
- Maintains temperature control
- Protects against injury from radiation and electricity
- Provides immunologic surveillance
MELANOCYTES
FACTORS AFFECTING THE SKIN

- Genetic makeup
- Aging
- Volume loss
- Sun exposure
- Muscle contraction
- Lifestyle
- Diet

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Traits are familial if they are shared by members of a family, for whatever reason.

Traits are heritable only when the similarity arises from shared genotypes.

Skin color is heritable.

Skin cancers are familial.
Normal aging: The normal aging of the skin leads to:

- atrophy
- decreased elasticity
- impaired metabolic and reparative responses.

These changes are separate from those due to sun exposure, so-called “photoaging.”
Facial compartments change over time
Lips thin
Jowls form
Cheeks and eyes hollow
Lines become etched into the skin

VOLUME LOSS

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### Fitzpatrick skin phototypes

<table>
<thead>
<tr>
<th>Skin type</th>
<th>Unexposed skin color</th>
<th>Reaction to sun exposure*</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>White</td>
<td>Always burns, never tans</td>
</tr>
<tr>
<td>II</td>
<td>White</td>
<td>Always burns, minimal tan</td>
</tr>
<tr>
<td>III</td>
<td>White to olive</td>
<td>Burns minimally, gradually tans</td>
</tr>
<tr>
<td>IV</td>
<td>Light brown</td>
<td>Burns minimally, tans well</td>
</tr>
<tr>
<td>V</td>
<td>Brown</td>
<td>Very rarely burns, tans profusely</td>
</tr>
<tr>
<td>VI</td>
<td>Dark brown to black</td>
<td>Never burns, tans deeply</td>
</tr>
</tbody>
</table>

Note: Slight variations on the definitions of the phototypes appear in the literature.
* After the first one hour of sun exposure on untanned skin on the first day of spring.
Shorter wavelengths are more biologically active (UVA and UVB)

UV light causes: DNA damage, decreased DNA repair, oxidative damage, altered collagen structure (breakdown, synthesis).

Infra-red wavelengths

THE EFFECTS OF UV RADIATION EXPOSURE
THE EFFECTS OF UV RADIATION EXPOSURE

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MUSCLES OF THE FACE

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MUSCLE CONTRACTION

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LIFESTYLE

- Smoking
- Hydration
- Sun exposure
- Excessive weight loss and/or gain
  - Laxity
  - Stretch marks

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A FEW WORDS ON DIET

- Nothing found in the literature regarding direct impact of certain foods on skin
- Healthy balanced diet theoretically keeps skin healthy and performing well
- Alcohol intake dehydrates the body, tissues and skin
- There are no randomized clinical studies connecting food or milk to acne breakouts although, stress has been implicated

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THE AGING FACE

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FAT LOSS AND REDISTRIBUTION

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BONE RESORPTION

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COLLAGEN, ELASTIN AND HYALURONIC ACID CHANGES

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VISIBLE SIGNS OF AGING

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Tied for first place:

- Dynamic wrinkles
- Volume loss
PHARMACOLOGY OF NEUROTOXINS
BOTULINUM TOXIN TYPE A: 3 FDA-APPROVED PRODUCTS IN US
<table>
<thead>
<tr>
<th>Product</th>
<th>Units per Vial</th>
<th>Molecular Size</th>
<th>Exipients</th>
<th>Stabilization</th>
<th>Storage Pre-reconstitution</th>
<th>Storage Post Reconstitution</th>
<th>Gliabellar Lines Approval</th>
<th>Lateral Canthal Lines Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>onabotulinumtoxinA</td>
<td>500 BOTOX© Cosmetic Units</td>
<td>&gt; 900 kDa</td>
<td>Human albumin: 0.5 mg per 100 Unit vials; 0.25 mg per 50 Unit vials; Sodium chloride: 0.9 mg per 100 Unit vials; 0.45 mg per 50 Unit vials</td>
<td>Vacuum drying</td>
<td>2°C to 8°C</td>
<td>24 hours, refrigerated</td>
<td>2002</td>
<td>2013</td>
</tr>
<tr>
<td>abobotulinumtoxinA</td>
<td>300 Dysport® Units</td>
<td>≤ 500 kDa</td>
<td>Human albumin: 0.125 mg per 300 Unit vials; Lactose: 2.5 mg per 300 Unit vials</td>
<td>Lyophilization</td>
<td>2°C to 8°C</td>
<td>4 hours, refrigerated</td>
<td>2009</td>
<td>Not approved</td>
</tr>
<tr>
<td>incobotulinumtoxinA</td>
<td>50 Xeomin® Units</td>
<td>150 kDa</td>
<td>Human albumin: 1 mg per 50 Unit or 100 Unit vials; Sucrose: 4.7 mg per 50 Unit or 100 Unit vials</td>
<td>Lyophilization</td>
<td>20°C to 25°C (room temperature); 2°C to 8°C (refrigerator); -20°C to -10°C (freezer)</td>
<td>24 hours, refrigerated</td>
<td>2011</td>
<td>Not approved</td>
</tr>
</tbody>
</table>
WARNING: DISTANT SPREAD OF TOXIN EFFECT

Postmarketing reports indicate that the effects of BOTOX® Cosmetic and all botulinum toxin products may spread from the area of injection to produce symptoms consistent with botulinum toxin effects. These may include asthenia, generalized muscle weakness, diplopia, ptosis, dysphagia, dysphonia, dysarthria, urinary incontinence and breathing difficulties. These symptoms have been reported hours to weeks after injection. Swallowing and breathing difficulties can be life threatening and there have been reports of death. The risk of symptoms is probably greatest in children treated for spasticity but symptoms can also occur in adults treated for spasticity and other conditions, particularly in those patients who have an underlying condition that would predispose them to these symptoms. In unapproved uses, including spasticity in children, and in approved indications, cases of spread of effect have been reported at doses comparable to those used to treat cervical dystonia and at lower doses.
WARNINGS AND PRECAUTIONS

- Hypersensitivity Reactions
- Cardiovascular System
- Pre-existing Neuromuscular Disorders
- Pre-existing Conditions at the Injection Site
- Human Albumin and Transmission of Viral Diseases
All are contraindicated in the presence of infection at the proposed injection site(s) and in individuals with known hypersensitivity to any botulinum toxin preparation or to any of the components in the formulation.

CONTRAINDICATIONS
Co-administration of neurotoxins and aminoglycosides or other agents interfering with neuromuscular transmission should only be performed with caution as the effect of the toxin may be potentiated.

Use of anticholinergic drugs after administration of neurotoxins may potentiate systemic anticholinergic effects.

Excessive weakness may also be exaggerated by administration of a muscle relaxant before or after administration of neurotoxins.
Neurotoxin treatment is not recommended for use in children or pregnant women.

It is not known whether neurotoxins are excreted in human milk. Caution should be exercised when neurotoxin is administered to a nursing woman.

SPECIAL POPULATIONS

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NORMAL FUNCTION

PHOTO: ALLERGAN GLOBAL MEDICAL AFFAIRS

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MECHANISM OF ACTION AT NMJ

PHOTO: ALLERGAN GLOBAL MEDICAL AFFAIRS

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PLACEMENT OF NEUROTOXINS
Aesthetic Considerations
Lateral canthal lines (Botox only FDA approved)

Glabellar lines (Botox, Dysport and Xeomin)

Common areas where neurotoxin may be used (off-label)

FDA APPROVED SITES FOR COSMETIC INJECTION

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LATERAL CANTHUS

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- Forehead
- Upper lip lines
- “Gummy” smile
- Platysmal bands
- Mentalis
- Depressor anguli oris

COMMON OFF LABEL SITES

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SIDE EFFECTS AND COMPLICATIONS

What You and Your Patients Need to Know
Aesthetics is a true medical discipline with potential for serious complications.

Disruptive to patient appearance in addition to potential for infection and other health issues.

Dysphagia and breathing difficulties in treatment of cervical dystonia.
There has not been one confirmed serious case of spread of toxin effect when botulinum toxin product when used cosmetically at the recommended dose to treat frown lines, crow’s feet lines, or both at the same time.

COMPLICATIONS
SIDE EFFECTS

- **Common:**
  - Swelling
  - Bruising
  - Redness
  - Slight pain at injection site
SIDE EFFECTS

- Uncommon:
  - Moderate pain at injection site
  - Asymmetrical outcome
- Lid edema with orbital treatment
- Lid ptosis with glabellar treatment
- Hematoma

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CONTRAINDICATIONS

- Hypersensitivity to any botulinum toxin preparation or to any of the components in the formulation
- Infection at the injection site
- Concomitant neuromuscular disorder may exacerbate clinical effects of treatment
- Use with caution in patients with compromised respiratory function or dysphagia

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TIPS FOR AVOIDING UNDESIRED AFFECT

- Understand the patient’s desires and preferences
- Avoid treating any one area in isolation without regard to its effect on other areas
- Consider gender differences when treating eyebrows or lips

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INCORRECT PLACEMENT – LATERAL CANTHUS

PHOTO: COURTESY BETH HANEY

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BEFORE AND AFTER NEUROTOXIN TREATMENT

PHOTO COURTESY KRISTIN GUNN

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BEFORE AND AFTER NEUROTOXIN TREATMENT  PHOTO COURTESY BETH HANEY

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BEFORE AND AFTER NEUROTOXIN TREATMENT

PHOTO: BEAUTYEDITOR.CA

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