Clostridium botulinum: Friend or Foe?
“The Fountain of Youth”  Deadly Pathogen
Clostridium botulinum

• Strict anaerobe
• Gram-positive
• Bacillus (rod) shape
• Ubiquitous in terrestrial environment
• Virulence factor = Botulinum toxin
What is Botulism?

• Flaccid paralysis of muscles
  – by toxin from *Clostridium botulinum*
• Three types – via route of entry of bacteria
  – Foodborne, infant, wound
• Mainly foodborne outbreaks
Symptoms of Botulism

Table 1. Symptoms and Signs of Food-borne and Wound Botulism

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Signs</th>
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<tbody>
<tr>
<td>Visual disturbances</td>
<td>Dilated, fixed pupils</td>
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<td>Blurred vision, diplopia, photophobia</td>
<td>Eye muscle paresis/paralysis (extraocular, eyelid)</td>
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<td>Dry mouth</td>
<td>Nystagmus</td>
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<td>Dysarthria</td>
<td>Dry mucous membranes in mouth/throat</td>
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<td>Dysphagia</td>
<td>Pharyngeal erythema</td>
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<tr>
<td>Dysphonia</td>
<td>Other specific muscle paresis/paralysis</td>
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<td>Sore throat</td>
<td>Decreased to absent deep tendon reflexes</td>
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<td>Difficulty with mastication</td>
<td>Ataxia</td>
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<td>Generalized weakness (usually bilateral)</td>
<td>Somnolence</td>
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<tr>
<td>Dizziness and/or vertigo</td>
<td>Hypotension (including postural)</td>
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<td>Nausea and/or vomiting</td>
<td>Ventilatory (respiratory) problems</td>
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<td>Abdominal pain, cramps, discomfort</td>
<td>Fever (typically absent in food-borne botulism but often present in wound botulism)</td>
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<td>Diarrhea</td>
<td>Sensory deficits (very rare)</td>
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<td>Constipation</td>
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<td>Problems with urination</td>
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<td>(retention or incontinence)</td>
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<td>Paresthesias</td>
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Classes of Botulinum Toxin

• Seven different subtypes of toxin
  – A, B, C1, D, E, F, and G

• Same general mechanism for muscular paralysis

• Vary in structure, target site, & toxicity

• Only two manufactured for commercial use
  – A and B
Transmission of Botulinum Toxin

- Mostly via improperly cooked food
- Conditions to produce toxin not completely understood
- Complex route of transmission
  - Ingestion/injection
  - Progenitor toxin complex
  - Absorbed into tissue → circulated in blood
  - Dock onto receptors of neuron → transcytosis → binds up acetylcholine → paralysis
Major Steps in Toxin Action

Toxin synthesized as single-chain polypeptide (inactive form)

Polypeptide cleaved by protease to create dichain structure (active form)

Toxin binds to epithelium, transcytosed, reaches general circulation

Receptor-mediated endocytosis at peripheral cholinergic nerve endings

In cytosol, toxin cleaves target, blocking neurotransmitter release = flaccid paralysis
Figure taken from: Arnon, et al. 2001.
Toxin as therapeutic agent

- Many cosmetic uses: Use Botulinum toxin type A (Botox®)

  Before Botox®  After Botox®

- Therapeutic use in muscular disorders: muscle hyperactivity/spasm
- Controlling pain-associated disorders: inhibiting neurotransmitters
Concluding Remarks

• Toxin = potential as therapeutic agent!

• However, repeated administration required and long-term effects not known

• Questionable if really needed in cosmetic treatments cause you have to remember…
Sometimes wrinkles aren’t all that bad!