Botulinum toxin / "sausage poison"

- Derived from clostridium botulinum (Gm +ve, anaerobic, produces neurotoxin, causes botulism)
- Botox Species are divided into 4 groups:
- Produces 7 different botulinum neurotoxin serotypes A to G:
  - Group I – A B F
  - Group II – B E F
  - Group III – C D
  - Group IV – G

**PHARMACOLOGY**

- 3 steps in toxin-mediated paralysis
  - Step 1: Binding
  - Step 2: Internalization – Internalized by endocytosis
  - Step 3: Inhibition of neurotransmitter release (Cleaves proteins required for release of Ach vesicles)
    - Inhibits calcium dependent neurotransmitter release. This is a multistep process

- Duration of neurotransmitter inhibition varies (Action Duration: A > C > B > F > E)
- Paralysis is seen 24-48 hours after injection
  - Presynaptic vesicles are depleted
- Recovery
  - Initially new axons sprout – 28 days
- Return of synaptic function of the initial NMJ – 91 days
- Muscle function usually present by 3 to 4 months

**MOLECULAR STRUCTURE OF BOTULINUM NEUROTOXIN:**

- These neurotoxins are synthesized as 150 kDa single chain protein molecules. These molecules when secreted are inert and must be cleaved by proteases for them to become active. These neurotoxin botulinum molecule when acted upon by proteases generates a dichain molecule. This dichain molecule is composed of a heavy chain about 100 kDa and a light chain which measures about 50 kDa. These two chains are held together by disulfide bond

**Botox Uses in the Laryngopharynx**
1. Stuttering
2. Vocal tics
3. Puberphonia
4. Ventricular dysphonia / Dysphonia plica Ventricularis
5. Dysphagia
6. TEP speech failure
7. Prevention of posterior glottic stenosis and
8. Recurrent vocal fold granuloma
9. Arytenoid Rebalancing
10. Bilateral vocal fold paralysis
11. Spasmotic Dysphonia

**STUTTERING**
- Affects children and adults
- Involuntary break in vocal fluency
- Larynx, pharynx, lips, oral cavity
- Decrease laryngeal contribution by injecting the Thyroarytenoid muscles
- Return of symptoms in 12 weeks

**VOCAL TICS**
- Tourette’s syndrome
- Repetitive dyskinetic movements of eyes, facial muscles, neck, oral cavity
- Dyskinetic movements of larynx-leads to grunts, abrupt breaks in fluency, and complex formations like screams, loud talking, repetitive word or vowel sounds, copralalia.
- Botox injections into thyroarytenoid muscles have shown clinical improvements

**PUBEROPHONIA**
- Also known as mutational dysphonia
- Men and adolescent boys
- Higher fundamental frequency of prepubescent years
- Speech and behavioral therapy
- Botox as adjunct into cricothyroid muscles
- – Enables larynx to relax and allow for lowering of pitch

**VENTRICULAR DYSPHONIA / DYSPHONIA PLICA VENTRICULARIS**
- Hyper functioning of Supragottic larynx
- Over adduction of false vocal folds
- Propagation of fundamental frequency from FVC’s
- Gravelly, wet, hoarse quality voice – prone to vocal fatigue
- Compensatory response after injury, cysts, sulci allowing air escape
- Botox injections into the false vocal folds – Aryepiglottic muscle

**DYSPHAGIA**
- Cricopharyngeal dysfunction and dyscoordination
- Botox into cricopharyngeus
- Identify patients that would benefit from CPM

**VOCAL FOLD GRANULOMA AND PREVENTION OF POSTERIOR GLOTTIC STENOSIS**
- Following repair of posterior glottis clefting (interarytenoid)
- Recurrent granulation/scarring
- Botox into the thyroarytenoid muscles to decrease the strength of vocal fold closure and allow more lateral position at rest
- Decreases strength of vocal fold closure to help in treatment of vocal fold granuloma (less local trauma)

**ARYTENOID REBALANCING**

- Arytenoid dislocation following traumatic intubation or blunt trauma to anterior neck.
- Hoarseness/breathiness after surgery
- Immobile vocal cord
- EMG analysis and operative endoscopy
- Endoscopic manipulation of arytenoid back into native position
- Botox injected into interarytenoid muscle, ipsilateral thyroarytenoid muscle, and lateral cricothyroid muscle
- Weakens ipsilateral adductor muscles, allowing ipsilateral adductor to provide traction on the arytenoid allowing a more physiologic position.

**BILATERAL VOCAL CORD PARALYSIS**

- Botox injected into the thyroarytenoid and interarytenoid muscles
- Weakens the adductor muscles, allowing increased patency of the airway at rest and with activity
- “Rebalance” position of the paralyzed cords to a more abducted position

**SPASMODIC DYSPHONIA**

- Mid 30’s, women (63%)
- Two types: ADductor and ABductor
- Dx based on careful history and examination of the glottis during a variety of laryngeal tasks

**Adductor Spasmodic Dysphonia**

- Most common type
- Hyperactivity of the thyroarytenoid m. (TA)
- Inappropriate closing or tightness of the glottis
- Strained voice

**Abductor Dysphonia**

- Less common
- Inappropriate glottal opening
- Produces hypophonia and breathy breaks
- Treatment alternatives to Botox:
  - Surgical denervation: crush, neurolysis
  - Speech therapy (adjunct)
  - Psychological therapy
**Injection Strategy**

- Adductor spasmodic dysphonia: EMG guided Transcutaneous injections of the Thyroarytenoid muscle, using equal amounts of Botox (1-1.25U initially)

**Adductor spasmodic dysphonia:**

- Injection Technique
  - Reclined position with neck extended
  - Local anesthesia unnecessary (hinder)
  - Bend needle 30-45° (esp in women)
  - Insert needle through skin just off midline at level of cricothyroid membrane
  - Characteristic ‘buzz’ when in airway
  - Advance superiorly and laterally
  - Patient asked to phonate for EMG confirmation
  - Botox injected

**Abductor spasmodic dysphonia:**

- EMG guided transcutaneous injection of one posterior crycoarytenoid muscle with Botox (3.75U initially)
- PCA may be reached in two ways:
  - Retrocricoid (lateral) approach
  - transcricoid (anterior) approach

**OTHER USES OF BOTOX**

- Facial Aesthetics i.e. hyperfunctional lines
- Control of autonomic dysfunction, as in Frey syndrome, sialorrhea, and rhinorrhoea
- Blepharospasm
- Hemifacial spasm
- Oromandibular dystonia
- Spasmodic torticollis
- Temporomandibular joint disorders
- Migraine
- Tension headache
- Achalasia cardia
- Paediatric incontinence due to over active bladder