# *Infant Botulism*

Environmental Health – Food Protection Services

BC Centre for Disease Control

# Topics

- History of Botulism
- Mode of Action
- Infant Botulism (Intestinal Botulism)
  - Symptoms & Diagnosis
  - Treatment - BabyBIG
  - Neurotoxin Types & Groups
  - Risk Factors
- Food Sources (honey)
- Laboratory Diagnosis
- References

# Botulism – a short history

- Emperor Leo VI of Byzantium (886-911 A.D.) forbade his people to eat blood sausages.
- 1793, southern Germany, 6 of 13 died, initially diagnosed as belladonna poisoning. "Blunze" - pig stomach/blood preserved by smoking.
- 1820-22 in Germany Justinus Kerner collected data on 230 cases of sausage poisoning due to "corpse acid".
- Recognized in Russia in 1818
  7 cases of paralytic illness in Yakutsk due to salted fish. Known as ichthyism!
- ~1900 Dr. van Ermengem isolated an anaerobic spore-forming bacillus from the spleen of a victim
  → described this organism as *Bacillus botulinus*

# 1924 – Albany, Oregon

- Home-canned string beans
- All 12 people family members died

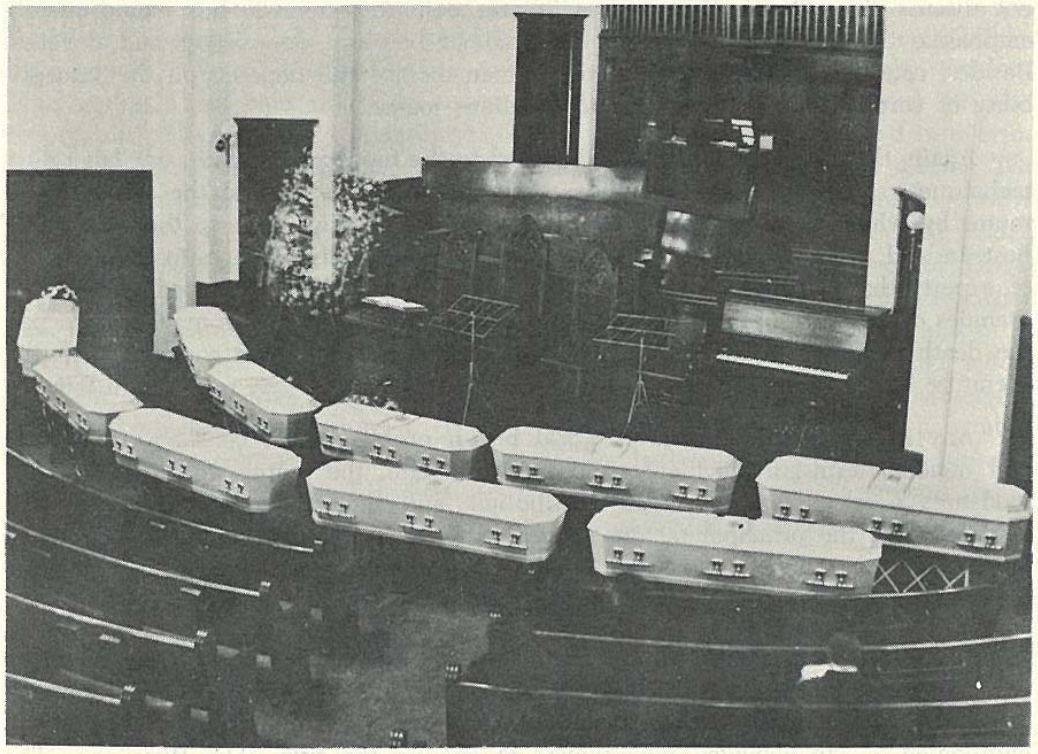


Figure 3 — Funeral of family wiped out by botulism caused by home-canned string beans at Albany, Oregon, in 1924. Altogether there were 12 deaths.
(Photo courtesy of Dr. Philip B. Cowles, Yale University.)

# *C. botulinum*

**Gram positive**

**Anaerobe**

**Spore Former**

**Oval subterminal endospores**

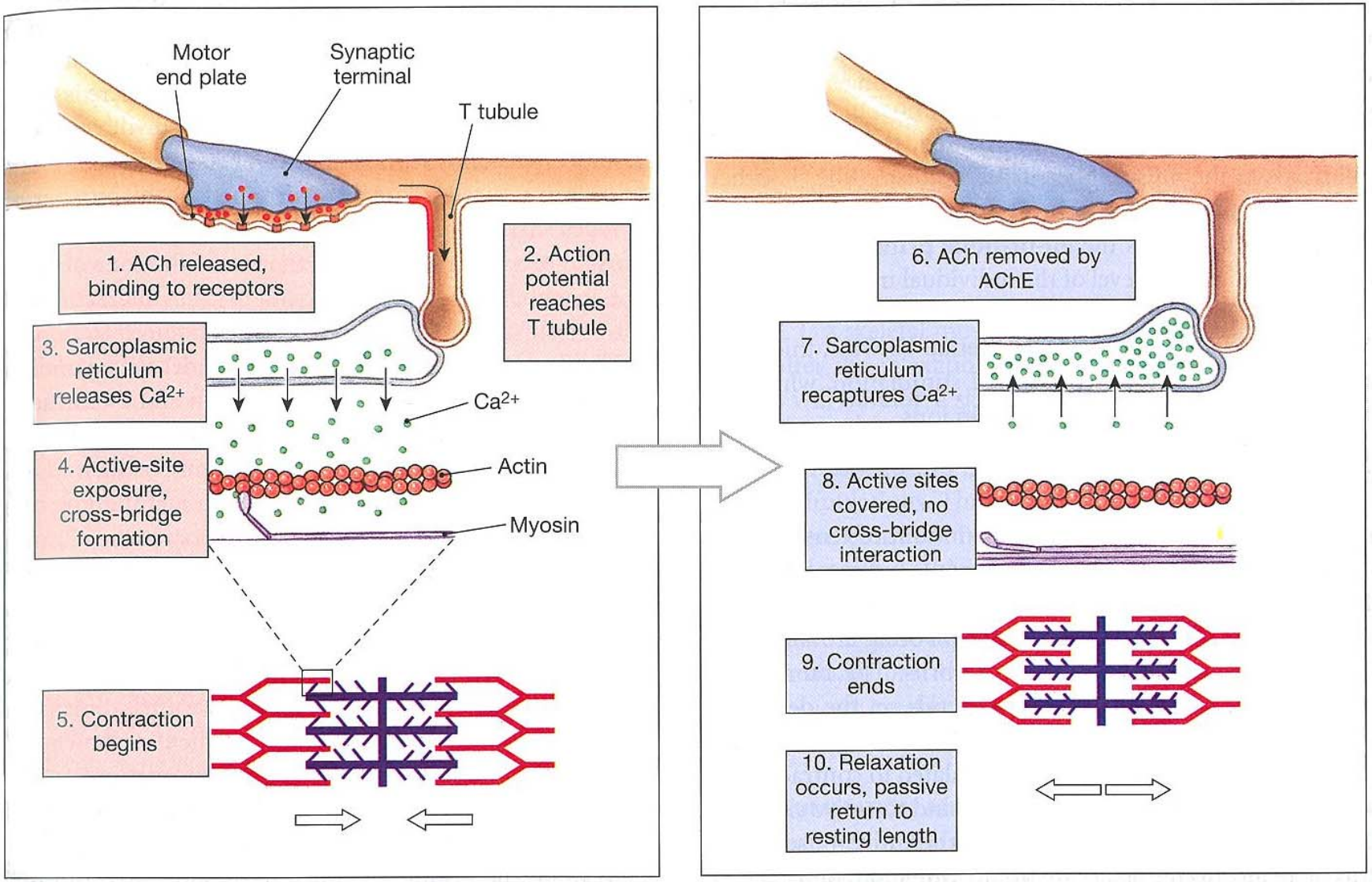
**Motile**

www.hpa.org CDC Public Images 2132, 1930

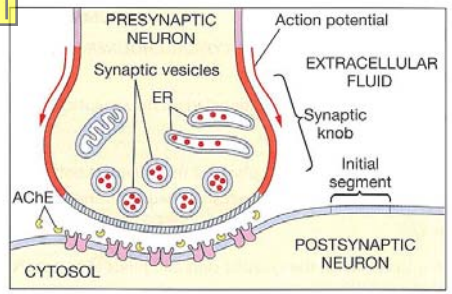
# Botulism – what is the disease?

- Botulism causes an intoxication that damages the nerves
- Ingestion of protein toxin blocks the release of acetylcholine at neuromuscular junctions
- This stops muscle contractions and paralyzes skeletal muscle cells – “muscular paralysis”.

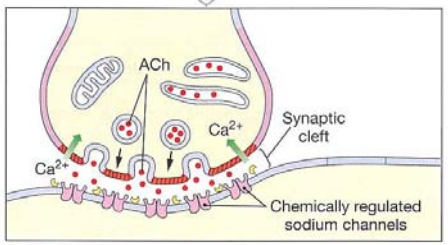
## SUMMARY TABLE 10–1 STEPS INVOLVED IN SKELETAL MUSCLE CONTRACTION



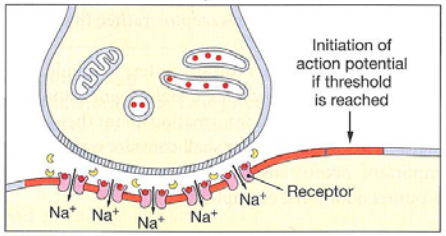

**Martini, Anatomy & Physiology, 6th ed.**



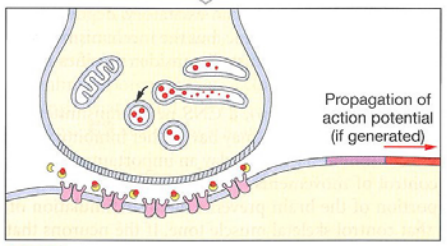

**STEP 1:** An action potential arrives and depolarizes the synaptic knob.




**STEP 2:** Extracellular $Ca^{2+}$ enters the synaptic cleft triggering the exocytosis of ACh.

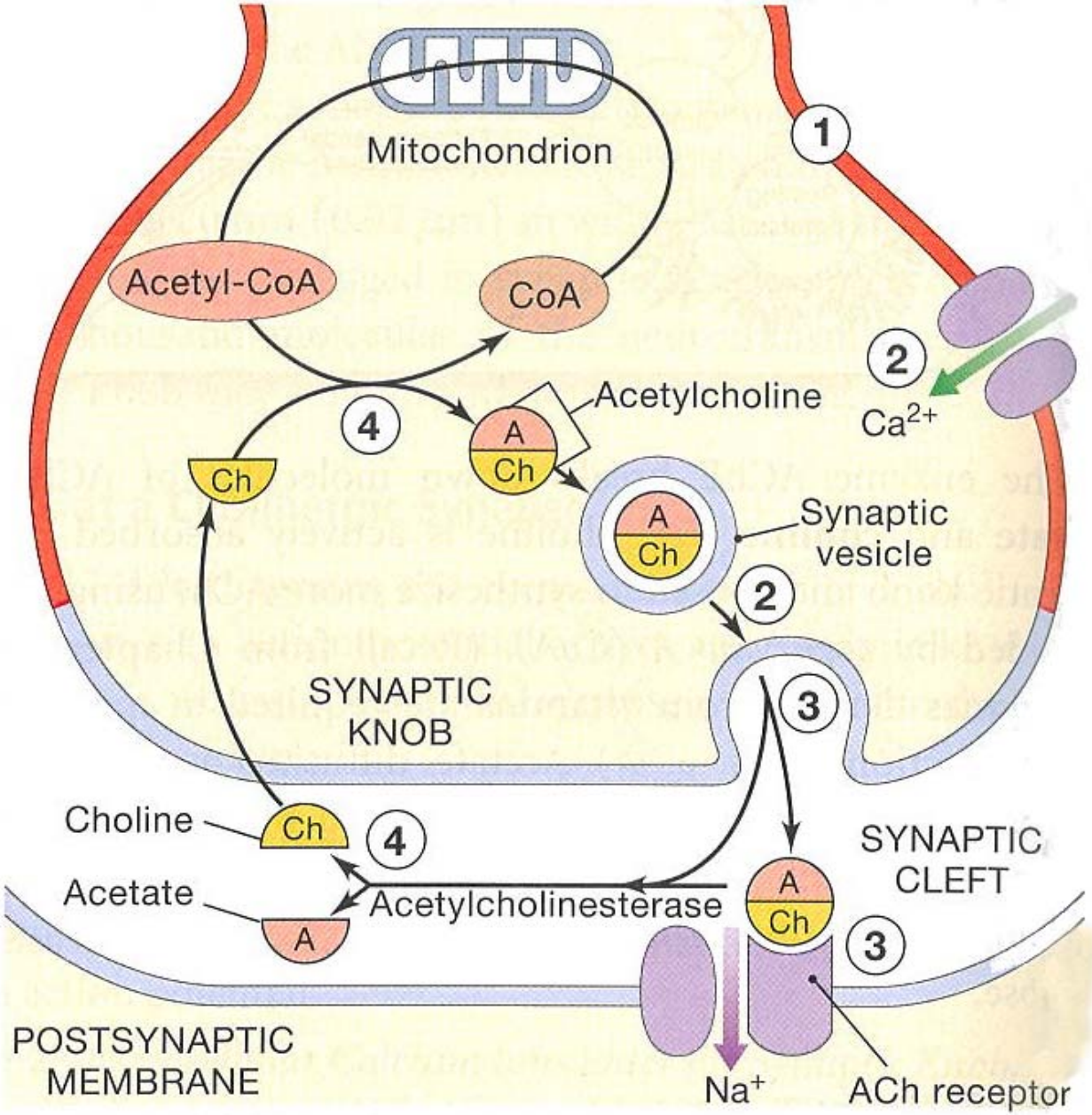



**STEP 3:** ACh binds to receptors and depolarizes the postsynaptic membrane.




**STEP 4:** ACh is removed by AChE (acetylcholinesterase).

**FIGURE 12–19**
**The Function of a Cholinergic Synapse**




**Martini, Anatomy & Physiology, 6th ed.**

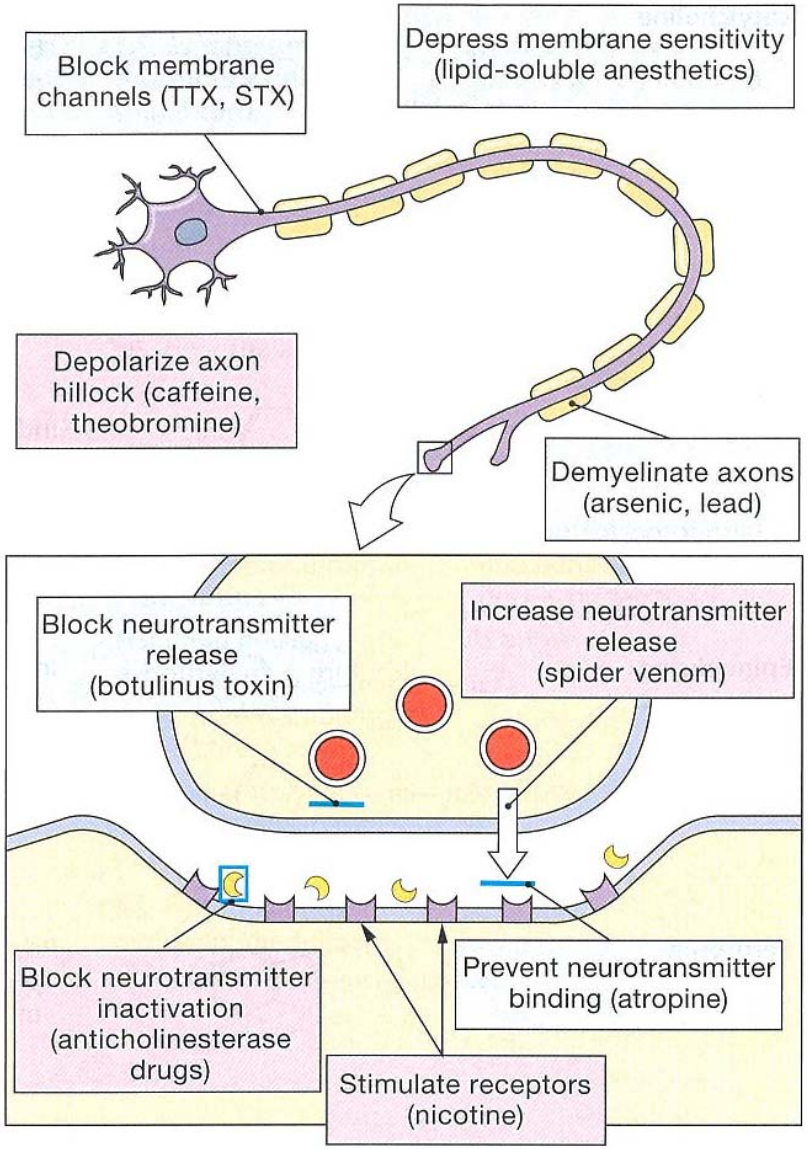



**FIGURE 12–20**
**The Mechanism of Drug Action at a Cholinergic Synapse.** Factors that facilitate neural function and make neurons more excitable are shown in violet. Factors that inhibit or depress neural function are in blue.

**Martini, Anatomy & Physiology, 6th ed.**

# Types of Botulism

- Food Botulism
- Wound Botulism
- Infant Botulism
- Child/Adult Botulism

} **Intestinal Botulism**

# Infant Botulism

- Affects children less than 12 months old
  - Median age: 10 wks (2 wks to 1 yr)
    - exception: 7.6 days for *C. baratti* (rapid progression)
- Ingestion of *C. botulinum* spores cause the illness (food or environmental)
  - *in situ* production of toxin by *Clostridium* bacteria, gut microflora fail to competitively inhibit outgrowth of spores
- Mild to severe illness
  - Feeding difficulties, mild hypotonia, floppy neck → respiratory failure, infant death
- Incubation period from 3 to 30 days after exposure

# Symptoms & Diagnosis

- 1st symptom constipation (95%)
- “Floppy baby”, listless, lethargic, poor head control
- Difficulty swallowing & sucking, weak cry
- Flaccid expression
- Pupils don’t react to light
- Weak gag reflex

Diagnosis:

- EMG – electromyogram
- Stool specimen

# Treatments

- Supportive and respiratory care
- Nasogastric feeding, mechanical respiration
- BabyBIG
- Wait until recovery of nerve function: regeneration of terminal motor neurons
- Hospital stays from one month to a year

# Differences in Outcomes of Infants Treated with BIG-IV (BabyBIG)

(Arnon *et al*, *N Engl J Med.* 2006;354:462-471)

**Randomized Placebo-Controlled Trial (129 Infants)**

| Duration of | Placebo | BIG-IV |
|---|---|---|
| Hospitalization | 5.7 wk | 2.6 wk |
| ICU care | 5.0 wk | 1.8 wk |
| Mechanical ventilation | 4.4 wk | 1.8 wk |
| Tube feeding | 10.0 wk | 3.6 wk |
| Total hospital charges | $163,000 | $74,800 |

**Open-Label Use (366 infants)**

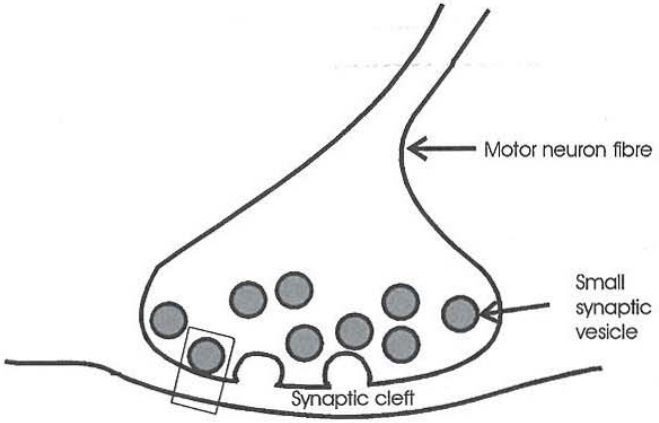
| | | |
|---|---|---|
| Hospitalization | BIG-IV @4-7 days hosp | BIV-IV@ <4 days hosp |
| | 2.9 wk | 2.0 wk |

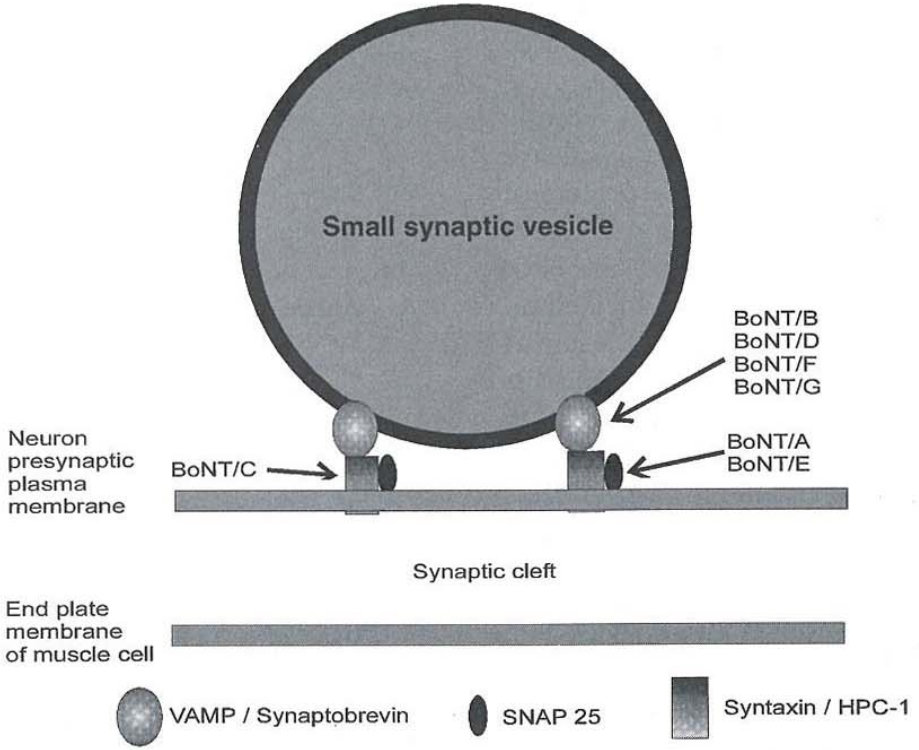
All differences statistically significant $p<0.001$

# Botulism neurotoxin types

- A, B, E, F affect humans
- $C_1$, $C_2$, D affect birds, mammals
- G not found to cause illness
- AB, BF dual toxin strains

(*C. butyricum, C. baratii* also known to produce type E & F toxins)


Motor neuron fibre
Small synaptic vesicle
Synaptic cleft
Muscle cell


Small synaptic vesicle
BoNT/B
BoNT/D
BoNT/F
BoNT/G
BoNT/A
BoNT/E
BoNT/C
Neuron presynaptic plasma membrane
Synaptic cleft
End plate membrane of muscle cell
VAMP / Synaptobrevin
SNAP 25
Syntaxin / HPC-1

# Botulism Groups

| | Group I | Group II | Group III | Group IV |
|---|---|---|---|---|
| | Proteolytic | Non-proteolytic | Non-proteolytic | |
| Neurotoxin | A, B, F | B, E, F | | |
| Optimal temp | 35-40°C | 18-25°C | 40°C | 37°C |
| **Range temp survival (min/max)** | 10-48°C | 3-45°C | ND | ND |
| pH | 4.6 | 5.0 | ND | ND |
| Salt | 10% | 5% | ND | ND |
| Aw | 0.94 | 0.97 | ND | ND |
| **Spore Inactivation Step†** | 25' @ 100°C<br>0.1-0.2' @ 121°C | <0.1' @ 100°C<br><0.001' | <0.1 to 0.9' @ 100°C | <0.8 to 1.1' @100°C |

†- Note: in commercial canning operations, a 12D (12 log reduction) process is typically 2.4 min at 121°C (250°F)

# Water Activities of various foods

| Food | $a_w$ |
|---|---|
| Fresh fruit, veg, meat, fish | >0.98 |
| Cooked meat, bread | 0.98 - 0.95 |
| Cured meat products, cheeses | 0.95 - 0.91 |
| Sausages, syrups | 0.97 - 0.87 |
| Flours, rice, beans | 0.87 - 0.80 |
| Jams, marmalades | 0.80 - 0.75 |
| Candies | 0.75 - 0.65 |
| Dried fruits | 0.65 - 0.60 |

# Minimal $a_w$ for growth of....

| Microorganims | $a_w$ |
|---|---|
| Most bacteria | 0.91 - 0.88 |
| Most yeasts | 0.88 |
| “Regular molds” | 0.80 |
| Halophilic bacteria | 0.75 |
| Xerotolerant molds | 0.71 |
| Osmophilic yeasts | 0.62 - 0.60 |

# Processing of Foods for $a_w$

Photo: BC Centre for Disease Control

# Processing of Foods for $a_w$


**Chilled mirror dew-point technique**

Photo: BC Centre for Disease Control

**Adult classical Botulism: BC case**

**“Stink Eggs”**

**Type E Botulism**

Photo: BC Centre for Disease Control

# Infant Botulism Types & Risk Factors

- Type A is found in the west / Type B is found in the east
- Risk factors and predisposing conditions…
  - ingestion of honey – risk of Type B
  - parent has daily contact with soil / living on a farm / living in area following an earthquake
  - windy, high soil water and alkaline content
  - possible seasonal trend: cases between March and October (not winter)
  - exclusively breast-fed infants during weaning (change in gut microflora)
  - introduction of first formula feeding
  - age onset differences:
    formula-fed: 7.6 weeks, breast-fed: 13.7 weeks (±8.4 weeks)
  - host factors role in pathogenesis

# Spores found in....

- Honey
- Yard soil
- Vacuum cleaner dust
- Infant Formulas

# Laboratory Investigation – Infant Botulism

- Specimen to be submitted:
  **stool

  NOT blood or serum (rarely does toxin circulate in infant blood)
  - Exception: early in course of infection

# Laboratory Methods

- Mouse assay – intraperitoneal Inject culture filtrates, food filtrates or serum into mice
- Look for symptoms
  - Wasp-like or constricted waist
  - Ruffled hair
  - Difficulty breathing, failure to right response
  - Death
- TAT for mouse assay
  - Serum: 48 hours minimum for negative result
    - If positive, signs may be observed within 4 to 8 hrs post-inoculation, usually 24 hrs is required.
  - Culture (stool, food): 5 to 7 days

# Infant Formula Problems

- Botulinum Type B in Infant Powder
  Ireland 2001
  (SMA nutrition: white infant formula)
- Thiamine Deficiency in Infant Formula, Israel, November 2003
- *Enterobacter sakazakii* in Powdered Infant Formulas, Canada, July 2002
- *Bacillus cereus* in Powdered Infant Formulas, Survey, Germany, 1994

Photo: BC Centre for Disease Control


Photo: BC Centre for Disease Control

# BCCDC Contacts for Case Management and Investigations

- When botulism is suspected, immediately inform the local Medical Health Officer
- Contact the on-call Physician for BCCDC at 604.312.9222 regarding provision of botulism antitoxin
- Contact the on-call Medical Microbiologist at Laboratory Services (BCCDC) 604.661.7033 for consultation and approval of sample testing
- Phone Food Poisoning Laboratory (BCCDC) 604.707.2611 for priority sample submission information
- Phone Food Protection (BCCDC) 604.707.2440 for consultation regarding Food Recalls & investigation

BCCDC Reference Links:

1. Communicable Disease Control Chapter 1 - Botulism
2. PHSA Programs and Services

# References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