

TOXICOLOGY TODAY



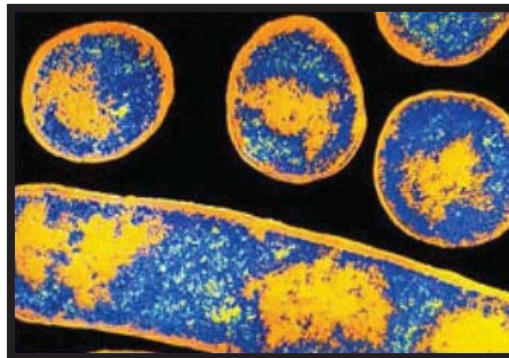
BOTULISM

by *Brieana Cox Buckley, PharmD*

Introduction

During July 2007 four people were diagnosed with botulism after ingestion of a commercially canned chili sauce.¹ This led to a nationwide recall of several commercially canned chili products. Botulism consists of a group of potentially fatal clinical syndromes that result from a potent neurotoxin produced by *Clostridium botulinum*. *C. botulinum* is a group of anaerobic, spore-forming, gram positive bacilli that form toxins with similar pharmacologic activity. *C. botulinum* spores are found worldwide in soil, air, freshwater, and seawater. They are very resistant to destruction. Ingestion of spores, except in infants, is generally harmless. The botulinum toxin is extremely potent and it is estimated as little as 0.05 mcg may be fatal in humans.

There are four forms of botulism that are classified based on how the toxin was acquired: food-borne, infant, wound and intestinal colonization. According to the Centers for Disease Control and Prevention



C. botulinum Source: <http://www.health.utah.gov>

(CDC), approximately 110 cases of botulism are reported each year, with the majority being infant botulism.² The incidence of food-borne and infant botulism has remained relatively constant while the incidence of wound botulism has increased. Food-borne botulism outbreaks have been reported in 46 states, Puerto Rico and Washington D.C, although over 50% of reports come from the states of Alaska, California, Colorado, Oregon and Washington. In Alaska, food-borne botulism is a significant public health concern due to improperly prepared and stored native foods.

There are eight different serotypes, not all of which produce disease in humans. The vast majority of cases are caused by botulinum toxin types A, B, and E.

Fatalities have been reported with all three types. Types A and B are most often associated with home-canned vegetable, fruits and meats while Type E is most often associated with marine products.

Mechanism of Toxicity

Botulin toxin binds irreversibly to the cell membrane of presynaptic nerve terminals and inhibits the release of acetylcholine in the peripheral nervous system.

Food-Borne Botulism

The oldest recognized form of botulism is the food-borne type. This type occurs after ingestion of foods that contain the preformed neurotoxin. In the past, poorly preserved meat was the most common cause of botulism, however, most current

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E - NEWSLETTER

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food-borne exposures result from improper home canning of vegetables. The bacterial spores are resistant to heat and may survive the home canning process at temperatures below 120° C (250° F). Foods most likely to enhance toxin production have low acidity (pH > 5), low oxygen, and high water content. Some foods most often implicated in transmission are vegetables such as corn, beets, carrots,

asparagus, and green beans. Food contaminated with *C. botulinum* types A and B usually will have signs of spoilage. However, food contaminated with *C. botulinum* type E may appear and taste normal. The toxin can be destroyed by heating food to 100° C (212° F) for 10 minutes. Longer boiling times or pressure cooking must be used at high altitudes to ensure

(cont. on pg. 2)

OUTREACH WITH OTHER PUBLIC HEALTH ENTITIES

One of the UPCC's major goals is to be "a state resource for accurate and up-to-date poison information and clinical toxicology consultation to the public, health-care professionals, emergency service personnel and public health officials. To that end, the UPCC works hard to support state and local public health efforts. The following are just a few of the examples of collaboration involving outreach education with other groups that share a common interest in poisonings and poison prevention:

- **Utah National Violent Death Reporting System (NVDRS)** is a state-wide database maintained by the Utah Department of Health which provides accurate and timely information to: 1) inform decision-makers about the magnitude, trends and characteristics of violent deaths; and 2) evaluate and continue to improve state-based violence prevention policies and programs. The

UPCC was invited to attend the NVDRS Technical Advisory Committee to discuss shared interests and share data.

- **State Epidemiology Outcomes Workgroup Project (SEOW)** reviews and analyzes data on drug abuse trends in order to assess substance abuse prevention needs throughout the state. This group which brings together experts in prevention, survey design and methodology, and epidemiology assists prevention workers to better understand their community's needs and apply effective prevention activities. The UPCC shares data on substance abuse reported to the UPCC to contribute to prevention efforts at the state level.
- **Utah Migrant Seasonal Farmworkers (UMSFW) Coalition** is a group of individuals and agencies that work together regarding health, safety, legal,

housing, and education to meet the needs of migrant and seasonal farmworkers and their families in Utah. The UPCC works with the coalition to evaluate their needs related to pesticide poison prevention to the workers.

Checkout our website for more poison prevention information at www.utahpoisoncontrol.org

FYI

TELECOMMUNICATIONS AND THE UPCC

All "emergency" calls to the UPCC are recorded. The digital recording becomes part of the patient's medical record. Digital recordings are valuable in training new employees and are an integral part of our continuous quality improvement program.

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destruction of the heat-labile toxin.

Patients with food-borne botulism usually have initial symptoms of nausea, vomiting, diarrhea, and abdominal pain. The onset of neurological signs and symptoms is usually delayed 12 to 36 hours. Cranial nerve involvement predominates with blurred vision, diplopia, ptosis, dysarthria, dysphagia, and dysphonia. A descending paralysis follows eventually affecting the respiratory muscles. Patients remain awake and alert and have no sensory loss.

Infant Botulism

Infant botulism is the most common form of botulism in the United States. It occurs in children less than one year of age, usually less than 6 months, and occurs following ingestion of clostridium spores from dirt or honey. Infant botulism is almost entirely Types A and B. It is thought that because infants lack bile acids and have less gastric acid that this environment allows for germination of the spores and production of the toxin. Infants who are breast fed may have increased susceptibility to infant botulism due to changes in gut flora. Because the spores germinate in the GI tract and the toxin is formed

slowly, symptoms are more gradual in onset as compared to the food-borne illness when all the toxin is absorbed at once. The main features are constipation, listlessness, difficulty sucking and swallowing, weak cry, pooled oral secretions, general muscle weakness, and loss of head control. The child is often noted to appear "floppy". Neurological findings can include ptosis, dysphagia, sluggish pupillary reaction to light, weak gag reflex, and decreased anal sphincter tone.

Wound Botulism

Until recently wound botulism was considered rare and almost exclusively associated with traumatic injury or surgical wounds. Since 1991 the number of wound botulism cases has increased dramatically, with 19 confirmed cases reported to the California Department of Health Services in 1995.³ The majority of these cases occurred in injecting-drug users, particularly involving subcutaneous injection or "skin popping" of black tar heroin. The most likely underlying causes are contamination of the heroin while it is being cut and poor hygiene during injection, resulting in the development of subcutaneous abscesses and subsequent infection. Patients with wound botulism have similar neurological findings as classic food-borne botulism but have fewer GI complaints, an increased incidence of fever, and an

extended incubation period (4 to 18 days).

Biological Warfare

C. botulinum toxin is considered a risk to national security and is a Category A agent by the CDC. Category A agents can be easily disseminated, are likely to produce significant mortality and have a high public health impact. They might cause public panic or require special preparedness needs.⁴ Botulism can not be transmitted from person to person and will not pass through intact skin. However, the toxin can be fatal after ingestion, and can also cause disease via inhalation. Botulism could be introduced into its target population by contaminating food or water supplies, but these routes are associated with significant limitations. As a result, most concerns are focused on the inhalational delivery of botulin toxin. Inhalation botulism has a dose dependent onset that typically occurs between 1 to 5 days after exposure.

Diagnosis

Botulism is under-diagnosed or delayed because symptoms can be mistaken for more common clinical entities (Table 1). Initial suspicion of botulism based on history and physical examination must be confirmed with detection of the toxin in the patients stool, *(cont. on pg. 3)*

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serum or wound. The suspected food, if available, should also be tested. The state health department can mobilize resources to facilitate testing. The toxin type can be identified using mouse bioassay studies with antitoxin neutralization. Testing is usually preformed by the state health departments or the CDC.

Treatment and Prognosis

The mainstay of treatment for botulism is supportive care. Because the primary concern is paralysis of respiratory muscles, patients must be in a health care facility with the capability of ventilatory support. In mild cases, ventilatory support may not be necessary. Because the botulinum toxin binds irreversibly, respiratory muscle weakness and paralysis will last until the nerve terminals can regenerate. Ventilatory support may be required for weeks to months. Antibiotics have very limited roles; aminoglycosides, clindamycin, and polymixin B, in particular, should be avoided because they have intrinsic neuromuscular blocking properties. Patients should be carefully observed for progression of limb and respiratory muscle weakness.

Gastrointestinal decontamination may be beneficial to remove spores (infants) or toxins from the GI tract. Because the toxin may still be present hours or even days after exposure, activated charcoal should be considered because it adsorbs type A toxin. Gastric lavage may be considered in an asymptomatic person who recently ingested a known contaminated food. Wound debridement and drainage may be appropriate in the management of wound botulism.

Antitoxins for food-borne and wound botulism are available from the CDC and are equine-derived products with IgG antibodies to toxin types A, B, and E (monovalent, bivalent and trivalent formulations). Antitoxin is not recommended for infant botulism. Contact the local or state health department to facilitate reporting and access to the antitoxin. Anaphylaxis and serum sickness are potential adverse effects following antitoxin administration. The antitoxin only neutralizes the toxin not bound at the nerve terminal and therefore must be given as soon as possible for maximum benefit. Its effectiveness is greatest if given within the first 24 hours of exposure. It is effective in preventing progression of illness and shortening the duration of respiratory failure in severe cases of botulism.

A human botulism immune globulin (BIG-IV) has been developed for the treatment of infant

botulism Types A and B. The product licensed as BabyBIG® is available through the Infant Botulism Treatment and Prevention Program of the California Department of Health Services.⁵ Botulism immune globulin has been demonstrated to reduce hospital length of stay and need for mechanical ventilation and tube feeding.⁶

The prognosis has greatly improved during the past 50 years as a result of modern supportive care measures. The case fatality rate for food borne botulism has decreased from 60% prior to 1950 to less than 10% in 1996.⁷

Summary

Botulism is a rare but potentially fatal illness where Clostridium botulinum toxin blocks acetylcholine release, resulting in acute symmetric diplopia, dysarthria, dysphagia, descending weakness and paralysis, which may impact respiratory function. Treatment consists of respiratory support and antitoxin or immunoglobulin administration. Rapid diagnosis and early antidotal therapy are important factors to improve patient outcomes. In the event C.

botulinum is used as a biological weapon, it is crucial for all health care professionals to be familiar with this disease, its proper evaluation, and timely treatment.

Table 1: Differential Diagnosis of Botulism in Adults and Infants

Adults

Bacterial food poisoning
Cerebrovascular accident
Diphtheria
Elapidae envenomation
Guillain-Barre syndrome
Myasthenia Gravis
Organophosphate poisoning
Paralytic shellfish

Infants

Congenital myopathy
Electrolyte abnormalities
Encephalitis
Meningitis
Reye's Syndrome
Sepsis

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POISON PEARLS

ADOLESCENT DRUG ABUSE

by Lorin Browne, DO
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The growth of the Internet in recent years has provided a revolutionary new means for interpersonal communication. Information on recreational drugs is readily available online. With this new source for the exchange of ideas, adolescent drug abuse patterns have begun to change at a rapid rate. The overall rate of adolescent drug abuse has decreased 14-30% from its peak in 1996. However, the Monitoring the Future Study's most recent survey of 8th, 10th and 12th graders identified showing increased rates of use in the last few years. Abuse of Ecstasy (MDMA), prescription narcotics (notably Oxycontin® and Vicodin®), and inhalants have increased modestly since 2004. The study implicates both increased availability and decreased perception of risk as two factors involved in the increased use of these substances among adolescents.

Source: <http://www.monitoringthefuture.org/pubs>

MEET THE UPCC STAFF



JULIE GERSTNER joined the UPCC as the Administrative Assistant in March 2005. Prior to that, she worked in the U of U Biology Advising office for 13 years. She is the proud mother of three grown daughters, Jamie, Janelle, and Jill. She is also a new grandmother

and loves it! She is a fan of U of U basketball and her license plate "UT MOM" reflects her loyalty to the U. She is a native of Salt Lake City and loves spending time at her family cabin in the Uintah Mountains. Her hobbies include "playing" with her two horses (Snowflake and Honey), traveling abroad, cooking, gardening, and being with her family (especially her grandson, Tanner). She enjoys working at the UPCC because of the variety in her job and the dedicated and caring people she works with.



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*CSPI denotes Certified Specialist in Poison Information.



THANK YOU

The Utah Poison Control Center expresses its sincere thanks to the health care professionals, public health officials and toxicology colleagues that work together to treat and prevent poisonings.



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