INFANT BOTULISM: A SUMMARY

Infant botulism is a rare paralytic disease caused by the microorganism *Clostridium botulinum*. If an infant swallows enough spores, the spores can colonize the large intestine, multiply and produce toxin. The toxin is absorbed into the body and carried to the nerve endings, which results in muscular impairment. Infant botulism differs from foodborne botulism in where and when the toxin is produced. In foodborne botulism, the toxin is pre-formed in the food and absorbed in the small intestine (making foodborne botulism a more acute and severe disease).

The common first symptoms of infant botulism include poor feeding, less than one bowel movement in three days and an altered cry. Other symptoms may include poor sucking, lethargy, lack of facial expression, irritability and progressive 'floppiness.' Any infant showing these symptoms should receive prompt medical treatment.

About 70 to 100 cases of infant botulism are reported annually in the United States. The incidence of this disease is decreasing which may reflect increasing awareness of the disease and specific actions taken to prevent it. Because of the ever-present nature of botulinum spores, particularly in dust and dirt, all babies, children and adults come into contact and swallow botulinum spores some of the time. Children and adults are not normally susceptible to this form of botulism because their digestive tracts are mature. Babies have yet to develop the necessary defense mechanisms.

It is not known how many spores are needed to cause infant botulism or why only some babies become ill. Chances of developing the disease depend upon conditions in the immediate environment of the infant (e.g., exposure to dust and geographic location) and individual characteristics of the baby (such as age and frequency of bowel movements). Botulinum spores can come from the baby's food, from surfaces in the baby's environment, or even from dust in the air. Although food is a vehicle for spores and certain diets may predispose an infant to growth of *Cl. botulinum*, the spores come predominantly from environmental sources.

The initial epidemiological research that followed the discovery of infant botulism identified honey as a risk factor for the disease and determined that honey can contain spores that cause botulism. About five percent of the thousands of samples of honey that have been analyzed contain botulinum spores. It is very difficult to remove bacterial spores from honey without appreciably changing or destroying the honey. Honey is occasionally a source of high numbers of botulinum spores. However, since most infants with infant botulism have not been exposed to honey, the development of infant botulism must involve additional factors. Nonetheless, honey should not be fed to anyone less than one year of age.

The National Honey Board, the Centers for Disease Control and Prevention, the American Academy of Pediatricians, the California Department of Public Health, Health Canada and other public health associations recommend that honey not be fed to infants under one year of age.

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INFANT BOTULISM: AN OVERVIEW

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BOTULISM - WHAT IS IT?

Botulism is a paralytic disease caused by a microorganism known as Clostridium botulinum. Cl. botulinum is a bacterium with two distinct life phases. The dormant phase is the spore form and, like the seed of a plant, it can germinate into the vegetative phase. During the vegetative phase the bacteria are capable of metabolism, growth, reproduction and can produce and release a potent toxin. Different strains of Cl. botulinum are distinguished by the different types of toxin that they produce. These are called "types" of Cl. botulinum and are used to identify the source of the bacteria that caused a specific incident of disease. In mammals, the toxin can bind to nerve endings and block the transmission of signals through the nervous system. Without signals from the nervous system the muscles will not function, paralysis results, and the ability to breathe is severely impaired. Medical care is needed until new nerve endings grow and reverse the effects.

Botulinal spores are distributed widely throughout nature. They are common in soil, water, raw agricultural and aquacultural products, and finished food products that are not sterilized. Spores are also found in the household and have been recovered from air, from carpets, from houseplants and from vacuum cleaners (Chin et al., 1979). The spores are distributed unevenly in the environment; one type may dominate in a given geographic location. Spores are extremely resistant to heat, drying and chemicals. As exposure to the spore is impossible to avoid. Disease-prevention is based on avoiding conditions that encourage germination of the spore, bacterial replication, and subsequent toxin production.

There are three forms of botulism. The food poisoning form occurs when the microorganism grows in a food and produces toxin in the food. If somebody eats this food, the toxin is absorbed into the bloodstream and carried to the nerve endings. This type of botulism poisoning can be prevented by using appropriate food processing and food handling techniques. Rigorous control of processing conditions in the food industry now makes this type of botulism a rare disease. The Centers for Disease Control and Prevention generally record less than 50 cases of food poisoning botulism per year (Centers for Disease Control, 1990). Wound botulism is the second form of botulism and is often associated with gunshot injury and puncture wounds. It occurs when Cl. botulinum enters a break in the skin, starts to grow, and produces toxin in the wound. This type of botulism is controlled by the use of standard medical procedures for treating wounds. The third form of botulism is infant botulism.
**WHAT IS INFANT BOTULISM?**

Infant botulism is different from the food poisoning botulism because the bacterium grows and produces toxin inside the body. If enough spores are swallowed by a susceptible individual, the spores can colonize the large intestine (Mills and Arnon, 1987, Miyazaki and Sakaguchi, 1978, and Sugiyarna and Mills, 1978), multiply, and produce toxin. The toxin is absorbed into the body and carried to the nerve endings with the usual result of muscular impairment.

Although infant botulism is less severe than foodborne botulism, and its mortality rate is lower, it may involve longer hospital stays. This is probably accounted for by the varying mechanisms of toxin production and toxin absorption. The toxin in infant botulism is produced in an area (the large intestine) that absorbs botulinum toxin very poorly (Bonventre, 1979); this lessens the severity of the disease. However, the bacterial growth and toxin production in the infant's intestine is a continuing process that may last for weeks.

Because of the ever-present nature of botulinum spores, particularly in dust and dirt, all babies, children, and adults come into contact and swallow botulinum spores some of the time. Children and adults are not normally susceptible to this form of botulism because their digestive tracts are mature. During the year after birth, the digestive system gains several defense mechanisms including higher numbers and more types of bacteria, a barrier of mucous and the capability of a local immune response (Walker, 1977). Infants (defined as individuals less than one year of age) lack these defenses and are more vulnerable to disease until they develop them. The development of higher numbers and more types of bacteria in the digestive tract has been shown to be particularly important in preventing *Cl. botulinum* from causing infant botulism (Sugiyarna and Mills, 1978). Adult cases of infant-type botulism are possible but are very rare (Chia et al., 1986 and McCroskey and Hatheway, 1988). Normal healthy children and adults routinely ingest botulinum spores without harm.

**WHAT ARE THE SYMPTOMS OF INFANT BOTULISM?**

The common first symptoms of infant botulism include poor feeding, less than one bowel movement in three days, and an altered cry (Spika et al., 1987). The disease is obscure because these symptoms are common to many maladies in infants. Other symptoms may include poor sucking, lethargy, lack of facial expression, irritability, and progressive 'floppiness.' Problems with the eyes, such as dilated and sluggish pupils, are often noted and respiratory arrests occur frequently but are seldom fatal (Dodds, 1992). Prompt medical treatment is essential and may include mechanical support for breathing. Effective treatment consists of "meticulous supportive care" with a focus on the child's "nutritional and respiratory needs" (Center for Disease Control, 1978). While antitoxins or antibiotics are of uncertain effectiveness (Centers for Disease Control, 1984), other drugs to counteract the disease in infants are being tested (California Morbidity, 1990).

The effects of infant botulism can range from mild to severe paralysis (Arnon and Chin, 1979). A few infants may temporarily carry botulinal spores without any overt symptoms and those infants with mild paralysis may go undiagnosed. Most documented cases of infant botulism are those with moderate to severe paralysis and require hospitalization until the symptoms are reversed. In rare instances the symptoms occur suddenly and are severe and the disease can be fatal.

Since "the prognosis is excellent with institution of appropriate supportive care" (Gay et al., 1988), medical attention should be sought when symptoms are first noticed. It is recommended that all "infants
who develop decreased ability to feed and in whom no other infectious cause is identified should have stool specimens submitted for culture of *Clostridium botulinum* and detection of toxin, particularly if there has been a change toward a less frequent bowel movement pattern" (Spika et al., 1989).

**HOW COMMON IS INFANT BOTULISM?**

Infant botulism is a rare disease; about 70 to 100 cases are reported annually in the United States (Centers for Disease Control and Prevention, 1995). Infant botulism was not recognized as a disease until 1976 and in the United States approximately 1,200 cases were reported between 1976 and 1993. The rate of disease dropped from 0.03 to 0.02 (per 100,000) from 1980 to 1989 (Centers for Disease Control, 1990). This decrease may reflect increasing awareness of the disease and specific actions to prevent it.

Cases from many nations have been reported but substantially less often than what is reported in the United States. Less than 100 cases have been reported, between 1975 and 1990, from 14 developed countries outside of the United States (Dodds, 1992). As botulinum spores are found around the world, this difference may be due to misdiagnosis, limited laboratory facilities, and under reporting. Not all physicians are aware of this disease and the symptoms are hard to associate clearly with infant botulism.

In California, pediatricians are very familiar with this disease and the state reports over half of the cases in the United States (California Morbidity, 1990). Additional factors accounting for this increased incidence include the high concentrations of botulinum spores in the state and the high birth rate in California. Utah and Pennsylvania also routinely report a higher number of cases than other states (Arnon et al., 1981). The difference may in part be explained by the higher concentration of botulinum spores in the soil in some states. The discrepancies may also lie in inconsistencies in reporting practices between the states and in as yet unknown regional factors.

**WHAT CAUSES INFANT BOTULISM?**

It is not known how many spores are needed to cause infant botulism or why only some babies become ill from exposure to the spores. Chances of developing the disease depend upon conditions in the immediate environment of the infant (e.g., exposure to dust and geographic location) and individual characteristics of the baby (such as age and frequency of bowel movements).

Based on studies using mice, it has been suggested that as few as 10 to 100 spores may induce disease in human infants (Sugiyama and Mills, 1978). Sugiyama (1979) reported that 170 to 700 spores were probably needed to infect half of the mice tested. Tabita et al. (1991) determined a 50 percent infective dose of 290 spores per mouse. It is likely that most infections would require exposure to several hundred spores.

Botulinum spores can come from the baby's food, from surfaces in the baby's environment, or even from dust in the air. Although food is a vehicle for spores and certain diets may predispose an infant to growth of *Clostridium botulinum*, the spores come predominantly from environmental sources (Dodds, 1992). Spores have been recovered from the home environment in places such as the dirt in houseplants (Chin et al., 1979) and dust in cribs (Istre et al., 1986). Infants exposed to dirt and dust may be more likely to develop infant botulism (Arnon et al., 1981, Long, 1985 and Thilo and Townsend, 1993) presumably by inhalation and swallowing dustborne particles. The geographic locale also influences the incidence of
disease probably because botulinum spores occur in high concentrations more often in one locale over another (Spika et al., 1989, Murrell and Stewart, 1983, and Long, 1985). Some scientists believe that the distribution of botulinic spores in the environment "is the most significant determinant of case rate" (Long, 1985).

Age is an important factor in determining the risk of developing infant botulism because defense mechanisms against this disease develop after birth. Infants are most frequently affected between two weeks and six months of age (Arnon, Damus and Chin, 1981) although infants as young as seven and eight days old have had this disease (Thilo and Townsend, 1993). Half of the reported cases are in infants less than two months old and the median age at onset of disease is two months (Spika et al., 1990). It is believed that protective defense mechanisms are present in the gut by six months of age; however, a safety factor of six months is added and one year of age is considered the maturation point at which protection against infant botulism is in place (Center for Disease Control, 1978).

Individual characteristics of the baby and his/her diet may determine susceptibility to infant botulism. Breast-feeding has been identified as a risk factor for the disease, but its role is ambiguous (Spika et al., 1989, Morris et al., 1983, Long et al., 1985). Breast milk may be protective by moderating the severity of the symptoms at onset of infant botulism (Arnon et al., 1982), but at the same time may change the pH microbial composition or motility of the intestines in a way that encourages growth of *Clostridium botulinum* (Gay et al., 1988). Many infants who develop infant botulism have been exclusively breast-fed which suggests that factors other than diet are important in determining the development of this disease. In other instances, weaning onto solid foods may encourage the growth of *Clostridium botulinum* in the intestines (Murrell and Stewart, 1983, Long et al., 1985). The microbiological composition of the gastrointestinal tract is a chief determinant of the ability of *Clostridium botulinum* to grow and produce toxin (Sugiyama and Mills, 1978). Decreased intestinal motility (as evidenced by decreased bowel movements) may contribute to the risk of developing infant botulism (Spika et al., 1989). Initial scientific research focused on dietary factors such as breast milk, infant formula, cereals, canned baby food, honey, and corn syrup. Some scientists believe that "preexisting host factors, such as intestinal flora and frequency of bowel movements, may be the most important risk factors for development of disease" and note that "food exposures account for a minority of infant botulism cases" (Spika et al., 1989).

**WHAT DOES HONEY HAVE TO DO WITH INFANT BOTULISM?**

The initial epidemiological research that followed the discovery of infant botulism identified honey as a risk factor for the disease and determined that honey can contain spores that cause botulism (Arnon, 1977, Arnon et al., 1979 and Chin et al., 1979). However, since most infants with infant botulism have not been exposed to honey, the development of infant botulism must involve additional factors (Arnon et al., 1979, Gay et al., 1988, Spika et al., 1989 and Center for Disease Control, 1978). Subsequent research has shown that the infecting spores are more likely to come from surfaces in the baby's environment or from dust in the air (Arnon et al., 1981, Dodds, 1992, Long, 1985, and Thilo and Townsend, 1993). Nonetheless, under no circumstances should honey be fed to an individual under one year of age.

The number of cases associated with honey has declined dramatically. This decline has been documented best in data from California (California Morbidity, 1990). Between 1976 and 1979, an estimated 34 percent of infant botulism cases involved babies who had been fed honey. This percentage dropped to 16.7 by 1987. In 1988 and 1989, the association with honey was as infrequent as three out of
Scientists have analyzed honey to determine if and how often botulinum spores can be detected (Aureli et al., 1983, Berry et al., 1987, Du et al., 1989, Flemmig and Stojanovic, 1980, Guilfoyle and Yager, 1983, Hartgen, 1980, Hauschild et al., 1988, Hetland, 1986, Huhtanen et al., 1981, Kautter et al., 1982, Kokubo et al., 1984, Midura et al., 1979, Nakano et al., 1990, Nakano and Sakaguchi, 1991, Pastoni et al., 1986, Sakaguchi, 1987 as cited in Nakano et al., 1990, Stier et al., 1982 and Sugiyama et al., 1978). Of a combined total of 2,519 honey samples from around the world, 105 (4.2 percent) contained detectable levels of spores. The analytical results vary widely; some studies detected no spores, most detected spores in less than 10 percent of their samples and one study detected spores in 62.5 percent of their samples. This variation is probably due to the difficulty in removing low numbers of spores from a viscous material. It is believed that "...the contamination of honey in general is low" (Dodds, 1992).

Data on the exact concentration of botulinum spores in honey is limited. As reported above, more than 95 percent of the honey that has been analyzed does not contain detectable levels of botulinum spores. There may, however, be spores at concentrations below the limit of detection which is generally reported as 100 - 1,000 spores/kilogram (kg). Scientists have found that samples of honey collected at random are usually at concentrations well below 1,000 spores/kg of honey (Sugiyama et al., 1978, Stier et al., 1982 and Nakano et al., 1990). The exceptions among these 547 samples are two randomly collected samples of honey where spores were detected at levels of 4,000 and 60,000 per kg (Nakano et al., 1990). This leads to the hypothesis that less than one percent (2/547) of honey samples contain high (over 1,000 spores/kg) concentrations of botulinum spores.

There is evidence that occasionally the concentration of botulinum spores in honey is very high. Studies of honey involving cases of infant botulism indicated spore levels ranging from 1,000 to 80,000 spores/kg (Midura et al., 1979, Canada Diseases Weekly Report, 1985 and Hauschild et al., 1988). It has been suggested that the honey supply usually contains concentrations of botulinum spores at levels well below 1,000/kg (perhaps as little as one to 10 spores/kg) but that infant botulism might be associated with concentrations of 1,000 to 10,000 spores/kg (Dodds, 1992). Less than half a tablespoon of honey with spores at a concentration of 10,000 spores/kg would be necessary to reach a dose of 100 spores. This is in contrast to the several hundred tablespoons of honey that would be necessary to reach the same dose if the honey contained 10 spores/kg. This is consistent with current epidemiological and scientific data.

WHERE DO THE BOTULINUM SPORES IN HONEY COME FROM?

Botulinum spores have been found just about everywhere there is soil or water. Microbiological spores may enter the beehive via airborne dust or via the legs of bees. Spores could also enter the hive through the digestive tracts of bees (Huhtanen et al., 1981) or along with the pollen that the bees carry. However, these routes of entry do not account for the very high concentrations of spores occasionally found in honey.

Botulinum spores cannot grow in nectar being converted to honey (Huhtanen et al., 1981) nor can they grow in ripe honey. Honey has numerous antimicrobial properties that completely inhibit bacterial growth (Snowdon and Giver, 1996). Toxin cannot be formed without bacterial growth and botulinal toxin has not been found in honey (Hartgen, 1980).
The fact that high concentrations of botulinum spores are found in honey only on an occasional basis and that only one bacterial serotype has been recovered from any single sample of honey leads scientists to think that high concentrations of spores are created under infrequent circumstances and in the hive (Hauschild et al., 1988, Dodds, 1992, Nakano et al., 1992). Some scientists believe that Cl. botulinum might multiply in dead bees in the hive (Nakano et al., 1994) possibly in symbiotic association with Bacillus alvei (an organism which is common in bees with European foulbrood disease).

**CAN BOTULINUM SPORES BE REMOVED FROM HONEY?**

It is difficult to remove bacterial spores from honey without appreciably changing or destroying the honey. Botulinal spores are extremely resistant to heat especially in concentrated sugar solutions such as honey. Any heat treatment that is sufficient to kill botulinal spores will caramelize the sugars in honey and produce undesirable flavor changes. Standard filtration processes will not remove botulinal spores because honey is highly viscous and will not readily pass through filters that are fine enough to remove bacterial spores. A process known as ultrafiltration, which is typically used to remove protein from honey, would work to remove the spores. However, ultrafiltration requires the dilution and then reconcentration of the honey, which alters the original nature of the honey.

Specialized irradiation techniques will destroy microbial spores. Bacillus spores have been inactivated by high velocity electron beams (Shimanuki et al., 1984) and Clostridium spores have been inactivated by gamma radiation (Huhtanen, 1991). These techniques are sophisticated, require additional expense and are not always well received by the consuming public.

Spores are inactivated when manufactured food products (such as cereals or nuts) receive a roasting heat treatment. Graham crackers or cereal, for example, would not contain any viable microbial spores. Likewise, food that is preserved by proper canning will have received enough heat to inactivate microbial spores. Food products which are not submitted to a heat treatment lethal to Cl. botulinum can be expected to be an occasional source of spores. Similarly the mild heat treatment of stirring honey into a cup of tea or a bowl of oatmeal will not inactivate botulnum spores.

Although bacterial spores are very stable, some scientists noted that Cl. botulinum spores in honey decreased in concentration after 100 days at 77°F and after five days at 149°F (Nakano et al., 1989). The routine processing and storage of honey (often months in warehouses ranging from 60 to 90°F) may decrease the bacterial spore concentration and may explain the low incidence of botulinum spores in retail supplies (Nakano et al., 1990).

Infants are exposed to botulinum spores primarily from environmental sources; food is not the predominant source of spores for an infant. However, the diet of an infant can be controlled and honey can, and should, be eliminated from an infant's diet. Honey is safe for toddlers, children, and adults. Honey should not be fed to anyone less than one year of age.

**CONCLUSIONS**

- The National Honey Board, the Centers for Disease Control and Prevention, the American Academy of Pediatricians, the California Department of Public Health, Health Canada and other public health associations recommend that honey not be fed to infants under one year of age.
• As infant botulism can strike even in the absence of honey, any infant showing symptoms of infant botulism – poor feeding, altered cry, constipation, lethargy – should receive medical attention promptly.

• Children and adults with normal intestinal systems are resistant to infant botulism and are able to ingest botulinum spores without harm. The Centers for Disease Control and Prevention state "the safety of honey as a food for older children and adults remains unquestioned" (Center for Disease Control, 1978).
ABOUT THE AUTHOR

Dr. Jill Snowdon completed her graduate studies at the University of Wisconsin-Madison. She holds a Ph. D. in Food Safety with a minor in Environmental Toxicology and a Master of Science in Food Chemistry. She completed her B.A. in Biology, in her native state of Pennsylvania, at Millersville State University. Dr. Snowdon has a broad academic background in biology, chemistry and food science and specializes in the study of diseases transmitted through food and water.

Dr. Snowdon's postgraduate experiences include a fellowship on Capital Hill as a Congressional Science Fellow and a stint at the United Fresh Fruit and Vegetable Association. Currently, Dr. Snowdon serves the egg industry as a communicator of technical information and as a liaison for regulatory affairs.
REFERENCES


