

Infant Botulism, Israel, 2007–2021

[Announcer] This program is presented by the Centers for Disease Control and Prevention.

[Sarah Gregory] Hello, I'm Sarah Gregory, and today I'm talking with Dr. Bar Goldberg at Schneider Children's Medical Center at Tel Aviv University. We'll be discussing cases of infant botulism in Israel.

Welcome, Dr. Goldberg.

[Bar Goldberg] Hi.

[Sarah Gregory] What is botulism?

[Bar Goldberg] Botulism is a rare but potentially lethal disease caused by a toxin produced by the bacterium *Clostridium botulinum*, a gram-negative, spore-forming anaerobic bacteria. And this toxemia leads to flaccid paralysis and even respiratory failure.

[Sarah Gregory] Are there different kinds?

[Bar Goldberg] Yes. There are six main kinds of botulism. The first is infant botulism (IB; the subject of our study), also known as "floppy baby syndrome", results from ingestion of *Clostridium botulinum* spores with subsequent colonization in the gut and releases botulism toxin, causing acute flaccid descending paralysis. And the second type is wound botulism, in which *Clostridium botulinum* spores get into wounds, especially after a traumatic injury, post-op, or IVDU. And the third type is foodborne botulism, especially in homemade preserved or canned or fermented food that has contained the toxin. Also, we have iatrogenic botulism (such as by Botox injections) and bioterrorism botulism...this is another type.

[Sarah Gregory] You just briefly mentioned some of the symptoms, but how serious of an illness can this cause?

[Bar Goldberg] The disease manifests in a wide clinical spectrum from mild symptoms to life-threatening conditions (such as respiratory failure) and often leads to a late diagnosis, but it can be pretty serious.

[Sarah Gregory] Is there a treatment for it?

[Bar Goldberg] Yeah. Botulism is generally treated with botulinum antitoxin (such as BabyBIG Botulism Immune Globulin) and supportive care. Supportive care includes mechanical ventilation, feeding by nasogastric tube, and monitoring. The antitoxins are actually antibodies that neutralize the circulatory toxins and prevent them from binding to the neuromuscular junction in the presynaptic acetylcholine release area. And the antitoxin does not reverse the neuromuscular junction blockade but prevents from additional attachment. And vaccines are under development also.

[Sarah Gregory] Your study is specifically about infant botulism. How is infant botulism different from other kinds?

[Bar Goldberg] So infant botulism is the most common type of botulism. It affects infants in their first year of life, especially in the first six months of age. And the common belief is that infant intestinal flora is insufficient to suppress *Clostridium botulinum* colonization. Honey

contains botulinum spores, and that's why it is recommended to avoid honey consumption until one year old.

[Sarah Gregory] Can it be fatal to these babies?

[Bar Goldberg] Yes, it can be fatal. Infant botulism is quite a rare disease, as I said, with a wide clinical spectrum so the diagnosis is often delayed, with rapid respiratory failure and need for intubation and mechanical ventilation. And the earlier the antitoxin treatment is given, the better and shorter the course of this disease and comorbidity.

[Sarah Gregory] What ages are at most risk? You mentioned under a year, but is it even more specific than that? Or just anything under a year?

[Bar Goldberg] Generally, infant botulism is described in infants under one years old, but the peak incidence worldwide is two to eight months of age. And in our study, infant median age of diagnosis was six and a half months (older than the previously reported three months).

[Sarah Gregory] What should parents or clinicians be on the lookout for? What are the signs that a baby is even sick with botulism?

[Bar Goldberg] Infant botulism is classically described as the "floppy baby syndrome" with flaccid descending symmetric paralysis, and recovery can take several weeks. The disease manifests in a wide clinical spectrum, from mild weakness and constipation and feeding difficulties, to a serious life-threatening hypotonia with respiratory failure. The most common clinical signs and symptoms in our study were hypotonia, poor feeding, and weak cry. Other symptoms such as mydriasis, drooling, and hoarseness were less common.

[Sarah Gregory] And globally, how common is it?

[Bar Goldberg] Since 1976, about 3,500 cases of infant botulism have been reported worldwide and 90% of them in the US, with an average incidence of two cases per 100,000 live births. We had some that's due to lack of awareness and laboratory tests, there's a lack of reports from Asia, Africa, and even the Middle East. The national incidence of infant botulism in Israel is relatively low—only 0.3 cases to 100,000 live births compared with two cases per 100,000 in the US or Argentina, and more similar to low-incidence countries, such as England or Germany.

[Sarah Gregory] California in the United States seems specifically to have the most cases worldwide. Do we know why?

[Bar Goldberg] California has a higher incidence of infant botulism compared to other states in the US, that is true. This is likely due to the presence of *Clostridium botulinum* spores in the soil and dust in California, as well as consumption of certain types of honey that may contain the bacteria. So I mean that this might be a matter of soil ecology and climate conditions. But this is just an assumption.

[Sarah Gregory] What was your study period?

[Bar Goldberg] The study period was during 2007 to 2021.

[Sarah Gregory] You want to take a minute to tell us about your study—why you did it and what was the main goal of it?

[Bar Goldberg] Yeah. Infant botulism is quite a rare disease, and we saw a cluster of cases in 2021, which was interesting and led us to investigate whether this is an increase in the national

incidence. So the main goal of our study was to evaluate the current incidence of infant botulism in Israel, and examine national epidemiologic and clinical data from the past two decades.

[Sarah Gregory] Tell us how you conducted this study—the number of patients, how you collected the data, and what tests were used...that sort of thing.

[Bar Goldberg] So we conducted a retrospective multicenter randomized cohort study, including all infants one week to one year of age who had IB diagnosed by Kimron Institute. In addition, we verified with all the pediatric infectious disease specialists that no other patients had IB diagnosed during the study period. And we performed laboratory testing for infant botulism by using the standard MLB (mouse lethality bioassay) procedures, and we used other diagnostic tools such as electromyography (EMG) tests, stool PCR, and EndoPep-MS. We retrieved medical records in six hospitals, and for each case we collected demographic data; clinical data; environmental exposure (such as living nearby a construction area, agricultural occupation of parents); and also...laboratory tests in honey, formula, and soil samples; and clinical manifestations.

We also collected information on treatment protocols, whether supportive care only or administration of antitoxin, use of antibiotics, etc.

[Sarah Gregory] Was it decided how these babies got sick from botulism in the first place?

[Bar Goldberg] We found several risk factors and hazardous exposures. Some infants lived near construction areas and had a history of traveling outside near the construction site a few days before symptoms began. Two patients had a history of being given homeopathic or plant-based traditional medicine such as yannsoon (which is anise leaf), a common traditional medicine for infantile colic among Bedouin population and another unrecognized mixture. One patient was exposed to contents of a vacuum cleaner. The father of one patient was an agriculturist and therefore exposed to soilborne pathogens. In only one case, actually, a sample taken from a honey cake that the infant had eaten tested positive via culture and mouse lethality bioassay to botulinum. Probably raw honey was poured over the topping of the cake after baking.

[Sarah Gregory] What were the most common clinical signs of botulism that you saw in these babies?

[Bar Goldberg] As I said, the most common clinical signs and symptoms were hypotonia, poor feeding, and weak cry. The classical descending paralysis was observed in 75% of the infants, and only two patients were intubated and five were fed by nasogastric tube.

[Sarah Gregory] So apparently honey is very popular in Israel, especially during some of the holidays. But you only found the one case of botulism related to honey consumption. Why do you think this is?

[Bar Goldberg] Yeah, it is true. We found only a modest link to honey consumption and infant botulism in our study, and no case occurred during the Jewish holiday around September, in which we do consume a lot of honey in Israel. A possible explanation might be an early and mandatory parental education program in outpatient infant clinics in Israel called Tipat Chalav that forbids honey products until the infant is one year of age. So it might be due to this.

[Sarah Gregory] What treatments did the infants receive?

[Bar Goldberg] So half of the infants were treated by antitoxin (equine-derived). Two infants were intubated, and five were fed by nasogastric tube.

[Sarah Gregory] Is one treatment more effective than another?

[Bar Goldberg] Our study is too small to conclude whether one treatment was superior to another. Half of the infants in our study were treated with antitoxin, whereas the rest showed clinical improvement and recovered without antitoxin treatment. Previous reports showed that antitoxin treatment shortened the length of hospitalization from 23 days to 13 days. In our study, infants who were treated with antitoxin were hospitalized for 17 days versus 13 days in those who weren't treated. And a possible explanation might be that the infant who received antitoxin had a more severe clinical picture, which necessitated the use of antitoxin, but also led to a more complex and prolonged hospitalization.

Another possible explanation might be the fact that in Israel we still use the equine-derived botulism antitoxin, whereas in the US, the common antitoxin is the human botulism immune globulin (the BabyBIG), which might be more effective.

[Sarah Gregory] Did they all recover? Were there any long-term complications?

[Bar Goldberg] Yes, they all recovered. The long-term prognosis was excellent, and no neurologic or other sequelae were found among our patients.

[Sarah Gregory] Did you find anything surprising?

[Bar Goldberg] Yes. First and foremost, we found that although infant botulism is a rare disease, the incidence in Israel might have increased, especially during the past three years. We also found that honey consumption is less prominent as a risk factor compared with environmental exposures, such as living nearby construction areas. Another surprising finding was that two infants had recovered spontaneously without any treatment. Another unique finding was a much older age of presentation in our study in contrast to previous reports (six and a half months versus three months of age). And we also found that nearly all of the cases occurred during spring or summertime, which is interesting.

[Sarah Gregory] Do you think the COVID pandemic affected incidence of infant botulism in Israel in any way?

[Bar Goldberg] Our sample is too small to conclude whether IB incidence increased during the COVID pandemic. However, as I mentioned, we showed a cluster of three cases that occurred during the pandemic. Personally, I think that there might be a connection. One assumption is that during quarantine, people were allowed to leave their homes for a few hundred meters and went for a short walk with their babies around the block and in construction areas. Another explanation is that common viral diseases decreased, so the physicians were more available to recognize the mild botulism cases that might have gone under the radar in a busy clinic.

[Sarah Gregory] What are the public health implications of this study?

[Bar Goldberg] First and foremost, increasing the awareness of infant botulism in Israel among clinicians. Secondly, we found that honey consumption is less prominent as a risk factor compared with environmental exposure (I mean, spores in soil, dust in construction areas) and we support further investigation on this soil ecology and epidemiological studies

[Sarah Gregory] Are there any further research studies do you think is needed on this topic?

[Bar Goldberg] Yeah. We support pediatricians and clinicians around the world—and especially in the Middle East, which lacks information on infant botulism prevalence and epidemiology—to

conduct studies similar to ours. The exact risk factors for infant botulism are still not fully understood, but there are several areas where further research could be valuable. First, I think that environmental exposure (and we're talking about spores in soil and dust)...and further research could explore potential environmental risk factors and help to identify ways to reduce the exposure.

Secondly, the second research area, in my opinion, is infant feeding practice and gut microbiome. The age of infant botulism presentation is around six months of age, when most babies start to consume solid food. There is some evidence to suggest that the gut microbiome composition or flora may affect the risk of infant botulism. Further research could clarify this relationship and examine whether breast feeding or certain foods might increase or decrease the risk of this condition.

And the third research area, in my opinion (in my view), is genetic factors, because we know that some infants may be more susceptible to infant botulism due to genetic factors that affect your immune system or digestive function. And the fourth area is prevention strategies, and even maybe vaccination for infant botulism.

[Sarah Gregory] Dr. Goldberg, tell us about where you work, what you do, and how you became involved in this study.

[Bar Goldberg] I'm a resident in Schneider Children's Medical Center of Israel. I graduated from the Technion Faculty of Medicine. I find an interest in immunology and infectious diseases as a research area. The head of my department (professor Oded Scheuerman) observed the cluster of infant botulism cases in our institute in 2021 and suggested to me to explore and examine whether this had occurred in other hospitals in Israel and to conduct the first comprehensive botulism study in Israel, and I agreed.

[Sarah Gregory] Well, thank you so much for taking the time to talk with me today, Dr. Goldberg.

[Bar Goldberg] Thank you so much. It was a pleasure.

[Sarah Gregory] And thanks for joining me out there. You can read the February 2023 article, *Infant Botulism, Israel, 2007–2021*, online at [cdc.gov/eid](https://www.cdc.gov/eid).

I'm Sarah Gregory for *Emerging Infectious Diseases*.

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