

INFANT BOTULISM

Scientists are baffled by how and why the poison infiltrates infants. But they know its onset is more than a freak occurrence — just how much more is what they fear.

The second of two articles on mysterious instances of infant death and disease.

BY JOEL GREENBERG

Case Study: A male baby born March 22, 1976, in Los Angeles had normal development until the onset of constipation occurred when he was 20 weeks of age. Two days later, his mother noted that he sucked poorly from her breast. By the following day, ptosis, generalized muscle weakness (particularly in the neck), a weak cry and shallow respirations developed. He appeared lethargic, irritable and floppy. After two days with no improvement on a regimen of oral ampicillin sodium, the infant was admitted to a local hospital for examination. When positioned for a lumbar puncture, he had a respiratory arrest, but he was easily resuscitated. Although muscle tone remained poor, the infant's condition improved during his nine-day hospital stay, with partial return of head control and reaching ability. He received no antibiotics during his hospitalization. ... Four days after discharge, the infant's condition deteriorated, with onset of increased weakness, shallow respirations and a poor cry.

He was then admitted to a metropolitan hospital. ... He appeared drowsy and had a weak, constant cry. The abdomen was soft, with active bowel sounds present. The infant had generalized decreased muscle tone and diminished spontaneous movements. Cranial nerve function was intact except for ... sluggishly reactive pupils; absent upward gaze; and a weak gag reflex. He withdrew from painful stimuli. Deep tendon reflexes were diminished or absent. Cerebrospinal fluid was normal.

Because botulism was suspected on the basis of admission ... findings, a fecal specimen was obtained, using sterile, nonbacteriostatic water. *Clostridium botulinum* type A toxin and organisms were found in the feces. The infant received no antitoxin, but was given a 14-day course of oral penicillin G sodium. He gradually recovered neurologic function and was discharged after a total hospitalization of 60 days.

JAMA, May 2, 1977, p. 1947

Photos: R. M. Wood. Inset: Stephen Arnon, Infectious Disease Section, Calif. Dept. of Health



Workers at the California Department of Health's Infectious Disease Section analyze samples for the presence of botulism. Spores and vegetative cells of *Clostridium botulinum* (above, stained with fluorescent antibodies) are found in fecal samples of stricken babies. The toxin is virtually unidentifiable in standard blood samples.

The possibility that the most potent poison known — botulism toxin — could strike, small, vulnerable infants seems almost unthinkable. Perhaps that is the major reason why, until recently, botulism has been overlooked as a potential cause of mysterious infant disease or death.

But since first being detected in five California infants and one New Jersey baby in 1976, infant botulism is rapidly becoming recognized in a growing number of illness cases. Currently, there are 63 recorded instances of the disease in the United States — two-thirds are in California, primarily because of the interest and facilities of that state's health department. Two of the victims have died.

Those investigating the disease, however, believe that the actual figures are considerably higher and that most cases have gone undetected. "We believe this is a worldwide problem, currently unrecognized, of undetermined magnitude in morbidity and mortality," says Stephen S. Arnon of the California Health Department's Infectious Disease Section. "Medical awareness is only beginning in the

world — Great Britain's first recorded case came in February 1978," says Arnon. "Awareness is still quite limited; it's [infant botulism] not in any textbooks as yet."

The critical, and frightening, difference between infant and adult botulism is that youngsters seem to become ill without having ingested contaminated food. The botulism spores — *Clostridium botulinum* — germinate in the child's intestine, where they grow the toxin. Among the recorded cases, botulism has struck infants between the ages of 3 weeks and 26 weeks, with a median of 10 weeks.

Botulism toxin attacks areas where motor nerves connect to muscles and blocks the release of the chemical transmitter acetylcholine. The disease can become fatal when the respiratory muscles become paralyzed. The strength of the poison is striking: Once in the bloodstream, the equivalent of one drop of botulin toxin per 8.7 million gallons of water can be lethal to an adult, Arnon says.

In infants, the potency is comparable, he says. "All we have to go on now are cases

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that have reached the hospital," says Arnon. "But we don't know how many other cases there are ... and we don't know the number of infants that may have died before reaching the hospital."

Because botulism cannot be detected in standard autopsies, Arnon believes the toxin may be responsible for an unknown number of Sudden Infant Death Syndrome (SIDS) cases (SN: 4/15/78, p. 234). Both of the recorded deaths involved respiratory arrest, the most apparent mechanism implicated in instances of SIDS.

"We're not sure as yet why certain children get infected and others don't," says the researcher. What is apparent, though, is a fairly standard progression of symptoms in the hospitalized botulism-infected baby: constipation, lethargy, poor

If a sample from the same feces that killed one mouse is heated and is not then fatal to another mouse, then the botulin toxin characteristically has been inactivated.

• The specific type of botulism in the sample is determined by testing which antitoxin counteracts the sample injected into a mouse.

"The toxin cannot be identified in a routine autopsy procedure—it is difficult to isolate," says Arnon. In infants, the poison travels almost instantaneously to the nerve-muscle connections and leaves almost no trace behind in the bloodstream, he explains. This could be a major factor in why botulism is potentially an undetected cause of SIDS, he adds. (In about one-third of adult cases, botulism traces can be found circulating in the serum. The reason for this is not fully un-

it." Along with California, the Center for Disease Control in Atlanta is among the handful of facilities that is equipped for botulism testing.

Once diagnosed in an infant, botulism is treated by relatively conventional means, which Arnon says are sufficient provided the disease is caught early enough. Antitoxin is not used with babies because of its potentially hazardous side effects. Manufactured in horses, the antitoxin can produce allergic shock (fatal in some cases), kidney inflammation and other problems.

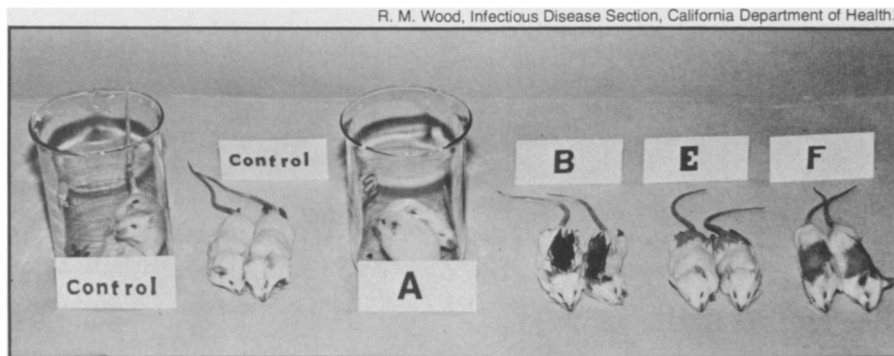
Infant victims require comprehensive supportive care in the hospital for the course of the disease—usually about three to four weeks. Some infants may require artificial breathing machines in respiratory emergencies, but treatment usually consists of close observation, tube or intravenous feeding until strength is regained and a nutritious diet. Penicillin and antibiotics have been used in various cases, but their role in the infants' ultimate recovery is unknown. In fact, says Arnon, "the mechanisms permitting recovering remain obscure."

On the basis of cases documented thus far, Arnon estimates there are about 250 infant botulism attacks a year that require hospitalization in the United States. Victims thus far generally have been products of normal gestation and delivery, he says. They had no congenital abnormalities and were healthy at the onset of illness. Slightly more than half of the victims so far have been males.

Just how many infant botulism cases never make it to a hospital—either because of the mildness of the infection or because they die—is not known. "We have reason to hold to our opinion that infant botulism could be a cause of sudden infant death," says Arnon.

Neither is there any solid indication as to how or why some babies make the toxin in their bodies. "We don't know," Arnon says simply. Botulin spores are present in soils and dust throughout the world, he says, but if there is a link between any specific land area and the onset of the disease, it is too early to tell.

"In terms of medical awareness and diagnostic techniques, we're still in the horse and buggy era," says the researcher. "We think we have a tiger by the tail." □



Mice studies are a major part of conclusive evidence for the existence and type of botulism present. The dead mice received untreated fecal extracts from victims. The live mice (in beakers) received antitoxin with the fecal extract.

feeding, swallowing problems, general weakness, loss of muscle tone and poor head control. The majority of young victims seen thus far have been classified as "floppy babies." The syndrome can evolve within the baby in anywhere from six hours to one week or more.

"The first case that occurred in California in February 1976 was a floppy baby," says Arnon. (The first six cases were reported in the May 2, 1977 JAMA.) The California lab is one of the few in the United States equipped to test for botulism. Feces samples extracted from the youngster must meet three criteria to be proven positive:

- They must prove fatal when injected into mice.
- They must be inactivated by heating.

derstood, but Arnon speculates that perhaps adults may ingest enough through food sources to make the toxin detectable in serum. In contrast, he says, infants do not appear to develop botulism as a result of contaminated food. That, combined with a baby's inability to verbally communicate symptoms, contributes to problems in diagnosing the disease, he says.)

Aside from the need for specialized, sophisticated equipment and facilities, another reason relatively few labs are capable of testing for the disease has to do with the potency of the toxin. "Some hospital labs just don't want to work with botulism," Arnon says, "and up until now there hasn't been a widespread need for

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nant, the best preventive is better education about human reproduction and birth control, Lopez asserts. A recent study conducted by Planned Parenthood of New York City shows that the reason some sexually active teens use birth control and others do not is that the former have been better informed about birth control, where to get it and how to use it. Abortion, in contrast, does not appear to be a solution to the teen pregnancy epidemic, Sullivan points out, as adolescent girls who solve one pregnancy with abortion often go on

to become pregnant a second, third, fourth or even fifth time.

Physicians also need to better inform themselves about laws regarding the dispensation of birth control to adolescents without parental consent, declares Harriet F. Pilpel, a lawyer with Planned Parenthood-World Population, so that they don't withhold contraceptives from sexually active teens who want them and have a legal right to them. Currently, teens have a legal right to birth control without their parents knowing about it through any agency sponsored by federal, state or city

funds. However, private hospitals, clinics and physicians have the right, if they so choose, to withhold birth control from adolescents who do not have parental consent to use it.

Probably the best solution to the teen pregnancy epidemic, though, is the strengthening of American family life, Lopez and Fontana concur, since those girls who get pregnant usually come from homes where sexual values and guidance are lacking. "There is no pregnant teenager," Lopez declares, "whose relationship with her parents has been ideal." □