Infant Botulism

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Although the worldwide incidence of infant botulism is rare, the majority of cases are diagnosed in the United States. An infant can acquire botulism by ingesting Clostridium botulinum spores, which are found in soil or honey products. The spores germinate into bacteria that colonize the bowel and synthesize toxin. As the toxin is absorbed, it irreversibly binds to acetylcholine receptors on motor nerve terminals at neuromuscular junctions. The infant with botulism becomes progressively weak, hypotonic and hyporeflexic, showing bulbar and spinal nerve abnormalities. Presenting symptoms include constipation, lethargy, a weak cry, poor feeding and dehydration. A high index of suspicion is important for the diagnosis and prompt treatment of infant botulism, because this disease can quickly progress to respiratory failure. Diagnosis is confirmed by isolating the organism or toxin in the stool and finding a classic electromyogram pattern. Treatment consists of nutritional and respiratory support until new motor endplates are regenerated, which results in spontaneous recovery. Neurologic sequelae are seldom seen. Some children require outpatient tube feeding and may have persistent hypotonia. (Am Fam Physician 2002;65:1388-92. Copyright© 2002 American Academy of Family Physicians.)

Pathophysiology

Infant botulism occurs when ingested spores germinate and colonize the infant’s gastrointestinal tract. The cecum is thought to be the initial site of activity and paralysis of the ileocecal valve might allow the colonizing bacteria to extend into the terminal ileum. Once the bacteria have colonized, toxin is produced and absorbed throughout the intestinal tract. The mechanism by which the toxin is transported to the nerve tissue is unknown. The toxin irreversibly binds to acetylcholine receptors on motor nerve terminals at neuromuscular junctions. The infant with botulism becomes progressively weak, hypotonic and hyporeflexic, showing bulbar and spinal nerve abnormalities. Presenting symptoms include constipation, lethargy, a weak cry, poor feeding and dehydration. A high index of suspicion is important for the diagnosis and prompt treatment of infant botulism, because this disease can quickly progress to respiratory failure. Diagnosis is confirmed by isolating the organism or toxin in the stool and finding a classic electromyogram pattern. Treatment consists of nutritional and respiratory support until new motor endplates are regenerated, which results in spontaneous recovery. Neurologic sequelae are seldom seen. Some children require outpatient tube feeding and may have persistent hypotonia. (Am Fam Physician 2002;65:1388-92. Copyright© 2002 American Academy of Family Physicians.)

Epidemiology

Ninety percent of the world’s cases of infant botulism are diagnosed in the United States, mainly because of physician awareness. As of 1996, the Centers for Disease Control and Prevention (CDC) has documented more than 1,400 cases. The prevalence of infant botulism has surpassed that of food-borne and wound botulism. It is estimated that more than 250 cases of infant botulism occur in the United States each year, but many go unrecognized. California, Utah and Pennsylvania have the highest incidence; nearly 50 percent of all cases are reported in California.

Soil and honey contamination are the two recognized sources of Clostridium botulinum spores.
1970s, researchers analyzed 555 samples of soil, household dust, cereals, baby foods, canned goods, sugar, corn syrup, honey and commercial formulas. Except in the samples of honey and soil, no spores were detected. In a study performed in New York, no spores were found in any of the 236 products that were tested. According to microbiologic testing, up to 25 percent of honey products have been found to contain spores. A history of honey consumption is seen in 15 percent of the botulism cases reported to the CDC. As a result, honey should not be given to infants younger than one year.

A prospective, case-controlled study was performed to determine the risk factors of infant botulism. The results showed that decreased frequency of bowel movements (less than one per day) and breast-feeding were risk factors for the development of disease in infants older than two months. For infants younger than two months, living in a rural farming area was the only significant risk factor, reported by 40 percent of the families studied. Presumably, these infants would more likely be exposed to aerosolized spores from clothing contaminated by soil or from disrupted soil.

The role of breast-feeding in infant botulism remains controversial. In various studies, breast-feeding occurs in 70 to 90 percent of infants with botulism. Breast-feeding may delay the clinical severity of this condition, allowing these infants to receive medical attention before the botulism becomes fatal. There is no evidence that breast-fed infants have an increased severity of disease when compared with formula-fed infants.

Historically, infant botulism was thought to contribute to sudden infant death syndrome (SIDS). If the disease went unrecognized, paralysis of the respiratory musculature could lead to rapid hypoxemia and respiratory arrest. Two studies identified postmortem colonization in 4 to 15 percent of deaths caused by SIDS. However, a recent 10-year prospective study did not find occult botulism to be a significant factor for SIDS.

### Clinical Presentation

Infants who acquire botulism range in age from six weeks to nine months, with the peak incidence occurring at two to three months of age. About 90 percent of infants with botulism are younger than six months. Infant botulism may be difficult to recognize because of its insidious onset. The classic clinical features include constipation, cranial nerve abnormalities, hypotonia, hyporeflexia and respiratory difficulties. The signs and symptoms commonly present at the time of hospital admission are listed in Table 1.

Constipation may be present in affected infants for a variable length of time and can precede weakness by several weeks. Hypotension, neurogenic bladder and other signs of autonomic dysfunction can occur early in the

### TABLE 1

<table>
<thead>
<tr>
<th>Signs and symptoms</th>
<th>Incidence (%)</th>
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<tbody>
<tr>
<td>Weakness or floppiness</td>
<td>88</td>
</tr>
<tr>
<td>Poor feeding</td>
<td>79</td>
</tr>
<tr>
<td>Constipation</td>
<td>65</td>
</tr>
<tr>
<td>Lethargy/decreased activity</td>
<td>60</td>
</tr>
<tr>
<td>Weak cry</td>
<td>18</td>
</tr>
<tr>
<td>Irritability</td>
<td>18</td>
</tr>
<tr>
<td>Respiratory difficulties</td>
<td>11</td>
</tr>
<tr>
<td>Seizures</td>
<td>2</td>
</tr>
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**Constipation is often the first symptom of infant botulism and can precede weakness by several weeks.**
Signs of weakness in the infant with botulism begin with cranial nerve involvement and loss of head control. The infant may develop a weak cry, poor sucking ability, impaired gag reflex, pooling of secretions and decreased oral intake. Loss of ocular motility, ptosis, mydriasis and facial weakness also may occur.\textsuperscript{14,15} The weakness progresses in a descending fashion in a matter of days. Affected infants become irritable and lethargic. In severe cases of infant botulism, respiratory difficulties begin as a late sign of disease, quickly leading to respiratory arrest.\textsuperscript{14}

### Differential Diagnosis

The differential diagnosis of infant hypotonia is extensive (Table 2).\textsuperscript{14} An infant with botulism is often diagnosed with sepsis or meningitis because of symptoms of lethargy and irritability on presentation. However, these infants are typically afebrile and the work-up for these entities will be negative.\textsuperscript{17} Dehydration and other metabolic causes should be properly investigated. Reye’s syndrome can be effectively ruled out by determining the serum ammonia level.\textsuperscript{14} Poisoning also must be considered. Poliomyelitis is often associated with asymmetric clinical findings and a cerebrospinal fluid pleocytosis, which is not seen in infant botulism.\textsuperscript{14,17} Infantile spinal muscular atrophy rarely causes pupillary or eye dysfunction.\textsuperscript{14} Congenital myasthenia gravis is rare and can be excluded by maternal and neonatal history. Guillain-Barré syndrome presents as an ascending paralysis and is usually not seen in children younger than one year.\textsuperscript{14,17} Lastly, acute upper airway obstruction should be considered in infants with poor feeding, an inability to handle secretions and respiratory distress.

### Diagnosis

A definitive diagnosis can be made with the detection of botulinum toxin and the isolation of \textit{C. botulinum} from stool samples. Additionally, electromyogram (EMG) studies can support an early diagnosis.
A passed stool is the preferred specimen for culture and toxin investigation. In a constipated infant, it may be necessary to perform colonic irrigation with limited amounts of sterile saline. A 25-g stool or a 25-mL effluent sample should be collected in a sterile container and refrigerated. A serum sample should be obtained for a toxin assay. Other potential source samples, such as dust, soil from clothing, honey, corn syrup or foods, should also be collected for investigation.

Testing is usually performed by state health departments or the CDC. Organism identification is established using conventional microbiologic techniques. Identification of botulinum toxin is completed using a mouse neutralization bioassay. Polymerase chain reaction and enzyme-linked immunosorbent assays have been developed to test for infant botulism. However, the unavailability of reagents and lack of standardization among laboratories have kept these tests from replacing the mouse bioassay as the preferred testing method.

Researchers have proposed that standardized electrodiagnostic testing be performed in infants with suspected botulism, looking for the EMG triad to aid in early confirmation of the diagnosis (Table 3). Hypermagnesemia is the only other consideration in infants who display all three diagnostic features. Because EMG results can be normal early in the disease, serial testing may be required, beginning one week to 10 days from the onset of symptoms. Also, resolution of EMG findings do not correlate with the recovery of spontaneous ventilation.

**Clinical Management**

Supportive care is the mainstay of therapy. Infants with botulism should stay in an intensive care unit because they frequently require airway management, nasogastric tube feedings, and physical and occupational therapy. Parents are usually permitted 24-hour visitation and should be encouraged to participate in the care of their infant.

A variety of complications can occur in these infants during hospitalization (Table 4). Aminoglycosides should be avoided because their use can lyse bacteria, releasing additional intracellular toxin into the infant gut. Cathartics have not been found to shorten the course of the illness.

Historically, administration of antitoxin involved an equine-derived product. Side effects, including anaphylaxis, occurred in 20 percent of patients, and the antitoxin is no longer considered beneficial given the self-limiting course of infant botulism. Recently, the California Department of Health Services conducted a five-year clinical investigation of botulinum immune globulin, a human-derived antitoxin for the treatment of infant botulism. The use of botulinum immune globulin in infants has successfully reduced the time spent in the hospital and the need for mechanical ventilation and tube feeding.

The prognosis is excellent, with a case-fatality rate of less than 2 percent. Recovery results from the regeneration of nerve terminals and  

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**TABLE 3**

**EMG Evaluation of Suspected Cases of Infant Botulism**

| EMG standard battery | Motor and sensory nerve conduction velocity in one arm and one leg  
| Two-Hz nerve stimulation to two distal muscles  
| Supramaximal single nerve stimulation, followed by 50-Hz tetanization for 10 seconds and immediately thereafter by single nerve stimuli at 30-second intervals until amplitude of compound muscle potentials return to baseline  
| Diagnostic triad for infant botulism | Compound muscle action potentials of decreased amplitude in at least two muscle groups  
| Tetanic and post-tetanic facilitation defined by an amplitude of more than 120 percent of baseline  
| Prolonged post-tetanic facilitation of more than 120 seconds and absence of post-tetanic exhaustion  

**EMG = electromyogram.**

motor endplates. Diaphragmatic function returns before peripheral muscle recovery.

For infants who require mechanical ventilation, the average duration is 23 days. On average, infants were able to feed orally 51 days from admission.2 Parents should be aware that the course of this illness consists of small improvements and setbacks. The average hospital stay is 44 days.2 Typically, neurologic sequelae is seldom seen. Persistent hypotonia may be present at the time of hospital discharge, but full recovery can be expected with time.14,15

Relapse of infant botulism has been reported in infants demonstrating complete resolution of symptoms.22 All relapses occurred within 13 days of hospital discharge. No predictors of relapse were identified.22 Therefore, close follow-up is important during the first month after discharge.

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REFERENCES

TABLE 4  
General Complications in Patients Hospitalized with Infant Botulism

<table>
<thead>
<tr>
<th>Complication</th>
<th>Incidence (%)</th>
</tr>
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<tbody>
<tr>
<td>Syndrome of inappropriate secretion of antidiuretic hormone</td>
<td>16</td>
</tr>
<tr>
<td>Autonomic instability</td>
<td>12</td>
</tr>
<tr>
<td>Apnea</td>
<td>12</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>11</td>
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<tr>
<td>Pneumonia</td>
<td>7</td>
</tr>
<tr>
<td>Sepsis</td>
<td>5</td>
</tr>
<tr>
<td>Seizure</td>
<td>5</td>
</tr>
<tr>
<td>Deterioration with gentamicin</td>
<td>4</td>
</tr>
<tr>
<td>Respiratory arrest</td>
<td>4</td>
</tr>
</tbody>
</table>