botulism, other than infant botulism. For suspected cases of infant botulism, the California Department of Public Health Infant Botulism Treatment and Prevention Program provides clinical consultation and access to the specific antitoxin licensed for treatment of infant botulism.

The recommendations in these guidelines address the conventional standard of care, in which medical resources are not limited, as well as settings of contingency and crisis standards of care, with limited medical resources. These guidelines focus on clinical management in the acute phase of illness and do not address long-term care, epidemiologic investigations, antitoxin for postexposure prophylaxis, and management of routine medical issues that are not specific to botulism. Clinicians, hospital administrators, state and local health officials, and planners can use the recommendations in these guidelines to assist in developing crisis protocols for national preparedness for botulism events ranging from sporadic (single) cases to large outbreaks.

Pathophysiology of Botulism

Botulism is caused by toxins formed by the anaerobic, gram-positive bacterium *C. botulinum* and, rarely, by strains of closely related species (*C. baratii* and *C. butyricum)* (*3*). These organisms form spores that are ubiquitous in the environment and capable of indefinitely surviving most naturally occurring conditions as well as boiling and other routine cooking practices. Spores are routinely ingested by humans but do not normally germinate in the intestine (*4*). Toxin is produced only when the spores germinate; this occurs under a rare confluence of circumstances that include anaerobic conditions, low acidity (pH >4.5), low salt and sugar content, and temperatures of 37°F–99°F (3°C–37°C), depending on the serotype. Botulinum toxins are the most potent biologic toxins known. Although the precise lethal dose for humans is unknown, extrapolations have been made from primate studies. The lethal doses for purified crystalline botulinum toxin type A for a 154-lb (70-kg) man are estimated to be 70 μg when introduced orally and 0.80–0.90 μg when inhaled (*2*). Lower doses were proposed in older studies (*5*–*7*).

Seven antigenically distinct botulinum toxins have been identified (A, B, C, D, E, F, and G), all during 1919–1970 (*3*); most strains of *C. botulinum* produce only a single toxin, although strains producing two toxin types have been identified (*8*). In addition, two novel botulinum-toxin–like proteins have been identified from gene sequences and assembled: one from a *C. botulinum* isolate and one from an *Enterococcus faecium* isolate (*9*–*11*). All botulinum toxin types share a similar structure, consisting of a zinc-endopeptidase protein formed by a heavy chain of approximately 100,000 daltons and a light chain of approximately 50,000 daltons. Botulinum neurotoxin enters the vascular circulation (through ingestion, absorption from colonized wound or intestine, inhalation, or injection) and is transported to peripheral cholinergic nerve terminals, including neuromuscular junctions, postganglionic parasympathetic nerve endings, and peripheral ganglia (*12*). All toxin types produce a similar clinical syndrome of cranial nerve palsies followed by descending symmetric flaccid paralysis of variable severity and extent through similar pharmacological mechanisms at the neuromuscular junction (*12*–*14*).

The sequence of botulinum neurotoxin activity at the neuromuscular junction includes heavy-chain binding to a neuronal cell followed by internalization by means of receptor-mediated endocytosis, translocation to the cytosol, and cleavage of the proteins (specific for each serotype) involved in the release of the neurotransmitter acetylcholine (*4*). The characteristic flaccid paralysis results from blocking acetylcholine transmission across the neuromuscular junction by inhibition of acetylcholine release from the presynaptic motor neuron terminal (*12*). The large molecular size of the botulinum toxin likely precludes its crossing the blood-brain barrier to the central nervous system (*4*). Botulinum toxin might be transported to the central nervous system axonally, similar to tetanus toxin, which it resembles, although direct effects on the central nervous system have not been documented in humans (*15*). Recovery, which takes weeks to months, occurs after sprouting of new nerve terminals.

Toxin serotypes A, B, E, and (more rarely) F cause human disease. Toxin type A produces the most severe syndrome, with the highest proportion of patients requiring mechanical ventilation (*14*,*16*,*17*). Toxin type B usually causes milder disease than type A (*14*,*16*,*17*). Only two cases of illness in humans from toxin type C and one outbreak caused by toxin type D have been reported, all in the 1950s (*18*,*19*). Although toxin type C blocks neuromuscular transmission in human tissue in laboratory experiments, this toxin type might not be absorbed in the human gastrointestinal tract (*20*,*21*). In studies of human tissue, toxin type D has been reported not to block neuromuscular transmission (*20*). No cases in humans have been reported from toxin type G (*3*). Toxin type E, usually associated with consumption of foods of aquatic origin, produces a syndrome of variable severity, which frequently includes gastrointestinal symptoms (*17*,*22*,*23*). Type F cases are rare and characterized by rapid progression, extensive paralysis, and respiratory failure but with earlier recovery (*24*,*25*). All toxin types readily produce botulism in experimental animal models.