not spread from person to person, the ease of production of the toxin coupled with its high morbidity and 60–100% mortality make it a close to ideal bioweapon.

Botulism can result from the growth of *C. botulinum* infection in a wound or the intestine, the ingestion of contaminated food, or the inhalation of aerosolized toxin. The latter two forms are the most likely modes of transmission for bioterrorism. Once toxin is absorbed into the bloodstream, it binds to the neuronal cell membrane, enters the cell, and cleaves one of the proteins required for the intracellular binding of the synaptic vesicle to the cell membrane, thus preventing release of the neurotransmitter to the membrane of the adjacent muscle cell. Patients initially develop multiple cranial nerve palsies that are followed by a descending flaccid paralysis. The extent of the neuromuscular compromise is dependent on the level of toxemia. The majority of patients experience diplopia, dysphagia, dysarthria, dry mouth, ptosis, dilated pupils, fatigue, and extremity weakness. There are minimal true central nervous system effects, and patients rarely show significant alterations in mental status. Severe cases can involve complete muscular collapse, loss of the gag reflex, and respiratory failure. Recovery requires the regeneration of new motor neuron synapses with the muscle cell, a process that can take weeks to months. In the absence of secondary infections, which may be common during the protracted recovery phase of this illness, patients remain afebrile. The diagnosis is suspected on clinical grounds and confirmed by a mouse bioassay or toxin immunoassay.

TREATMENT BOTULISM

Treatment for botulism is mainly supportive and may require intubation, mechanical ventilation, and parenteral nutrition (Table 261e-3). If diagnosed early enough, administration of equine antitoxin may reduce the extent of nerve injury and decrease the severity of disease. At present, a heptavalent botulinum antitoxin (HBAT) is available through the CDC as an investigational agent for treatment of naturally occurring noninfant botulism. HBAT contains horse serum–derived antibody fragments to all seven known botulinum toxins (A–G). It is composed of <2% intact immunoglobulin and ≥90% Fab and $F(ab')_2$ immunoglobulin fragments. A single dose of antitoxin is usually adequate to neutralize any circulating toxin. Repeat dosing may be needed in a setting of continued toxin exposure. Given that this product is derived from horse serum, one needs to be vigilant for hypersensitivity reactions, including serum sickness and anaphylaxis following its administration. Once the damage to the nerve axon has been done, however, there is little possible in the way of specific therapy. At this point, vigilance for secondary complications such as infections during the protracted recovery phase is of the utmost importance. Due to their ability to worsen neuromuscular blockade, aminoglycosides and clindamycin should be avoided in the treatment of these infections.

Vaccination and Prevention A botulinum toxoid preparation has been used as a vaccine for laboratory workers at high risk of exposure and in certain military situations; however, it is not currently available in quantities that could be used for the general population. At present, early recognition of the clinical syndrome and use of appropriate equine antitoxin is the mainstay of prevention of full-blown disease in exposed individuals. The development of human monoclonal antibodies as a replacement for equine antitoxin antibodies is an area of active research interest.

CATEGORY B AND C AGENTS

The category B agents include those that are easy or moderately easy to disseminate and result in moderate morbidity and low mortality rates. A listing of the current category B agents is provided in Table 261e-2. As can be seen, it includes a wide array of microorganisms and products of microorganisms. Several of these agents have been used in bioterrorist attacks, although never with the impact of the category A agents described above. Among the more notorious of these was the contamination of salad bars in Oregon in 1984 with *Salmonella typhimurium* by the religious cult Rajneeshee. In this outbreak, which many consider to be the first bioterrorist attack against U.S. citizens, >750 individuals were poisoned and 40 were hospitalized in an effort to influence a local election. The intentional nature of this outbreak went unrecognized for more than a decade.

Category C agents are the third highest priority agents in the biodefense agenda. These agents include emerging pathogens to which little or no immunity exists in the general population, such as the severe acute respiratory syndrome (SARS) or Middle East respiratory syndrome (MERS) coronavirus or pandemic-potential strains of influenza that could be obtained from nature and deliberately disseminated. These agents are characterized as being relatively easy to produce and disseminate, having high morbidity and mortality rates, and having a significant public health impact. There is no running list of category C agents at the present time.

PREVENTION AND PREPAREDNESS

As noted above, a large number and diverse array of agents have the potential to be used in a bioterrorist attack. In contrast to the military situation with biowarfare, where the primary objective is to inflict mass casualties on a healthy and prepared militia, the objectives of bioterrorism are to harm civilians as well as to create fear and disruption among the civilian population. Although the military need only to prepare their troops to deal with the limited number of agents that pose a legitimate threat of biowarfare, the public health system needs to prepare the entire civilian population to deal with the multitude of agents and settings that could be used in a bioterrorism attack. This includes anticipating issues specific to the very young and the very old, the pregnant patient, and the immunocompromised individual. The challenges in this regard are enormous and immediate. Whereas military preparedness emphasizes vaccines toward a limited number of agents, civilian preparedness needs to rely on rapid diagnosis and treatment of a wide array of conditions.

The medical profession must maintain a high index of suspicion that unusual clinical presentations or the clustering of cases of a rare disease may not be a chance occurrence but rather the first sign of a bioterrorist event. This is particularly true when such diseases occur in traditionally healthy populations, when surprisingly large numbers of rare conditions occur, and when diseases commonly seen in rural settings appear in urban populations. Given the importance of rapid diagnosis and early treatment for many of these conditions, it is essential that the medical care team report any suspected cases of bioterrorism immediately to local and state health authorities and/or to the CDC (888-246-2675). Enhancements made to the U.S. public health surveillance network after the anthrax attacks of 2001 have greatly facilitated the rapid sharing of information among public health agencies.

A series of efforts are in place to ensure the biomedical security of the civilian population of the United States. The Public Health Service has a more highly trained, fully deployable force. The Strategic National Stockpile (SNS) maintained by the CDC provides rapid access to quantities of pharmaceuticals, antidotes, vaccines, and other medical supplies that may be of value in the event of biologic or chemical terrorism. The SNS has two basic components. The first of these consists of "push packages" that can be deployed anywhere in the United States within 12 h. These push packages are a preassembled set of supplies, pharmaceuticals, and medical equipment ready for immediate delivery to the field. Given that an actual threat may not have been precisely identified at the time of stockpile deployment, they provide treatment for a variety of conditions. The contents of the push packs are constantly updated to ensure that they reflect current needs as determined by national security risk assessments; they include antibiotics for treatment of anthrax, plague, and tularemia as well as a cache of vaccine to deal with a smallpox threat. The second component of the SNS comprises inventories managed by specific vendors and consists of the provision of additional pharmaceuticals, supplies, and/or products tailored to the specific attack.