Botulism and tetanus

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Abstract
Botulism and tetanus are diseases caused by neurotoxins produced by *Clostridium botulinum* and *Clostridium tetani* respectively. The bacteria and the toxins they produce are closely related. Both diseases are rare in the UK and the developed world but tetanus in particular is a major cause of death in the developing world causing between 100,000 and 200,000 deaths each year.
In botulism a descending flaccid paralysis occurs whereas in tetanus generalized muscle spasms develop. Autonomic nervous system dysfunction may occur in either disease and in tetanus cardiovascular parameters may fluctuate widely. Early involvement of respiratory muscles means that rapid recognition and prompt institution of supportive measures are important in improving survival.

Keywords
botulism; *Clostridium botulinum*; *Clostridium tetani*; tetanus

Botulism
Definition
Botulism is characterized by a descending flaccid paralysis. Several forms of botulism are recognized depending on aetiology.

Epidemiology
Food-borne botulism occurs after ingestion of food contaminated with botulinum toxin. This is usually the result of inadequate cooking of food, home canning or fermenting of meat.
Wound botulism occurs after a wound is contaminated with *Clostridium botulinum* spores. A particular risk group is people who inject drugs (particularly 'skin popping'). In anaerobic conditions of the wound, spores germinate and bacteria multiply releasing botulinum toxin.
Infantile botulism occurs between 1 week and 1 year of life and is usually a result of ingestion of environmental dust or food by *C. botulinum*.(1) An adult form of intestinal colonization by *C botulinum*, intestinal toxaemia, has also been recognized but is very rare.

Pathology and pathogenesis
Seven serotypes of botulinum toxin have been identified. They are structurally similar to tetanus toxin and act by enzymatically cleaving members of the SNARE family of proteins, which are involved in acetylcholine release at the neuromuscular junction, resulting in neuromuscular block.(2)

Course of the disease
Botulism presents as a symmetrical descending flaccid paralysis. Severity of disease depends on toxin dose and can range from mild disease to rapid death due to respiratory failure.

Diagnosis
In wound botulism, incubation periods are longer as spores need to germinate before toxin can be released. However most cases occur in injecting drug users and incubation periods are difficult to determine. Food-borne botulism typically presents 18–36 hours after ingestion of contaminated food; symptoms of botulism are often preceded by abdominal symptoms such as nausea, vomiting and diarrhoea, which are absent in wound botulism.
Invariably, cases start with symptoms and signs of cranial nerve palsy. Ocular muscle involvement results in blurred vision and signs of ptosis and pupillary dysfunction, and facial nerve paresis causes loss of facial expression. Lower cranial nerve paralysis produces dysphagia, dysphonia and dysarthria, often associated dry mouth due to autonomic involvement.

A symmetrical descending flaccid paresis follows, associated with loss of deep tendon reflexes. The autonomic system may be involved, producing constipation, urinary retention and haemodynamic dysfunction. Cognitive and sensory systems are intact.

Differential diagnosis (Table 1)
Management: antitoxin should be given as quickly as possible to neutralize any remaining toxin. If wound botulism is suspected wounds should be carefully cleaned. Infant botulism is treated with human-origin antitoxin (BIV-Ig) whereas other forms can be treated with equine-source antitoxin, although equine preparations are reported to be associated with higher rates of allergic reactions. Antibiotics (metronidazole) should be given if on-going infection with *C. botulinum* is suspected.

Further management is supportive with special attention to respiratory and airway support as there may be few warning signs of impending respiratory failure. Patients are best managed on high-dependency units where staff can respond rapidly to changes in condition. Severe cases may need respiratory support for several weeks.

Long-term sequelae are rare.

Prevention: no vaccine is available for the prevention of botulism. Food hygiene and good wound care are the main methods of preventing the disease.

Tetanus

Definition
Tetanus is caused by tetanus toxin, produced by the bacterium *Clostridium tetani*. It triggers characteristic skeletal muscle rigidity and spasm, often accompanied by cardiovascular disturbance.

Epidemiology
Spores of *C. tetani* are widespread throughout the world, mainly in soil or human/animal faeces. The bacterium itself can survive only in strictly anaerobic conditions but its spores are much more resistant and survive normal disinfection and heating. If a wound is contaminated with tetanus spores, they are able to germinate allowing bacterial multiplication and toxin release. Vaccination protects against tetanus. In the developed world most cases occur in the elderly or injecting drug users.
Neonatal tetanus occurs in infants of unvaccinated mothers. Contamination is usually via the umbilical stump, often as a result of practices such as applying dung or cutting the cord with grass.(3)

Pathology and pathogenesis
Tetanus toxin prevents release of neurotransmitter at γ-aminobutyric acid (GABA) and glycinergic inhibitory interneurone terminals in the central nervous system. These neurones normally inhibit alpha motor neurone discharge.[5] Toxin action results in loss of normal inhibitory control of skeletal muscle producing increased muscle activity and spasms. The autonomic nervous system may also be involved.

Course of the disease
Tetanus develops over a period of days to weeks. A generally milder localized form may occur but usually generalized muscle spasms evolve. Severe cases require full supportive care for several weeks.

Diagnosis

Initial symptoms include muscle stiffness and pain. Trismus is almost a universal symptom and gives rise to the condition's common name, 'lock jaw' (Figure 1). Facial muscle spasm is also characteristic and produces a sardonic smile or 'risus sardonicus'. Spasm of the extensor muscles of the trunk produces opisthotonus. Respiratory failure occurs secondary to laryngeal and respiratory muscle involvement. Without mechanical ventilation this is the usual cause of death.

Neonatal tetanus presents usually between 5 and 14 days of life with symptoms of inability to suck and dysphagia followed by generalized muscle spasms. (4)
Autonomic disinhibition occurs in more severe cases of tetanus, associated with increased mucus secretion and wide fluctuations in heart rate and blood pressure.

Investigations (Figure 2)
Tetanus is a clinical diagnosis. Bacteria may be cultured from a wound (although in most cases this is not possible). Polymerase chain reaction detection of tetanus toxin may also be used as a method of confirming clinical diagnosis. Serum antibody titres can also be measured and presence of protective levels are generally considered to rule out the diagnosis.

Differential diagnosis (Table 2)
Management: the principles of management are similar to those of botulism although, in addition to supportive care, muscle spasms must be treated. Antitoxin should be given as soon as possible. In the developed world, this is usually human-origin (tetanus immune globulin or human immunoglobulin) but equine forms are also available although similar to botulinum antitoxin these are associated with increased risk of adverse events. (5)

Wound debridement and antibiotic administration (penicillin or metronidazole) are important in removing any remaining bacteria.
Respiratory support and intervention should be performed early. Muscle relaxants may be used to control spasms; non-depolarizing neuroblocking agents, benzodiazepines and magnesium sulphate as first-line agents.

Cardiovascular instability, apparent as rapid changes in blood pressure and heart rate, may occur and are managed using short-acting agents.

Prevention: tetanus is prevented by vaccination. Common protocols include three or four doses in infancy followed by a pre-school booster and one later. A total of 5 adequately spaced vaccinations is believed to provide long-lasting protection. Individuals sustaining tetanus-prone wounds should have their immunization status checked and a booster given if needed. People sustaining high-risk wounds likely to be contaminated by *C. tetani* should also be given antitoxin. Vaccination of pregnant women prevents neonatal tetanus. Ideally two doses at least 2 months apart are given.

Key Points
•Tetanus and botulism are caused by closely related neurotoxins but differences in their site of action account for differing clinical pictures.
•A flaccid paralysis occurs in botulism whereas muscle rigidity and spasms occur in tetanus
•Autonomic dysfunction can occur in both although is most marked in tetanus
•Severe cases of either are fatal without good medical care
•Treatment consists of antitoxin, antibiotics and supportive care. In tetanus, spasms and autonomic instability must also be controlled
•Tetanus can be prevented by vaccination whereas no readily available vaccine for botulism currently exists

What's new?
•Global health initiatives to eradicate tetanus continue, with particular emphasis on reducing maternal and neonatal tetanus mainly through vaccination. Work continues to develop and effective botulism vaccine.
•No new treatments have been evaluated but clinical trials and meta-analyses have strengthened the evidence base for commonly used therapies
•Enhanced understanding of the pathophysiology of tetanus and botulinum toxins has led to the proposal of potential neuroprotective or drug-transporting rolls of tetanus toxin

Differential diagnosis of botulism

Guillain–Barré syndrome	Nerve conduction studies, CSF analysis
Myasthenia gravis	EMG, antibody testing, edrophonium (Tensilon®) testing
Stroke syndromes	CT/MR scanning
Shellfish/tetrodotoxin poisoning	History of fish/shellfish ingestion, paraesthesia common – often within minutes of ingestion
Poliomyelitis	Prolonged fever, isolation of virus
Tick paralysis	Ascending paralysis
Inflammatory myopathy	Serum CK, EMG
Eaton–Lambert syndrome	EMG, nerve conduction studies

EMG, electromyography; CK, creatine kinase; CSF, cerebrospinal fluid; CT, computerized tomography; MR, magnetic resonance.

Table 1

Differential diagnosis of tetanus

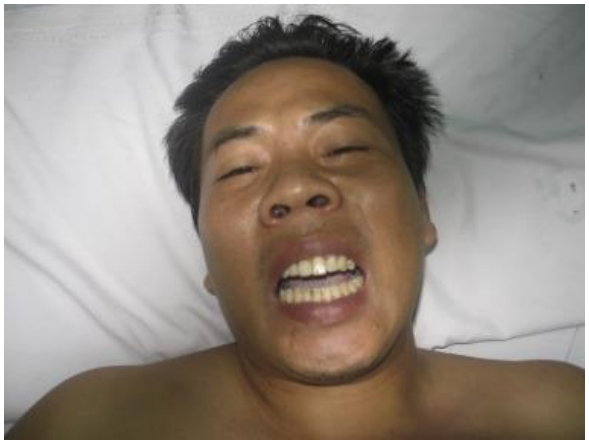
Strychnine poisoning	History of ingestion, toxicology
Drug-induced dystonia	History, response to anticholinergics
Acute abdomen	Localized rigidity, raised WBC
Dental infection	Signs of local infection, raised WBC
Organophosphate ingestion	History, toxicology
Neonatal convulsions (e.g. hypoglycaemia, meningitis)	Serum calcium, plasma glucose, CSF

WBC, white blood cell count; CSF, cerebrospinal fluid.

Table 2

Figure 1

Trismus in tetanus.



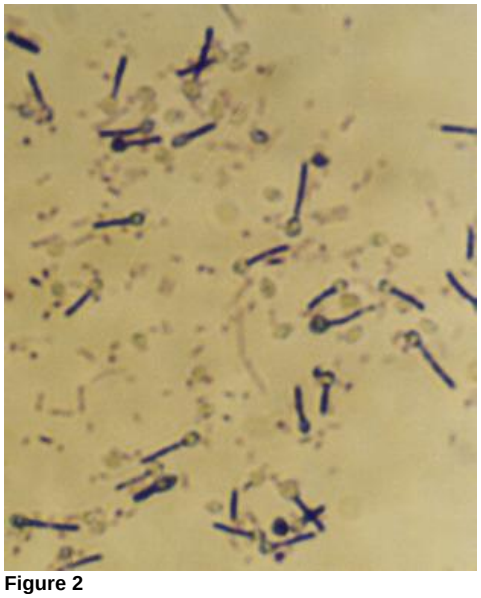


Figure 2

Gram-positive rod-shaped clostridia with terminal spores.

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We are no longer publishing long lists of references but are now asking authors to submit 5 key references cited within the text.

A further reading list can be added with a total of 5 entries

FURTHER READING

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