Tetanus: an ever-present infection risk

Christopher Brightman, Consultant Microbiologist (retired); Locum GP, Lincoln

Tetanus was recognised as far back as the 5th century BC, when it was first described by Hippocrates. Today, immunisation has reduced the incidence of tetanus infection, but the bacteria responsible remains active in soil and manure. Although most people in the UK are covered by immunisation, the elderly and some immigrants, may be at risk.

The word tetanus comes from the Greek tetanos, meaning ‘stretched’ or ‘rigid’ in regards to a muscle spasm. Though tetanus must have existed for millennia, the antiquity of the disease is not known as it does not leave characteristic changes in skeletal remains. Hippocrates (ca. 460–ca. 370 BC) recognised the disease, and its association with wounds has been known for centuries.

The German Jewish physician Arthur Nicolaier, in 1884, produced tetanus in mice by injecting them with garden soil. He saw a bacillus in the pus from these animals which he assumed was the cause of the disease, but was not able to isolate it in culture. In 1889, Japanese physician and bacteriologist Kitasato Shibasaburo isolated the tetanus bacillus, and showed that it could only grow in the absence of oxygen.

Tetanus has always been a complication of wounds in wartime. There is a dramatic painting of a wounded soldier with tetanus among the paintings and sketches produced by Sir Charles Bell between 1809–1815. During the Peninsular War of 1808–1814, 13 out of every 1000 wounded soldiers developed tetanus. This fell to 2 per 1000 during the Crimean War of 1853–1856, but rose to 1 in 100 during the first two months of the First World War. However, the incidence fell to 1.47 per 1000 after the introduction of passive immunisation.

Active immunisation against tetanus became available in about 1926, as a result of which the incidence of tetanus among wounded soldiers fell. The incidence of tetanus among troops of the British Expeditionary Force between 1939–1940 was 0.43 per 1000, and among Allied soldiers in Northwest Europe between 1944–1945, 0.06 per 1000.

Tetanus spores are present in the faeces of horses, and have also been detected in human faeces. The advent of the motor car, and the decline in the use of horses for transport, contributed to the fall in the incidence of tetanus in both civilian and military life.

Dominique Jean Larrey (1766–1842), surgeon to Napoleon I, recommended that wounds should be cauterised to prevent tetanus. He also recommended amputation to prevent tetanus in soldiers who had a wound in the distal part of a limb. However, the effective treatment of tetanus did not become available until the introduction of intermittent positive pressure respiration and paralysis in the middle of the twentieth century.

Figure 1. It is the potent neurotoxin tetanospasmin produced by Clostridium tetani that causes the characteristic spasms of tetanus.
Infections

Bacteriology
Tetanus is caused by a toxin produced by *Clostridium tetani* (Figure 1), a motile Gram-positive strictly anaerobic bacillus that produces subterminal spores, although not every strain is sporogenic. The organism grows under strictly anaerobic conditions on laboratory media.

Though vegetative forms of *C. tetani* are easily killed by heat, the spores are more resistant. Some are killed by boiling for 15 minutes, whereas others may survive for up to three hours. Most spores are killed within a few hours by a 1% aqueous solution of iodine, or by a 10-volume solution of hydrogen peroxide. The difficulty in killing spores explains why cases of postoperative tetanus have been caused by inadequately sterilised catgut – spores can survive for years under the right environmental conditions. Spores of tetanus have been isolated in soils throughout the world, and can survive dry heat at 100 degrees Celsius for one hour.

A case of tetanus has been reported in which spores of *C. tetani* were isolated from abdominal scar tissue in a woman who had had an abdominal hysterectomy 10 years before developing tetanus.

Epidemiology
It is estimated that each year at least 100,000 cases of tetanus occur globally. This is probably an underestimate, as the majority of cases occur in countries with poor medical facilities, in which cases are likely to go unreported. About 60% of cases occur in neonates and children under five years old.

Between January and December 2013, seven cases of tetanus were reported in England and Wales. The patients were aged between 35–82. Two were intravenous drug addicts, three cases sustained lacerations in the home or garden, and one was injured on a farm. The seventh patient had no recorded injury. None of the patients died.

Intravenous drug addicts who ‘dilute’ heroin by mixing it with quinine are at risk from tetanus, as this causes tissue necrosis, thereby providing an ideal environment for the germination of spores and the growth of the vegetative organism. Elderly patients are also at risk due to the decline in antibody levels following immunisation in their youth.

Pathogenesis
All the symptoms of tetanus arise from a toxin produced by the vegetative organism: they do not arise from invasion of tissues by *C. tetani*. Spores of *C. tetani* have been isolated from soil, street dust and, in the past, the dust in operating theatres. They enter the body through a wound, which can be as minor as the prick from a thorn. In some cases, the patient may not remember the injury, hence the difficulty in estimating the incubation period of the disease. Spores will start to germinate if the conditions in the tissue are appropriate, the most important of these being a low oxygen tension. This is the case in deep, necrotic wounds; hence the frequency with which tetanus occurs in wounded soldiers. *C. tetani* produces the toxin tetanospasmin, a protein responsible for the clinical features of tetanus. It is only slightly less toxic than botulin, one of the most poisonous chemicals known. The toxin enters peripheral nerves from adjacent muscle. Evidence supports the theory that it reaches the central nervous system by transport in the axons of motor nerves. It is probable that it is also disseminated to distant sites via lymphatic vessels and the bloodstream. After entering presynaptic nerves, it binds to neuronal gangliosides, inhibiting the release of neurotransmitters. Its main action is to inhibit the action of interneurons, responsible for the inhibition of motor neurones, with the result that the patient develops muscular rigidity and spasm.

Clinical features of tetanus
It is difficult to give an incubation period for tetanus, as spores may remain dormant in tissues for weeks to years, until conditions are suitable for exosporulation to take place. In a deep wound contaminated with soil, the incubation period will be a matter of days. The incubation period for tetanus neonatorum, or neonatal tetanus, is usually less than a week.

The characteristic clinical signs of tetanus are spasm and rigidity of the voluntary muscles, in particular the masseters, the abdominal muscles and the erector spinae. Muscular rigidity persists throughout the illness, and can be detected by palpation. Spasms are intermittent. They may only involve the muscles of the mouth and face, giving rise to *risus sardonicus* (rictus grim), but can also be generalised. Localised tetanus can occur in which the rigidity and spasm are confined to muscles near an infected wound. This is usually seen under wartime conditions in soldiers who are partially immune.

In some patients the signs of tetanus do not progress beyond trismus (lockjaw), but in others generalised convulsions occur in which the muscles of the trunk and limbs go into violent spasm. The neck may become extended so that the shoulders are lifted off the bed. This is shown in the painting by Sir Charles Bell referred to previously.

The frequency of convulsions vary, and may be continuous in severe cases. The patient remains mentally alert and there are no signs of generalised toxaemia. Difficulty in passing urine, together with constipation, is common.

Cephalic tetanus can follow wounds of the head and neck. Dysphagia is usually a prominent symptom; diagnosis can be difficult as generalised convulsions may be absent.

There are few complications in cases of mild or moderately severe tetanus that are only managed by
sedation. The main danger arises from aspiration of secretions, which can occur during or after a spasm. This can lead to collapse of part of a lung, or to pneumonia. The latter is the most common cause of death in tetanus neonatorum.

Bone fractures, including compression fractures of vertebrae, can occur as a result of muscular spasm. Several complications can occur in patients with severe tetanus who are paralysed and on respiratory support. Cardiovascular complications, in particular a labile blood pressure, is probably due to the action of tetanospasmin on the brainstem. This can be accompanied by severe sweating, which may be followed by failure of the peripheral circulation.

Hyperpyrexia, with temperatures reaching 40 degrees Celsius (104 degrees Fahrenheit), can be seen in patients who have been paralysed, and is a bad prognostic sign. Again, this is probably due to tetanospasmin acting on the brainstem. Dilatation of the stomach and intestines can also occur in severe cases: this is usually fatal. The metabolic rate is increased in patients with severe tetanus, resulting in weight loss. This can be difficult to prevent.

There are no permanent sequelae in patients who have recovered from tetanus. In countries where intensive care facilities are good, most patients should recover. However, an attack of tetanus, however severe, does not confer immunity to further episodes of the illness.

**Diagnosis**

Diagnosis is based on clinical signs and symptoms. Laboratory investigations are of no value. It may be possible to isolate *C. tetani* from material taken from a wound; however, by the time the organism has been grown in the laboratory, an astute clinician will have already made the diagnosis.

There are other conditions that may simulate the clinical features of tetanus. Strychnine poisoning can cause spasms similar to those of tetanus, but there is complete muscular relaxation between spasms. The symptoms of rabies can also be similar, but the spasms tend to be localised to the muscles of the neck, mouth and pharynx. Diagnosis can be difficult if trismus is the main symptom, as painful conditions affecting the oropharynx can make it difficult for the patients to open their mouths.

**Treatment**

Skilled nursing is essential in the treatment of tetanus. Close attention should be paid to oral hygiene. The patient must be kept in a darkened room in which there is little noise, and it is important to monitor the patient’s weight together with fluid balance.

Human anti-tetanus immunoglobulin should be given to neutralise any toxin that is still in the circulation. There is evidence that intrathecal administration diminishes the severity of the illness. Anti-toxin will have no effect on toxin that is already bound to gangliosides. Metronidazole should be given to eradicate vegetative stages of *C. tetani* that may still be in the wound. This antibacterial agent is preferable to penicillin as the latter can act as a competitive inhibitor of gamma-amino butyric acid, one of the neuroinhibitors affected by tetanospasmin.

Muscular spasms should be controlled with diazepam. The autonomic nervous system should be ‘stabilised’ with sedatives and, if necessary, drugs to control a labile blood pressure.

The patient may need to be paralysed and put on a ventilator; however, this may not be possible in some countries with less well developed medical facilities, in which tetanus is common. The author looked after a patient in a remote part of Africa in which the only active treatment available was sedation with diazepam.

**Prevention**

Immunisation with tetanus toxoid is very effective at preventing the disease. In the UK the first dose is given at two months of age, followed by a second and third dose at monthly intervals. Booster doses are given at three to five years, and at 13–18. No further doses are given unless a patient has a wound that is likely to give rise to tetanus (Box 1).

All wounds should be thoroughly cleaned and debrided if necessary. It may be appropriate to give anti-toxin, with or without tetanus immunisation, if the patient has a deep wound contaminated with soil.

A booster tetanus injection is recommended for people travelling to an area with limited medical facilities whose last tetanus injection was more than 10 years ago.

**Declaration of interests:** none declared.

---

**Box 1. Tetanus-prone wounds as defined by Public Health England**

- Wounds or burns that need surgery, but where surgery cannot be performed within 24 hours
- Wounds or burns where a significant amount of tissue has been removed, or puncture-type injuries such as animal bites, particularly if they have had contact with soil or manure
- Wounds containing any substance that should not be there, such as dust or dirt (foreign bodies)
- Serious fractures where the bone is exposed and prone to infection (compound fractures)
- Wounds and burns in people who have systemic sepsis