5 Tetanus

5.1 Introduction

Tetanus has long been known as the scourge of parturient women, newborn babies and wounded soldiers. In the 18th century one out of every six infants born at the Rotunda Hospital in Dublin died from neonatal tetanus. Hippocrates described tetanus, but the cause was not recognised until 1884 and the toxin not purified until 1890. The toxoid (chemically inactivated toxin) was first prepared in 1924.

5.2 The illness

Tetanus is a clinical diagnosis, and is characterised by muscular rigidity and very painful contraction spasms. When severe, it is associated with a characteristic facial grimace (risus sardonicus) and arching of the back (opisthotonus). The patient suffering from tetanus remains alert unless they become severely hypoxic. A toxin produced by *Clostridium tetani* (a gram positive, spore forming, motile, anaerobic bacillus) causes the disease. The toxin reaches the central nervous system via the axons and irreversibly binds to nerve terminals at the neuromuscular junction, blocking release of inhibitory neurotransmitters and leading to the tetanic muscle spasms.

The incubation period is between four and 21 days, commonly about 10 days, but has been reported to vary from one day to several months. The bacteria need an anaerobic environment to grow, and this is often found in damaged and necrotic tissue.

Initial symptoms include weakness, stiffness or cramps, and difficulty chewing or swallowing food. Reflex muscle spasms usually occur within one to four days of the initial symptoms. The interval between initial symptoms and reflex spasms is called the onset period. The shorter the incubation and onset periods, the more severe the disease. Even with modern intensive care tetanus mortality is about 10 percent overall, and much higher in older people.

Neonatal tetanus, from infection of the umbilical stump, is the commonest form of disease in non-industrialised countries.

5.3 Epidemiology

Tetanus spores are ubiquitous in the environment, and are particularly common in soil and the alimentary tracts of animals. They can easily be introduced into a wound at the time of injury, even when the injury is quite trivial. The incidence of tetanus varies inversely with immunisation coverage.

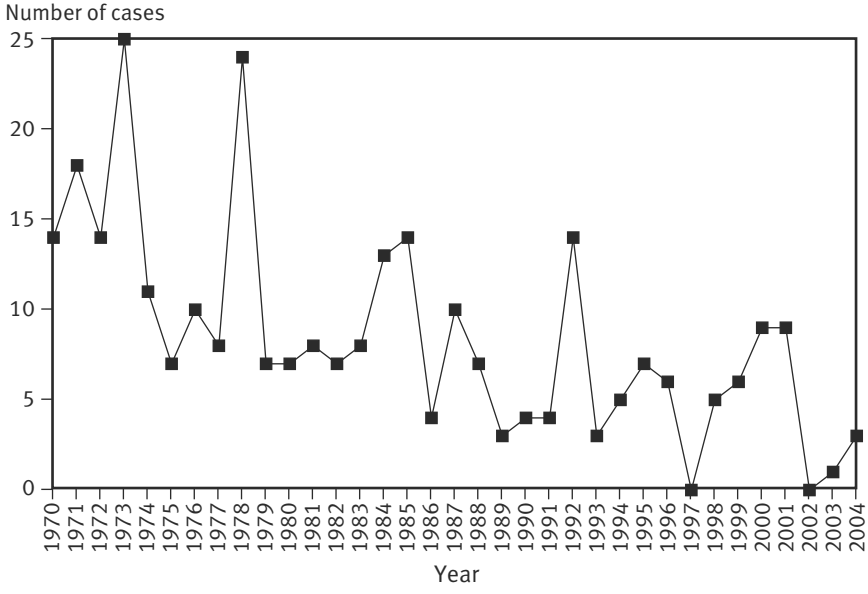
Tetanus is not infectious, and vaccination provides only individual protection and no herd immunity.

New Zealand epidemiology

During 1980–92, 86 cases of tetanus occurred in New Zealand and there were eight deaths, a case fatality rate of 9.3 percent.[1] Of all cases of tetanus, 79 percent were over 40 years of age. Of those who died, seven were over 70 years of age and one was 58 years; seven of the eight were female. The average incidence in New Zealand of 0.20 per 100,000 for the 13-year period compares with a 1992 rate of 0.08 in Australia, 0.01 in Canada, 0.02 in England, 0.04 in Scotland and 0.02 in the United States (US).

From 1993 to 2000 there were 18 cases of tetanus notified to the medical officers of health, a range of zero to six cases a year. Six cases were reported in 1999; two were in the age group 40–49 years and four were over 70 years of age. Four of the cases were unimmunised, and there was no information on the immunisation history of the other two cases. A total of eight cases were notified from 2001 to 2004, and among these was an unimmunised child aged one year diagnosed with tetanus in 2001. The single case notified in 2004 was a female aged 60–65 years with an unknown immunisation history, although there were five cases hospitalised with tetanus. Not all cases of tetanus are notified, as illustrated in the hospitalisations data shown in Figure 5.1.

Figure 5.1: Tetanus hospitalisations, by year, 1970–2004



History of the New Zealand Immunisation Schedule

The history of tetanus vaccine use prior to the introduction of diphtheria, tetanus and whole cell pertussis (DTwP) vaccine in 1960 is not well recorded, but tetanus vaccine was widely used, in World War II and subsequently, by the armed forces.

In New Zealand, universal infant immunisation with tetanus toxoid started in 1960 with the use of three doses of triple vaccine. Anyone born before 1960 is less likely to have received a primary series, unless they were in the armed forces. Older women appear to be at particular risk. The first scheduled vaccine used for infants (from 1960) was the DTwP vaccine, with three doses at monthly intervals at three, four and five months of age; and a diphtheria tetanus (DT) booster before school entry (at five years of age). A DT booster at 18 months of age was added in 1964, primarily to enhance protection against tetanus. There was a change to a more immunogenic adsorbed vaccine in 1971 and the dose given at four months of age was dropped.

In 1980 the dose of DT given at five years of age was replaced by the monovalent tetanus toxoid (TT) given at 15 years of age, as part of a move from 10-yearly to 20-yearly boosters for tetanus. It was considered that more frequent boosters were unnecessary and the cause of significant local reactions. There was a return to a three dose primary series of DTwP (by the addition of a six weeks of age vaccination) in 1984, because two doses had been inadequate to control pertussis. In 1996 the booster of adult tetanus diphtheria vaccine (Td), previously given at age 15 years, was changed to age 11 years.

In 2002 the primary schedule for tetanus, given in combination vaccines at age six weeks, three months and five months followed by a dose at 15 months, was changed when a further dose was introduced at age four years before school entry. The Td given at age 11 years continued.

The adult tetanus diphtheria vaccine (Td) replaced the tetanus toxoid (TT) vaccine in 1994 and 10 yearly boosters were recommended. The change was recommended to maintain the adult population's immunity to diphtheria, in response to outbreaks overseas affecting adults and the absence of natural boosting because the disease had become rare. From 2002 adult boosters have been recommended at 45 and 65 years of age (instead of 10 yearly) as a pragmatic attempt to increase coverage in the adult population.

Whether routine booster doses of tetanus vaccine, unrelated to the treatment of an injury, are necessary following the primary series in childhood is debated. As discussed above, the policy recommending boosters has changed over time. The population coverage for adult Td immunisation in New Zealand is unknown but is thought to be low. The change in 2002 to Td immunisation at 45 and 65 years of age aimed to increase the proportion of the population who receive boosters. The age specific recommendations may facilitate the linkage of adult immunisation with the delivery of other preventive health measures.

5.4 Vaccines

Tetanus immunisation protects by stimulating the production of antitoxin, providing immunity against the effects of the toxin. It does not prevent organisms growing in a contaminated wound. The tetanus vaccine is prepared from cell free toxin treated with formaldehyde to produce a toxoid. The toxoid is adsorbed onto an aluminium salt adjuvant to improve immunogenicity.

Tetanus vaccine is available as a single antigen or in combination with other vaccines. A primary immunisation course consists of three doses of vaccine. The adult Td vaccine, which has a reduced dose of diphtheria toxoid, is used in individuals seven years of age and older. (See also sections 4.4, 6.4 and 8.4.)

Efficacy

The tetanus vaccine was 100 percent effective when given to pregnant women to protect against neonatal tetanus in a randomised controlled trial (RCT). Tetanus in adults is too rare for vaccine efficacy to be tested in an RCT, but the vaccine was shown to be efficacious before RCTs became the standard. The efficacy of tetanus vaccine was clearly demonstrated in World War II, when only 12 cases of tetanus occurred among the 2.7 million wounded US army personnel (0.44 per 100,000), compared to 70 cases out of 520,000 wounded in World War I (13.4 per 100,000). Of the 12 cases, only four had completed primary immunisation. Immunised cases have less severe disease and a lower case fatality.

In most studies, 100 percent of infants have protective levels of tetanus antibody after three doses of vaccine given at intervals of one month or longer. The duration of antibody persistence depends on the initial antibody level. Calculations of tetanus antibody decay have shown that a three dose primary schedule in infancy will provide protection for at least five years, and a booster at five years will provide protection for at least another 21 years.[2] Additional doses increase the duration of protection, but the immune response gets slower and lower in older people.

Dosage

The dose of DTaP-IPV, dTap-IPV, DT, Td and TT is 0.5 mL given by intramuscular injection. (See section 2.3 for needle sites and sizes.)

5.5 Recommended immunisation schedule

Usual childhood schedule

From 2006 a primary course of tetanus is given as DTaP-IPV at six weeks, three months and five months of age followed by a dose of DTaP-IPV at four years of age, before school entry. From 2006 the booster given at age 11 years (school year 7) includes a pertussis component given as the vaccine diphtheria, tetanus, acellular pertussis and inactivated polio vaccine (dTap-IPV, BOOSTRIX®-IPV, GSK). If pertussis vaccine is contraindicated (see sections 6.6 and 6.7), DT, or adult tetanus diphtheria

vaccine (Td) in older children and IPV should be substituted (see section 4.5). Note that the dTap-IPV vaccine given at age 11 years contains the smaller adult doses of diphtheria and pertussis antigens compared with the vaccines given to infants and children up to age seven years. The dTap-IPV vaccine will be given to children aged 11 years in 2006/07, as these children have not received four doses of polio vaccine. After this it is expected dTap will be given.

Maximum number of doses for children

Children who did not receive the pertussis vaccine as infants, but subsequently request to have pertussis vaccine, will receive additional doses of diphtheria and tetanus vaccine, because pertussis vaccine is only available as diphtheria, tetanus, acellular pertussis and inactivated polio (DTaP-IPV). In general, children should not have more than six doses of tetanus and diphtheria vaccine by their fourth birthday. For an individual child, the vaccinator may be guided by the extent of any local reaction when determining whether to give further doses. The only danger from the additional doses is a local reaction, and this needs to be balanced against the need to protect against pertussis.

Adults and children from seven years of age

For adults and children who present with a tetanus prone wound, boosters should be offered according to the guidelines in section 5.7 and Table 5.1.

For previously unimmunised adults and children from seven years of age, a primary immunisation course consists of three doses of 0.5 mL of Td at intervals of not less than one month. This is shorter than the manufacturer's recommended schedule of zero, one and six months but is likely to increase compliance. A booster dose should be given 10 years later. Alternatively three doses of dTap-IPV may be given, plus the booster in 10 years (see section 4.5).

For children given a primary course as infants and a booster at age four years, a further booster of tetanus toxoid containing vaccine is given at age 11 years as dTap-IPV vaccine.

Adults are recommended to have booster doses of adult tetanus diphtheria (Td) vaccine at 45 and 65 years of age. Protection against tetanus is expected to last at least 20 years following a booster dose after the primary series. The recommendation for a booster dose at 45 and 65 years of age is intended to ensure ongoing protection, and to facilitate delivery by recommending the booster at a time when routine preventive care for adults may be taking place.

Note that the recommendations for diphtheria vaccine include: if someone is travelling to an endemic area, or there is another reason to ensure immunity, a booster dose of Td should be given if it is more than 10 years since the last dose (see section 4.5).

People born before 1960 are less likely to have had a primary series of tetanus vaccine. General practitioner visits at or around 45 and 65 years of age should be used to check on the immunisation history. If there is no reliable history of the patient having received a primary series, the vaccine at that episode should be considered the first of a primary series. The next two injections should be given at monthly intervals or at zero, one and six months. A booster dose should be scheduled in 10 years' time.

Prior clinical tetanus does not usually confer immunity, and immunisation is required. In 1995 a 40-year-old man developed tetanus for a second time because he failed to complete the recommended course of immunisation after the first episode of tetanus.[3]

Dose intervals between Td and dTap-IPV

It is recommended that for students who have recently received a tetanus diphtheria (Td) vaccine booster, eg, at the time of an injury, the age 11 (year 7), dTap-IPV immunisation should be delayed until two years after the dose of Td, and offered before the student reaches the age of 16 years. Students who would normally receive the year 7 event at school should be referred to their general practitioner for follow up and recall.

Prevention of tetanus following injury

Following injury it is essential that all wounds receive adequate surgical toilet. Tetanus bacteria can only grow in anaerobic conditions. Further treatment must depend on the circumstances of each case. Tetanus prone injuries include those that are contaminated with dirt, saliva or faeces, puncture wounds (including unsterile injections), missile injuries, burns, frostbite, avulsions and crush injuries. Guidelines for management are shown in Table 5.1.

Table 5.1: Prevention of tetanus following injury

The following are offered as guidelines.

(i) Recipients should be divided into four categories.

Category 1: completed a course of tetanus toxoid (TT or Td), with the most recent dose within the last five years

Category 2: completed a course of tetanus toxoid (TT or Td), with the most recent dose between five and 10 years ago

Category 3: completed a course of tetanus toxoid (TT or Td) with the most recent dose more than 10 years ago.

Category 4: never had a complete course of tetanus toxoid or immune status is unknown.

(ii) Wounds should then be classified as 'clean' or 'dirty'.

(a) 'clean' wounds – wounds less than six hours old, non-penetrating with negligible tissue damage

(b) 'dirty' wounds – wounds not classified as clean, which may be contaminated, infected, penetrating, more than six hours old and with tissue damage.

Recommendations based on the category of patient and the kind of wound are summarised below.

From the person's tetanus immunisation history, put them into one of the four categories as stated above, and identify the time since a previous booster. Classify the wound as clean or dirty and use the table to identify the need for Td or tetanus immunoglobulin (TIG).

Category based on history of tetanus course and/or booster	1	2	3	4
Number of years since completing tetanus toxoid course or booster	< 5	5–10	> 10	Never or unknown
(a) Clean wound	Nil	Nil	Booster Td*	Course Td*
(b) Dirty wound	Nil	Booster Td**	Booster Td*	TIG plus course Td*

* A tetanus immunisation course consists of three doses at not less than monthly intervals.

** For children age 7–15 years, dTap-IPV may be used, if a booster is indicated and they have not received a fifth pertussis dose and fourth IPV dose.

Immunised individuals respond rapidly to a booster injection of adsorbed tetanus or tetanus diphtheria vaccine, even after a prolonged interval. Toxoid and TIG should be given at the same time but into different limbs and using separate syringes.

Tetanus immunoglobulin (TIG) availability and storage

TIG is issued in ampoules, each containing 250 IU. (Ampoules of 2000 IU are used for treatment and not for prophylaxis.) These should be protected from light and stored in a refrigerator at +2° to +8°C. They must never be frozen. TIG is given intramuscularly.

TIG dose

The recommended dose to prevent tetanus is 250 IU of TIG for recent injuries, but this should be increased to 500 IU if more than 24 hours have elapsed since injury, or if there is a risk of heavy contamination or following burns.

There is no need to test the patient's sensitivity before administering TIG, but caution is necessary if the patient is known to suffer IgA deficiency. In this situation, specialist help should be sought (see section 1.8).

Patients with impaired immunity who suffer a tetanus-prone wound may have failed to respond to prior vaccination and may therefore require TIG.

5.6 Expected responses and adverse events following immunisation (AEFI)

Expected responses

Local reactions such as pain, redness and swelling around the injection site have been reported in 0–95 percent of recipients. Local reactions generally increase with the number of doses given. The local reactions are usually minor and only last a day or so. In a small percentage of vaccine recipients the reactions will be severe enough to limit movement of the arm and may last for about a week.

High levels of antibody before immunisation (usually from an excessive number of immunisations) are associated with more severe local reactions. The reaction may be due to some of the other vaccine constituents (eg, aluminium).

See chapter 6: Pertussis for information on reactions following the fourth and fifth dose of a diphtheria, tetanus, pertussis antigen containing vaccine.

Sterile abscesses and persistent nodules at the injection site may develop if the injection is not given deeply enough into the muscle. The deeper the injection, the less the risk of reaction.[4]

The change from TT to Td was associated with the reporting of more local as well as other reactions. Generalised reactions after Td are uncommon, but may include headache, lethargy, malaise, myalgia and pyrexia.

Adverse events following immunisation

Anaphylaxis was reported at a rate of 1.6 per million doses of Td in the US from 1991 to 1995. There have been no reports of anaphylaxis after Td was introduced

in New Zealand. The 1994 US Institute of Medicine[5] review of adverse events from tetanus vaccine concluded that the evidence supported a link with brachial plexus neuropathy at a rate of 0.5 to 1 per 100,000 doses within one month of immunisation. No evidence has been found for a connection between receipt of tetanus vaccine and the Guillain-Barré syndrome in a large population based study. The study found no link in an estimated 730,000 children who were of eligible age to receive DTwP in a population of 2.2 million children under 15 years of age, or in adults who received tetanus containing vaccines.[6]

Any severe or unexpected reactions should be reported to CARM, PO Box 913, Dunedin, using the prepaid postcard HP3442 (see section 2.4) or via online reporting at http://carm.otago.ac.nz. If the patient or parent/caregiver does not consent to being identified, the report should be made without personal identification. When reporting local reactions, state the size of the redness and/or swelling, as well as the number of previous doses of vaccine.

5.7 Contraindications

See section 1.9 for general contraindications for all vaccines.

Although there is the general contraindication to administering a vaccine when a patient has a febrile illness, protection against the risk of tetanus is paramount if the wound is thought to be tetanus prone. Immunisation should not be postponed because the patient has a minor infection.

Immunisation with Td (or tetanus toxoid) should not be repeated in individuals who have had previous severe hypersensitivity reactions. Most cases of hypersensitivity have been reported in individuals who have had excessive numbers of booster injections outside the guidelines noted above. (See also sections 4.7 and 6.7.)

5.8 Control measures

All cases of tetanus, together with an accurate immunisation history, should be notified to the local medical officer of health.

References

1 Galloway Y. 1994. Tetanus: still a problem for over 35s. *NZ Public Health Report* 1: 19.

2 Simonsen O, Bentzon MW, Kjeldsen K, et al. 1987. Evaluation of vaccination requirements to secure continuous antitoxin immunity to tetanus. *Vaccine* 5: 115–22.

3 Smith J. 1995. Tetanus infection may not confer immunity. *NZ Public Health Report* 6: 53.

4 Mark A, Carlsson RM, Granstrom M. 1999. Subcutaneous versus intramuscular injection for booster DT vaccination of adolescents. *Vaccine* 17: 2067–72.

5 Vaccine Safety Committee, Institute of Medicine. 1994. Diphtheria and tetanus toxoids. In: KR Stratton, CJ Howe, RB Johnston (eds). *Adverse Events Associated with Childhood Vaccines: Evidence bearing on causality*. Washington, DC: National Academy Press, pp. 67–117.

6 Tuttle J, Chen RT, Rantala H, et al. 1997. The risk of Guillain-Barré syndrome after tetanus-toxoid-containing vaccines in adults and children in the United States. *Am J Public Health* 87: 2045–8.