19 Tetanus

Key information

Mode of transmission	Environmental exposure to the bacillus, usually through contaminated wounds. The disease is not directly transmitted from person to person.
Incubation period	Between 3 and 21 days, commonly about 10 days; may vary from 1 day to several months.
Period of communicability	A person with tetanus is not infectious to others.
Burden of disease	In older individuals, usually women, who are less likely to have received a primary series of tetanus vaccine.
Funded vaccines	DTaP-IPV-HepB/Hib (Infanrix-hexa). DTaP-IPV (Infanrix-IPV). Tdap (Boostrix). Td (ADT Booster).
Dose, presentation, route	0.5 mL per dose. DTaP-IPV-HepB/Hib: pre-filled syringe and glass vial. The vaccine must be reconstituted prior to injection. DTaP-IPV, Tdap, Td: pre-filled syringe. Intramuscular injection.
Funded vaccine indications and schedule	6 weeks, 3 months and 5 months: DTaP-IPV-HepB/Hib. 4 years: DTaP-IPV. 11 years: Tdap. 45 and 65 years: Td. During each pregnancy (from 16 weeks' gestation): Tdap. For individuals with tetanus-prone wounds. For (re-)vaccination of eligible patients: DTaP-IPV-HepB/Hib, DTaP-IPV, Tdap or Td. For testing for primary immune deficiencies: Td.
Dose interval between Td and Tdap	No minimum interval is required between Td and Tdap, unless Tdap is being given as part of the primary immunisation course.
Wound control	If an injury is considered to be tetanus prone *and* there is any doubt about previous tetanus immunisation, the individual must be given tetanus immunoglobulin (TIG) and a 3-dose primary immunisation course.

19.1 Bacteriology

Tetanus is caused by the action of tetanus toxin released by *Clostridium tetani*, a spore-forming gram-positive, motile, anaerobic bacillus. The most common source of environmental exposure to *C. tetani* spores and bacilli is soil. However, soil is not the only reservoir of the organism. Animals, both herbivores and omnivores, can carry *C. tetani* bacilli and spores in their intestines, and the organism is readily disseminated in their faeces. Once introduced into the relatively anaerobic conditions found in wound tissue, they germinate and produce toxin.

Tetanus spores or bacilli can easily be introduced into a wound at the time of injury, even when the injury is quite trivial. Contaminated wounds, especially wounds with devitalised tissue and deep-puncture trauma, are at greatest risk.

19.2 Clinical features

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.

The *C. tetani* toxin reaches the central nervous system via the axons and irreversibly binds to nerve terminals at the neuromuscular junction, blocking the release of inhibitory neurotransmitters and leading to the tetanic muscle spasms.

The incubation period is between 3 and 21 days, commonly about 10 days, but it has been reported to vary from one day to several months. The bacteria need an anaerobic environment in which to grow, and this is often found in damaged and necrotic tissue, although the inoculation site may appear insignificant. 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 being 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 the disease in some low-income countries, particularly where births take place at home without adequate sterile procedures.[1]

A person with tetanus is not infectious to others, and vaccination provides individual protection only, with no herd immunity. Suffering tetanus does not confer immunity. See section 19.5.2.

19.3 Epidemiology

19.3.1 Global burden of disease

The estimated total number of tetanus cases (including neonatal cases) globally has fallen from more than 110,000 in 1980 to 10,000 in 2015.[2] India, Uganda, Nepal, the Philippines and Pakistan had the highest number of cases in 2015, representing more than 60 percent of the cases worldwide.[3] Of the estimated 3,500 cases of neonatal tetanus worldwide in 2015, half of them occurred in Pakistan, India, the Democratic Republic of Congo and China.[4]

Worldwide, all countries are committed to 'elimination' of maternal and neonatal tetanus; that is, a reduction of neonatal tetanus incidence to below one case per 1,000 live births per year in every district.[1] However, the goal of eliminating maternal and neonatal tetanus by 2015 has not been reached.

The incidence of tetanus reflects the effectiveness of the local immunisation programme, with low incidence in regions with high immunisation coverage. In 2015, 126 countries (65 percent of the 194 WHO member states) had immunisation coverage rates of 90 percent or more for three doses of a diphtheria, tetanus, and pertussis-containing vaccine (DTP) given in the first year of life.[5] Almost 40 percent of the 19.4 million children worldwide who did not receive three doses of DTP vaccine lived in India, Nigeria and Pakistan.

19.3.2 New Zealand epidemiology

One case of tetanus was notified in New Zealand in 2015.[6] The case was a female in the 70 years and older age group (the vaccination status was not known). No cases were reported in 2014.

There were 32 tetanus cases notified between 1997 and 2015.[6] Immunisation status was recorded for 21 of the 32 notified cases (ESR data, 9 February 2017). There were four cases in unvaccinated children (aged under 10 years), 14 cases in unvaccinated adults and three cases in vaccinated adults (the time since vaccination is not known). Two females in the 70 years and older age group died (one was not vaccinated and the vaccination status of the other was unknown).[6]

19.4 Vaccines

Tetanus immunisation protects by stimulating the production of antitoxin, providing immunity against the effects of the toxin. It does not prevent *C. tetani* 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.

19.4.1 Available vaccines

Funded vaccines

Tetanus vaccine as a single antigen is no longer available in New Zealand. It is only available in combination with other vaccines.

The tetanus toxoid-containing vaccines funded as part of the Schedule are:

- DTaP-IPV-HepB/Hib (Infanrix-hexa, GSK): diphtheria, tetanus, acellular pertussis, inactivated polio, hepatitis B and *Haemophilus influenzae* type b vaccine
- DTaP-IPV (Infanrix-IPV, GSK): diphtheria, tetanus, acellular pertussis and inactivated polio vaccine
- Tdap (Boostrix, GSK): a smaller adult dose of diphtheria and pertussis vaccine, together with tetanus vaccine
- Td (ADT Booster, Seqirus (NZ) Ltd): a smaller adult dose of diphtheria vaccine together with tetanus vaccine.

See section 5.4.1 for more detailed vaccine information.

Other vaccines

Other tetanus toxoid-containing vaccines registered (approved for use) and available (marketed) in New Zealand are:

- Tdap: Adacel (Sanofi)
- Tdap-IPV: Adacel Polio (Sanofi).

19.4.2 Efficacy and effectiveness

Efficacy and effectiveness

Tetanus toxoid vaccine administered to pregnant women can prevent tetanus in their newborns (neonatal tetanus). Subsequent field assessments of the efficacy of two or more tetanus toxoid doses using data collected during neonatal tetanus mortality surveys demonstrated effectiveness of 70–100 percent.

A systematic review and meta-analysis concluded that immunisation of pregnant or childbearing-age women with two or more doses of tetanus toxoid reduces neonatal tetanus mortality by 94 percent (95% CI: 80–98).[7]

Tetanus in adults is too rare for vaccine efficacy to be tested in a clinical trial. However, the effectiveness 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).[7] Of the 12 cases, only four had completed primary immunisation. Immunised cases have less severe disease and a lower case fatality.

Duration of protection

In most studies, 100 percent of infants have protective levels of tetanus antibody after three doses of vaccine given at intervals of four weeks 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.[8] By mid-life, around 50 percent of vaccinated people have low or undetectable antibody levels;[9, 10, 11, 12] a single dose of tetanus toxoid produces a rapid anamnestic response.[13, 14, 15, 16]

(See also sections 5.4.2 and 14.4.2.)

19.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017*.[17] Store at +2°C to +8°C. Do not freeze.

DTaP-IPV-HepB/Hib and Td should be stored in the dark.

DTaP-IPV-HepB/Hib (Infanrix-hexa) must be reconstituted by adding the entire contents of the supplied container of the DTaP-IPV-HepB vaccine to the vial containing the Hib pellet. After adding the vaccine to the pellet, the mixture should be shaken until the pellet is completely dissolved. Use the reconstituted vaccine as soon as possible. If storage is necessary, the reconstituted vaccine may be kept for up to eight hours at 21°C.

19.4.4 Dosage and administration

The dose of DTaP-IPV-HepB/Hib, DTaP-IPV, Tdap and Td is 0.5 mL administered by intramuscular injection (see section 2.2.3).

Co-administration with other vaccines

DTaP-IPV-HepB/Hib, DTaP-IPV, Tdap and Td can be administered simultaneously (at separate sites) with other vaccines or IGs.

19.5 Recommended immunisation schedule

Table 19.1: Immunisation schedule for tetanus-containing vaccines (excluding catch-up)

Age	Vaccine	Comment
6 weeks	DTaP-IPV-HepB/Hib	Primary series
3 months	DTaP-IPV-HepB/Hib	Primary series
5 months	DTaP-IPV-HepB/Hib	Primary series
4 years	DTaP-IPV	Booster
11 years	Tdap	Booster
45 years	Td[a]	Booster
65 years	Td[a]	Booster
Pregnant women (recommended from 16 weeks' gestation of every pregnancy, preferably in the second trimester, but at least two weeks before birth; funded when given any time in second or third trimester)	Tdap	Booster[b]

a The Td vaccine is funded at ages 45 and 65 years, but not the administration.

b The Tdap booster during pregnancy is for protection against pertussis (see section 4.1.2).

19.5.1 Usual childhood schedule

A primary course of tetanus vaccine is given as DTaP-IPV-HepB/Hib (Infanrix-hexa) at ages 6 weeks, 3 months and 5 months, followed by a

dose of DTaP-IPV (Infanrix-IPV) at age 4 years (Table 19.1). A booster is given at age 11 years (school year 7), which includes a pertussis component, given as the vaccine Tdap (Boostrix).

If a course of immunisation is late or interrupted for any reason, it may be resumed without repeating prior doses (see Appendix 2).

Alternatives to combination pertussis-containing vaccines

Some parents or guardians may ask about alternatives to pertussis-containing vaccines. The recommended and funded vaccines for children are those described above. There are no diphtheria-only or tetanus-only vaccines available. The Td vaccine contains half the amount of tetanus toxoid and one-fifteenth the amount of diphtheria toxoid compared to the DTaP-containing vaccines. Td was not clinically designed or tested for use to provide the primary vaccine course in children and it is not registered for use in children aged under 5 years. Although there are no safety concerns relating to administration of the vaccine, there is no data on the use of this vaccine for a primary course in children and it is not recommended.

19.5.2 Catch-ups for individuals aged 10 years and older

For adults and children who present with a tetanus-prone wound, boosters are recommended in accordance with the guidelines in the following sections and Table 19.2.

For partially immunised or previously unimmunised individuals aged 10 years and older, a primary immunisation course consists of three doses of a tetanus toxoid-containing vaccine at intervals of not less than four weeks (see Appendix 2). For children aged under 18 years, a booster dose is recommended at least six months after the third dose (which, depending on the age of the child, may be given as the scheduled Tdap vaccine at age 11 years).

Children aged under 18 years may receive Tdap (funded from age 7 to under 18 years); adults aged 18 years and older may receive Td (funded) or Tdap (unfunded). Although Tdap and Td are not approved for use (registered) as a primary course, there are expected to be no safety concerns.

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.[18]

Dose intervals between Td and Tdap

When Tdap is to be given to adolescents or adults to protect infants or other vulnerable individuals from pertussis, no minimum interval between Td and Tdap is required,[19, 20, 21] – unless Tdap is being given as part of a primary immunisation course.

19.5.3 Booster doses for adults

Adults are recommended to have their tetanus immunisation status assessed at ages 45 and 65 years, and either given a booster dose of tetanus toxoid-containing vaccine if more than 10 years has elapsed since the previous dose, or a primary course if there is any doubt about the adequacy of previous tetanus immunisation (uncertain or no history of a prior primary course).

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 ages 45 and 65 years is intended to ensure ongoing protection, and to facilitate delivery by recommending the booster during routine preventive care for adults.

Offer a booster dose of Td for someone travelling overseas if it has been more than 10 years since the last dose (not funded) (see section 5.5.3).

19.5.4 Pregnancy and breastfeeding

Pregnant women should receive a dose of Tdap (funded) from 28 to 38 weeks' gestation. This should be given during each pregnancy[22] to protect the mother against pertussis and so that antibodies can pass to the fetus (see section 4.1.2).

Td vaccine is not routinely recommended for pregnant women but it can be given under certain circumstances, such as when catch-up is needed for an under-immunised woman, or for management of a tetanus-prone

wound[12, 22] (see section 19.5.5). However, Tdap is the preferred vaccine in pregnancy.

Td or Tdap vaccines can be given to breastfeeding women.[12]

19.5.5 Prevention of tetanus following injury

Following injury, it is essential that all wounds be adequately cleaned and devitalised tissue removed. Further treatment depends on the circumstances of each case.

If the injury is considered to be tetanus-prone and there is any doubt about the adequacy of previous tetanus immunisation, the individual must have tetanus immunoglobulin (TIG) and the recommended primary course of three doses of a tetanus toxoid-containing vaccine (Td or Tdap – the latter is not funded for adults aged 18 years and older).

The definition of a tetanus-prone injury is not straightforward, because tetanus can occur after apparently trivial injury, such as from a rose thorn, or with no history of injury. However, there are certain types of wounds likely to favour the growth of tetanus organisms. These include:

- compound fractures
- bite wounds
- deep, penetrating wounds
- wounds containing foreign bodies (especially wood splinters)
- wounds complicated by pyogenic (pus-forming) infections
- wounds with extensive tissue damage (eg, crush injuries, avulsions, contusions or burns)
- any superficial wound obviously contaminated with soil, dust or horse manure (especially if topical disinfection is delayed more than four hours)
- re-implantation of an avulsed tooth – minimal washing and cleaning of the tooth is conducted to increase the likelihood of successful re-implantation.

General measures for the treatment of tetanus-prone wounds

Wounds or injuries should be classified as tetanus-prone or non-tetanus-prone as follows (see Table 19.2):

- non-tetanus-prone wounds – clean, minor wounds that are less than six hours old, non-penetrating and with negligible tissue damage
- tetanus-prone wounds – all wounds that may be contaminated or infected, and are penetrating, more than six hours old and with tissue damage.

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

See also the IMAC factsheet *Guidelines for the management of tetanus-prone wounds* (available for download from: www.immune.org.nz/resources/written-resources).

Table 19.2: Guide to tetanus prophylaxis in wound management

History of tetanus vaccination[a]	Time since last dose	Type of wound	Td or Tdap as appropriate[b,c]	TIG[d]
≥3 doses	<5 years	Tetanus-prone wounds	No	No
≥3 doses	5–10 years	Clean minor wounds	No	No
≥3 doses	5–10 years	Tetanus-prone wounds	Booster dose[e]	No
≥3 doses	>10 years	Tetanus-prone wounds	Booster dose[e]	No
≥3 doses	>10 years	Clean minor wounds	Booster dose[e]	No
<3 doses or uncertain		Clean minor wounds	Complete the course[f]	No
<3 doses or uncertain		Tetanus-prone wounds	Complete the course[f]	Yes

a People who have experienced Arthus-type hypersensitivity reactions (see section 19.7.2) or temperature >39.4°C after a previous dose of a tetanus toxoid-containing preparation should not receive tetanus toxoid-containing preparation more frequently than every 10 years, even if they have a wound that is neither clean nor minor.

b See Appendix 2 for catch-up schedules for previously unimmunised children. DTaP-containing vaccine may be used in children aged under 10 years.

c Td is funded. Tdap may be given to, but is not funded for, individuals aged 18 years and older.

d TIG = tetanus immunoglobulin. The recommended dose is 250 IU given by IM injection as soon as practicable after injury. If more than 24 hours has elapsed, 500 IU is recommended.

e If appropriate, this may count as the age 45 or 65 years booster dose.

f To complete the 3-dose primary immunisation course, give 1 to 3 doses at not less than 4-weekly intervals.

Tetanus immunoglobulin (TIG) availability and storage

TIG is issued in ampoules, each containing 250 IU of human tetanus antitoxin. (Ampoules of 2,000 IU are used for treatment and not for prophylaxis.) These should be protected from light and stored in a refrigerator at +2°C 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 has 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 complete immunoglobulin A (IgA) deficiency. In this situation, specialist help should be sought (see section 4.3).

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

19.5.6 (Re-)vaccination

Tetanus toxoid-containing vaccines are funded for (re-)vaccination of eligible patients, as follows. See also sections 4.2 and 4.3.

DTaP-IPV-HepB/Hib (Infanrix-hexa) and DTaP-IPV (Infanrix-IPV)

An additional four doses (as appropriate) of DTaP-IPV-HepB/Hib (for children aged under 10 years) or DTaP-IPV are funded for (re-)vaccination of patients:

- post-HSCT or chemotherapy
- pre- or post-splenectomy
- pre- or post-solid organ transplant
- undergoing renal dialysis
- with other severely immunosuppressive regimens.

Up to five doses of DTaP-IPV-HepB/Hib (for children aged under 10 years) or DTaP-IPV are funded for children requiring solid organ transplantation.

Tdap (Boostrix)

An additional four doses (as appropriate) of Tdap (Boostrix) are funded for patients:

- post-HSCT or chemotherapy
- pre- or post-splenectomy
- pre- or post-solid organ transplant
- undergoing renal dialysis
- with other severely immunosuppressive regimens.

Td (ADT Booster)

Td is funded for patients following immunosuppression.

19.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

19.6.1 Contraindications

Immunisation with Td, Tdap or another tetanus toxoid-containing vaccine should not be repeated in individuals who have had previous severe hypersensitivity reactions to the vaccine or a vaccine component. Most cases of hypersensitivity have been reported in individuals who have had an excessive number of booster injections outside the guidelines noted above.

19.6.2 Precautions

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.

People who have experienced Arthus-type hypersensitivity reactions (see section 19.7.2) or temperature greater than 39.4°C after a previous dose of a tetanus toxoid-containing preparation should not receive tetanus toxoid-containing preparation more frequently than every 10 years, even if they have a wound that is neither clean nor minor.[23]

GBS within six weeks of a tetanus toxoid-containing vaccine weeks is a precaution to receiving a further dose[24] (see section 19.7.2).

See section 14.6.2 for precautions to pertussis-containing vaccines, including DTaP-IPV-HepB/Hib.

19.7 Expected responses and AEFIs

See also sections 5.7 and 14.7 for expected responses and AEFIs with Td, DTaP-IPV-HepB/Hib, DTaP-IPV and Tdap vaccines.

19.7.1 Expected responses

Tetanus toxoid combination vaccines have not been associated with any safety concerns. Sterile abscesses and persistent nodules at the injection site may develop if the injection is not given deeply enough into the muscle.[25] Mild discomfort or pain at the injection site persisting for up to a few days is common.[12]

Tdap has a safety profile similar to Td and both vaccines are generally well tolerated.[26, 27]

19.7.2 AEFIs

Anaphylaxis was reported at a rate of 1.6 per million doses of Td in the US from 1991 to 1995.

The 1994 US Institute of Medicine 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 four weeks of immunisation.[28]

Severe local reactions (including large injection site swelling, called Arthus reactions, which are presumed to be immune-complex mediated reactions) are hypersensitivity reactions that have been associated with vaccines containing tetanus and diphtheria toxoids. Historical data on multiple doses of Td and tetanus toxoid vaccines indicate that hypersensitivity was associated with higher levels of pre-existing antibody.[7, 29] People who have experienced Arthus-type hypersensitivity reactions or temperature greater than 39.4°C after a previous dose of a tetanus toxoid-containing preparation usually have very high serum tetanus antibody concentrations and should not receive tetanus toxoid-containing preparation more frequently than every 10 years, even if they have a wound that is neither clean nor minor.[23]

No increased risk of GBS has been observed with use of tetanus toxoid-containing vaccines, and therefore a history of GBS is not a contraindication to receiving a tetanus toxoid-containing vaccine. However, out of prudence, it is recommended that having GBS within six weeks of a tetanus toxoid-containing vaccine is a precaution to receiving a further dose.[24]

19.8 Public health measures

All cases of tetanus must be notified immediately on suspicion to the local medical officer of health, who should be provided with as accurate an immunisation history as possible.

See section 19.5.5 'Prevention of tetanus following injury'. See also the 'Tetanus' chapter of the *Communicable Disease Control Manual 2012*.[30]

19.9 Variations from the vaccine data sheets

Td (ADT Booster) vaccine is not approved for use (registered) for primary immunisation. However, adults aged over 18 years may receive Td (funded) for catch-up of the primary schedule (see Appendix 2).

See section 14.9 for variations from the DTaP-IPV-HepB/Hib (Infanrix-hexa), DTaP-IPV (Infanrix-IPV) and Tdap (Boostrix) data sheets.

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