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.	
Incidence and burden of disease	Older individuals, usually women, who are less likely to have received a primary series of tetanus vaccine; and in unvaccinated children.	
Funded vaccines	DTaP-IPV-HepB/Hib (Infanrix-hexa). DTaP-IPV (Infanrix-IPV). Tdap (Boostrix).	
Dose, presentation, route	Intramuscular injection. 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: pre-filled syringe.	
Funded vaccine indications and schedule	During each pregnancy (recommended from 16 weeks' gestation) for pertussis protection	Tdap
	6 weeks, 3 months and 5 months	DTaP-IPV-HepB/Hib
	4 years	DTaP-IPV
	11 years	Tdap
	45 years (catch-up, if individual has not received 4 previous tetanus doses)	Tdap
	65 years	Tdap
	Parents or primary caregivers of infants admitted to neonatal intensive or specialist baby care units for more than 3 days and whose mothers had not received Tdap at least 14 days prior to birth for pertussis protection	Tdap
	For vaccination of previously unimmunised or partially immunised patients	DTaP-IPV-HepB/Hib, DTaP-IPV or Tdap
	For (re)vaccination of eligible patients	
	For boosting of patients with tetanus-prone wounds	Tdap
Post-exposure prophylaxis	If an injury is 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. (see section 19.5.6).	

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

The clinical diagnosis of tetanus 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 and antenatal screening and immunisation programmes are disrupted.[1]

A person with tetanus is not infectious to others, and vaccination provides individual protection only, with no herd immunity. Protective immunity can only be conferred by vaccination with tetanus toxoid and not through exposure to the natural pathogen or suffering tetanus. See section 19.5.2.

19.3 Epidemiology

19.3.1 Global burden of disease

Tetanus infection continues to occur globally but is rare in high income countries. The estimated total number of tetanus cases (including neonatal cases) globally fell from more than 110,000 in 1980 to 15,000 in 2018.[2] The highest numbers of cases were in India, Uganda and other sub-Saharan African countries.[2] Tetanus in males in some sub-Saharan countries has been associated with voluntary circumcision aimed at reducing the risk of HIV infection.[3]

There were 1,803 neonatal tetanus cases reported worldwide in 2018, two-thirds of which were in Africa, and all the cases of tetanus reported in Afghanistan, Chad and Yemen were neonatal.[4] Maternal and neonatal tetanus is described as a silent killer, since many cases are unreported.[5] 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, this goal has not yet been reached in 14 countries.

The incidence of tetanus reflects the effectiveness of the local immunisation programme, with low incidence in regions with high immunisation coverage. Global immunisation coverage for DTP is around 86 percent and 129 countries have reached at least 90 percent coverage for three doses of the DTP vaccine. In 2018, an estimated 19.4 million children aged under 1 year did not receive DTP. Of these, 13.5 million lack access to vaccination service and live in the poorest most fragile or conflicted states, and 60 percent live in 10 countries: Nigeria, India, Pakistan, Indonesia, Ethiopia, Philippines, Brazil, Angola and Vietnam.[6]

19.3.2 New Zealand epidemiology

No cases of tetanus were notified during 2017-2019. There were 33 tetanus cases notified between 1997 and 2017.[7] 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 aged 70 years or older died (one was not vaccinated and the vaccination status of the other was unknown).[8]

For further information, see to the ESR's notifiable disease reports (available at **surv.esr.cri.nz/surveillance/surveillance.php**).

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 lower adult dose of diphtheria and pertussis 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).[9]

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).[9] Of the 12 cases, only four had completed primary immunisation. Immunised cases have less severe disease and a lower case-fatality.

Duration of protection

Serological studies show that the three-dose primary series of a tetanus vaccine given in infancy plus a booster during the second year of life, provide 3–5 years of protection against tetanus. WHO recommends six doses of tetanus-containing vaccine before age 18 years to induce immunity that lasts for much of adulthood.[1] It is recommended that adults receive at least one booster dose, particularly where fewer than six doses have been given in childhood.

Over the last two decades, there has been a significant increase in the proportion of the adult population with protective antitoxin levels by mid-life.[10] One mathematical model estimated protection to last for at least 30 years in most adults after vaccination.[11] But as age increases, by every 10 years there is an associated 50 percent reduction in antitoxin levels.[12, 13] Even if documented as fully immunised, older adults are likely to have had fewer tetanus doses in their lifetime than adults younger than 30 years.[14] Protection against the effects of tetanus toxin may be insufficient in adults who have not been adequately primed, and those aged over 65 years are at particularly increased risk of tetanus.[10]

A single dose of tetanus toxoid produces a rapid anamnestic response.[15, 16, 17, 18] To ensure that there is adequate antitoxin to neutralise tetanus toxin in the case of a tetanus-prone injury, a booster dose is advised if it has been longer than 10 years since the last tetanus vaccine dose. The extent of wound contamination and delays in seeking medical assistance can result in high levels of tetanus toxin being released. (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 (2nd edition)* (available at **www.health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017**).

Store at +2°C to +8°C. Do not freeze. DTaP-IPV-HepB/Hib and Tdap 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 or Tdap is 0.5 mL administered by intramuscular injection (see section 2.2.3).

Co-administration with other vaccines

DTaP-IPV-HepB/Hib, DTaP-IPV and Tdap 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
Pregnant women: recommended from 16 weeks' gestation of every pregnancy, preferably in the second trimester (funded when given any time in second or third trimester)	Tdap	Booster for mother Passive immunity for infant
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 (individuals who have not received 4 tetanus vaccinations in their lifetime)	Tdap	Booster
65 years	Tdap	Booster

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 further booster is given at age 11 years (school year 7) as 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).

19.5.2 Catch-up immunisation 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.

See Appendix 2 for detailed catch-up immunisation information.

Tdap may be used for primary immunisation of children aged 7 to under 18 years. Tdap can be given for vaccination of previously unimmunised or partially immunised adult patients.

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.[19]

Dose intervals between Td and Tdap

When Tdap is to be given to adolescents or adults, no minimum interval between Td and Tdap is required,[20, 21, 22] unless Tdap is being given as part of a primary immunisation course.

19.5.3 Booster doses for adolescents and adults

Adults are recommended to have their tetanus immunisation status assessed at ages 45 and 65 years, and given either 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.

Tdap is recommended and funded:

- as a booster dose to all adolescents at school year 7 or age 11 years
- as a single dose for vaccination of individuals aged 65 years old
- as a single dose for catch-up vaccination of individuals aged 45 years old who have not had four previous tetanus doses.

These age-specific recommendations may facilitate the linkage of adult immunisation to the delivery of other preventive health measures. Offer a booster dose of Tdap for someone travelling overseas if it has been more than 10 years since the last dose (unfunded) (see section 5.5.3).

The administration of tetanus and diphtheria (Tdap) boosters given at ages 45 and 65 years, is also funded.

19.5.4 Pregnancy and breastfeeding

Pregnant women should receive a dose of Tdap in every pregnancy so that antibodies can pass to the fetus to provide pertussis protection from birth (funded when given any time in second or third trimester). It is recommended to be given from 16 weeks' gestation of every pregnancy, preferably in the second trimester to protect both the mother and her infant from pertussis (see section 14.5.2).[23]

Tdap vaccine may also be given to pregnant women when catch-up is needed for an under-immunised woman, or for management of a tetanus-prone wound (see section 19.5.5).[23, 24]

Tdap can be given to breastfeeding women.[24]

19.5.5 (Re)vaccination

Tetanus toxoid-containing vaccines are funded for (re)vaccination of eligible patients as follows, including prior to planned immunosuppression regimes or following immunosuppression. 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
- prior to planned or following 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
- prior to planned or following other severely immunosuppressive regimens.

A single dose of Tdap is funded for parents or primary caregivers of infants admitted to a neonatal intensive care unit or special care baby unit for more than three days and whose mothers had not received Tdap at least 14 days prior to baby's birth.

19.5.6 Prevention of tetanus following injury

Following injury, it is essential that all wounds be adequately cleaned and devitalised tissue removed to reduce the level of contamination and tetanus toxin release. 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 commence or complete the recommended primary course of three doses of a tetanus toxoid-containing vaccine (depending on age and other antigens required: DTaP-containing vaccine or Tdap).

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)
- wounds associated with vascular insufficiency (eg, leg or foot ulcers in the elderly)
- 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 – in this case, 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 at **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	Tdap[b]	TIG[c]
≥3 doses	<5 years	Tetanus-prone wounds	No	No
≥3 doses	>5 years	Clean minor wounds	No	No
≥3 doses	>5 years	Tetanus-prone wounds	Booster dose[d]	No
≥3 doses	>10 years	Clean minor wounds	Booster dose[d]	No
<3 doses or uncertain		Clean minor wounds	Complete the course[e]	No
<3 doses or uncertain		Tetanus-prone wounds	Complete the course[e]	Yes

a. People who have experienced Arthus-type hypersensitivity reactions (see 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. 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.

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

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

Tetanus immunoglobulin availability and storage

Tetanus immunoglobulin (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.

19.6 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 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) 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. Arthus-type reactions are rare in children and did not occur during the clinical trial of Tdap vaccines.[25]

Guillain–Barré Syndrome within six weeks of a tetanus toxoid-containing vaccine weeks is a precaution to receiving a further dose (see section 19.7.2).[22]

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

19.7 Potential responses and AEFIs

See also sections 5.7 and 14.7 for potential responses and AEFIs to DTaP-IPV-HepB/Hib, DTaP-IPV and Tdap vaccines.

19.7.1 Potential 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.[26] Mild discomfort or pain at the injection site persisting for up to a few days is common.[24]

Tdap has a safety profile similar to Td and is generally well tolerated.[27, 28]

19.7.2 AEFIs

The 1994 US Institute of Medicine review of adverse events from tetanus vaccine concluded that the evidence supported a link with brachial plexus neuropathy (brachial neuritis) at a rate of 0.5–1 per 100,000 doses within four weeks of immunisation.[29] Occurrence of brachial neuritis following vaccination does not preclude the future use of a tetanus-toxoid containing vaccine in the same person.[22]

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 older tetanus and diphtheria toxoid-containing vaccines. Historical data on multiple doses of Td and tetanus toxoid vaccines indicate that hypersensitivity was associated with very high levels of pre-existing antibody.[9, 30]

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.[9, 30]

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 19.5.6 'Prevention of tetanus following injury'. See also the 'Tetanus' chapter of the *Communicable Disease Control Manual* (available at **www.health.govt.nz/publication/communicable-disease-control-manual-2012**).

19.9 Variations from the vaccine data sheets

Tdap vaccine is not approved for use (registered) for primary immunisation. However, adults aged over 18 years may receive Tdap (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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