

3.21 TETANUS

Bacteriology

Tetanus is caused by *Clostridium tetani*, a motile, non-capsulated, Gram-positive rod that forms endospores. Spores of the bacillus are found in manured soil and can enter wounds. Once in a wound site, the bacillus can grow anaerobically. *C. tetani* produces a potent protein toxin which has 2 components, tetanospasmin (a neurotoxin) and tetanolysin (a haemolysin).

Clinical features

Tetanus is an acute, often fatal, disease caused by the toxin produced by *C. tetani*. The neurotoxin acts on the central nervous system to cause muscle rigidity with painful spasms. The disease usually occurs after an incubation period of 3 to 21 days (range 1 day to several months), with a median time of onset after injury of 10 days. Generally, a shorter incubation period is associated with a more heavily contaminated wound, more severe disease and a worse prognosis. Generalised tetanus, the most common form of the disease, is characterised by increased muscle tone and generalised spasms. Early symptoms and signs include increased tone in the masseter muscles (trismus, or lockjaw), dysphagia, stiffness or pain in the neck, shoulder and back muscles. Some patients develop paroxysmal, violent, painful, generalised muscle spasms. A constant threat during generalised spasms is reduced ventilation or apnoea or laryngospasm. The patient may be febrile, although many have no fever; mental state is unimpaired. Sudden cardiac arrest sometimes occurs, but its basis is unknown. Other complications include pneumonia, fractures, muscle rupture, deep vein thrombophlebitis, pulmonary emboli, decubitus ulcers and rhabdomyolysis. Death results from respiratory failure, hypertension, hypotension or cardiac arrhythmia.

Tetanus is rare in people who have received 5 doses of a tetanus-containing vaccine (1 in 90 cases in the United Kingdom from 1984–2000).¹ However, individual cases have been reported^{2,3} and clinicians should consider tetanus when there are appropriate symptoms and signs, irrespective of the person's vaccination record. A high level of diagnostic awareness of tetanus is particularly important in the elderly in industrialised countries, including Australia, as most deaths occur in people over 70 years of age, especially women, and may be associated with apparently minor injury.^{1,4}

Neonatal tetanus usually occurs as the generalised form and is usually fatal if left untreated. It develops in children born to inadequately immunised mothers, frequently after unsterile treatment of the umbilical cord stump. Its onset generally occurs during the first 2 weeks of life. Poor feeding, rigidity, and spasms are typical features of neonatal tetanus.

Epidemiology

In Australia, tetanus is rare, occurring primarily in older adults who have never been vaccinated or were vaccinated in the remote past. There were 18 notified cases of tetanus during 2001–2005, but 120 hospitalisations (July 2000–June 2005) where tetanus was the principal diagnosis.^{4,5} This discrepancy suggests under-notification. During 2001–2005, there were 2 deaths from tetanus.^{4,5} The case-fatality rate in Australia is about 3%. Neonatal tetanus is a frequent cause of infant mortality in parts of Asia, Africa and Latin America.

Effective protection against tetanus can be provided only by active immunisation. Tetanus vaccine was introduced progressively into the childhood vaccination schedule after World War II. The effectiveness of the vaccine was demonstrated in that war; all Australian servicemen were vaccinated against tetanus and none contracted the disease. As tetanus can follow apparently trivial, even unnoticed wounds, active immunisation is the only certain protection.¹ A completed course of vaccination provides protection for many years.

Vaccines

The acronym DTPa, using capital letters, signifies child formulations of diphtheria, tetanus and acellular pertussis-containing vaccines. The acronym dTpa is used for adolescent/adult formulations which contain substantially lesser amounts of diphtheria toxoid and pertussis antigens (see formulations).

Formulations for children aged <8 years

- **Infanrix hexa** – GlaxoSmithKline (DTPa-hepB-IPV-Hib; diphtheria-tetanus-acellular pertussis-hepatitis B-inactivated poliomyelitis vaccine-*Haemophilus influenzae* type b (Hib)). The vaccine consists of *both* a 0.5 mL pre-filled syringe containing 30 IU diphtheria toxoid, 40 IU tetanus toxoid, 25 µg pertussis toxoid (PT), 25 µg filamentous haemagglutinin (FHA), 8 µg pertactin (PRN), 10 µg recombinant HBsAg, 40 D-antigen units inactivated polioviruses type 1 (Mahoney), 8 D-antigen units type 2 (MEF-1) and 32 D-antigen units type 3 (Saukett) adsorbed onto aluminium hydroxide/phosphate; phenoxyethanol as preservative; traces of formaldehyde, polymyxin and neomycin *and* a vial containing a lyophilised pellet of 10 µg purified Hib capsular polysaccharide (PRP) conjugated to 20–40 µg tetanus toxoid. The vaccine *must be reconstituted* by adding the entire contents of the syringe to the vial and shaking until the pellet is completely dissolved. May also contain yeast proteins.

- **Infanrix-IPV** – GlaxoSmithKline (DTPa-IPV; diphtheria-tetanus-acellular pertussis-inactivated poliomyelitis vaccine). Each 0.5 mL pre-filled syringe contains 30 IU diphtheria toxoid, 40 IU tetanus toxoid, 25 µg PT, 25 µg FHA, 8 µg PRN, 40 D-antigen units inactivated polioviruses type 1 (Mahoney), 8 D-antigen units type 2 (MEF-1) and 32 D-antigen units type 3 (Saukett) adsorbed onto aluminium hydroxide; phenoxyethanol as preservative; traces of formaldehyde, polymyxin and neomycin.
- **Infanrix Penta** – GlaxoSmithKline (DTPa-hepB-IPV; diphtheria-tetanus-acellular pertussis-hepatitis B-inactivated poliomyelitis vaccine). Each 0.5 mL pre-filled syringe contains 30 IU diphtheria toxoid, 40 IU tetanus toxoid, 25 µg PT, 25 µg FHA, 8 µg PRN, 10 µg recombinant HBsAg, 40 D-antigen units inactivated polioviruses type 1 (Mahoney), 8 D-antigen units type 2 (MEF-1) and 32 D-antigen units type 3 (Saukett) adsorbed onto aluminium hydroxide/phosphate; phenoxyethanol as preservative; traces of formaldehyde, polymyxin and neomycin. May also contain yeast proteins.

Formulations for people aged ≥8 years

Adsorbed diphtheria-tetanus vaccine

- **ADT Booster** – Statens Serum Institut/CSL Biotherapies (dT; diphtheria-tetanus, adult formulation). Each 0.5 mL pre-filled syringe or monodose vial contains ≥2 IU diphtheria toxoid and ≥20 IU tetanus toxoid adsorbed onto 0.5 mg aluminium hydroxide.

Combination vaccines

- **Adacel** – Sanofi Pasteur Pty Ltd (dTpa; diphtheria-tetanus-acellular pertussis). Each 0.5 mL monodose vial contains ≥2 IU diphtheria toxoid, ≥20 IU tetanus toxoid, 2.5 µg PT, 5 µg FHA, 3 µg PRN, 5 µg pertussis fimbriae (FIM) 2+3; 1.5 mg aluminium phosphate; phenoxyethanol as preservative; traces of formaldehyde.
- **Adacel Polio** – Sanofi Pasteur Pty Ltd (dTpa; diphtheria-tetanus-acellular pertussis-inactivated poliomyelitis vaccine). Each 0.5 mL monodose vial contains ≥2 IU diphtheria toxoid, ≥20 IU tetanus toxoid, 2.5 µg PT, 5 µg FHA, 3 µg PRN, 5 µg FIM 2+3, 40 D-antigen units inactivated polioviruses type 1 (Mahoney), 8 D-antigen units type 2 (MEF-1) and 32 D-antigen units type 3 (Saukett); 1.5 mg aluminium phosphate; phenoxyethanol as preservative; traces of formaldehyde, polymyxin, neomycin and streptomycin.

- **Boostrix** – GlaxoSmithKline (dTpa; diphtheria-tetanus-acellular pertussis). Each 0.5 mL monodose vial or pre-filled syringe contains ≥ 2 IU diphtheria toxoid, ≥ 20 IU tetanus toxoid, 8 μg PT, 8 μg FHA, 2.5 μg PRN, adsorbed onto 0.5 mg aluminium hydroxide/phosphate; 2.5 mg phenoxyethanol as preservative. May contain traces of formaldehyde.
- **Boostrix-IPV** – GlaxoSmithKline (dTpa-IPV; diphtheria-tetanus-acellular pertussis-inactivated poliomyelitis vaccine). Each 0.5 mL pre-filled syringe contains ≥ 2 IU diphtheria toxoid, ≥ 20 IU tetanus toxoid, 8 μg PT, 8 μg FHA, 2.5 μg PRN, 40 D-antigen units inactivated polioviruses type 1 (Mahoney), 8 D-antigen units type 2 (MEF-1) and 32 D-antigen units type 3 (Saukett) adsorbed onto aluminium hydroxide/phosphate; traces of formaldehyde, polymyxin and neomycin.

Tetanus vaccination stimulates the production of antitoxin, which protects against the toxin produced by the organism. The immunogen is prepared by treating a cell-free preparation of toxin with formaldehyde, thereby converting it into the innocuous tetanus toxoid. Tetanus toxoid is usually adsorbed onto an adjuvant, either aluminium phosphate or aluminium hydroxide, to increase its immunogenicity. Antigens from *Bordetella pertussis*, in combination vaccines, also act as an effective adjuvant.

Complete immunisation (5 doses) induces protective levels of antitoxin lasting throughout childhood but, by middle age, about 50% of vaccinees have low or undetectable levels.⁶⁻⁸ A single dose of tetanus toxoid produces a rapid anamnestic response in such vaccinees.⁹⁻¹¹

Tetanus toxoid is available in combination with other antigens. Production of the previously available tetanus toxoid vaccine was discontinued by the manufacturer in February 2006. Production of the previous DT (CDT vaccine), registered for use in children <8 years of age, ceased in June 2005. ADT Booster can be used for the booster dose of dT in people aged ≥ 8 years or, if necessary, for the primary dT course (see 'Variations from product information' below).

Transport, storage and handling

Transport according to *National Vaccine Storage Guidelines: Strive for 5*.¹² Store at +2°C to +8°C. Protect from light. Do not freeze.

Dosage and administration

The dose of tetanus-containing vaccine is 0.5mL by IM injection.

Do not mix DTPa-containing vaccines, dTpa or dT vaccine with any other vaccine in the same syringe, unless specifically registered for use in this way.

Recommendations

(i) Vaccination in childhood

Vaccination against tetanus is part of the National Immunisation Program (NIP) schedule, with tetanus toxoid being given in combination with diphtheria toxoid and acellular pertussis as DTPa vaccine. The recommended primary course of vaccination is at 2, 4 and 6 months of age. A booster dose of DTPa is given at 4 years of age. Immunity to tetanus will not be compromised before the booster dose, as the serological response to the primary course of vaccination is usually sufficient for those years. A second booster, using the adolescent/adult formulation, dTpa, at 12–17 years of age, is essential for maintaining immunity to tetanus in adults. By the age of 17 years, young adults should have received 5 doses of a tetanus toxoid-containing vaccine, and may have received an extra dose if they have experienced a tetanus-prone wound during childhood.

For details on the management of children who have missed doses in the NIP schedule, see Section 1.3.5, *Catch-up*.

(ii) Vaccination of adults

Booster vaccination

Routine 10-yearly booster doses in adults who have previously received 5 doses of a tetanus-containing vaccine have *not* been recommended in Australia since 2000. All adults who reach the age of 50 years and have not received a booster dose of a tetanus-containing vaccine in the previous 10 years should be given dT or dTpa vaccine. This stimulates further production of circulating tetanus antibodies at an age when waning of diphtheria and tetanus immunity is commencing in the Australian population.⁶ The adolescent/adult formulation dTpa is preferred, if not given previously, as it provides additional protection against pertussis (see Chapter 3.14, *Pertussis*).

Primary vaccination

Where an adult has not received a primary course of tetanus toxoid previously, 3 doses of dT should be given, at minimum intervals of 4 weeks, followed by booster doses at 10 and 20 years after the primary course. Give the first of these doses as dTpa, to provide boosting to natural immunity from exposure to pertussis, which is almost universal in unvaccinated adults. In the event that dT vaccine is *not* available, dTpa can be used for all primary doses. However, this is not recommended routinely because there are no data on the safety, immunogenicity or efficacy of dTpa in multiple doses for primary vaccination.

Tetanus-prone wounds

Adults who have sustained injuries deemed to be tetanus prone should receive a booster dose of dT, if more than 5 years have elapsed since the last dose. In the event that dT vaccine is *not* available, dTpa can be used (see Table 3.21.1 below).

(iii) Other people at special risk

Adults who were born in countries without adequate vaccination programs may never have received primary vaccination against tetanus. Older adults may have inadequate antitoxin levels, due to incomplete primary vaccination against tetanus. Injecting drug users are at risk of tetanus, particularly if skin ‘popping’ is practised.¹³

Travellers to countries where health services are difficult to access should be adequately protected against tetanus before departure. They should receive a booster dose of dT, if more than 10 years have elapsed since the last dose, or dTpa if not given previously.

Tetanus-prone wounds

In the event of a tetanus-prone injury (defined below), a booster dose of vaccine should be given if more than 5 years have elapsed since the last dose. If there is any doubt about the adequacy of previous tetanus immunisation, tetanus immunoglobulin (see below) should be given as well as tetanus toxoid (see Table 3.21.1). In children <8 years of age, this dose of vaccine should be given as DTPa or a DTPa-combination vaccine, consistent with the child’s vaccination history and the NIP schedule. For details on the management of children who have missed doses in the NIP schedule, see Section 1.3.5, *Catch-up*.

The definition of a tetanus-prone injury is not straightforward, as tetanus may 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 infections, wounds with extensive tissue damage (eg. contusions or burns) and any superficial wound obviously contaminated with soil, dust or horse manure (especially if topical disinfection is delayed more than 4 hours). Reimplantation of an avulsed tooth is also a tetanus-prone event, as minimal washing and cleaning of the tooth is conducted to increase the likelihood of successful reimplantation.

General measures for treatment of tetanus-prone wounds¹⁴⁻¹⁹

Table 3.21.1: Guide to tetanus prophylaxis in wound management

History of tetanus vaccination	Time since last dose	Type of wound	DTPa, DTPa-combinations, dT, dTpa, as appropriate	Tetanus immunoglobulin* (TIG)
≥3 doses	<5 years	All wounds	NO	NO
≥3 doses	5–10 years	Clean minor wounds	NO	NO
≥3 doses	5–10 years	All other wounds	YES	NO
≥3 doses	>10 years	All wounds	YES	NO
<3 doses or uncertain [†]		Clean minor wounds	YES	NO
<3 doses or uncertain [†]		All other wounds	YES	YES

* The recommended dose for TIG is 250 IU, given by IM injection using a 21 gauge needle, as soon as practicable after the injury. If more than 24 hours has elapsed, 500 IU should be given.

† Individuals who have no documented history of a primary vaccination course (3 doses) with a tetanus toxoid-containing vaccine should receive all missing doses. See Section 1.3.5, *Catch-up*.

As an alternative to dT vaccine after a tetanus-prone wound, adults can receive a single dose of dTpa vaccine to provide additional protection against pertussis (providing they have not received a dose of dTpa previously).²⁰

Whatever the immune status of an individual with a tetanus-prone wound, local disinfection and, where appropriate, surgical treatment of tetanus-prone wounds, must never be omitted. The use of antibiotics (such as penicillin or metronidazole) for preventing infection is a matter for clinical judgement.

The recommended use of booster tetanus vaccines and the use of human tetanus immunoglobulin are set out in Table 3.21.1. These should be administered as soon as possible after the injury.

Tetanus immunoglobulin

Tetanus immunoglobulin (human) for intramuscular use

- **Tetanus Immunoglobulin-VF (TIG)** – CSL Bioplasma. 160 mg/mL solution of immunoglobulin from selected human plasma with high concentration of antibodies to tetanus toxin, 250 IU.

- (i) TIG should be used for passive protection of individuals who have sustained a tetanus-prone wound, where the person has not received 3 or more doses of a tetanus toxoid-containing vaccine or where there is doubt about their tetanus vaccination status. TIG provides immediate protection, for a period of 3 to 4 weeks.
- (ii) The recommended dose for TIG is 250 IU by IM injection, to be given as soon as practicable after the injury. If more than 24 hours have elapsed, 500 IU should be given. A tetanus toxoid-containing vaccine should be given at the same time in the opposite limb with a separate syringe, and arrangements should be made to complete the full course of tetanus toxoid-containing vaccinations.
- (iii) Because of its viscosity, TIG should be given to adults using a 21 gauge needle. For children, it can be given slowly, using a 23 gauge needle.
- (iv) For wounds not categorised as tetanus-prone, such as clean cuts that have been treated appropriately, TIG is unnecessary.

Tetanus immunoglobulin (human) for intravenous use

- **Tetanus Immunoglobulin-VF** (human, for intravenous use) – CSL Bioplasma. 60 mg/mL solution of immunoglobulin fraction of selected human plasma with high concentration of antibodies to tetanus toxin, 4000 IU.

This product is used in the management of clinical tetanus. The recommended dose is 4000 IU given by slow intravenous infusion. Detailed protocols for administration of this product and management of adverse events should be consulted if its use is contemplated.

Contraindications

The only absolute contraindications to tetanus vaccine are:

- anaphylaxis following a previous dose of the vaccine, or
- anaphylaxis following any vaccine component.

If an individual has a tetanus-prone wound and has previously had a severe adverse event following tetanus vaccination, alternative measures, including the use of human tetanus immunoglobulin, can be considered.

Precautions

In previously vaccinated people, administration of more than 1 dose of a tetanus-containing vaccine in a 5-year period may provoke adverse events.

Adverse events

Mild discomfort or pain at the injection site persisting for up to a few days is common. Uncommon general adverse events following dT vaccine include headache, lethargy, malaise, myalgia and fever. Anaphylaxis, urticaria and peripheral neuropathy very rarely occur (brachial neuritis occurs in 0.001% of

cases). For specific adverse events following combination vaccines containing both tetanus and pertussis antigens, see Chapter 3.14, *Pertussis*.

Use in pregnancy

Refer to Chapter 2.3, *Groups with special vaccination requirements*, Table 2.3.1 *Vaccinations in pregnancy*.

Variations from product information

The product information for both Infanrix hexa and Infanrix Penta states that these vaccines may be given as a booster dose at 18 months of age. NHMRC recommends that a booster dose of DTPa (or DTPa-containing vaccines) is not necessary at 18 months of age. However, DTPa-containing vaccine may be used for catch-up of the primary schedule in children <8 years of age.

The product information for Infanrix-IPV states that this vaccine may be used as a booster dose for children ≤6 years of age who have previously been vaccinated against diphtheria, tetanus, pertussis and poliomyelitis. NHMRC recommends that booster doses of DTPa and IPV be given at 4 years of age; however, this product may be used for catch-up of the primary schedule or as a booster in children <8 years of age.

The product information for ADT Booster states that this vaccine is indicated for a booster dose only in children aged ≥5 years and adults who have previously received at least 3 doses of diphtheria and tetanus vaccines. NHMRC recommends that, where a dT vaccine is required for any person ≥8 years of age, ADT Booster can be used, including for primary immunisation against diphtheria and tetanus.

The product information for adolescent/adult formulations of dTpa-containing vaccines states that these vaccines are indicated for booster doses only. NHMRC recommends that, where dT is unavailable for the primary course, dTpa can be used.

The product information for Adacel and Boostrix (adolescent/adult formulations of dTpa) states that these vaccines are recommended for use in those aged >10 years. However, NHMRC recommends that they may be used in people aged ≥8 years. The product information also states that dTpa should not be given within 5 years of a tetanus toxoid-containing vaccine. However, NHMRC recommends that dTpa vaccines can be administered at any time following receipt of a diphtheria and tetanus toxoid-containing vaccine.

References

Full reference list available on the electronic *Handbook* or website <http://immunise.health.gov.au>.