

# 30

## Tetanus

NOTIFIABLE

### The disease

Tetanus is an acute disease caused by the action of tetanus toxin, released following infection by the bacterium *Clostridium tetani*. Tetanus spores are present in soil or manure and may be introduced into the body through a puncture wound, burn or scratch – which may go unnoticed. Neonatal tetanus is due to infection of the baby's umbilical stump. The bacteria grow anaerobically at the site of the injury and have an incubation period of between four and 21 days (most commonly about ten days).

The disease is characterised by generalised rigidity and spasms of skeletal muscles. The muscle stiffness usually involves the jaw (lockjaw) and neck and then becomes generalised. The case–fatality ratio ranges from 10 to 90%; it is highest in infants and the elderly. It varies inversely with the length of the incubation period and the availability of intensive care.

Tetanus can never be eradicated because the spores are commonly present in the environment, including soil. Tetanus is not spread from person to person.

### History and epidemiology of the disease

Tetanus immunisation was first provided in the UK to the Armed Forces in 1938. From the mid-1950s it was introduced in some localities as part of the primary immunisation of infants, then nationally in 1961. The disease had almost disappeared in children under 15 years of age by the 1970s (Galbraith *et al.*, 1981). In 1970, it was recommended that people with tetanus-prone wounds should routinely be offered passive immunisation and complete a primary immunisation course.

Between 1984 and 2004, there were 198 cases of tetanus (combined data from notifications, deaths and laboratory reports) in England and Wales (Rushdy *et al.*, 2003). Seventy-four per cent occurred in individuals aged 45 years or over, and 16% were in individuals aged from 25 to 44 years. The highest incidence of tetanus was in adults over 65 years of age, with no cases of tetanus reported in infants or children under five years of age. Three cases were notified in Northern Ireland between 1984 and 2002.

Twenty cases of tetanus were reported in injecting drug users (IDUs) between July 2003 and February 2004 (Health Protection Agency (HPA), 2004). Seven

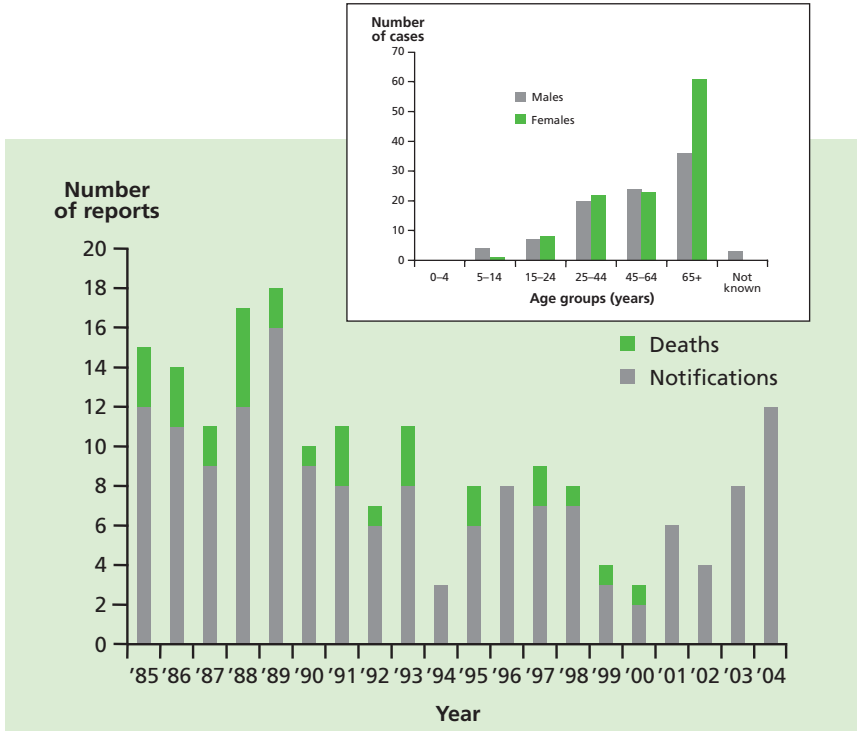


Figure 30.1 Tetanus cases and deaths in England and Wales (1984–2004)

were closely clustered in time and possibly caused by a contaminated batch of illicit drugs (HPA, 2003). Tetanus in IDUs had previously been reported rarely in the UK, in contrast to the US, where IDUs accounted for 15 to 18% of cases reported between 1995 and 2000 (Centers for Disease Control and Prevention (CDC), 2003).

Neonatal tetanus is an important cause of death in many countries in Asia and Africa due to infection of the baby’s umbilical stump. Worldwide elimination of neonatal tetanus by 1995 was one of the targets of the World Health Organization (WHO), and the number of countries in which neonatal tetanus occurs is progressively decreasing. Turkey was the only country in the WHO European Region still reporting cases, with 32 cases in 2002 ([www.nt.who.int/immunization\\_monitoring/en/globalsummary/countryprofilelect.cfm](http://www.nt.who.int/immunization_monitoring/en/globalsummary/countryprofilelect.cfm)).

## The tetanus vaccination

The vaccine is made from a cell-free purified toxin extracted from a strain of *C. tetani*. This is treated with formaldehyde that converts it into tetanus toxoid. This is adsorbed onto an adjuvant, either aluminium phosphate or aluminium hydroxide, to improve its immunogenicity.

Tetanus vaccines contain more than 20IU of tetanus toxoid.

The tetanus vaccine is only given as part of combined products:

- diphtheria/tetanus/acellular pertussis/inactivated polio vaccine/*Haemophilus influenzae* type b (DTaP/IPV/Hib)
- diphtheria/tetanus/acellular pertussis/inactivated polio vaccine (DTaP/IPV or dTaP/IPV)
- tetanus/diphtheria/inactivated polio vaccine (Td/IPV).

The above vaccines are thiomersal-free. They are inactivated, do not contain live organisms and cannot cause the diseases against which they protect.

Td/IPV vaccine should be used where protection is required against tetanus, diphtheria or polio in order to provide comprehensive, long-term protection against all three diseases.

### Storage

Vaccines should be stored in the original packaging at +2°C to +8°C and protected from light. All vaccines are sensitive to some extent to heat and cold. Heat speeds up the decline in potency of most vaccines, thus reducing their shelf life. Effectiveness cannot be guaranteed for vaccines unless they have been stored at the correct temperature. Freezing may cause increased reactivity and loss of potency for some vaccines. It can also cause hairline cracks in the container, leading to contamination of the contents.

### Presentation

Tetanus vaccine should only be used as part of combined products. It is supplied as a cloudy white suspension either in a single dose ampoule or in a pre-filled syringe. The suspension may sediment during storage and should be shaken to distribute the suspension uniformly before administration.

### Administration

Vaccines are routinely given intramuscularly into the upper arm or anterolateral thigh. This is to reduce the risk of localised reactions, which are more common when vaccines are given subcutaneously (Mark *et al.*, 1999; Diggle and Deeks, 2000; Zuckerman, 2000). However, for individuals with a bleeding disorder,

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vaccines should be given by deep subcutaneous injection to reduce the risk of bleeding.

Tetanus-containing vaccines can be given at the same time as other vaccines such as MMR, MenC and hepatitis B. The vaccines should be given at a separate site, preferably in a different limb. If given in the same limb, they should be given at least 2.5cm apart (American Academy of Pediatrics, 2003). The site at which each vaccine was given should be noted in the child's records.

### Dosage and schedule

- First dose of 0.5ml of a tetanus-containing vaccine.
- Second dose of 0.5ml, one month after the first dose.
- Third dose of 0.5ml, one month after the second dose.
- Fourth and fifth doses of 0.5ml should be given at the recommended intervals (see below).

### Disposal

Equipment used for vaccination, including used vials or ampoules, should be disposed of at the end of a session by sealing in a proper, puncture-resistant 'sharps' box (UN-approved, BS 7320).

## Recommendations for the use of the vaccine

The objective of the immunisation programme is to provide a minimum of five doses of tetanus-containing vaccine at appropriate intervals for all individuals. In most circumstances, a total of five doses of vaccine at the appropriate intervals are considered to give satisfactory long-term protection.

To fulfil this objective, the appropriate vaccine for each age group is determined also by the need to protect individuals against diphtheria, pertussis, Hib and polio.

### Primary immunisation

#### Infants and children under ten years of age

The primary course of tetanus vaccination consists of three doses of a tetanus-containing vaccine with an interval of one month between each dose. DTaP/IPV/Hib is recommended to be given at two, three and four months of age but can be given at any stage from two months up to ten years of age. If the primary course is interrupted it should be resumed but not repeated, allowing an interval of one month between the remaining doses.

## Children aged ten years or over, and adults

The primary course of tetanus vaccination consists of three doses of a tetanus-containing vaccine with an interval of one month between each dose. Td/IPV is recommended for all individuals aged ten years or over. If the primary course is interrupted it should be resumed but not repeated, allowing an interval of one month between the remaining doses.

## Reinforcing immunisation

Children under ten years should receive the first tetanus booster combined with diphtheria, pertussis and polio vaccines. The first booster of a tetanus-containing vaccine should ideally be given three years after completion of the primary course, normally between three and a half years and five years of age. When primary vaccination has been delayed, this first booster dose may be given at the scheduled visit provided it is one year since the third primary dose. This will re-establish the child on the routine schedule. DTaP/IPV or dTaP/IPV should be used in this age group. Td/IPV should not be used routinely for this purpose in this age group because it has been shown not to give equivalent diphtheria antitoxin response when compared with other recommended preparations.

Individuals aged ten years or over who have only had three doses of a tetanus-containing vaccine, with the last dose at least five years ago, should receive the first tetanus booster combined with diphtheria and polio vaccines (Td/IPV).

The second booster dose of Td/IPV should be given to all individuals ideally ten years after the first booster dose. When the previous doses have been delayed, the second booster should be given at the school session or scheduled appointment provided a minimum of five years have lapsed between the first and second boosters. This will be the last scheduled opportunity to ensure long-term protection.

If a person attends for a routine booster dose and has a history of receiving a vaccine following a tetanus-prone wound, attempts should be made to identify which vaccine was given. If the vaccine given at the time of the injury was the same as that due at the current visit and was given after an appropriate interval, then the routine booster dose is not required. Otherwise, the dose given at the time of injury should be discounted as it may not provide long-term protection against all antigens, and the scheduled immunisation should be given. Such additional doses are unlikely to produce an unacceptable rate of reactions (Ramsay *et al.*, 1997).

Intravenous drug users are at greater risk of tetanus. Every opportunity should be taken to ensure that they are fully protected against tetanus. Booster doses should be given if there is any doubt about their immunisation status.

### Vaccination of children with unknown or incomplete immunisation status

Where a child born in the UK presents with an inadequate immunisation history, every effort should be made to clarify what immunisations they may have had (see Chapter 11 on vaccination schedules). A child who has not completed the primary course should have the outstanding doses at monthly intervals. Children may receive the first booster dose as early as one year after the third primary dose to re-establish them on the routine schedule. The second booster should be given at the time of leaving school to ensure long-term protection by this time, provided a minimum of five years is left between the first and second boosters.

Children coming to the UK who have a history of completing immunisation in their country of origin may not have been offered protection against all the antigens currently used in the UK. They will probably have received tetanus-containing vaccines in their country of origin ([www-nt.who.int/immunization\\_monitoring/en/globalsummary/countryprofileselect.cfm](http://www-nt.who.int/immunization_monitoring/en/globalsummary/countryprofileselect.cfm))

Children coming from developing countries, from areas of conflict or from hard-to-reach population groups may not have been fully immunised. Where there is no reliable history of previous immunisation, it should be assumed that they are unimmunised, and the full UK recommendations should be followed (see Chapter 11).

Children coming to the UK may have had a fourth dose of a tetanus-containing vaccine that is given at around 18 months in some countries. This dose should be discounted as it may not provide satisfactory protection until the time of the teenage booster. The routine pre-school and subsequent boosters should be given according to the UK schedule.

### Travellers and those going to reside abroad

All travellers should ensure that they are fully immunised according to the UK schedule (see above). Additional doses of vaccines may be required according to the destination and the nature of travel intended (see Departments of Health, 2001 (the Yellow Book) for more information).

For travellers to areas where medical attention may not be accessible and whose last dose of a tetanus-containing vaccine was more than ten years previously, a booster dose should be given prior to travelling, even if the individual has received five doses of vaccine previously. This is a precautionary measure in case immunoglobulin is not available to the individual should a tetanus-prone injury occur.

Where tetanus, diphtheria or polio protection is required and the final dose of the relevant antigen was received more than ten years ago, Td/IPV should be given.

## Tetanus vaccination in laboratory workers

Individuals who may be exposed to tetanus in the course of their work, in microbiology laboratories, are at risk and must be protected (see Chapter 12).

### Contraindications

There are very few individuals who cannot receive tetanus-containing vaccines. When there is doubt, appropriate advice should be sought from a consultant paediatrician, immunisation co-ordinator or consultant in communicable disease control rather than withholding the vaccine.

The vaccines should not be given to those who have had:

- a confirmed anaphylactic reaction to a previous dose of a tetanus-containing vaccine, or
- a confirmed anaphylactic reaction to neomycin, streptomycin or polymyxin B (which may be present in trace amounts).

Confirmed anaphylaxis occurs extremely rarely. Data from the UK, Canada and the US point to rates of 0.65 to 3 anaphylaxis events per million doses of vaccine given (Bohlke *et al.*, 2003; Canadian Medical Association, 2002). Other allergic conditions may occur more commonly and are not contraindications to further immunisation. A careful history of the event will often distinguish between anaphylaxis and other events that either are not due to the vaccine or are not life-threatening. In the latter circumstance, it may be possible to continue the immunisation course. Specialist advice must be sought on the vaccines and circumstances in which they could be given. The risk to the individual of not being immunised must be taken into account.

### Precautions

Minor illnesses without fever or systemic upset are not valid reasons to postpone immunisation.

If an individual is acutely unwell, immunisation should be postponed until they have fully recovered. This is to avoid wrongly attributing any new symptom or the progression of symptoms to the vaccine.

### Systemic and local reactions following a previous immunisation

This section gives advice on the immunisation of children with a history of a severe or mild systemic or local reaction within 72 hours of a preceding vaccine. Immunisation with tetanus-containing vaccine **should** continue following a history of:

- fever, irrespective of its severity
- hypotonic-hyporesponsive episodes (HHE)
- persistent crying or screaming for more than three hours
- severe local reaction, irrespective of extent.

Children who have had severe reactions, as above, have continued and completed immunisation with tetanus-containing vaccines without recurrence (Vermeer-de Bondt *et al.*, 1998; Gold *et al.*, 2000).

In Canada, a severe general or local reaction to DTaP/IPV/Hib is not a contraindication to further doses of the vaccine (Canadian Medical Association, 2002). Adverse events after childhood immunisation are carefully monitored in Canada (Le Saux *et al.*, 2003), and experience there suggests that further doses were not associated with recurrence or worsening of the preceding events (S Halperin and R Pless, pers. comm., 2003).

### Pregnancy and breast-feeding

Tetanus-containing vaccines may be given to pregnant women when protection is required without delay. There is no evidence of risk from vaccinating pregnant women or those who are breast-feeding with inactivated virus, bacterial vaccines or toxoids (Plotkin and Orenstein, 2004).

### Premature infants

It is important that premature infants have their immunisations at the appropriate chronological age, according to the schedule. The occurrence of apnoea following vaccination is especially increased in infants who were born very prematurely. The potential risk of apnoea and the need for respiratory monitoring for 48-72 hours should be considered when administering the primary immunisation series to infants who were born very prematurely (born  $\leq$  28 weeks of gestation) and particularly for those with a previous history of respiratory immaturity (Pfister *et al.*, 2004; Ohlsson *et al.*, 2004; Schulzke *et al.*, 2005; Pourcyrous *et al.*, 2007; Klein *et al.*, 2008).

The first immunisation of a child born very prematurely should be administered in hospital. If the child reacts to the first immunisation, they should return to hospital for their second immunisation.



As the benefit of vaccination is high in this group of infants, vaccination should not be withheld or delayed.

## Immunosuppression and HIV infection

Individuals with immunosuppression or HIV infection (regardless of CD4 count) should be given tetanus-containing vaccines in accordance with the recommendations above. These individuals may not make a full antibody response. Re-immunisation should be considered after treatment is finished and recovery has occurred. Specialist advice may be required.

Further guidance is provided by the Royal College of Paediatrics and Child Health ([www.rcpch.ac.uk](http://www.rcpch.ac.uk)), the British HIV Association (BHIVA) *Immunisation guidelines for HIV-infected adults* (BHIVA, 2006) and the Children's HIV Association of UK and Ireland (CHIVA) Immunisation guidelines ([www.bhiva.org/chiva](http://www.bhiva.org/chiva)).

## Neurological conditions

### Pre-existing neurological conditions

The presence of a neurological condition is not a contraindication to immunisation. Where there is evidence of a neurological condition in a child, the advice given in the flow chart in Figure 30.2 should be followed.

If a child has a stable, pre-existing neurological abnormality such as spina bifida, congenital abnormality of the brain or perinatal hypoxic ischaemic encephalopathy, they should be immunised according to the recommended schedule. When there has been a documented history of cerebral damage in the neonatal period, immunisation should be carried out unless there is evidence of an evolving neurological abnormality.

If there is evidence of current neurological deterioration, including poorly controlled epilepsy, immunisation should be deferred and the child should be referred to a child specialist for investigation to see if an underlying cause can be identified. If a cause is not identified, immunisation should be deferred until the condition has stabilised. If a cause is identified, immunisation should proceed as normal.

A family history of seizures is not a contraindication to immunisation. When there is a personal or family history of febrile seizures, there is an increased risk of these occurring after any fever, including that caused by immunisation. Seizures associated with fever are rare in the first six months of life and most common in the second year of life. After this age, the frequency falls and they are rare after five years of age.

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When a child has had a seizure associated with fever in the past, with no evidence of neurological deterioration, immunisation should proceed as recommended. Advice on the prevention and management of fever should be given before immunisation.

When a child has had a seizure that is not associated with fever, and there is no evidence of neurological deterioration, immunisation should proceed as recommended. When immunised with DTP vaccine, children with a family or

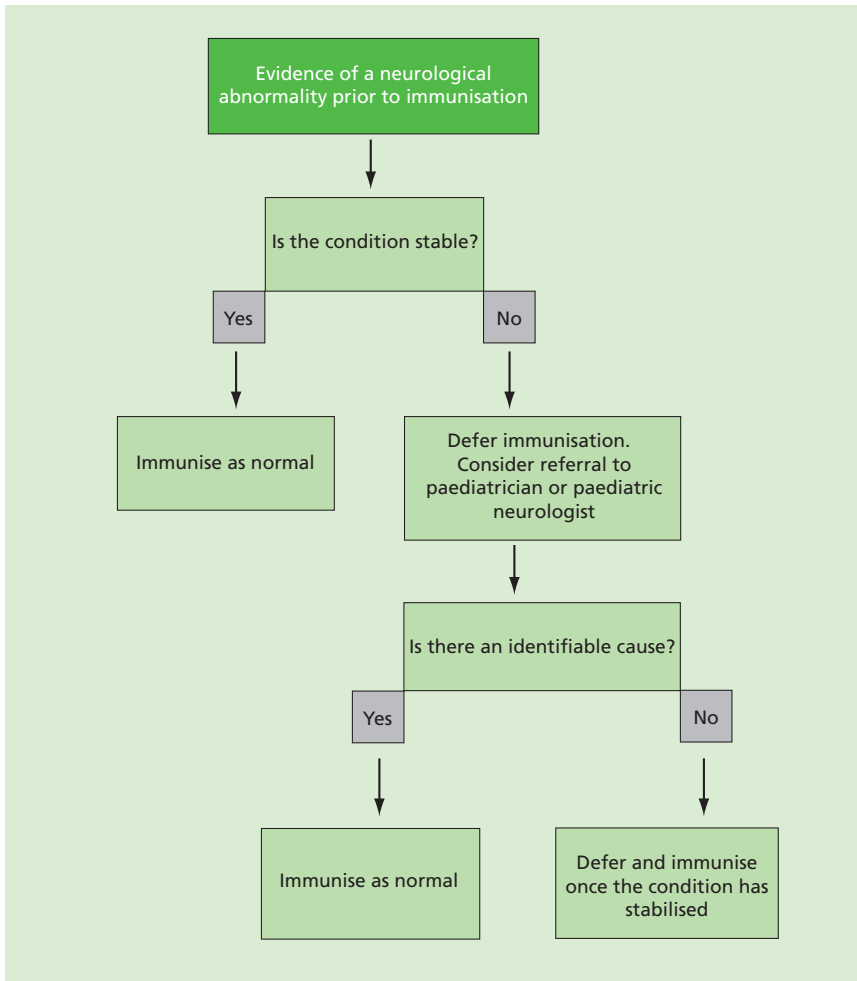


Figure 30.2 Flow chart for evidence of a neurological condition before immunisation

personal history of seizures had no significant adverse events and their developmental progress was normal (Ramsay *et al.*, 1994).

### Neurological abnormalities following immunisation

If a child experiences encephalopathy or encephalitis within seven days of immunisation, the advice in the flow chart in Figure 30.3 should be followed. It is unlikely that these conditions will have been caused by the vaccine and they should be investigated by a specialist. Immunisation should be deferred in children where no underlying cause is found, and the child has not recovered completely within seven days, until the condition has stabilised. If a cause is identified or the child recovers within seven days, immunisation should proceed as recommended.

If a seizure associated with a fever occurs within 72 hours of an immunisation, further immunisation should be deferred if no underlying cause has been found and the child did not recover completely within 24 hours, until the condition is stable. If a cause is identified or the child recovers within 24 hours, immunisation should continue as recommended.

### Deferral of immunisation

There will be very few occasions when deferral of immunisation is required (see p 45). Deferral leaves the child unprotected; the period of deferral should be minimised so that immunisation can commence as soon as possible. If a specialist recommends deferral, this should be clearly communicated to the general practitioner, who must be informed as soon as the child is fit for immunisation.

## Adverse reactions

Pain, swelling or redness at the injection site are common and may occur more frequently following subsequent doses. A small painless nodule may form at the injection site; this usually disappears and is of no consequence. The incidence of local reactions is lower with tetanus vaccines combined with acellular pertussis vaccines than with whole-cell pertussis vaccines and is similar to that after DT vaccine (Miller, 1999; Tozzi and Olin, 1997).

Fever, convulsions, high-pitched screaming and episodes of pallor, cyanosis and limpness (HHE) occur with equal frequency after both DTaP and DT vaccines (Tozzi and Olin, 1997).

Confirmed anaphylaxis occurs extremely rarely. Data from the UK, Canada and the US point to rates of 0.65 to 3 anaphylaxis events per million doses of vaccine given (Bohlke *et al.*, 2003; Canadian Medical Association, 2002).

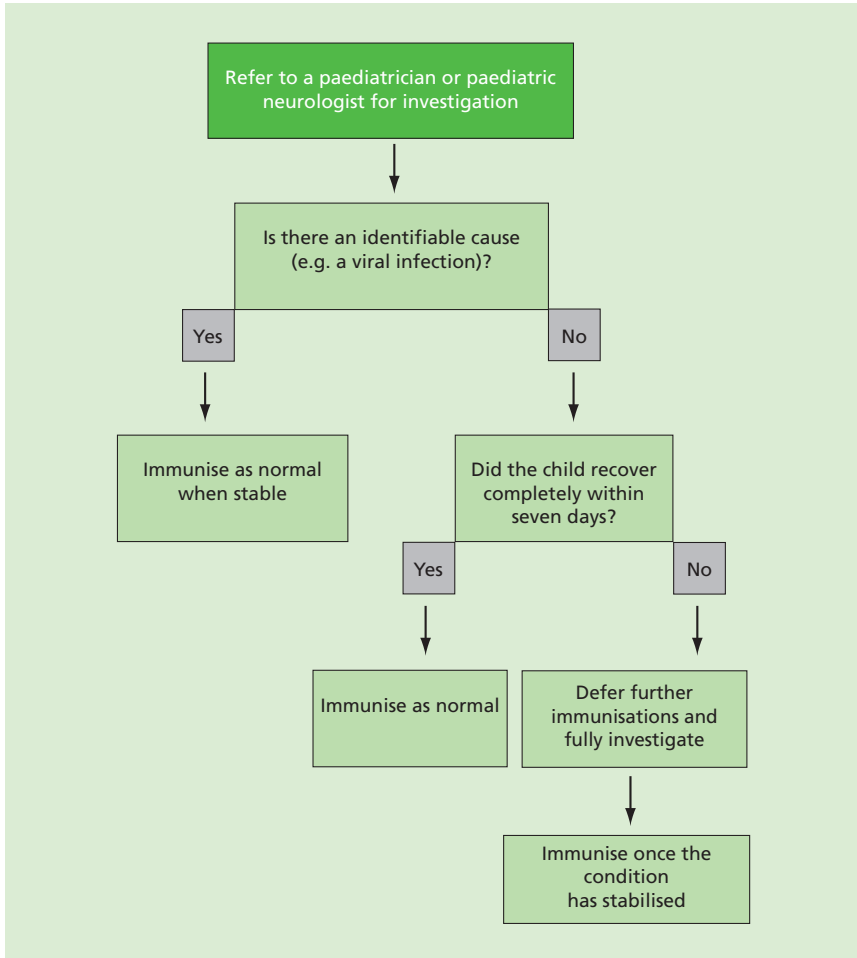


Figure 30.3 Flow chart for encephalitis or encephalopathy occurring within seven days of immunisation

Other allergic conditions may occur more commonly and are not contraindications to further immunisation.

All suspected adverse reactions to vaccines occurring in children, or in individuals of any age to vaccines labelled with a black triangle (▼), should be reported to the Commission on Human Medicines through the Yellow Card scheme. Serious suspected adverse reactions to vaccines in adults should be reported through the Yellow Card scheme.

## Management of patients with tetanus-prone wounds

Tetanus-prone wounds include:

- wounds or burns that require surgical intervention that is delayed for more than six hours
- wounds or burns that show a significant degree of devitalised tissue or a puncture-type injury, particularly where there has been contact with soil or manure
- wounds containing foreign bodies
- compound fractures
- wounds or burns in patients who have systemic sepsis.

Thorough cleaning of wounds is essential. If the wound, burn or injury fulfils the above criteria and is considered to be high risk, human tetanus immunoglobulin should be given for immediate protection, irrespective of the tetanus immunisation history of the patient. This is a precautionary recommendation since there is insufficient current evidence to support other alternatives. High risk is regarded as heavy contamination with material likely to contain tetanus spores and/or extensive devitalised tissue.

Injecting drug users may be at risk from tetanus-contaminated illicit drugs, especially when they have sites of focal infection such as skin abscesses that may promote growth of anaerobic organisms (Health Protection Agency, 2003).

Although any wound can give rise to tetanus, clean wounds are considered to have a low likelihood of harbouring tetanus spores and of developing the anaerobic and acidic conditions that promote spore germination (Wassilak *et al.*, 2004). Therefore, in the case of wounds such as clean cuts, human tetanus immunoglobulin need not be given.

Tetanus vaccine given at the time of a tetanus-prone injury may not boost immunity early enough to give additional protection within the incubation period of tetanus (Porter *et al.*, 1992). Therefore, tetanus vaccine is not considered adequate for treating a tetanus-prone wound. However, this provides an opportunity to ensure that the individual is protected against future exposure (see Table 30.1).

Patients who are immunosuppressed may not be adequately protected against tetanus, despite having been fully immunised. They should be managed as if they were incompletely immunised.

For those whose immunisation status is uncertain, and individuals born before 1961 who may not have been immunised in infancy, a full course of immunisation is likely to be required.

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### Dosage of human tetanus immunoglobulin

For prevention: 250IU by intramuscular injection, or 500IU if more than 24 hours have elapsed since injury or there is a risk of heavy contamination or following burns. This preparation is available in 1ml ampoules containing 250IU.

### Management of cases

Early recognition and treatment may be life saving but few clinicians in the UK now have experience of managing tetanus. Recent experience has pointed to injecting drug users as being at significant risk of tetanus. But injecting drug users are often reluctant to present to health services. Awareness of the risk and value of vaccination in this group, and awareness among those working with them, is extremely important.

For **treatment**: The dose of tetanus immunoglobulin for intravenous use is 5000–10,000IU by infusion. If intravenous administration is not possible, 150IU/kg of the intramuscular preparation may be given in multiple sites.

### Supplies

#### Vaccines

- Pediacel (diphtheria/tetanus/5-component acellular pertussis/ inactivated polio vaccine/*Haemophilus influenzae* type b (DTaP/IPV/Hib)) – manufactured by Sanofi Pasteur MSD.
- Repevax (diphtheria/tetanus/5-component acellular pertussis/ inactivated polio vaccine (dTaP/IPV)) – manufactured by Sanofi Pasteur MSD.
- Infanrix IPV (diphtheria/tetanus/3-component acellular pertussis/ inactivated polio vaccine (DTaP/IPV)) – manufactured by GlaxoSmithKline.
- Revaxis (diphtheria/tetanus/inactivated polio vaccine (Td/IPV)) – manufactured by Sanofi Pasteur MSD.

These vaccines are supplied by Healthcare Logistics (Tel: 0870 871 1890) as part of the national childhood immunisation programme.

In Scotland, supplies should be obtained from local childhood vaccine-holding centres. Details of these are available from Scottish Healthcare Supplies (Tel: 0141 282 2240).

In Northern Ireland, supplies should be obtained from local childhood vaccine-

<b>IMMUNISATION STATUS</b>	<b>CLEAN WOUND</b>	<b>TETANUS-PRONE WOUND</b>	
	<b>Vaccine</b>	<b>Vaccine</b>	<b>Human tetanus immunoglobulin</b>
Fully immunised, i.e. has received a total of five doses of vaccine at appropriate intervals	None required	None required	Only if high risk (see p 379)
Primary immunisation complete, boosters incomplete but up to date	None required (unless next dose due soon and convenient to give now)	None required (unless next dose due soon and convenient to give now)	Only if high risk (see p 379)
Primary immunisation incomplete or boosters not up to date	A reinforcing dose of vaccine and further doses as required to complete the recommended schedule (to ensure future immunity)	A reinforcing dose of vaccine and further doses as required to complete the recommended schedule (to ensure future immunity)	Yes: one dose of human tetanus immunoglobulin in a different site
Not immunised or immunisation status not known or uncertain	An immediate dose of vaccine followed, if records confirm the need, by completion of a full five-dose course to ensure future immunity	An immediate dose of vaccine followed, if records confirm the need, by completion of a full five-dose course to ensure future immunity	Yes: one dose of human tetanus immunoglobulin in a different site

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holding centres. Details of these are available from the regional pharmaceutical procurement service (Tel: 028 90 552368).

### Human tetanus immunoglobulin

#### Intravenous product

Human tetanus immunoglobulin for intravenous use is available on a named-patient basis from the Scottish National Blood Transfusion Service (Tel: 0131 536 5300, Fax: 0131 536 5781).

In England and Wales it is available from Bio Products Laboratory (Tel: 020 8258 2342).

In Northern Ireland, the source of anti-tetanus immunoglobulin is the Northern Ireland Blood Transfusion Services (Tel: 028 90 439017) (issued via hospital pharmacies).

#### Intramuscular products

Human tetanus immunoglobulin for intramuscular use is available from Bio Products Laboratory (Tel: 020 8258 2342) and as Liberim T from the Scottish National Blood Transfusion Service (Tel: 0131 536 5300, Fax: 0131 536 5781).

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