

# 24

## Pertussis

NOTIFIABLE

### The disease

Whooping cough is a highly infectious disease that is usually caused by *Bordetella pertussis*. A similar illness is caused by *B. parapertussis*, but this is not preventable with presently available vaccines.

There is an initial catarrhal stage, followed by an irritating cough that gradually becomes paroxysmal, usually within one to two weeks. The paroxysms are often followed by a characteristic ‘whoop’, often accompanied by vomiting. In young infants, the typical ‘whoop’ may never develop and coughing spasms may be followed by periods of apnoea. The illness often lasts for two to three months. In older children and adults, the disease may be mild and not recognised as whooping cough.

Pertussis may be complicated by bronchopneumonia, repeated vomiting leading to weight loss, and cerebral hypoxia with a resulting risk of brain damage. Severe complications and deaths occur most commonly in infants under six months of age. Minor complications include subconjunctival haemorrhages, epistaxis (nosebleeds), facial oedema, ulceration of the tongue or surrounding area, and suppurative otitis media.

Transmission of the infection is by droplet, and cases are most infectious during the early catarrhal phase. The incubation period is between six and 20 days and cases are infectious from six days after exposure to three weeks after the onset of typical paroxysms.

### History and epidemiology of the disease

Before the introduction of pertussis immunisation in the 1950s, the average annual number of notifications exceeded 120,000 in the UK.

By 1972, when vaccine coverage was around 80%, there were only 2069 notifications of pertussis. Because of professional and public anxiety about the safety and efficacy of the vaccine, coverage fell to about 30% in 1975 and major epidemics occurred in 1977–79 and 1981–83. In 1978, there were over 68,000 notifications and 14 deaths. The actual number of deaths due to

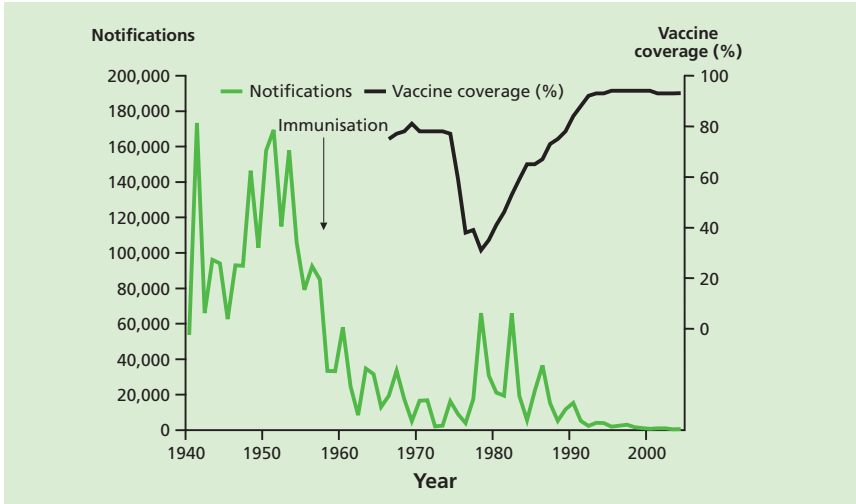


Figure 24.1 Pertussis notifications and vaccine coverage of children by their second birthday, England and Wales (1940–2003)

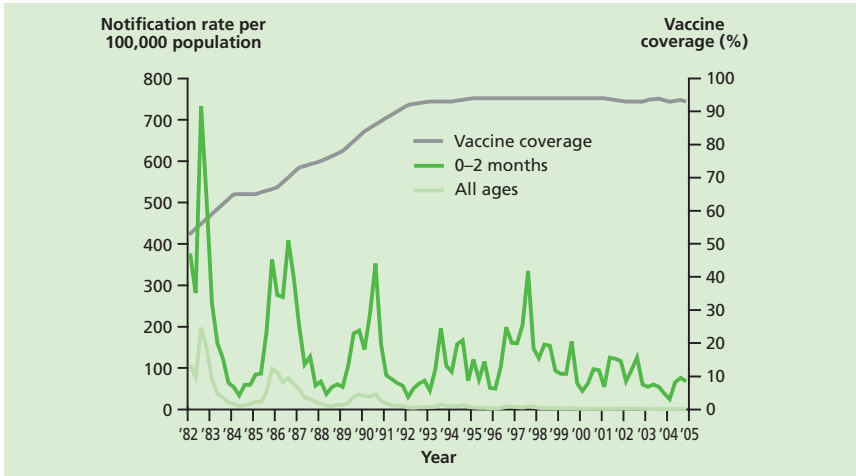


Figure 24.2 Notification rates of whooping cough (in all ages and infants aged under three months) and vaccine coverage at two years of age, England and Wales (1982–2005)

pertussis is higher, since not all cases in infants are recognised (Miller and Fletcher, 1976). These two major epidemics illustrate the impact of the fall in coverage of an effective vaccine.

The return of professional and public confidence resulted in increased vaccine uptake. Since the mid-1990s, coverage has been consistently over 90% by the second birthday, with fewer than 6000 notifications per year. In 2002, only 1051 cases were reported. The most recent estimate of deaths in England is nine deaths per year (Crowcroft *et al.*, 2002).

Despite the current low levels of disease, pertussis in the very young remains a significant cause of illness and death. The majority of hospitalisations following pertussis have occurred in those under six months of age, some of whom were seriously ill and required admission to paediatric intensive care units (Crowcroft *et al.*, 2003).

As the morbidity and mortality are highest in infants, high coverage must be maintained to protect those who are too young to be immunised. Adults and older children may infect younger members of their family who are too young to be immunised (Crowcroft *et al.*, 2003).

## The pertussis vaccination

The acellular vaccines are made from highly purified selected components of the *Bordetella pertussis* organism. These components are treated with formaldehyde or glutaraldehyde and then adsorbed onto adjuvants, either aluminium phosphate or aluminium hydroxide, to improve immunogenicity.

Acellular vaccines differ in source, number of components, amount of each component, and method of manufacture, resulting in differences in efficacy and in the frequency of adverse effects (Edwards and Decker, 2004). The vaccine chosen for primary immunisation in the UK programme (Pediace) contains five purified pertussis components. This vaccine has been shown to offer equal or better protection against clinically typical pertussis disease than the whole-cell pertussis vaccine previously used in the UK (Miller, 1999). The incidence of local and systemic reactions is lower with acellular pertussis vaccines than with whole-cell pertussis vaccines (Miller, 1999). The five-component vaccine contains pertussis toxoid (PT), filamentous haemagglutinin (FHA), fimbrial agglutinogens (FIM) 2 and 3, and pertactin (PRN). The three-component vaccine contains PT, FHA and PRN.

Three- and five-component pertussis-containing vaccines are provided according to their suitability for pre-school boosting. The pre-school vaccines are not provided for the purpose of primary immunisation. The three-component preparation (DTaP/IPV – Infanrix-IPV) does not provide the same

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level of protection against whooping cough in primary immunisation. The five-component pre-school preparation (dTaP/IPV– Repevax) does not contain the recommended strength of diphtheria vaccine for primary immunisation.

The pertussis vaccines are 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).

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

Monovalent pertussis vaccine is not available.

## 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 reactogenicity and loss of potency for some vaccines. It can also cause hairline cracks in the container, leading to contamination of the contents.

## Presentation

Pertussis-containing vaccines are available only 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.

## Dosage and schedule

- First dose of 0.5ml of a pertussis-containing vaccine.
- Second dose of 0.5ml, one month after the first dose.
- Third dose of 0.5ml, one month after the second dose.
- A fourth dose of 0.5ml should be given at the recommended interval.

## Administration

Vaccines are routinely given intramuscularly into the upper arm or antero-lateral 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, vaccines should be given by deep subcutaneous injection to reduce the risk of bleeding.

Pertussis-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 patient's records.

## 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 four doses of a pertussis-containing vaccine at appropriate intervals for all individuals up to ten years of age.

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

## Primary immunisation

### Infants and children under ten years of age

The primary course of pertussis vaccination consists of three doses of a pertussis-containing product with an interval of one month between each dose. DTaP/IPV/Hib is recommended for all infants 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. DTaP/IPV/Hib should be used to complete a primary course that has been started with a whole-cell or another acellular pertussis preparation.

Children of one to ten years who have completed a primary course (which includes three doses of diphtheria, tetanus and polio), but have not received three doses of a pertussis-containing vaccine should be offered a dose of combined DTaP/IPV (or DTaP/IPV/Hib) vaccine to provide some priming

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against pertussis. The DTaP/IPV vaccine, which contains a lower dose of pertussis antigen, should only be used as a booster in fully primed children. They should then receive the first reinforcing dose as scheduled, also as DTaP/IPV (or DTaP/IPV/Hib), preferably allowing a minimum interval of one year.

Similarly, children who present first for the pre-school booster without any pertussis, should also receive DTaP/IPV (or DTaP/IPV/Hib) as priming and reinforcing doses, preferably allowing a minimum interval of one year.

Children of one to ten years who have completed the primary course plus a reinforcing dose (which includes four doses of diphtheria, tetanus and polio), but have not received four doses of pertussis-containing vaccine, may be offered a dose of combined DTaP/IPV or DTaP/IPV/Hib (if appropriate) to provide some or additional protection against pertussis, preferably allowing an interval of one year from the previous dose.

These children will therefore receive an extra dose of diphtheria, tetanus or polio vaccines. Such additional doses are unlikely to produce an unacceptable rate of reactions (Ramsay *et al.*, 1997).

### Children aged ten years or over, and adults

Currently immunisation against pertussis is not recommended.

### Reinforcing immunisation

Children under ten years of age should receive the first pertussis booster combined with diphtheria, tetanus and polio vaccines. Either of the recommended pre-school vaccines should be used to boost a primary course of whole-cell or acellular pertussis preparations. The first booster of pertussis-containing vaccine should ideally be given three years after completion of the primary course, normally between three years and four months to 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 in 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 does not contain pertussis and has not been shown to give an equivalent diphtheria antitoxin response to other recommended preparations.

If a child attends for a 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 was the same as that due at the current visit and at an appropriate interval, then the booster dose is not required. Otherwise, the dose given at the time of injury should be discounted as it may not provide satisfactory 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).

Individuals aged ten years or over who have only had three doses of pertussis vaccine do not need further doses of pertussis-containing vaccine.

### **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). 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.

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 pertussis-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 on vaccine schedules).

Children coming to the UK may have had a fourth dose of a pertussis-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.

### Contraindications

There are very few individuals who cannot receive pertussis-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 withhold vaccine.

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

- a confirmed anaphylactic reaction to a previous dose of a pertussis-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 are either not due to the vaccine or 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 confusing the differential diagnosis of any acute illness by wrongly attributing any signs or symptoms to the adverse effects of 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 pertussis-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.

Previous experience suggested that the above events occurred more often after whole-cell DTP vaccine than after DT alone or after DTaP. Following the replacement of whole-cell pertussis vaccine with an acellular pertussis vaccine (DTaP/IPV/Hib) in Canada, there was a significant reduction in the number of reports of febrile seizures collected through the Immunization Monitoring Program – ACTive (IMPACT) (Le Saux *et al.*, 2003). When DTaP vaccines were compared with DT alone, severe general and local reactions occurred at the same rate (Tozzi and Olin, 1997). Therefore, these reactions were not due to the acellular pertussis components.

Children who have had severe reactions, as above, have continued and completed immunisation with pertussis-containing vaccines without recurrence of these reactions (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, 1998). Adverse events after childhood immunisation are carefully monitored in Canada (Le Saux *et al.*, 2003), and experience there suggests that further doses are not associated with recurrence or worsening of the preceding events (S Halperin and R Pless, pers. comm., 2003).

Since local or general reactions are less frequent after acellular than whole-cell pertussis vaccines, the number of children with such events will be small. There is no benefit in withholding acellular pertussis-containing vaccines in order to reduce the risks of adverse events, and there is additional protection from completing pertussis immunisation; this should be carried out in accordance with the routine immunisation schedule. Children who have had a local or general reaction after whole-cell pertussis vaccine should complete their immunisation with acellular pertussis preparations.

## Pregnancy and breast-feeding

Pertussis-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 viral or 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; Pourcyrus 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 and HIV infection (regardless of CD4 count) should be given pertussis-containing vaccines in accordance with the routine recommended schedule. 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 24.3 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

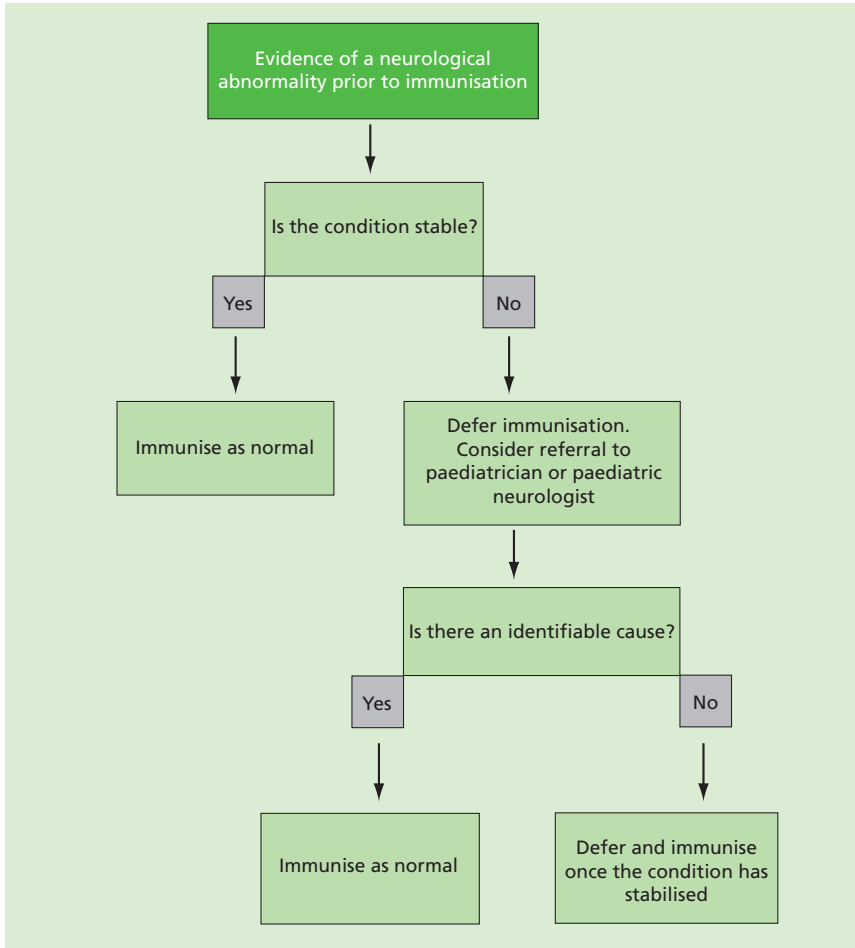


Figure 24.3 Flow chart for evidence of a neurological condition before immunisation

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.

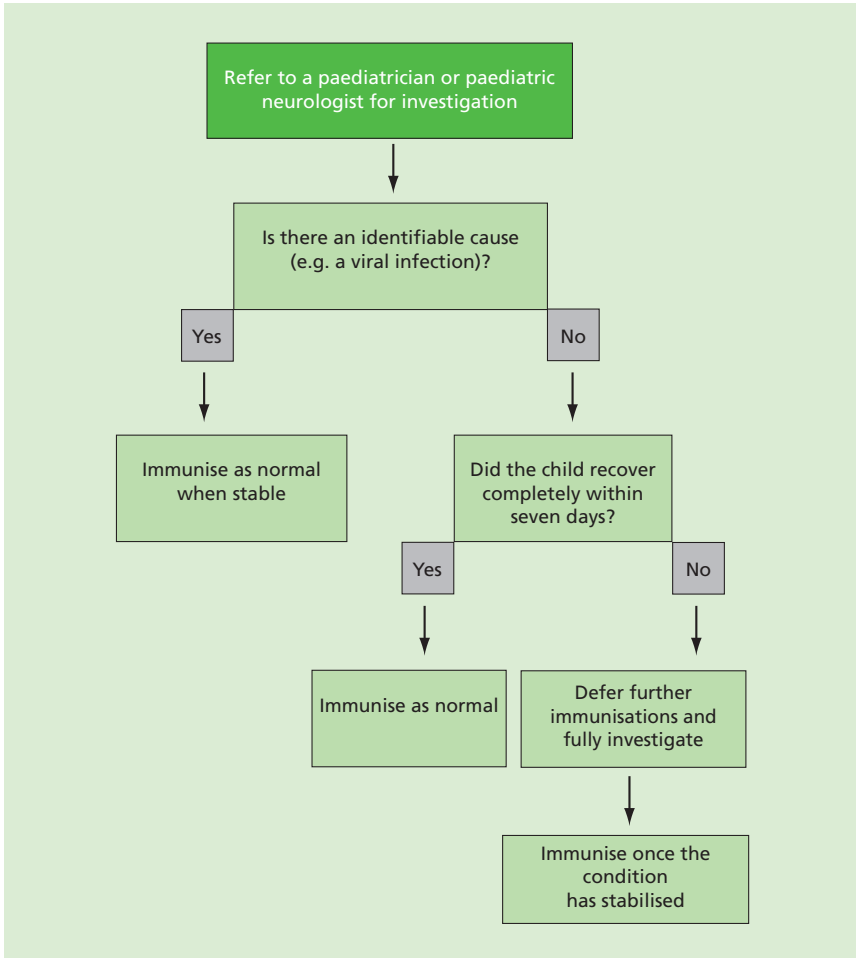


Figure 24.4 Flow chart for encephalitis or encephalopathy occurring within seven days of immunisation

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.

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 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 24.4 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 until the condition has stabilised in children where no underlying cause was found **and** the child did not recover completely within seven days. 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 until the condition is stable if no underlying cause has been found **and** the child did not recover completely within 24 hours. 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 above). 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 vaccines combined with acellular pertussis than with whole-cell pertussis, and is similar to that after DT vaccine (Miller, 1999; Tozzi and Olin, 1997).

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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 (Bohlke *et al.*, 2003; Canadian Medical Association, 2002). 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 after vaccines labelled with a black triangle (▼), should be reported to the Commission on Human Medicines using the Yellow Card scheme. Serious suspected adverse reactions to vaccines in adults should be reported through the Yellow Card scheme.

### Conditions historically associated with pertussis vaccine

In the past, there was public and professional anxiety that whole-cell pertussis vaccine contributed to the onset of neurological problems in young children. Between 1976 and 1979, a total of 1182 children with serious neurological illnesses were reported to the National Childhood Encephalopathy Study (NCES). Only 39 of these children had recently received whole-cell pertussis vaccine. The study concluded that whole-cell pertussis vaccine may very rarely be associated with the development of severe acute neurological illness in children who were previously apparently normal; most of these children suffered no apparent harm. The occurrence of a severe encephalopathy after whole-cell pertussis immunisation was sometimes associated with long-term residual neurological damage, but the evidence was insufficient to indicate whether or not whole-cell DTP increased the overall risk of chronic neurological dysfunction.

A major review of studies on adverse events after pertussis vaccine was published by the United States Institute of Medicine in 2001 (Howson *et al.*, 2001). This concluded that the evidence did not indicate a causal relationship between pertussis vaccine and infantile spasms, hypsarrhythmia, Reye's syndrome and sudden infant death syndrome (SIDS).

Cot deaths (SIDS) occur most commonly during the first year of life and may therefore coincide with the giving of pertussis-containing vaccines. Studies have established that this association is not causal (Fleming *et al.*, 2001).

It has been suggested that pertussis vaccine is linked with the development of asthma and allergy (Odent *et al.*, 1994). A recent double-blind study of pertussis vaccines found no significant differences in wheezing, itchy rash or sneezing between DTP-immunised children and controls (Nilsson *et al.*, 2003; DeStefano *et al.*, 2002). Asthma or allergy are not contraindications to the completion of pertussis immunisation.

## Management of outbreaks and contacts of cases

Because three injections are required to protect against pertussis, the vaccine cannot be used to control outbreaks (Dodhia *et al.*, 2002). In outbreaks affecting children under ten years of age, those who have not received four doses of pertussis-containing vaccines should receive an additional dose(s) of dTaP/IPV (DTaP/IPV may be used if there is no dTaP/IPV available).

Antibiotic prophylaxis should be offered to unimmunised or partially immunised vulnerable contacts of cases after discussion with the local health protection unit (Dodhia *et al.*, 2002).

## Supplies

- 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.

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 holding centres. Details of these are available from the regional pharmaceutical procurement service (Tel: 02890 552368).

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