26

Poliomyelitis

NOTIFIABLE

The disease

Poliomyelitis is an acute illness that follows invasion through the gastro intestinal tract by one of the three serotypes of polio virus (serotypes 1, 2 and 3). The virus replicates in the gut and has a high affinity for nervous tissue. Spread occurs by way of the bloodstream to susceptible tissues or by way of retrograde axonal transport to the central nervous system. The infection is most frequently clinically inapparent, or symptoms may range in severity from a fever to aseptic meningitis or paralysis. Headache, gastrointestinal disturbance, malaise and stiffness of the neck and back, with or without paralysis, may occur. The ratio of inapparent to paralytic infections may be as high as 1000 to 1 in children and 75 to 1 in adults, depending on the polio virus type and the social conditions (Sutter *et al.*, 2004).

Transmission is through contact with the faeces or pharyngeal secretions of an infected person. The incubation period ranges from three to 21 days. Polio virus replicates for longer periods and it can be excreted for three to six weeks in faeces and two weeks in saliva (Gelfand *et al.*, 1957). Cases are most infectious immediately before, and one to two weeks after the onset of paralytic disease (Sutter *et al.*, 2004).

When the infection is endemic, the paralytic disease is caused by naturally occurring polio virus – 'wild virus'. The live attenuated vaccine virus retains the potential to revert to a virulent form that can rarely cause paralytic disease. This is called vaccine-associated paralytic polio (VAPP). When wild viruses have been eliminated, VAPP cases can occur rarely where live attenuated vaccines are used.

History and epidemiology of the disease

During the early 1950s, there were epidemics of poliomyelitis infections with as many as 8000 annual notifications of paralytic poliomyelitis in the UK.

Routine immunisation with inactivated poliomyelitis vaccine (IPV – Salk) was introduced in 1956. This was replaced by live attenuated oral polio vaccine (OPV – Sabin) in 1962. The introduction of polio immunisation was accompanied by mass campaigns targeted at all individuals aged less than 40 years.

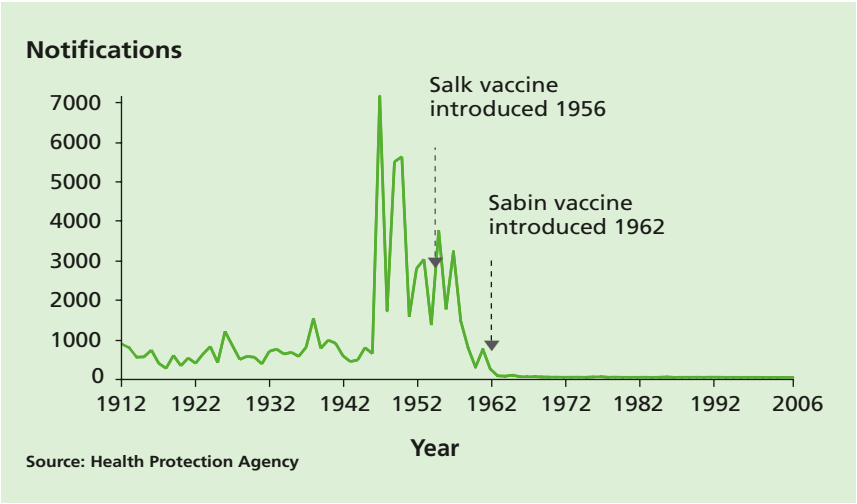

Figure 26.1 Polio notifications in England and Wales (1912–2006)

Following the introduction of polio immunisation, cases fell rapidly to very low levels. The last outbreak of indigenous poliomyelitis was in the late 1970s. The last case of natural polio infection acquired in the UK was in 1984. Between 1985 and 2002, a total of 40 cases of paralytic polio were reported in the UK (Figure 26.2). Thirty cases were VAPP; six cases had wild virus infection acquired overseas; and in a further five cases, all occurring before 1993, the source of infection was unknown but wild virus was not detected.

The number of reported cases of polio worldwide fell from 35,251 in 1988 to 677 in 2003 (reported by January 2004) (WHO, 2004a). International commissions have certified that polio virus transmission has been interrupted in three World Health Organization (WHO) regions: the Americas, the Western Pacific and Europe. WHO has included the UK among the countries that are likely to have eliminated indigenous poliomyelitis due to wild virus (WHO, 2004b).

By 2004, poliomyelitis remained endemic in only a small number of developing countries and, therefore, the risk of importation to the UK had fallen to very low levels. Following a resurgence of polio in Nigeria, poliomyelitis was reported during 2005 and 2006 from several countries that have previously been polio-free. In these countries, intensive efforts to interrupt transmission and to establish control are being undertaken, and the risk of importation to the UK is still considered low.

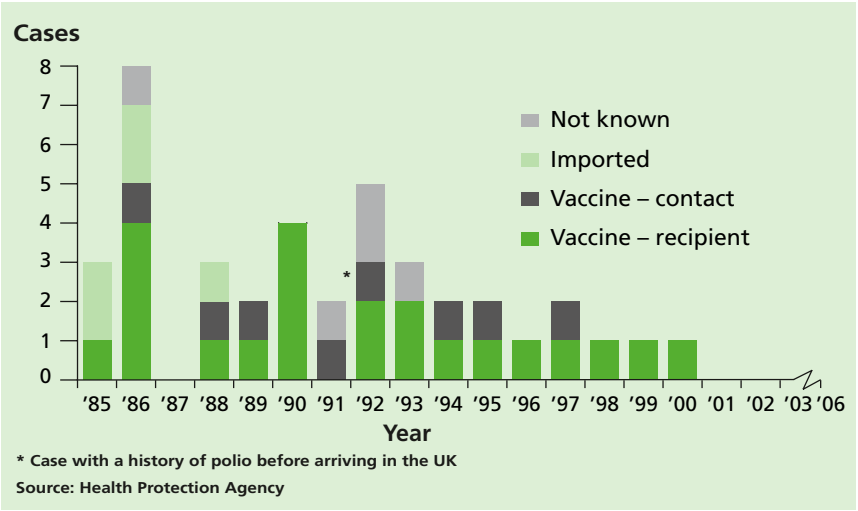

Figure 26.2 Reported cases of paralytic poliomyelitis by aetiology (all sources England and Wales 1985–2006)

Until 2004, OPV was used for routine immunisation in the UK because of the continuing risk of importation of wild virus. Both OPV and IPV provide excellent individual immunity. In addition, OPV provides community benefit as contacts of recently immunised children could be protected through acquisition of vaccine virus (Ramsay *et al.*, 1994a). OPV also promotes antibody formation in the gut, providing local resistance to subsequent infection with wild poliomyelitis virus. This reduces the frequency of symptomless excretion of wild viruses. The risks of wild polio virus being imported and the benefits of OPV need to be balanced against the risks of VAPP from OPV use and the efficacy of IPV. Since 2004, this balance favours the use of inactivated polio vaccine for routine immunisation in the UK.

The poliomyelitis vaccination

Inactivated polio vaccine (IPV) is made from polio virus strains Mahoney (Salk serotype 1), MEF-1 (Salk serotype 2) and Saukett (Salk serotype 3) grown in Vero cell culture. These components are treated with formaldehyde and then adsorbed onto adjuvants, either aluminium phosphate or aluminium hydroxide, to improve immunogenicity. The final vaccine mixture contains 40, 8 and 32 D-antigen units of serotypes 1, 2 and 3 respectively.

The polio 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.

OPV is no longer available for routine use and will only be available for outbreak control. OPV contains live attenuated strains of poliomyelitis virus types 1, 2 and 3 grown in cultures of monkey kidney cells or in human diploid (MRC-5) cells.

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

Presentation

Polio vaccine is only available 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 polio-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).

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

IPV-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 five doses of a polio-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 tetanus, pertussis, Hib and diphtheria.

Primary immunisation

Infants and children under ten years of age

The primary course of polio vaccination consists of three doses of an IPV-containing product 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. Those who commenced vaccination with oral polio vaccine can complete the course with IPV-containing vaccines.

Children aged ten years or over, and adults

The primary course of polio vaccination consists of three doses of an IPV-containing product 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. Those who commenced vaccination with oral polio vaccine can complete the course with IPV-containing vaccines.

Individuals born before 1962 may not have been immunised or may have received a low-potency polio vaccine; no opportunity should be missed to immunise them. Td/IPV is the appropriate vaccine for such use.

Reinforcing immunisation

Children under ten years should receive the first polio booster combined with diphtheria, tetanus, and pertussis vaccines. The first booster of an IPV-containing vaccine should ideally be given three years after completion of the primary course, normally between three years and four months 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 does not contain pertussis and has not been shown to give equivalent diphtheria antitoxin response compared with other recommended preparations.

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

The second booster dose of Td/IPV should be given to all individuals ideally ten years after the first booster dose. Where 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).

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. The second booster should be given at the time of leaving school to ensure long-term protection by this time. Wherever possible a minimum of five years should be 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 polio-containing vaccines in their country of origin (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 polio-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 to epidemic or endemic areas 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 Department of Health, 2001). 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.

Polio vaccination in laboratory and healthcare workers

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

Contraindications

There are very few individuals who cannot receive IPV-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 IPV-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 confusing the differential diagnosis of any acute illness by wrongly attributing any sign 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 receiving a

preceding vaccine. Immunisation with IPV-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.

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 were not associated with recurrence or worsening of the preceding events (S Halperin and R Pless, pers comm, 2003).

Pregnancy and breast-feeding

IPV-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 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.

Very premature infants (born ≤ 28 weeks of gestation) who are in hospital should have respiratory monitoring for 48-72 hrs when given their first immunisation, particularly those with a previous history of respiratory immaturity. If the child has apnoea, bradycardia or desaturations after the first immunisation, the second immunisation should also be given in hospital, with respiratory monitoring for 48-72 hrs (Pfister *et al.*, 2004; Ohlsson *et al.*, 2004; Schulzke *et al.*, 2005; Pourcyrous *et al.*, 2007; Klein *et al.*, 2008).

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 IPV-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), 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).

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 26.3 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 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.

When a child has had a seizure associated with fever in the past, with no evidence of neurological deterioration, immunisation should proceed as

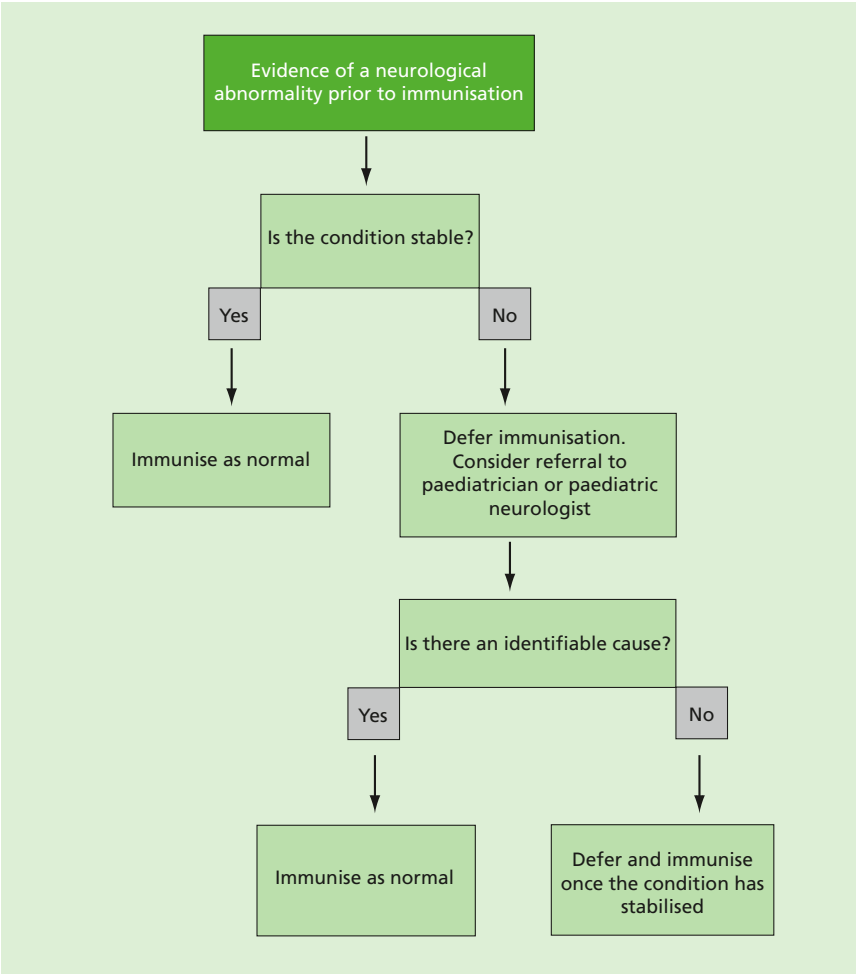

Figure 26.3 Flow chart for evidence of a neurological condition before immunisation

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.*, 1994b).

Neurological abnormalities following immunisation

If a child experiences encephalopathy or encephalitis within seven days of immunisation, the advice in the flow chart in Figure 26.4 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 is found, and the child has not recovered 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 if no underlying cause has been found, and the child has not recovered 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 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 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). Other allergic conditions may occur more commonly and are not contraindications to further immunisation.

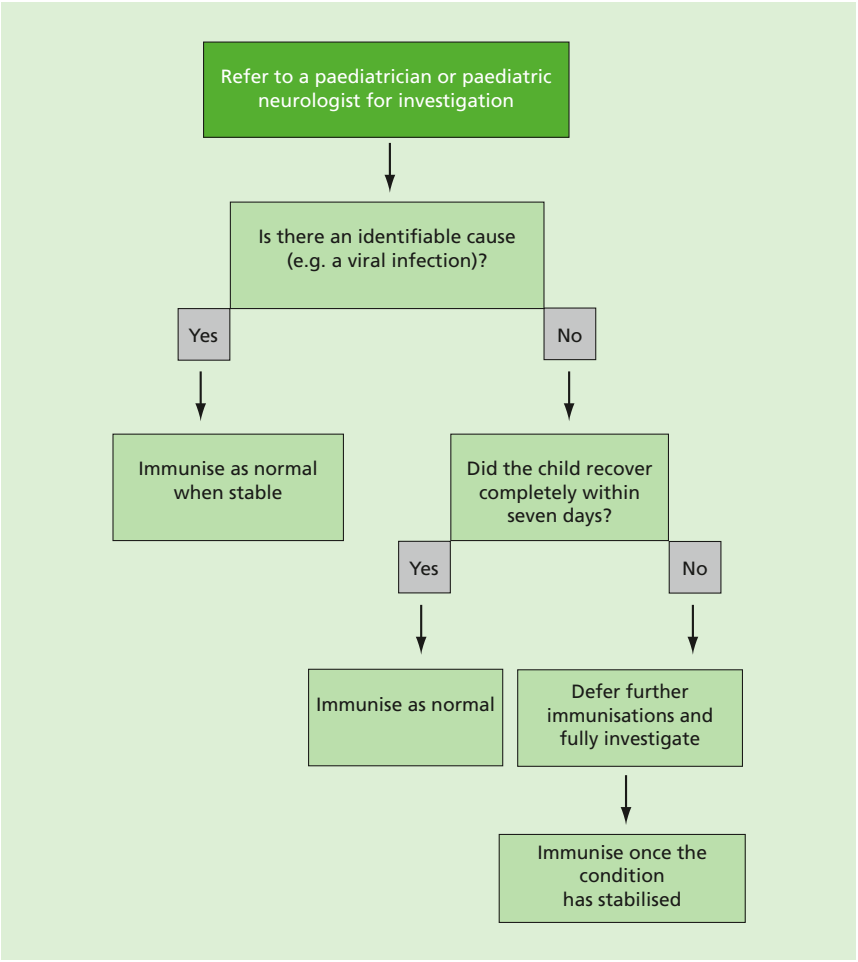

Figure 26.4 Flow chart for encephalitis or encephalopathy occurring within seven days of immunisation

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 suspected cases and outbreaks

Cases of suspected polio and other acute flaccid paralyses, including cases of Guillain-Barré syndrome, should be fully investigated. Two faecal samples for

virology should be taken in the first week of illness, 24 to 48 hours apart. Ideally, faecal samples should also be obtained from household and other close contacts. Advice on the investigation and management of suspected cases is available from the Communicable Disease Surveillance Centre (CDSC) / Enteric, Respiratory and Neurological Virus Laboratory (ERNVL) (or the Health Protection Scotland (HPS) in Scotland). Suspected cases should be reported immediately to a consultant in communicable disease control (or consultant of public health medicine (CPHM) in Scotland) and should not await culture confirmation.

To prevent ongoing transmission, OPV should be administered to household contacts of people with suspected polio immediately (after stool samples have been obtained). A stock of OPV is retained centrally for this purpose, and will be issued on the advice of the Health Protection Agency (HPA) or HPS. OPV may also need to be given immediately, after a case of paralytic poliomyelitis from wild virus, to other individuals in the neighbourhood of the case, regardless of a previous history of immunisation against poliomyelitis. Individuals with genuine contraindications to OPV, such as immunodeficiency or immunosuppression, should receive IPV-containing vaccine.

Appropriate control measures should be instituted in discussion with ERNVL (HPS in Scotland) and will depend upon the nature of the case and the likely vaccine coverage in the locality.

Maintaining polio-free status

Continued demonstration of the adequacy of clinical surveillance in the UK is required by WHO. Information on all suspected cases of polio is therefore being collated by CDSC and HPS for the UK Eradication Panel.

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

References

American Academy of Pediatrics (2003) Active immunization. In: Pickering LK (ed.) *Red Book: 2003 Report of the Committee on Infectious Diseases*, 26th edition. Elk Grove Village, IL: American Academy of Pediatrics, p 33.

Bohlke K, Davis RL, Marcy SH *et al.* (2003) Risk of anaphylaxis after vaccination of children and adolescents. *Pediatrics* **112**: 815–20.

British HIV Association (2006) *Immunisation guidelines for HIV-infected adults:* www.bhiva.org/pdf/2006/Immunisation506.pdf.

Canadian Medical Association (1998) Pertussis vaccine. In *Canadian Immunisation Guide*, 5th edition. Canadian Medical Association, p 133.

Canadian Medical Association (2002) General considerations. In *Canadian Immunisation Guide*, 6th edition. Canadian Medical Association, p 14.

Department of Health (2001) *Health information for overseas travel*, 2nd edition. London: TSO.

Diggle L and Deeks J (2000) Effect of needle length on incidence of local reactions to routine immunisation in infants aged 4 months: randomised controlled trial. *BMJ* **321**: 931–3.

Gelfand HM, LeBlanc DR, Fox JP and Conwell DP (1957) Studies on the development of natural immunity to poliomyelitis in Louisiana II. Description and analysis of episodes of infection observed in study households. *Am J Hyg* **65**: 367– 85.

Klein NP, Massolo ML, Greene J *et al.* (2008) Risk factors for developing apnea after immunization in the neonatal intensive care unit. *Pediatrics* **121**(3): 463-9.

Mark A, Carlsson RM and Granstrom M (1999) Subcutaneous versus intramuscular injection for booster DT vaccination in adolescents. *Vaccine* **17**: 2067–72

Miller E (1999) Overview of recent clinical trials of acellular pertussis vaccines. *Biologicals* **27**: 79–86.

Ohlsson A and Lacy JB (2004) Intravenous immunoglobulin for preventing infection in preterm and/or low-birth-weight infants. *Cochrane Database Syst Rev*(1): CD000361.

Pfister RE, Aeschbach V, Niksic-Stuber V *et al.* (2004) Safety of DTaP-based combined immunization in very-low-birth-weight premature infants: frequent but mostly benign cardiorespiratory events. *J Pediatr* **145**(1): 58-66.

Plotkin SA and Orenstein WA (eds) (2004) *Vaccines* 4th edition. Philadelphia: WB Saunders Company, Chapter 8.

Pourcyrous M, Korones SB, Arheart KL *et al.* (2007) Primary immunization of premature infants with gestational age <35 weeks: cardiorespiratory complications and C-reactive protein responses associated with administration of single and multiple separate vaccines simultaneously. *J Pediatr* **151**(2): 167-72.

Ramsay ME, Begg NT, Ghandi J and Brown D (1994a) Antibody response and viral excretion after live polio vaccine or a combined schedule of live and inactivated polio vaccines. *Pediatr Infect Dis J* **13**: 1117–21.

Ramsay M, Begg N, Holland B and Dalphinis J (1994b) Pertussis immunisation in children with a family or personal history of convulsions: a review of children referred for specialist advice. *Health Trends* **26**: 23–4.

Ramsay M, Joce R and Whalley J (1997) Adverse events after school leavers received combined tetanus and low dose diphtheria vaccine. *CDR Review* **5**: R65–7.

Le Saux N, Barrowman NJ, Moore DL *et al.* (2003) Canadian Paediatric Society/Health Canada Immunization Monitoring Program – Active (IMPACT). Decrease in hospital admissions for febrile seizures and reports of hypotonic-hyporesponsive episodes presenting to hospital emergency departments since switching to acellular pertussis vaccine in Canada: a report from IMPACT. *Pediatrics* **112**(5): e348.

Schulzke S, Heininger U, Lucking-Famira M *et al.* (2005) Apnoea and bradycardia in preterm infants following immunisation with pentavalent or hexavalent vaccines. *Eur J Pediatr* **164**(7): 432-5.

Sutter RW, Cochi S and Melnick JL (2004) Live attenuated polio virus vaccines. In: Plotkin SA and Orenstein WA (eds) *Vaccines*, 4th edition. Philadelphia: WB Saunders Company.

Tozzi AE and Olin P (1997) Common side effects in the Italian and Stockholm 1 Trials. *Dev Biol Stand* **89**: 105–8.

WHO (2004a)
www.polioeradication.org/casecount.asp (accessed October 2006).

WHO (2004b) *Polio News*, Issue 16, September 2002, p 1.
www.who.int/vaccines-documents/DocsPDF02/polio16.pdf (accessed 10 February 2004)

Zuckerman J N (2000) The importance of injecting vaccines into muscle. *BMJ* **321**: 1237–8.