



Chapter 9

Adverse events following immunisation and Anaphylaxis

9.1 Objectives

- To define the categories of adverse reactions that can occur following immunisation
- To identify minor reactions to immunisation and appropriate management
- To identify rare and serious adverse reactions following immunisation
- To define “anaphylaxis” and recognise signs and symptoms of anaphylaxis
- To recognise the signs and symptoms of faints, anxiety attacks, breath holding episodes and distinguish from signs and symptoms of anaphylaxis
- To distinguish between adverse reactions following immunisation and anaphylaxis
- To identify the appropriate management of an anaphylaxis reaction
- To outline the reporting of adverse reactions to the Irish Medicines Board

9.2 Adverse events following immunisation

Very rarely, people experience serious adverse events following immunisation.

Adverse events following immunisation (AEFI) can be divided into common uncommon, rare and very rare reactions. Most vaccine reactions are common, mild, settle without treatment and have no long term consequences.

The frequency of reactions can be classified as follows

- Very common > 1 in 10
- Common >1 in 1,000 and < 1 in 10
- Uncommon > 1 in 1,000 and < 1 in 100
- Rare > 1/10,000 and < 1 in 1,000
- Very rare < 1/10,000

The World Health Organisation has classified AEFIs into 4 main categories

- Programme related
- Vaccine-induced
- Coincidental
- Unknown

Programme related AEFIs

Programme errors are attributable to the vaccinator and therefore preventable through training and supervision. A programme error if undetected can lead to a clustering of events.

Examples include

- Wrong vaccine given
- Diluent only given
- Wrong dose of vaccine administered
- Vaccines used after their expiry date
- Vaccines used at inappropriate intervals
- Inappropriate route, site of injection or technique of administration
- Vaccine reconstituted with inappropriate diluent
- Wrong amount of diluent used
- Vaccine prepared incorrectly
- Mixing into inappropriate combinations
- Drug substituted for vaccine or diluent
- Vaccine or diluent contaminated
- Vaccine or diluent stored incorrectly
- Contraindications not elicited or ignored
- Reconstituted vaccine kept beyond the recommended period.

Vaccine Induced AEFIs

These are reactions that occur in individuals as a direct effect of the vaccine or its component parts. They can occur if the recipient has an underlying medical condition or has an idiosyncratic reaction to the vaccine.

Local reactions (redness, fever and swelling) that occur at the injection site are common. General reactions such as fever irritability loss of appetite etc usually occur within 24-48 hours of vaccination. Reactions that occur later include "mini measles" (temperature and rash) seven to ten days post MMR vaccination and swelling of the salivary glands that can occur three weeks post MMR vaccination.

Vaccine induced paralysis can follow the use of live attenuated oral polio vaccine in less than 1 in a million doses administered. This is the reason inactivated polio vaccine is used in primary childhood immunisation programme.

Idiopathic reactions to vaccination include idiopathic thrombocytopenic purpura (ITP) which can occur 30 days post MMR vaccine. This category also includes medical conditions that would have occurred at some point in an individual but are triggered by vaccination. This may include febrile convulsions in a child with a family history of febrile convulsions.

An anaphylactic reaction to a vaccine can also be considered as an idiosyncratic reaction.

Coincidental AEFIs

These are not true adverse reactions to vaccination but have a temporal relationship to the vaccination process. The event would have occurred in that individual even if they had not been vaccinated. A common coincidental AEFI is the development of upper respiratory tract infection in individuals post influenza vaccination.

Unknown AEFIs

This is a "catch all" category for AEFI that do not fit in to the three categories mentioned above.

9.3 Summary of minor reactions following immunisation

A vaccine produces immunity against a disease by causing the recipient's immune system to react to the vaccine. It is therefore not surprising that vaccination causes mild side effects. Local –injection site (pain, redness and swelling) and systemic (fever, irritability and malaise) symptoms are therefore not uncommon after vaccination and could be considered part of the body's normal immune reaction. An effective vaccine reduces these reactions to a minimum whilst also conferring maximum immunity. Common reactions to vaccines are outlined in Table 9.1.

Table 9.1: Summary and frequency of minor reactions following immunisation

Vaccine	Local reaction (pain, swelling, redness)	Fever	Irritability, malaise and non-specific symptoms
BCG	Common	Rare	Rare
DTP/IPV	Common	Common	Common
MMR	Common	Common	Uncommon
Hib	Common	Uncommon	Uncommon
Men C	Common	Common	Common
Hep B	Common	Uncommon	Uncommon
Pneumococcal	Common	Common	Uncommon

Source: Summary of Product Characteristics

Local reactions generally occur within hours of receiving the vaccine and are usually mild and self-limiting. Recent evidence has shown that reactogenicity is dramatically reduced with correct needle length. Occurrence of a local reaction **does not contraindicate** the administration of this vaccine subsequently.

The timing of systemic reactions will vary according to the type of vaccine received. . Fever can occur commonly within a few hours of administration of tetanus containing vaccines, whereas the rash associated with MMR vaccine occurs 7-10 days later. The presence of a systemic reaction does not contraindicate the administration of this vaccine subsequently.

9.4 Management of common reactions following immunisation

Parents should be informed both verbally and with the provision of information leaflets of expected common events post-vaccination and should be informed how to treat them. Advice should be given on the appropriate use of paracetamol or ibuprofen to prevent or treat a fever. Aspirin or aspirin-containing medication should not be administered to children under 18 years of age due to the possibility of developing Reye's syndrome.

Parents whose children receive BCG vaccination should be advised that 3 – 6 weeks after vaccination, in almost all cases small red pustules will appear at the site of the injection. The pustules will remain for a number of weeks and may discharge slightly. The area may appear scaly, crusty or look bruised. This is a normal reaction and will resolve leaving a flat scar. If a more serious reaction should occur parents should contact their HSE health centre or public health nurse for advice.

9.5 Rare and serious AEFI.

Some vaccines can very rarely produce more serious AEFI. The majority are either neurological or immune-mediated and include seizures, hypotensive-hyporesponsive episodes (HHE), idiopathic thrombocytopenic purpura and anaphylaxis. Some of the more rare and serious complications are outlined in Table 9.2.

Table 9.2: Examples of minor reactions following immunisation

Vaccine	Reaction Type	Onset interval	Rate per million doses
BCG	Suppurative lymphadenitis	2-6 months	100-1000
	BCG Osteitis	1-12 months	1-700
	Disseminated BCG-itis	1-12 months	2
MMR	Febrile convulsions	5-12 days	333
	Thrombocytopenia	15-35 days	33
	Anaphylaxis	0-1 hours	1-50

9.6 Anaphylaxis

Anaphylaxis can be defined as severe systemic (whole body) allergic reaction. The key issues in the management of anaphylactic reaction are


- Awareness that anaphylaxis though rare can occur
- Early recognition
- Early treatment.

Anaphylaxis is an extremely rare event occurring about once every million doses of vaccine given. Most people who vaccinate will never see an anaphylactic reaction. However, it can be a life threatening event and must be diagnosed and treated appropriately.

9.6.1 Signs and Symptoms of an anaphylactic reaction

The signs and symptoms of mild to severe anaphylactic reactions are outlined in Table 9.3.

Table 9.3: Signs and Symptoms of an anaphylactic reaction

Clinical Progression	Signs and Symptoms
Mild early warning signs	Itching of skin, rash and swelling around the injection site. Dizziness and general feeling of warmth
	Painless swelling in parts of the body e.g. face or mouth. Flushed, itchy skin, nasal congestion, sneezing tears
	Hoarseness, feeling sick, vomiting
	Swelling in the face, difficulty breathing, abdominal pain
Life threatening symptoms	Wheezy, difficulty breathing, collapse, low blood pressure, weak pulse

It is important that an anaphylactic reaction is differentiated from other more common and less serious reactions to vaccination e.g. simple faints, anxiety attacks and breath holding episodes. The differential features are outlined in Table 9.4.

Table 9.4. Differentiation of anaphylaxis from common post immunisation reactions

Faint or Syncopal episode	Anxiety Attack	Breath Holding Episode	Anaphylaxis
Good central pulse but may be breathing very fast (Tachypnoeic)	May appear fearful	Mostly in young children	Poor central pulses, usually sinus tachycardia
Respiration continues	Tachypnoea	Generally distressed/ crying prior to episode	Possible apnoea especially in children
Pallor	Hyperventilation	Facial flushing and cyanosis	Upper airways oedema, sneezing
Warm skin	Pallor	Can briefly become unconscious during which breathing returns	Hive like (Urticarial) lesions
Unusual in preschool children	Tingling of face and extremities		Itching
No itching	Complains of feeling light headed. Dizzy or numb		Sense of impending doom Flushed sweating cold skin Patient does not revive on lying down
Patient regains consciousness whilst lying down			

9.6.2 Management of anaphylaxis

The following outlines the management of anaphylaxis in the community setting

- Send for additional medical assistance
- Get a responsible adult to dial the emergency services 999 OR 112 and state that there is a case of anaphylaxis
- Lie patient down, ideally with legs raised unless the patient has breathing difficulties
- Administer oxygen if available
- If the patient is unconscious an airway should be inserted
- If the patient stops breathing, mouth to mouth resuscitation should be performed but preferably bag valve mask ventilation should be performed.

If the patient suffers clinical signs of shock, airway swelling or definite breathing difficulties they should be given adrenaline (epinephrine, 1:1000) administered by IM injection. For dose of adrenaline see Table 9.5. This can be repeated every 5-10 minutes for up to three doses.

Table 9.5: Recommended dose of adrenaline by age-group

Adrenaline(Epinephrine) 1:1000 (1mg(1000µcg)/ml) IM⁴	
Child: Dose by weight (0.01ml/kg) or age	
<6 months	0.05ml (50µcg)
7-18 months	0.1ml (100µcg)
18-36 months	0.15ml (150µcg)
4-7 years	0.2ml (200µcg)
8-10 years	0.3ml (300µcg)
11-12 years	0.4ml (400µcg)
> 12 years	0.5ml (500µcg)
Adult:	0.5ml (500µcg) ⁵
Those ≥ 100 kgs can be given 1mg IM (use green needle, 37mm)	

All cases should be sent to hospital for observation and/or treatment even if it appears that they have made a good recovery.

Chlorpheniramine maleate (piriton) and hydrocortisone are given to prevent the delayed manifestations of allergy and are not the first line treatment of anaphylaxis. Chlorpheniramine maleate is used three times daily for 48 hours to prevent recurrence (Table 9.6).

Table 9.6: Recommended dose of Chlorpheniramine maleate and hydrocortisone by age-group

Chlorpheniramine maleate			
Dose	<1 year	0.25mgs/kg	IM
	1-5 years	2.5-5mgs	IM
	6-12 years	5-10mgs	IM
	> 12 years and adult	10-20mgs	IM
Hydrocortisone.			
Dose	<1 year	25mgs	IM or slow IV
	1- 5 year	50mgs	IM or slow IV
	6-12 years	100mg	IM or slow IV
	> 12 years and adult	100-500mgs	IM or slow IV

In the hospital setting nebulised adrenaline 5mls of 1 in 1000 can be given and repeated every 10 minutes. Hydrocortisone can be given as outlined in table 9.6.

For less severe reactions in hospital when wheeze is present give nebulised salbutamol 2.5mg if less than 5 years or 5mg if more than 5 years. Consideration may also be given to the administration aminophylline 5mg/kg intravenously over 15 minutes or intravenous salbutamol.

9.7 Reporting of adverse events following immunisation

In Ireland, the Irish Medicines Board (IMB) is responsible for monitoring adverse reactions to medicines and vaccines. Of particular importance are all suspected reactions to newly authorised products, serious reactions to established products and all suspected reactions to vaccines.

Pharmaceutical companies are obliged, under the conditions of authorisation to market medicines in Ireland, to also submit adverse reaction reports associated with use of their products to the IMB.

All suspected adverse reactions should be reported to the Irish Medicines Board, Kevin O' Malley House, Earlsfort Terrace, Dublin 2, using the Adverse Reaction Report (Yellow) Card System (Appendix 9).

This is a "Freepost" system and cards are available from the Irish Medicines Board at the above address, or may be downloaded from their website. In addition, an on-line version of the report form is available from the IMB website (<http://www.imb.ie>.)

Reports must be as detailed as possible and include the batch number of the vaccine. All the data requested on the Yellow Card may not be available however this should not deter a health service provider from sending in a report. The possibility of adverse reactions must continually be borne in mind and, once suspected, such reactions should be reported.

9.8 Useful resources

American Academy of Paediatrics. 2006 Report of the Committee on Infectious Diseases–The Red Book. <http://aapredbook.aappublications.org/>

Department of Health UK. November 2006. Immunisation against infectious disease. http://www.dh.gov.uk/en/Policyandguidance/Healthandsocialcaretopics/Greenbook/DH_4097254

Ewan P.W. ABC of allergies: Anaphylaxis. BMJ1998 (316) 1442-1445

Health Protection Surveillance Centre, Ireland. www.hpsc.ie

Irish Medicines Board. <http://www.imb.ie>

National Immunisation Office. Health Service Executive, Ireland. <http://www.immunisation.ie>.

Royal College of Physicians of Ireland. Immunisation Guidelines for Ireland. Available at www.hpsc.ie

World Health Organisation. Adverse events following immunisation http://www.who.int/immunization_safety/aefi/en/

World Health Organisation. Geneva 2000. Supplementary information on vaccine safety <http://www.who.int/vaccines-documents/DocsPDF00/www562.pdf>

World Health Organisation. May 2007. Mass Measles Immunization Campaigns- reporting and investigating adverse events following immunization http://www.who.int/immunization_safety/aefi/managing_AEFIs/en/index6.html