Adverse events following immunisation

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While most vaccines cause frequent minor adverse events local to the injection site, more serious systemic and allergic reactions are relatively rare. Overall, the adverse events are far outweighed by the benefits conferred by immunisation.

An adverse event following immunisation (often known as an AEFI) is an unwanted or unexpected event following administration of a vaccine.[1] These events may occur because of the inherent nature of a vaccine constituent or as the result of the incorrect administration of the vaccine or the physical action of the needle, or they may be anxiety related or merely coincidental and unrelated to the vaccine. It is vital for any medical practitioner administering vaccines to be fully aware of the potential for adverse consequences of vaccination in order to minimise their occurrence and to be prepared for appropriate management when they occur. This article will consider some of the more common issues practitioners are likely to face.

Types of adverse events

Adverse events may be local to the injection site or generalised, and are listed in Table 1 as the categories used in the current NHMRC *Australian Immunisation Handbook* (8th edition, 2003).[1] Any serious or unexpected adverse events following immunisation should be reported to the Therapeutic Goods Admistration on 1300 134 237 or via the website (www.tga.gov.au/problem/index.htm).

Vasovagal episodes

Virtually every medical practitioner will be very familiar with vasovagal episodes, especially in settings associated with medical procedures, venesection and immunisations. In a mechanism that is not fully understood, the puncturing of a vein or the skin in some people is thought to result in a spinal reflex consisting of excitation of afferent nerve fibres and efferent nerve impulses mediated via the vagus nerve. The vagus nerve impulses cause bradycardia and also a sudden dilatation of the blood vessels in the legs, with blood pooling, which together cause hypotension. The ensuing decreased cerebral blood flow results in a prodrome of feeling light headed, blurred vision, nausea and sweatiness, and if immediate action is not taken, a loss of consciousness ensues – that is, a faint.

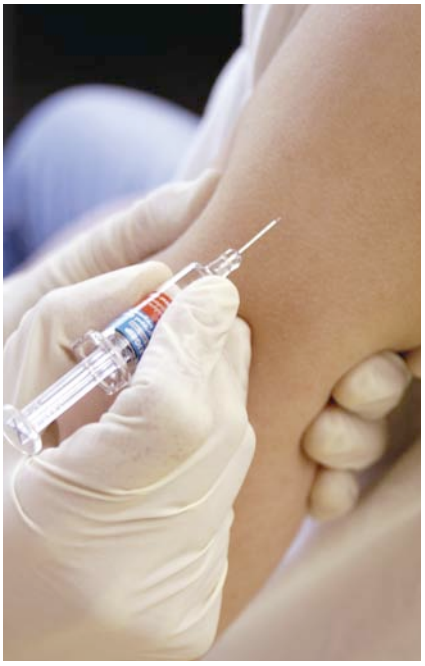

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Figure. Medical practitioners administering vaccines should be aware of the possible adverse reactions to vaccinations and prepared to manage them when they occur.

It is, therefore, important before vaccination to elicit in each patient any previous history of fainting at the time of or soon after the procedure, and to undertake steps to prevent a recurrence. Relative dehydration increases the risk of a vasovagal episode, so patients who are prone to fainting should be encouraged to ensure adequate fluid intake before vaccination.

In almost all cases, fainting may be prevented by having the patient lying down during the vaccination procedure, and remaining supine for five to 10 minutes before sitting up gradually and then remaining under observation for the next 20 to 30 minutes. If fainting does occur in a nonsupine patient, he or she should be caught and helped to the supine position as quickly as possible, even if on the floor, with attention paid to airways and the legs elevated to increase venous return to the heart. Vital signs should be regularly

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Table 1. Adverse events following immunisation*

Abscess
Acute flaccid paralysis
Allergic reaction
Anaphylaxis
Arthralgia
Arthritis
Brachial neuritis
Death
Disseminated BCG
Encephalopathy
Encephalitis
Extensive limb swelling
Fever
Guillain–Barré syndrome
Hypotonic–hyporesponsive episode
Local reaction (severe)
Lymphadenitis
Meningitis
Nodule
Orchitis
Osteitis
Osteomyelitis
Parotitis
Rash
Screaming (persistent)
Seizure
Sepsis
Subacute sclerosing panencephalitis
Thrombocytopenia
Toxic shock syndrome
Vaccine associated paralytic poliomyelitis
Other severe or unusual events

* Categories used in the *Australian Immunisation Handbook*, *8th edition*.[1]

recorded and the patient not left alone at any time. It is important to be alert for the development of indicators of this not being a vasovagal episode but instead anaphylaxis, a seizure or hyperventilation. Despite all appropriate action, a vasovagal episode in some patients may induce a clonic seizure; such seizures are almost always quite benign. As soon as the patient regains consciousness, it is important to explain in simple terms what has happened and to reassure him or her, followed by a period of observation.

As the specific triggers of vasovagal syncope have not been clearly elucidated, several medications may be used to treat recurrent syncopal episodes, although the evidence base for this is poor. Options to consider include beta blockers, anticholinergic agents, adenosine receptor blockers, selective serotonin reuptake inhibitors, mineralocorticoids and anticonvulsants.

Anxiety

Vasovagal events should be clearly distinguished from an anxiety disorder, which primarily occurs before vaccination. Relevant anxiety disorders to consider include panic disorder, generalised anxiety disorder and specific phobias.[2] Panic disorders may be associated with hyperventilation, with consequent changes in consciousness, and, conversely, hyperventilation can induce panic in prone individuals.

If simple reassurance is not adequate, it may be appropriate to consider aids such as dermal anaesthesia using EMLA (lignocaine plus prilocaine) patches or cream, anxiolytic medication and cognitive behavioural therapy.

Allergic reactions and anaphylaxis

An allergic reaction is defined in the *Australian Immunisation Handbook*, *8th edition*, as 'a non-anaphylactic, generalised reaction characterised by one or more symptoms or signs of skin and/or gastrointestinal tract involvement without respiratory or cardiovascular involvement'.[1] Simple allergic reactions may be readily managed with a corticosteroid cream for localised skin reactions and antihistamines for more systemic reactions. Because of the small but real risk of anaphylaxis, the patient should be cautioned to obtain medical assistance urgently if symptoms or signs progress.

Anaphylaxis is defined as a rapidly evolving allergic reaction with respiratory involvement (breathing difficulties, swelling of tongue or throat, hoarse voice, difficulty breathing, wheeze or persistent cough) and/or cardiovascular involvement (loss of consciousness, collapse, hypotension), and involvement of other systems such as the skin or gastrointestinal tract.[1]

Allergic reactions and anaphylaxis may occur as a result of exposure to any vaccine constituent. In contrast to vasovagal reactions, indicators of anaphylaxis are: occurrence of symptoms more than a few minutes after administration (vasovagal responses are immediate or within minutes); tachycardia (compared with bradycardia in vasovagal responses); weak central pulse; association with allergic symptoms such as itch, urticaria, hoarse voice or stridor; vomiting or diarrhoea; and loss of consciousness not responding to being placed in the supine condition.

Adrenaline remains the cornerstone of management of anaphylaxis. Even though anaphylaxis is rare, every medical practitioner giving a vaccine should ensure they have immediately available to hand an up-to-date supply of adrenaline with a 1 mL graduated syringe. Adrenaline is provided free of charge for the treatment of anaphylaxis as part of the doctor's bag supplies. The recommended approach to managing anaphylaxis and the dosages of adrenaline are documented in the *Australian Immunisation Handbook, 8th edition*.[1] Oxygen, masks and other appropriate resuscitation equipment should also be available. After emergency treatment of a patient with an anaphylactoid reaction, the patient should be sent to a hospital casualty department for a period of observation, and further treatment or admission if necessary.

Adverse reactions to specific vaccinations

The risks of some diseases and the side effects of vaccinations against them are

continued

Table 2. Risks of disease and vaccination*[1,3]

Disease	Disease characteristics and risks	Side effects of vaccination
Diphtheria	• Bacterial infection spread by nasal droplets. Two to five day incubation period. Severe sore throat with swollen glands; swallowing and breathing may become difficult. • About 7% of patients die.	Up to 50% of vaccine recipients have injection site pain, redness, swelling or fever. Side effects less common with the combined preparation DTPa (diphtheria toxoid, tetanus toxoid, acellular pertussis vaccine).
Hepatitis A	• Viral infection of the liver spread from person to person (faeco-oral route) or by contaminated food and water. Two to six week incubation period. Jaundice, abdominal pain, fever and malaise for up to three months. Severity worse with increasing age. • About 3% of patients die. Up to 2% of travellers affected.	Few adverse reactions. Mild local reactions of short duration (soreness, redness, swelling at injection site) are most common; systemic reactions (fever, malaise, headache, nausea, loss of appetite) much less common. No serious adverse reactions reported to date.
Hepatitis B	• Viral infection of the liver spread by contact with infected body fluids, especially blood (needle sharing) or semen (intercourse). Six to 12 week incubation period. Acute infection with jaundice, abdominal pain, fever and malaise for up to six months. • Up to 50% of patients die from cancer of the liver later in life or liver failure.	About 5 to 15% of patients have injection site soreness; about 2 to 3%, fever, nausea, dizziness, malaise, muscle or joint aches. Anaphylaxis extremely rare in adults.
Influenza	• Viral infection spread by droplets. Fever, muscle and joint pains, pneumonia. • Elderly, diabetic and immunosuppressed patients most at risk; increased hospitalisation.	Up to 10% of vaccine recipients have local reactions. Guillain–Barré syndrome occurs in about one in one million recipients.
Japanese encephalitis	• Viral infection spread by mosquitoes. Usually asymptomatic but may be fits or reduced conscious state. • About 25% of patients die; up to 30% of survivors have long term neurological or psychiatric damage. Risk of acquiring infection is about 0.02% per month of travel.	About 10% of vaccine recipients have fever, headache, malaise, rash, dizziness, muscle aches, nausea and vomiting. About 20% have injection site tenderness, redness and swelling. About 0.1% have severe generalised reactions, including anaphylaxis, which can be delayed (up to 14 days).
Measles	• Viral infection spread by droplets. Fever, cough, rash. • About 4% of paediatric patients develop pneumonia; about 0.05%, encephalitis, with risk of brain damage or death.	About 10% of vaccine recipients have injection site pain or fever; about 1%, rash. About one in one million recipients develops encephalitis.
Meningococcal infections	• Bacterial infection spread by nasal droplets. Fever, headache, stiff neck, vomiting. • Sepsis and meningitis. About 10% of patients die.	Significant general reactions are rare. About 2% of paediatric recipients have local injection site redness and tenderness or fever.
Mumps	• Viral infection spread by saliva. Swollen salivary glands and fever. • About 0.5% of paediatric patients develop encephalitis, with risk of deafness. About 20% of male patients past puberty develop testicular inflammation, with risk of infertility.	About 1% of vaccine recipients have swollen salivary glands. About one in three million recipients develop mild encephalitis.
Pertussis	• Bacterial infection spread by droplets. Whooping cough and vomiting, lasting up to three months. • About 0.5% of whooping cough patients under six months of age die from pneumonia or brain damage.	Up to 50% of vaccine recipients have injection site pain, redness, swelling or fever. Side effects less common with DTPa.

Disease	Disease characteristics and risks	Side effects of vaccination
Pneumococcal infections	• Bacterial infection spread by droplets. Fever, pneumonia, septicaemia, meningitis. • About 10% of patients with meningitis die.	Up to 10% of vaccine recipients have pain or a local reaction.
Polio	• Viral infection spread by faeces and saliva. • About 0.5% of those hospitalised die; about 50% of survivors have permanent paralysis.	About 33% of Salk vaccine (inactivated polio vaccine) recipients have erythema; about 13%, pain; about 1%, induration. About 5 to 10% paediatric recipients have fever, crying, anorexia.
Rabies and Australian bat lyssavirus infection	• Viral infection contracted by animal bite – usually dogs but also monkeys, bats and other mammals. Irritation or pain at wound, progresses to muscle spasms and death. • Survival unlikely once clinical symptoms present.	Some 74% of vaccine recipients have local reactions (pain, redness, swelling, itching). About 5 to 40% have mild headache, nausea, abdominal pain, muscle aches, dizziness. Much less reaction when vaccine administered intradermally rather than intramuscularly.
Rubella	• Viral infection spread by droplets. About 50% of patients have rash, fever, swollen glands; about 50% of adolescent and adult patients have painful joints. Bruising, bleeding and encephalitis are rare. • High risk of infected pregnant women having babies with severe malformations (deafness, blindness, brain damage, heart defects).	About 10% of vaccine recipients have injection site pain or fever; about 5%, swollen glands, joint pains or stiff neck; about 1%, rash. Bruising and bleeding are much less common.
Tetanus	• Toxin from bacteria in soil. Three to 21 day incubation period. Painful muscle spasms (lockjaw) and convulsions. • Risk of disease with even minor skin wounds. About 10% of patients die. Risk greatest for the very young and very old.	Up to 50% of vaccine recipients have injection site pain, redness, swelling or fever. Side effects less common with DTPa.
Tuberculosis	• Bacterial infection spread by aerosol droplets. Usually lungs affected, but can be any organ; common in developing countries. Cough, sometimes with blood, fever, sweats, weight loss. • Higher risk of disease in long term travellers to areas of high risk.	About 2.5% of vaccine recipients develop injection site abscess; about 1%, lymphadenitis, anaphylaxis, disseminated infection, keloid.
Typhoid	• Bacterial infection of gut and blood, spread by contaminated food or water related to poor hygiene. Abdominal cramps, nausea, diarrhoea, rash and fever. • Up to 20% of patients die if untreated.	Reactions include abdominal cramps, nausea, diarrhoea, rash; rare and mild with the newer vaccines.
Varicella–zoster	• Viral infection spread by droplets. Vesicular rash. • Complications include pneumonia, encephalitis and, less commonly, gut, joint and blood. Causes about 1200 hospitalisations and more than four deaths each year in Australia. More severe in adults and those who are immunocompromised.	Up to 20% of vaccine recipients have local reactions (injection site pain, swelling); fever or rash are less common. Adverse events more frequent in immunosuppressed people.
Yellow fever	• Viral infection spread by mosquitoes. Two to five day incubation period. Symptoms include fever, vomiting, jaundice, severe malaise and bleeding. • Up to 50% of patients die.	About 2 to 5% of vaccine recipients have mild headaches, muscle pains, fever within 10 days. Severe reactions including anaphylaxis very rare. Vaccine associated neurological and viscerotropic disease very rare, although more frequent in the elderly.

* It is important to note that side effects of vaccinations are relatively rare and far outweighed by the benefits. For further information, referral to a travel clinic is recommended.

listed in Table 2. Further details are available in the *Australian Immunisation Handbook, 8th edition*, and the product information for each vaccine.[1] A few comments follow on four specific vaccines, which, in the author's opinion, should only be given by practitioners with considerable experience in administration of these vaccines, such as those in a travel clinic.

Yellow fever vaccine

Yellow fever vaccine contains live virus and is therefore contraindicated during pregnancy, in infants under 9 months of age, and in patients with immune suppression or egg allergy. As immediate hypersensitivity reactions, including anaphylaxis, are well recorded, the patient should be monitored for at least 30 minutes after vaccination, and advised to avoid air travel and remain within easy reach of a medical facility for the next 10 days. Vaccine related viscerotropic and neurotropic disease have been increasingly reported recently, with 28 deaths noted in the last few years. The risk of this appears to be increased with older age groups, and is therefore thought to be immune suppression related.

Japanese encephalitis vaccine

Japanese encephalitis vaccine has been associated with a significant range of local and systemic side effects and for this reason was removed from the Australian market during the 1990s. It has since been recognised that there is a real need for this vaccine. Because the risk of hypersensitivity reactions, including anaphylaxis, may remain for up to two weeks after vaccination, postvaccination precautions similar to those recommended after yellow fever vaccination should be followed. The risk of reactions increases with successive doses.

Rabies vaccine

Rabies vaccine is similarly associated with both local and systemic reactions, the risk of which increases with successive doses, including booster doses given years later. However, in a postexposure dose situation, because of the absolute need to prevent rabies or Australian bat lyssavirus infection, allergic reactions are not contraindications and may be managed with prophylactic antihistamines.

BCG vaccine

BCG vaccine may be associated with local abscess formation or more extensive lymphadenitis sometimes requiring long term antibiotic treatment, especially if more extensive disease develops. Scarring tends to be the norm, with keloid formation in patients who are prone to this.

Conclusion

Although the administration of vaccines often results in adverse reactions, the more serious of these side effects are usually rare. Overall the adverse events are far outweighed by the benefits conferred by the vaccines. MT

DECLARATION OF INTEREST: Dr Cohen is Medical Director, Travel Clinics Australia.

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3. Cohen J. The traveller's pocket medical guide and international certificate of vaccination, 5th ed. Melbourne: Travel Clinics Australia; 2005.

Further reading

1. Centers for Disease Control and Prevention. National Immunization Program. www.cdc.gov/nip (accessed February 2006).
2. World Health Organization. Adverse events following immunization. www.who.int/immunization_safety/aefi/en (accessed February 2006).