Marc Shaw
Claire Wong *Editors*

The Practical Compendium of Immunisations for International Travel

Adis

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‘When going on a journey it is not just the strength of a man’s legs, but the provisions he prepares for the trip’

–Abbot Kaoze (Dr Congo, 1890)

Marc Shaw • Claire Wong
Editors

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Preface

Over one billion overseas visits are made by travellers worldwide each year to a myriad of destinations and for a huge variety of reasons. Each traveller will face different dangers which require individualised risk assessment and appropriate preventative advice. As such, travellers' health and medicine is an evolving, multifaceted specialty requiring travel health professionals to be knowledgeable and confident in advising travellers.

A major focus of travel medicine is vaccines and a knowledge of vaccinology is essential. Health professionals providing travel health advice need to be able to access authoritative and current health information in order to make decisions about appropriate vaccines for travellers going abroad, often into quite remote regions. Decisions on vaccines to be administered are made on analysis of a traveller's projected itinerary, and the 'any number' of vaccine-preventable diseases that the traveller may encounter.

This book serves as a guide for travel health professionals in the primary care medical setting; however, the 'practical compendium of immunisations for international travel' will also be of benefit to all healthcare professionals. It provides comprehensive practical travel vaccine advice, together with solutions to situations when the administration of vaccines is unclear.

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Chapter 1
Introduction

Marc Shaw and Claire Wong

In 2014, over one billion travellers crossed international borders. Whilst most visited industrialised or developed countries, increasing numbers are seeking new destinations that challenge them. These may be in isolated, remote or hazardous regions that contribute to the desire for an adrenaline rush. They may be secluded beaches in well-known tourist resort countries that equally put the traveller well outside their comfort zone. Like the armies of Genghis Khan, the global traveller is looking for new conquests, and as such these travellers need learned and secure travel health advice before spending time in foreign climes, whether this be for days or months.

Immunisation and immunisation programmes are a major success within medical science, for they have become a public health intervention with an immense impact on both national and global health. The year 1796 can arguably be dated as the birth of immunisation, for on the 14th of May Edward Jenner inoculated 8-year-old James Phipps, the son of Jenner's gardener. Jenner had noted the common observation of the time that milkmaids were generally immune to smallpox, so he hypothesised that the pus in the blisters that milkmaids received from cowpox (a similar disease to smallpox) protected them from the more virulent smallpox.

Jenner took pus scraped from cowpox blisters that were on the hands of Sarah Nelmes, a milkmaid who had caught cowpox from a cow called Blossom.

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Incidentally Blossom's hide now hangs on the wall of the St George's medical school library. Jenner inoculated James in both arms on that historical day, and this subsequently produced in the boy a fever and some malaise but no full-on infection. Later, he injected Phipps with variolous material (usually by inserting or rubbing powdered smallpox scabs or fluid from pustules into superficial scratches made in the skin). This was the routine method of immunisation at that time previously used in China and the Middle East and brought to Europe and the United States in the 1700s. No disease followed the procedure, and the boy was later challenged again with variolous material with a similar negative result.

Since this fortuitous development of cowpox 'vaccination' by Edward Jenner, human longevity has been increased, and the burden of disease borne by mankind greatly reduced through the implementation of vaccination programmes.

Travellers' health and medicine is a young discipline that brings focus onto the health and safety of international travellers. Over the last two decades, especially, it has developed into a distinct domain with parameters of responsibility growing in response to the increasing numbers of overseas travellers. As the demand for travel health advice increases, so too has the number of travel medicine service providers.

The discipline is an energetic one that attracts health professionals because it counsels positive social prevention on health issues whilst travelling. With this development has come the need for guidelines and standards with respect to vaccines and immunisation. To this end, in order to provide appropriate, accurate and up-to-date advice for travellers, the travel health professional needs to:

- Be trained
- Have experience in travel
- Be familiar with the guidelines within which they may practise vaccinology

There are a wealth of textbooks and Web-based guidelines available including those from the World Health Organization (Switzerland), the Centers for Disease Control and Prevention (United States) and the National Travel Health Network and Centre (United Kingdom). Bodies such as the Faculty of Travel Medicine of the Royal College of Physicians and Surgeons of Glasgow, the Infectious Diseases Society of America and the International Society of Travel Medicine have published standards and guidelines for the practice of travel health and medicine.

Whilst these resources are valuable to all practitioners, they are generic for the limitations of the discipline. This compendium has an intended focus for those working in primary care travel health and medicine. It is essential that professionals have the availability of good practical information for their day-to-day practice. Vaccine availability, advice and recommendations do differ between countries, and this compendium seeks to bring uniformity of practice to those in Australia, New Zealand and Singapore. No such text is available for those practising in these regions. This is the first and as such needs to encompass the diverse field of 'vaccinology for dummies': vaccine types, names, contents, effects, and contraindications. They are all here and made simple to understand and easy to refer to, easily. The authors are practical individuals and this is the manner in which we edited this text.

We are grateful to the contributors to this compendium. They are some of the region's best writers in the specialty, and we are indeed fortunate to have their thoughts and contributions to what we trust will be a worthy tome on vaccine knowledge for primary care travel health and medicine.

Chapter 2
The Anatomy of Immunity

Helen Petousis-Harris

Key Points

- Vaccines introduce antigens to the immune system in the form of live, dead/inactivated or subunit vaccines.
- Successful immune responses occur following the appropriate response to a foreign antigen:
  - The first response is rapid and non-specific.
  - Specialised but non-specific cells transport and present the vaccine antigen to antigen-specific T cells and B cells within the lymph nodes and spleen.
  - The first wave of antibodies produced by plasma B cells is short-lived and of low affinity.
  - Immune memory takes at least 4 months to develop, but the antibody and memory cells that develop are of high affinity.
- Immune memory is long-lived and can be boosted by further doses of vaccine or natural infection.
- A memory (secondary) immune response is rapid and the antibody of higher magnitude and higher affinity than that produced in the primary response.
- Polysaccharide vaccines do not induce immune memory and are associated with hypo-responsiveness to later doses. Conjugate vaccines overcome these problems.

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Introduction

The primary objective of vaccination is to induce immunological memory against a specific disease. Most vaccines achieve this well, some more effectively than others. Understanding some key aspects of the immune system as well as vaccine types can be helpful when managing vaccine schedules for travellers. The development of the immune response occurs over time, and timing of vaccine doses will need to be considered whenever possible.

Key Words in Immunology

Although immunology is a vast and often complex subject, there are a few key aspects which are useful to keep in mind when considering vaccination. This section introduces some basic principles of immunology that are pertinent when considering vaccination and then discusses the core components that relate to the response to different types of vaccines. Understanding these first principles should assist vaccinators in their use of a diverse and growing catalogue of vaccines.

The Bare Essentials of the Immune System

While complex with many interrelated components, the immune system is broadly comprised of organs, specialised cells and molecules. There is interconnection with other body systems with a diverse range of molecules serving as chemical messengers.

Immune Recognition

Protection against pathogens is not the only function of the immune system. A variety of housekeeping functions remove debris, dead cells and the like; specialised cells identify and destroy cancer cells, and the recognition of foreign material results in the rejection of nonself, such as splinters and organ transplants.

One of the primary mechanisms by which the immune system achieves these functions is through the ability to distinguish ‘self’ from ‘nonself’. The cells in our body have a ‘me’ tag much like a barcode. The absence of this tag will generally result in the destruction of the cell.

The immune response is driven by ‘antigen’ derived from the words *anti*body *gen*erator. Antigen is usually protein based or sugar based. Vaccines often contain purified antigen. The immune system responds to antigens based on their shape, in other words ‘molecular shape recognition’ as it occurs at the amino acid level.

A foreign antigen (such as a fragment of a pathogen or a vaccine component) in combination with a 'me tag' enables the immune system to mount an effective and appropriate response.

Organs of the Immune System

The immune system has organs distributed throughout the body. The primary immune organs are the thymus and bone marrow, where lymphoid tissue is generated. The secondary organs are the spleen, which is a white pulp rich in immune cells, and lymph nodes of which there are 500–600 distributed throughout the body. These swell during infection due to the increased number of white blood cells (lymphocytes) being produced.

Most vaccines (non-live) induce an immune response at the draining lymph node or nodes closest to the site of injection. The spleen and lymph nodes are densely populated with T cells and B cells (*see below*) which are important effectors of a successful immune response. Both lymph and blood flow through the nodes, and the lymph brings with it captured vaccine antigen which comes into contact with the T cells and B cells.

Innate Immunity: Recognition and Response to Nonself

Innate immunity includes a range of cells that recognise nonself. Their reaction when coming into contact with a cell without a 'me' tag or a microbial product is to initiate an immune response. Depending on the warning signal, this response may involve taking up a pathogen and degrading it or destroying virally infected cells. Cells called neutrophils can spit out nets that bind bacteria. Others called macrophages extend projectile-like tentacles to sense and capture foreign proteins or bacteria, and dendritic cells have spiny arms that give them a large surface area in which to take up foreign material. Innate immunity is a first line of defence and can result in the collateral damage of healthy cells and tissue.

In the process of recognising and neutralising foreign material, these cells of the innate immune system take up the material-antigen, degrade it, display it on their surface and transport it to the secondary immune organs (spleen and/or lymph nodes). Such cells are called *antigen-presenting cells*.

Adaptive (Specific) Immunity: Recognition and Effector Response to Target

Adaptive immunity (also called specific immunity) is comprised of two key cell types: T cells and B cells. These cells are specific for a single molecular shape, and each of us has a potential repertoire of some 10^{16} possibilities.

T cells are specific to a single antigen. While one type of T cell assists in B-cell responses, another kills infected cells, while others serve to reside as long-term immune memory for the future.

B cells are also specific to a single antigen. While one type of B cell (B-plasma cell) produces antibody, another type (B memory) resides as long-term memory.

Antibody (also called immunoglobulin or Ig) is secreted by B-plasma cells. Antibodies are molecules which have a highly variable region that recognises just one specific antigen and a constant region that binds to other immune effectors. Many cells in the body have receptors for antibody, which have a range of neutralising functions. The concentration of antibody in the blood is often used to measure the immune response to a vaccine or to assess a person's immunity to a disease.

There are five classes of antibody: IgG, IgM, IgA, IgE and IgD. IgG is generally considered the most important class of antibody and is also the main class that crosses the placenta to confer passive temporary protection to the neonate. IgM is the most predominant in the early primary immune response, and IgA is found primarily in secretions such as breast milk, tears, saliva and mucosal membranes. IgE provides protection against certain parasitic infections; however, in developed countries this is more commonly associated with allergic disease. The function of IgD has remained obscure since the discovery of IgD in 1965. It is co-expressed with IgM on the surface of the majority of mature B cells before antigenic stimulation and functions as a transmembrane antigen receptor.

Innate and Adaptive Immunity Work Together

Microbes have highly conserved features that distinguish them from multicellular organisms, and innate immunity has evolved to exploit these. Special receptors for microbial pattern recognition exist on some cell types, and microbial products such as viral RNA and bacterial lipopolysaccharide are recognised as danger signals by the immune system.

When a pathogen evades the physical barriers such as mucous, skin and tears – or a vaccine is administered – it will be identified as 'nonself' by innate immunity. The innate immune system then alerts the specific arm of the immune system via antigen-presenting cells within the lymph nodes and/or spleen. The specific arm in turn identifies only molecular shape. The first response is delayed, but it results in immune memory in the form of T cells and B cells (Fig. 2.1).

Acquisition and Duration of Specific Immunity

Specific immunity can be acquired either naturally or artificially. Naturally acquired immunity occurs either actively by experiencing the disease or passively through the transfer of maternal antibodies from mother to fetus or infant (transplacental or breast milk). Artificially acquired immunity is either active through vaccination or passive administration of immunoglobulin (such as rabies or tetanus Ig). While

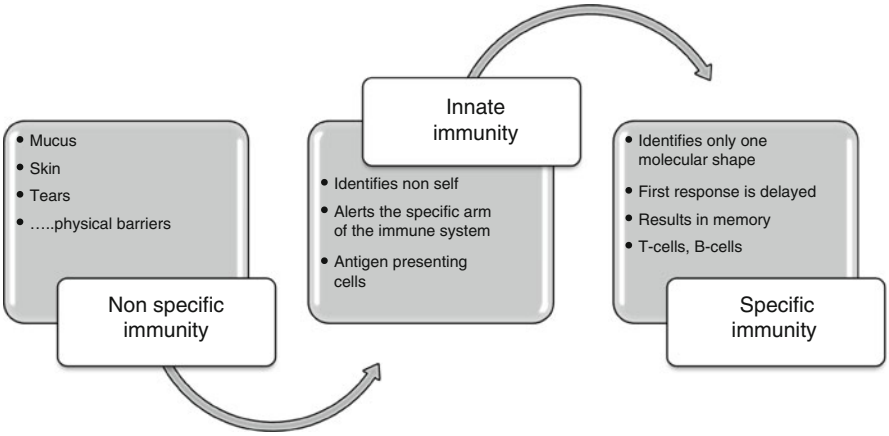

Fig. 2.1 Summary of non-specific innate and specific immunity

active immunity lasts years and often for life, passively acquired immunity lasts weeks to months as the transferred antibodies decay.

Primary and Secondary Immune Responses

A primary immune response is the specific immune response that occurs on first contact with a new antigen. This response results in a rapid appearance of low levels of low-affinity antibody that has a short life span. This tends to peak at 4 weeks then decline. A secondary response can only occur if there is immune memory to stimulate. During a secondary immune response (such as a booster vaccine or contact with disease), there is a rapid production of large amounts of highly specific, high-quality antibody which persists for longer than that produced during a primary response. A secondary immune response can only occur if there is pre-existing immune memory. Figure 2.2 summarises the pattern of antibody responses to primary and booster exposures.

The primary objective of vaccination is to induce an immune memory against a specific pathogen so that should exposure occur in the future, a rapid and specific secondary response prevents disease.

Classification of Vaccines

While many classifications of vaccine types exist, there are generally just three broad vaccine types:

1. *Live attenuated (weakened)*: Live vaccines have been weakened (attenuated) so that they stimulate an immune response qualitatively similar to natural infection but are unable to cause disease. Immunity from these vaccines is usually long-lived.

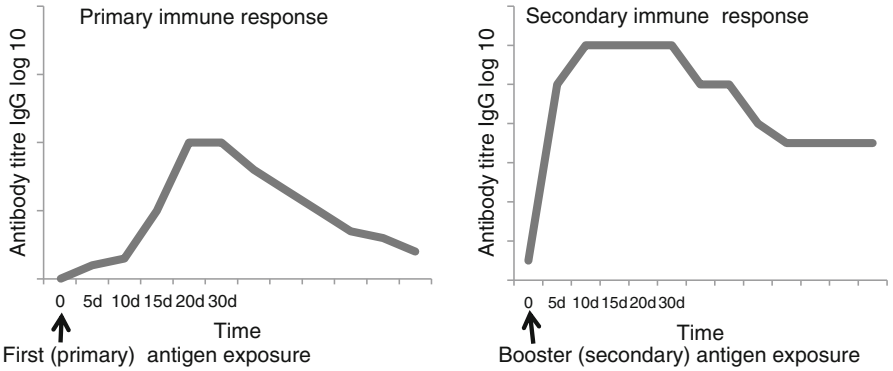

Fig. 2.2 Comparison of primary and booster (secondary) antibody responses to protein-containing vaccines. Booster responses are faster (peaking at day 7) and the antibody titres are higher, more prolonged and of higher neutralising capacity

Live attenuated	Killed/Inactivated	Sub unit
• Viral • Measles • Mumps • Rubella • Varicella • Zoster • Rotavirus • Polio (OPV) • Influenza • Yellow fever • Bacterial • BCG • Oral typhoid	• Killed refers to bacterial • wPertussis • Cholera • Inactivated refers to viral • Polio (IPV) • Influenza • Hepatitis A • Cell mediated rabies vaccines	• Excreted toxins: • Tetanus • Diphtheria • Pertussis • Selected antigens • Hepatitis B • Hib • Pneumococcal • aPertussis • HPV • Meningococcal • Typhoid polysaccaride

Fig. 2.3 Broad classification of vaccine types with examples

2. *Killed/inactivated*: Killed vaccines are those that consist of whole but dead bacteria, while inactivated vaccines consist of viruses that have been inactivated – as viruses are not 'alive', they cannot be killed, hence the term 'inactivated'.
3. *Subunit and toxoid*: Subunit vaccines are those that use a part of a disease causing pathogen that generates protective immunity. Subunit vaccines include those that are microbial fragments, those that consist of genetically engineered proteins, purified toxins treated to detoxify them (toxoids) and purified sugars (polysaccharides). Examples of different types of vaccines are summarised in Fig. 2.3.

The Immune Response to Vaccines

Immune Response to Protein-Based Non-live Vaccines

Once the vaccine is injected into the muscle or subcutaneous tissue, a local inflammatory response ensues, and antigen-presenting cells migrate to the injection site. The antigen (and adjuvant[1] if present) is taken up by these cells and digested into fragments only a few amino acids, or peptides, long. These tiny peptides are then displayed on the cell surface along with other important molecules including the 'self-identification' tag. The antigen-presenting cells then migrate, via the lymph, to a local lymph node.

Within the lymph node there is interaction between the antigen-bearing cells and the antigen-specific T cells and B cells. Once T and B cells recognise the antigen, two important things occur:

1. Some B cells rapidly develop into B-plasma cells and produce small amounts of low-affinity antibody which can be detected in the blood just a few days after vaccination.
2. T cells trigger other B cells to migrate towards further specialised cells, and a germinal centre is initiated. This centre induces B cells to proliferate and undergo class switching (i.e. from IgM to IgG or IgA) and affinity maturation, becoming more highly specific towards the antigenic shape originally presented. There will also be differentiation into more B-plasma cells which secrete very large amounts of highly specific antibody. Some of these cells will be long-lived. In parallel to the generation of plasma cells, memory B cells are also generated and persist in the blood, spleen and nodes until re-exposed to their specific antigens at which time they rapidly divide and differentiate into antigen-producing plasma cells. When this occurs large amounts of high-affinity antibody can be measured in the blood within a few days.

The germinal centre reaction takes around 4 months to occur. Therefore, the development of immune memory takes around 4 months. This is important to keep in mind when considering vaccine schedules as boosters are not boosters in the absence of immune memory.

Vaccine schedules for protein-based vaccines consist of one to three priming doses possibly followed by a booster dose, particularly in infancy. Highly immunogenic vaccines may only require a single dose.

Safety of Protein-Based Subunit Vaccines Because subunit vaccines are unable to cause infection, they cannot possibly cause disease. The response to them occurs locally at the injection site, and injection site reactions can occasionally be extensive and normally occur on the day of injection lasting up to a few days. This is as a result of the inflammatory response and unless it causes excessive discomfort is a

[1] Adjuvant – substance that enhances the immune response to the antigen, usually an aluminium salt

positive indication that the immune system is responding to the vaccine. As a result of this inflammatory response, a fever, headache and malaise may occur, but these are much less common than local reactions and usually only last a few hours. While anaphylaxis can occur after any vaccine, the risk is usually around one per million doses. Other serious events following these vaccines are very rare.

Immune Response to Live Vaccines

Unlike protein-based vaccines above, live vaccines do not deposit locally in the muscle. Instead they disseminate in a pathogen-specific manner to replicate. The specific immune response is multifocal with a more generalised activation of lymph nodes. However, like the protein-based vaccines, live vaccines induce long-term immune memory, possibly life-long in the case of measles, rubella and yellow fever vaccines.

Safety of Live Vaccines Because live vaccines do not depend on a local inflammatory response, injection site reactions after administration of these vaccines are less common and generally milder than those associated with killed, inactivated and subunit vaccines. However, systemic reactions do occur and are generally associated with viral replication, and timing of onset of these events coincides with this. For example, most events associated with administration of measles-containing vaccines, such as MMR, occur 7–14 days after administration.

Persons who have certain immunosuppressive conditions may be contraindicated for some live vaccines as they may be unable to control the limited viral replication that occurs with these vaccines.

Immune Response to Polysaccharide Vaccines

Polysaccharide vaccines behave differently from both protein-based and live vaccines. Once injected the antigen diffuses into the blood and comes into direct contact with antigen-specific B cells in the absence of antigen-presenting cells. There is no T-cell involvement in the immune response. Within the spleen and/or lymph nodes, the antigen-specific B cells will be activated, proliferate and differentiate into plasma cells which produce small amounts of low-affinity antibody. The plasma cells will survive for weeks or months. No T-cell or B-cell immune memory is produced in response to polysaccharide vaccines.

When polysaccharide vaccines are used more than once (multiple doses), they have been associated with a hypo-responsiveness (lowered immune response) whereby the antibody response reduces after successive doses. There is also concern that repeated doses could result in ‘clonal exhaustion’ where the specific B-cell pool becomes depleted due to successive primary responses and cannot be replenished.

It is important to understand that the polysaccharide and conjugate vaccines are very different. Polysaccharide vaccines are available against meningococcal groups A, C, W135 and Y and 23 serotypes of pneumococcus. These vaccines are relatively cheap and provide effective short-term protection in older children and adults. However, they are both associated with hypo-responsiveness to later doses. This includes a lowered immune response to the superior conjugate. The routine use of polysaccharide vaccines is not recommended, and vaccinees need to be aware that there is only very short-term protection offered which cannot be boosted at a later date.

Booster Responses (Secondary Responses)

Once a primary immune response has occurred, such as through a primary dose or doses of vaccine, then this can be boosted – provided there has been time for affinity maturation and immune memory to have developed (at least 4 months). Immune memory can be boosted by revaccination with the same vaccine or by exposure to the disease. While polysaccharide vaccines can also be used as boosters, this is not generally recommended any longer.

Overcoming the Problems of Polysaccharide Vaccines

The problem of polysaccharide vaccines has been overcome by the technology of conjugation whereby the polysaccharide (sugar) is chemically linked to an immunogenic protein, effectively converting it into a protein-based vaccine. The first of these vaccines was against *Haemophilus influenzae* type b (Hib) followed by vaccines against *Neisseria meningitidis* and then *Streptococcus pneumoniae.* The differences between polysaccharide vaccines and conjugate vaccines are summarised in Table 2.1.

Table 2.1 Key differences between polysaccharide vaccines and conjugate vaccines

	Polysaccharide vaccine	Conjugate vaccine
Immunogenicity: older children – adult	High	High
Immunogenicity: very young children (especially <2 years)	Poor	High
Booster response	Poor	High
Antibody avidity in children	Low	High
Antibody bactericidal activity (bacterial 'killing' ability) in children	Low	High
Induction of immune memory	No	Yes
Effect on colonisation (prevents carriage and transmission)	No	Yes

Further Reading

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Chapter 3
Common Vaccine-Preventable Travel-Related Diseases

Practical Information: What the Traveller Wants to Know and Now!

Marc Shaw

Key Points

- Many travellers are not properly immunised before travel. Often this is because they do not understand the significance of the diseases that they may encounter.
- In addition to individual consequences, vaccine-preventable travel diseases (VPD) can have public health consequences if they are introduced or reintroduced by infected travellers returning to areas with susceptible populations.
- Travellers suffering from VPD are frequently hospitalised.
- More people are travelling to more destinations, becoming exposed to the health and safety issues of that destination and also having the potential to impact the health and safety of that destination.

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Introduction

In 2014, over a billion tourists will cross international borders. Whilst travel to industrialised countries predominates, travel to less-developed regions is increasing and anticipated to approximate that of many developed countries by 2020. Like the armies of Alexander and Genghis Khan, the global traveller is looking for new territories to explore and take business to. Such travellers will need travel health advice before going forth.

Vaccination is a major success of medical science, being a public health intervention with a massive impact on national and global health. Since the incidental development of smallpox 'vaccine' by Edward Jenner, human longevity has been increased, and the burden of vaccine-preventable disease greatly reduced through the implementation of vaccination programmes.

This chapter will punch-point ten common vaccine-preventable diseases, so guiding the travel health professional to their simple explanation and for the traveller, an easy understanding.

Cholera

Medical

Cholera is an acute bacterial enteric disease causing severe diarrhoea and dehydration. It is caused by the toxin-producing bacterium *Vibrio cholerae* serogroups O1 and O139. *V. cholerae* serogroup O1 causes the majority of cholera outbreaks and has two biotypes, classical and El Tor. Each biotype has two serotypes, Inaba and Ogawa. The symptoms of infections are similar, although more people infected with the El Tor biotype remain asymptomatic or with only a mild illness.

Cholera is invariably a disease of poverty and is associated with poor sanitation. It is generally acquired from contaminated water or food, particularly undercooked or raw fish or shellfish. Direct transmission from person to person is possible but it is not common. It has a short incubation period, from less than 1 day to 5 days, and produces an enterotoxin that causes a profuse, painless, watery diarrhoea and nausea and vomiting. This can quickly lead to severe dehydration and hypovolaemic shock and ultimately death in a short time, if treatment is not promptly given. Case fatality ranges from 50 % or more without treatment to less than 1 % among adequately treated patients. The spectrum of disease is wide, with mild and asymptomatic illness occurring more frequently than severe disease.

Incidence

The World Health Organization (WHO) estimates that approximately 3–5 million cholera cases occur annually, with up to 120,000 deaths. However, the risk to travellers is low (0.2 cases per 100,000 travellers). For long-term travellers in areas of outbreaks,

the rate may be as high as 500 cases per 100,000 travellers. Cholera is endemic in many countries. A map of the areas reporting cholera risk is available from the WHO (http://gamapserver.who.int/mapLibrary/Files/Maps/Global_ChoeraCases_ITHRiskMap.png?ua=1).

About 75 % of people infected with *V. cholerae* do not develop any symptoms, although the bacteria are present in their faeces for 7–14 days after infection and are shed back into the environment, potentially infecting other people. Among people who develop symptoms, 80 % have mild or moderate symptoms, whilst around 20 % develop acute watery diarrhoea with severe dehydration.

Treatment

Rehydration is the basis of the treatment for cholera. Oral rehydration salts, or intravenous fluids and electrolytes in severe cases, administered appropriately will keep the case fatality rate to below 1 %. Antimicrobials may be considered: doxycycline, azithromycin or fluoroquinolone.

Prevention

Safe food and water precautions. For example, drink only water that has been boiled or disinfected with chlorine or iodine. Drinks such as hot tea or coffee, wine, beer, carbonated water and bottled or packaged juices are usually safe to drink. Avoid ice, unless there is certainty that it is made from safe water. Eat food that has been thoroughly cooked and is hot when served. Avoid raw seafood and other raw foods, except fruits and vegetables that are personally peeled or shelled. Boil unpasteurised milk before drinking. Ice cream from unreliable sources is frequently contaminated. Frequent handwashing is critical in preventing cholera.

An oral cholera vaccine is available.

What the TRAVELLER Needs to Know

Cholera is a sudden-onset disease caused by infection of the intestine with bacteria and is characterised by severe watery diarrhoea, vomiting and leg cramps. The risk of the traveller getting the disease is very low, approximately 1/50,000–200,000. It tends to be a disease of mass migratory populations (refugees) or where the sanitary infrastructure has broken down rather than one affecting the casual traveller.

The best prevention is to be vigilant with personal hand hygiene.

Immunisation is recommended only in limited circumstances and can be considered for:

- Relief and disaster workers
- Those travelling to remote areas or where there is limited access to medical care
- Those working in areas of cholera endemicity or epidemicity
- Those with gastrointestinal or suppressed immune medical problems, inflammatory bowel disease, irritable bowel syndrome or malabsorption
- Military personnel

Hepatitis A

Medical

Hepatitis A virus (HAV) is transmitted via the oral-faecal route by way of direct person-to-person contact, through contaminated food or water or contamination of an environment or objects. Transmission through infected blood, or blood products, has also been reported. Symptoms appear after an incubation period of 15–50 days (average 28 days). Cases are typically infectious 2 weeks before the onset of symptoms and remain infectious until a week after the onset of jaundice. The virus may remain infectious in the environment for several weeks – HAV can survive up to 7 days in ambient temperatures and 10 months in water. Viral shedding can be greatly prolonged in immunocompromised individuals.

Only a small proportion of infected children develop jaundice, but 75 % of infected adults develop classic icteric disease with fever, fatigue, nausea and anorexia. The case fatality rate varies with age and is highest in older individuals: approximately 2 % in those over 40 years and up to 4 % in those over 60 years. Older individuals tend to have a more protracted illness.

The virus is present in bile, blood, stools and liver during the late incubation period and the early phase of the illness. During this time, HAV is shed in the faeces. The average duration of the illness is one month, but symptoms of the disease may last up to a year.

Incidence

The incidence of HAV infection is approximately 1.4 million known cases per year, though the real incidence is probably as least double this. The risk of developing HAV for nonimmune travellers to developing countries has previously been cited as approximately three to five cases per 1,000 per month of travel. However, the changing epidemiology of HAV in many previously high-risk countries has provided a newer and much lower estimate of 6–30 cases per 100,000. An individual's risk relates to the destination region, the duration of stay, the local hygienic conditions and the degree of contact with the local population.

A map of the areas reporting HAV risk is available from the WHO (http://gamapserver.who.int/mapLibrary/Files/Maps/Global_HepA_ITHRiskMap.png?ua=1).

Treatment

Hepatitis A is a viral infection. There is no specific treatment. Management is conservative.

Prevention

Long-term protection from HAV infection can be achieved through active, pre-exposure vaccination with HAV vaccine. In addition, there is a combined hepatitis A and B vaccine that will give added protection against hepatitis B virus (HBV). All vaccines are produced from HAV grown in cell culture, inactivated with formalin and formulated with alum adjuvant, in adult and paediatric dosages. They are effective in preventing clinical disease in adults and adolescents when administered according to recommended schedules.

What the TRAVELLER Needs to Know

Hepatitis A is the second most common vaccine-preventable disease in travellers behind seasonal influenza. Protection against HAV is recommended for all travellers to developing countries, especially to rural areas or places with inadequate sanitary facilities. Given the long incubation period for hepatitis A and the demonstrated efficacy of postexposure use of vaccine, administration of hepatitis A vaccine even up to the day of departure is considered appropriate and effective.

Food, drink and personal hygiene precautions will reduce the risk of HAV infection.

Immunisation is advised for global travel. The vaccine is safe and effective, and immunity develops quickly.

Hepatitis B

Medical

Hepatitis B virus (*HBV*) is transmitted through contact with infectious body fluids such as blood and semen or through blood transfusions of HBV contaminated blood products. In addition, HBV can be transmitted from infected mothers to infants

perinatally, from family member to an infant in early childhood, through contaminated injections during medical procedures or through injecting drug use. It is therefore a risk to healthcare workers who may sustain needlestick injuries from infected individuals and also to those receiving haemodialysis. Major routes of transmission among adults in Western countries are intravenous drug use and sexual contact. The risk of HBV infection is notably high in promiscuous men who have sex with men.

Modes of transmission are thus the same as for HIV but HBV is 50 to 100 times more infectious. Unlike HIV, HBV can survive outside the body for at least 7 days. During that time, HBV can still cause infection if it enters the body of a nonimmune person.

HBV can produce either asymptomatic or symptomatic infection. The average incubation period is 90 days (range 60–150) from exposure to onset of jaundice and 60 days (range 40–90) from exposure to onset of abnormal liver enzymes. The onset of acute disease is usually insidious. Infants and children below 10 years of age are typically asymptomatic

Incidence

An estimated 240 million people have chronic HBV infection globally. Published reports of travellers acquiring hepatitis B are rare, and the risk for travellers without high-risk exposures is low. It is estimated that 25 % of travellers to endemic countries are at high risk for HBV exposure during their travel. This exposure is often unpredictable. Growing 'health tourism' brings a special risk of HBV in those returning from surgery in disease-endemic countries.

Among long-term residents of endemic areas, the incidence of symptomatic HBV infection ranges from 0.2/1,000 in Africa and Latin America to 0.6/1,000 in Asia. The rates of seroconversion including asymptomatic infection are 0.8 and 2.4, respectively.

A map of the areas reporting HBV risk is available from the WHO (http://gamapserver.who.int/mapLibrary/Files/Maps/Global_HepB_ITHRiskMap.png?ua=1).

Treatment

There is no specific treatment for acute viral hepatitis B. The use of adrenocorticosteroids in the management of acute, uncomplicated hepatitis B is not indicated because they have no effect on the resolution of the underlying disease process and may increase the rate of relapse. The therapeutic effectiveness of interferon on the course and prognosis of acute hepatitis B is not known.

Prevention

Immunisation with hepatitis B vaccine is the most effective means of preventing HBV infection and its consequences.

What the TRAVELLER Needs to Know

Hepatitis is an inflammation of the liver. HBV infection can be self-limiting or can progress to scarring, cirrhosis or liver cancer. Hepatitis viruses are the most common cause of hepatitis in the world, but other infections, alcohol, certain drugs and autoimmune diseases can also cause hepatitis.

Hepatitis B (and C and D) usually occurs as a result of contact with infected body fluids. Common modes of transmission for these viruses include sexual contact, receipt of contaminated blood (through blood transfusions) or blood products, invasive medical procedures (including dental work, cosmetic procedures or injections) using contaminated equipment, tattoos, body piercings, acupuncture or any activity that is likely to result in abrasions or broken skin. HBV and other pathogens can be transmitted if the equipment is not adequately sterilised or if the operators do not follow proper infection control. Hepatitis B transmission can occur from mother to baby at birth and from family member to child.

Immunisation is advised for global travellers. The vaccine is safe and effective, and immunity develops quickly.

Japanese Encephalitis

Medical

Japanese encephalitis (JE) is an arthropod-borne viral (arboviral) disease endemic throughout Asia and Northwest Oceania. JE virus is transmitted to humans primarily through the bite of mosquitoes infected from hosts such as pigs and wild birds, which then transmit the virus to noninfected hosts (e.g. humans and horses). The principal vectors are *Culex* species mosquitoes which generally tend to bite in the evening and night.

Larvae of *Culex* mosquitoes develop in standing water, such as rice fields. Consequently, JE virus transmission occurs principally in rural agricultural areas where there is flooding irrigation. Occasionally, however, cases have sporadically been reported from urban areas.

The incubation period is 5–15 days. In hyperendemic regions, seroprevalence studies indicate nearly universal exposure by adulthood. Children are thus more

likely to present with the signs and symptoms of JE. Approximately 1 in 250 infections in susceptible individuals is symptomatic.

The main clinical feature of JE is encephalomyelitis presenting as seizures in children but only as headaches and meningism in adults. The case fatality rate of symptomatic JE is approximately 30 %. Of those that survive, 30–50 % will have serious neurological, cognitive or psychiatric sequelae. It is estimated that more than 50,000 JE cases occur annually, with 10,000 deaths and 15,000 cases of long-term neuropsychiatric sequelae. From 1973 until 2011, there have been 58 published reports of travel-associated JE among travellers from non-endemic countries.

Humans usually do not develop sufficient viraemia to infect mosquitoes, and direct person-to-person spread of JE does not occur except, rarely, through intrauterine transmission. Nevertheless, transmission could theoretically occur through blood transfusions or even organ transplantation.

Incidence

1. *For short-term travel*: The overall incidence of JE reported among people from non-endemic countries travelling to Asia is <1 case per 1 million travellers.
2. *For long-term travel*: Expatriates and travellers staying for long periods in rural areas with active JE transmission have similar risk as a susceptible resident population: 0.1–2 cases per 100,000 persons per week of travel. This equates to a risk for travellers spending time in rural destinations during the rainy season of between 1 case/5,000/week (epidemic) and 1 case/20,000/week (endemic).

A map of the areas reporting JE risk is available from the WHO (http://gamapserver.who.int/mapLibrary/Files/Maps/Global_JE_ITHRiskMap.png?ua=1).

Treatment

There is no specific antiviral management for JE, and the treatment thus is supportive conservative care.

Prevention

Mosquito prevention measures remain paramount in prevention of JE. An inactive vaccine currently available (Jespect or Ixiaro) has a seroconversion rate of 98 % following two doses, whilst a live single-dose vaccine (Imojev or JE-ChimeriVax) has a seroconversion rate of 99 %.

What the TRAVELLER Needs to Know

JE virus is the most common vaccine-preventable cause of encephalitis (brain infection) in local populations throughout most of Asia and parts of the Western Pacific. The disease is not found in Europe, in Africa or in the Americas. Transmission principally occurs in rural agricultural areas, often associated with rice cultivation and flood irrigation.

In temperate areas of Asia, transmission is seasonal, with human JE usually peaking in summer and autumn. In the tropics and subtropics, transmission varies with both monsoon rains and irrigation practices; thus, it may occur year-round.

For most travellers to at-risk regions, the incidence of JE is extremely low but varies based on destination, duration, season and activities. Travel-related JE can occur among people of any age.

It is important that travellers are careful to avoid being bitten by mosquitoes by using insect repellents, using mosquito nets where possible and wearing appropriate clothes.

Immunisation is recommended only in limited circumstances, such as for when travellers spend time in rural or remote regions of Asia.

Meningococcal Meningitis

Medical

Invasive meningococcal disease (IMD) is an acute and serious communicable disease caused by the gram-negative bacterium *Neisseria meningitidis*, resulting in meningitis, septicaemia (meningococcemia) or both. IMD disease is endemic in all countries, but recurring epidemics of the disease occur in certain regions of the world, particularly in the 'meningitis belt' region of sub-Saharan Africa and adjacent regions to this belt and also around the Rift Valley and Great Lakes in Africa. Immunisation before travel to high-risk meningococcal destinations is advised.

Meningococci can be classified based on the immunologic reactivity of the polysaccharide capsule into 13 different serogroups, of which 5 (A, B, C, W-135 and Y) are associated most frequently with IMD globally. Of these, serogroups A and C are most commonly associated with epidemics of meningitis, especially in Africa in the dry winter months from December to June. Nasopharyngeal colonisation with *N. meningitides* occurs naturally in 5–10 % of healthy individuals although many of the strains are nonpathogenic. Person-to-person transmission of the disease occurs by close contact with respiratory secretions or saliva. Crowding, low humidity and smoke exposure indoors all favour transmission of infection. Whilst the disease may affect all ages, there are two peaks in age distribution: 1–5 years and 15–19 years.

The Hajj pilgrimage to Saudi Arabia has been associated with outbreaks of IMD in returning pilgrims and their contacts.

Incidence

During non-epidemic periods, the rate of meningococcal disease approximates 5–10 cases per 100,000 population per year. During epidemics this rate can climb to 1 % of the populace, or 1,000 per 100,000 population. Risk for travellers is low, depending on the region to be visited. Mortality rate of approximately 10 % makes prevention realistic for at-risk travellers.

A map of the areas reporting meningitis risk is available from the WHO (http://gamapserver.who.int/mapLibrary/Files/Maps/Global_MeningitisRisk_ITHRiskMap.png?ua=1).

Treatment

IMD is potentially fatal and is considered a medical emergency. Prompt antibiotic therapy is essential, and cases of the disease need to be hospitalised.

Prevention

Immunisation against the disease is advised for those travelling to, or residing in, countries where *Neisseria meningitidis* is hyperendemic or epidemic. This is especially so if contact with the local population is envisaged and prolonged.

A quadrivalent vaccine including the serogroups ACYW135 is required for travel to the Hajj and Umrah pilgrimages in Saudi Arabia.

What the TRAVELLER Needs to Know

Meningitis is an inflammation of the brain and is a medical emergency. There are a number of vaccines available, depending on whether short- or long-term exposure to the disease is anticipated. Vaccines are 85–90 % effective against serotypes A, C, Y and W135. Immunity is effective in 10–14 days.

Immunisation is required for travel to the Hajj and Umrah. It is recommended for travel to much of sub-Saharan Africa and for students travelling to Western nations who may be residing in student accommodation.

Poliomyelitis

Medical

Poliomyelitis, also known as polio or infantile paralysis, is a disease of the central nervous system. Following primary asymptomatic infection of the alimentary tract, less than 1 % develop paralytic disease. In developing countries, 65–75 % of cases occur in children under 3 years of age and 95 % in children under 5 years of age. The resulting paralysis is permanent, although some recovery of function is possible.

Poliovirus is a member of the enterovirus subgroup of the *Picornaviridae* family. There are three serotypes of wild-type poliovirus (WPV): type 1, type 2 and type 3. Wild-type 2 poliovirus has been eliminated from global circulation. In rare cases, polio infection can occur due to circulating vaccine-derived poliovirus (cVDPV). This is a strain of poliovirus that has genetically mutated from the strain in the oral polio vaccine (OPV), a vaccine that contains live-attenuated virus. The WHO is planning on withdrawing OPV globally by 2019/2020.

Polioviruses are spread predominantly by the faecal-oral route and less commonly by the oral-oral and respiratory routes. The incubation period for paralytic cases of polio is generally 7–14 days. Communicability is greatest around the onset of illness when the virus is present in high concentrations in the throat and faeces. After the first week of illness, the concentration of poliovirus in the throat decreases. However, poliovirus can continue to be excreted in faeces for 3–6 weeks. In individuals who have received oral polio vaccine (OPV), poliovirus can be present in the throat 1–5 weeks following immunisation and can remain in the faeces for several weeks. In some cases, including immunocompromised persons, poliovirus (from natural infection or OPV vaccine) can be excreted over sustained periods of time, e.g. 6 months to many years. A rare side effect of the usage of OPV is vaccine-associated paralytic poliomyelitis (VAPP), which is a rare event (0.5 cases per one million first-time OPV doses). It occurs among first-time OPV recipients and contacts of first-time OPV recipients in roughly equal frequencies.

In temperate climates, polio infection generally increases in the late summer and autumn months.

In rare cases, individuals can develop vaccine-derived polio following immunisation with the OPV. The OPV contains a live, attenuated (weakened) vaccine virus. Upon vaccination, the attenuated vaccine virus replicates in the intestine before entering into the bloodstream to trigger a protective immune response. It is possible for the virus to become genetically altered during replication resulting in a new form of the virus. This cVDPV can in rare cases cause paralysis. Vaccine-derived paralytic poliomyelitis occurs in an estimated 1 in 2.7 million children receiving their first dose of oral polio vaccine.

Polio remains endemic in three countries – Afghanistan, Nigeria and Pakistan as of February 2015. In 2013 and 2014, outbreaks following importation of wild poliovirus

from endemic countries occurred in Cameroon, Somalia, Equatorial Guinea, Ethiopia, Kenya, Iraq, Syria and Israel. Polio cases due to cVDPV were reported in 2013 from Nigeria, Niger, Chad, Cameroon, Pakistan, Afghanistan, Somalia and Yemen.

Incidence

Globally in 2013, 416 cases occurred – 160 in endemic countries and 256 in non-endemic countries.

A map of the areas reporting polio risk is available from the WHO (http://gamapserver.who.int/mapLibrary/Files/Maps/Global_PolioRisk_ITHRiskMap.png?ua=1).

Treatment

Only symptomatic treatment is available, ranging from pain and fever relief to intubation and mechanical ventilation for patients with respiratory insufficiency.

Prevention

Until worldwide eradication of polio has been achieved, routine vaccination to prevent poliomyelitis needs to continue. Childhood immunisation is a priority as is primary immunisation for nonimmune adults. A booster is recommended for adults travelling to epidemic or endemic areas or for those with other exposure risks. Travellers should practise strict food, water and personal hygiene. Travellers visiting countries where cases of WPV and cVDPV are being reported need to receive a booster dose of polio-containing vaccine if they have not received one within the past 10 years.

What the TRAVELLER Needs to Know

Travellers can be important carriers of polioviruses and infect contacts when they return from travelling. Those who receive an initial series of vaccinations against the disease, together with a booster, can expect around 95 % immune protection.

Immunisation is recommended for travel to sub-Saharan Africa, South Asia and the Middle East, for regions where WPV and cVDPV is being reported and for healthcare workers at possible exposure to the disease.

Rabies

Medical

Rabies is an acute progressive fatal encephalitis caused by neurotropic RNA viruses in the family *Rhabdoviridae*, genus *Lyssavirus*. There are 13 recognised or proposed lyssaviruses estimated to cause at least 55,000 human rabies-related deaths worldwide each year, a figure likely greatly underestimated, mostly in Asia and Africa. The virus attacks the central nervous system, causing progressive paralysis, encephalitis and coma. Once symptoms are present, rabies is almost always fatal.

Rabies occurs in mammals (both domestic and wild) and is transmitted to humans, usually by a bite from an infected dog, bat, cat or monkey with the former being responsible for over 90 % of exposures. Notwithstanding transmission that occurs in this most common and typical manner, it can also variably occur by way of mucous membrane, saliva-contaminated scratches, rarely via aerosol transmission or via transplantation of an infected organ. The higher the density of nerves in the region of the bite or lick, the higher the risk of rapidly developing encephalitis. Typically the hands and face are most prone because of the concentration of nerve endings in those areas.

In many regions of the world where the risk of rabies is high, access to standard WHO asserted postexposure prophylaxis (PEP) is limited. The incidence of imported rabies in travellers has been estimated at 2 per year.

Information about the risk of rabies for travellers to tropical countries and recommendations for the use of preventive measures are often neglected in the pre-travel advice provided by healthcare practitioners. This lack of information provided usually results from a lack of knowledge about the risk of acquiring rabies during a journey to countries endemic for the disease.

Incidence

The incidence of injuries to travellers caused by potentially rabid animals has been estimated to be 0.4 % per month of stay, whilst the risk of acquiring fatal rabies following exposure to a rabid animal reportedly varies from a low of 0.1 % in persons experiencing non-bite exposures to a high of 60 % in persons with penetrating wounds or hand or face lesions. Annually, it is estimated that over ten million people are exposed to potentially rabid animals.

A map of the areas reporting rabies risk is available from the WHO (http://gamapserver.who.int/mapLibrary/Files/Maps/Global_Rabies_ITHRiskMap.png?ua=1).

Treatment

There is no specific treatment for rabies once symptoms appear.

Prevention

1. *Pre-exposure*: Among the rabies vaccine products, the modern cell culture vaccines (CCV) are the safest and the most immunogenic. Human diploid cell vaccine, purified chick embryo cell vaccine, and purified vero cell rabies vaccine are the CCVs most commonly available globally. They are interchangeable. The older neural cell vaccines, still used in some countries though not advised, are not as effective as the CCVs and are associated with more side effects from vaccination. They are to be avoided.
2. *Postexposure*. Prompt and appropriate postexposure treatment, including the use of rabies immunoglobulin (RIG) and rabies CCV vaccine, virtually eliminates rabies fatalities.

What the TRAVELLER Needs to Know

Rabies is a deadly illness caused by a virus that spreads to humans through penetrating contact (e.g. broken skin) with the saliva of an infected mammal, usually a dog, most often from licks, bites or scratches. If there is a risk to the traveller of having had an exposure, then immediate medical attention is required.

The risk of being exposed to a rabid animal depends upon the following:

1. Intended destination: The disease is more common in Asia, Africa and the Indian subcontinent.
2. Duration of travel: Approximately half of all potential exposures occur within the first 2 weeks of travel.
3. Remoteness of the destination: Accessing postexposure treatment is more difficult in remote areas.
4. Personal activities: Risk is higher with activities that may enable close contact with animals – hunting, camping, cycling and caving. Travellers in close contact with animals are at higher risk.
5. Age of the traveller: Children are considered at higher risk as they often play with animals never before seen alive, are less likely to report bites or scratches and are more likely to be bitten in the head and neck area. Rabies is most common in children under the age of 15 years.
6. Access to medical care.

Immunisation is recommended for travellers to regions where rabies occurs who are at increased risk (see above) and for those concerned about the disease.

Travellers' Diarrhoea

Medical

WHO defines travellers' diarrhoea (TD) as greater than or equal to 3 loose bowel motions within 8 h or 4 or more within 24 h plus 1 of nausea, vomiting, abdominal cramps, mild fever or tenesmus.

The point of the definition is that many travellers assume that ANY loose motion is TD, and they may tend to self-treat unnecessarily. TD can vary from just a few extra-loose bowel movements per day to an illness with profuse bloody diarrhoea and fever (dysentery). Dysentery occurs in up to 10 % of persons. Of those affected, it is estimated that 30 % will be confined to bed, and over 40 % will have to curtail their activities. In warm climates dehydration can be severe, even fatal, particularly in children.

Most episodes of TD are mild and self-limited although the illness can be debilitating and particularly difficult to manage in remote or unfamiliar surroundings. Some travellers experiencing more severe acute inflammatory gastroenteritis may develop persistent gastrointestinal symptoms, but long-term sequelae resulting from noninflammatory gastroenteritis such as that caused by enterotoxigenic *Escherichia coli* (ETEC) are very uncommon.

Though viruses and parasites cause TD, bacterial causes such as ETEC remain the most common source of TD. Many ETEC strains produce a heat-labile enterotoxin that is similar to cholera toxin. ETEC is transmitted by contaminated food and, less often, contaminated water. The incubation period is usually 24–72 h though excretion of ETEC may be prolonged.

The most important determinants of risk for TD are the travel destination and the type of travel (e.g. backpacking vs. five-star accommodations). Factors associated with a higher probability of acquiring TD include gastric hypochlorhydria and the relative lack of gut immunity seen in small children. In addition, specific groups of travellers are at increased risk of serious consequences of TD:

- Persons with chronic illnesses, such as immunodeficiency diseases
- Individuals with chronic renal failure
- Persons with congestive heart failure
- Individuals with insulin-dependent diabetes mellitus
- Persons with inflammatory bowel disease

Incidence

It is estimated that 30–70 % of travellers from high-income countries who visit low-income countries will be affected by TD. The highest rates are seen in Latin America, Africa and the Indian subcontinent, whilst intermediate rates of 8–15 % are seen for travellers to China, Russia, the Middle East and Southeast Asia.

Treatment

The most important aspect of TD management at any age is adequate hydration, by either oral or intravenous administration as appropriate to the level of the traveller's dehydration. Various commercially made or homemade fluid preparations can be used. Whilst antibiotics can also be given, it needs to be noted that fluid replacement is *the* most important first-line management. Travellers are advised to plan a management schedule along the following lines, in case they get TD whilst abroad.

TD is usually treated with a series of measures such as:

- *Fluids to replace* the amounts lost through diarrhoea and vomiting, e.g. electrolytes and juices
- *Antidiarrhoeal medication* such as loperamide
- *Antibiotic medication* such as fluoroquinolone, azithromycin or co-trimoxazole, which needs to be taken in more severe disease with medical supervision

Prevention

With food and water precautions, e.g. drink only water that has been boiled or disinfected with chlorine or iodine. Drinks such as hot tea or coffee, wine, beer, carbonated water and bottled or packaged juices are usually safe to drink. Avoid ice, unless there is certainty that it is made from safe water. Eat food that has been thoroughly cooked and is hot when served. Avoid raw seafood and other raw foods, except fruits and vegetables that are personally peeled or shelled. Boil unpasteurised milk before drinking. Ice cream from unreliable sources is frequently contaminated.

What the TRAVELLER Needs to Know

TD is the most common infectious disease experienced by travellers, affecting approximately 50 % of travellers from high-income to low-income countries each year. Diarrhoea in travellers can have many different causes and may not necessarily be due to microbes. It is best treated by preventative measures such as food and water precautions. Medication can be used to help reduce the duration of a TD episode, but this needs to be taken with medical guidance.

The oral cholera vaccine 'Dukoral' provides some protection (approximately 10 %) against heat-labile ETEC. Immunisation may be recommended for travel to high-risk regions, but consultation needs to stress that the vaccine has very limited protection against traveller's diarrhoea.

Typhoid Fever

Medical

Typhoid fever is an acute, febrile bacterial infection. It is transmitted through the ingestion of food or water that has been contaminated with the faeces of people with the bacterium *Salmonella typhi* or those who are chronic carriers of *S. typhi*. Typhoid fever is still common in the developing world, where it affects about 21.5 million persons each year.

The incubation period ranges from 3 days to 2 months but is usually 8–14 days. Individuals infected with *S. typhi* are infectious as long as they are excreting the bacilli, usually from the first week of infection until symptoms have resolved. However, 10 % of untreated individuals excrete the bacilli for 3 months or more after initially contracting the disease and 2–5 % of untreated individuals become asymptomatic chronic carriers.

Symptoms of typhoid include lasting high fevers, weakness, stomach pains, headache and loss of appetite. Some patients have constipation, and some have a rash. Internal bleeding and death can occur but are rare.

Incidence

Typhoid fever is common in most parts of the world *except* in the industrialised regions of North America, Western Europe, Australasia and Japan. Travellers to Asia, Africa and Latin America are especially at risk, with the highest risk for typhoid being in South Asia. In the Pacific region, Samoa and Tonga have been experiencing variable outbreaks over the last 2 years.

The estimated risk of developing travel-associated typhoid is about 1/3,500 travellers to South Asia (high risk), 1/50,000–100,000 for travel to sub-Saharan African and South America (intermediate risk) and less than 1/300,000 for travel to the Caribbean and Central America (low risk).

Treatment

Empiric treatment in most regions of the world is with a fluoroquinolone; however, resistance to fluoroquinolones is high in South Asia. Azithromycin and third-line cephalosporins are increasingly prescribed because of emerging multidrug-resistant strains of bacteria. With appropriate antibiotic therapy, the fatality rate reduces to around 1 % (from 10 to 30 % in untreated cases.)

Prevention

Both the oral and injectable forms of the typhoid vaccine are approximately 70 % protective against typhoid fever. The vaccine does not give protection against paratyphoid fever.

Paratyphoid fever is a similar, but usually less severe, condition.

Some people become chronic carriers of typhoid fever and continue to shed the bacteria in the faeces without experiencing symptoms.

What the TRAVELLER Needs to Know

Travellers are ordinarily at low risk of contracting typhoid fever. The most consistent predictor of typhoid risk in travellers is destination of travel with the greatest risk for travellers being those going to sub-Saharan Africa, India, Nepal, Indonesia and parts of Latin America. The Pacific region also presents a destination of increasing risk. Travellers are advised to make sure that their food is hot and their water is bottled or purified with iodine, chlorine, sodium dioxide or UV light sources. Ice and tap water are to be avoided.

Immunisation is recommended for travellers to at-risk countries in Africa, Asia, the Pacific Nations of Samoa and Tonga and South America.

Yellow Fever

Medical

Yellow fever (YF) is a haemorrhagic fever caused by a ribonucleic acid (RNA) virus from the family *Flaviviridae.* Transmission occurs via the bite of an infected mosquito, primarily *Aedes* or *Haemagogus* spp.

Humans infected with YF virus experience the highest levels of viraemia and are infectious to mosquitoes shortly before the onset of fever and for 3–5 days afterwards. Because of the high level of viraemia in humans, blood-borne transmission of YF virus can occur through transfusion of blood products, intravenous drug use and needlestick injuries.

Clinical illness follows a short incubation period of 3–6 days and varies in severity from asymptomatic to fatal. When symptomatic, YF is typically characterised by an acute onset of fever, chills, headache, backache, muscle pain, joint pain, nausea, vomiting, photophobia, mild jaundice and epigastric pain. In about 85 % of YF cases, the disease resolves when the acute symptoms subside. For others, after a brief remission lasting anywhere between hours to a day, symptoms worsen and the disease advances, eventually leading to renal failure, haemorrhagic symptoms and thrombocytopenia.

A traveller's risk of contracting YF depends upon factors such as prior immunisation status, use of personal protective measures against mosquito bites, location of travel (rural and forested regions are more likely to harbour the virus) and the local rate of virus transmission, duration of exposure and activities, whilst travelling, e.g. participating in outdoor activities, increases the potential of exposure.

YF is endemic and intermittently epidemic in parts of sub-Saharan Africa and South and Central America and the Caribbean. YF virus transmission in rural West Africa is seasonal, with a higher risk during the end of the rainy season and the beginning of the dry season (usually July–October). Nevertheless, the virus may be intermittently transmitted by *Ae. aegypti* even during the dry season in both rural and densely settled urban areas. The risk for infection in the Americas is highest during the rainy season (January–May, peak incidence in February–March).

In the Americas, transmission of YF virus occurs mainly in forest areas rather than in urban areas. In Africa, the majority of outbreaks have been reported from West Africa. The mosquito vectors are present in Asia; however, there have been no documented cases of transmission.

Incidence

WHO estimates that approximately 200,000 YF cases occur annually, with up to 30,000 deaths in at-risk populations. From 1970 to 2011, a total of 9 cases of yellow fever were reported in unvaccinated travellers from Europe/USA who travelled to West Africa (5 cases) or South America (4 cases). Eight of these nine travellers died. There has been only one documented case of yellow fever in a vaccinated traveller.

For a 2-week stay, the risks for illness and death due to YF for an unvaccinated traveller visiting an endemic area in:

- West Africa is 50 per 100,000 and 10 per 100,000, respectively
- South America is 5 per 100,000 and 1 per 100,000, respectively

These estimates are an approximate and based on the risk to indigenous populations, often during peak transmission season. Most travellers, however, have a different immunity profile, take precautions against getting bitten by mosquitoes, have less outdoor exposure and thus undoubtedly have less danger of YF.

The risk of acquiring YF in South America is lower than that in Africa, because the mosquitoes that transmit the virus between monkeys in the forest canopy in South America do not often come in contact with humans.

A map of the areas where yellow fever vaccination is recommended can be found at:

http://gamapserver.who.int/mapLibrary/Files/Maps/ITH_YF_vaccination_africa.png?ua=1

Treatment

Treatment is symptomatic and supportive. There are no specific medications to treat YF virus infections. Rest, fluids and use of analgesics and antipyretics may ease symptoms.

Infected people need to be prevented from further mosquito exposure during the first few days of illness, so they do not contribute to the transmission cycle.

Prevention

YF is preventable by a relatively safe, live-attenuated viral vaccine. This needs to be administered before travel to YF endemic or epidemic regions, and passage into these regions will be dependent upon producing certified proof of vaccination against YF. YF is unique among diseases in that it is subject to International Health Regulations which outline the requirements for proof of vaccination when travelling to specific areas.

What the TRAVELLER Needs to Know

YF vaccination is required by travellers to certain countries and is recommended for all travellers to countries or areas with risk of YF transmission. The vaccine has a good safety record, but there are specific potential adverse events, particularly in the elderly and those with certain medical conditions. Specialist YF vaccination advice is essential.

Immunisation is recommended and may be required, for travellers to at-risk countries in sub-Saharan Africa, the Caribbean and Central and South America.

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Chapter 4
Risk Assessing for Vaccine Administration

Hilary Simons

Key Points
- Inclusive and wide-ranging risk assessment, with an understanding of how to manage identified risks, is fundamental to the travel health consultation.
- Assessment, at consultation, must be made of the likelihood of any traveller encountering hazards that may result in harm (i.e. an adverse health event).
- The travel health professional needs to identify travel-related hazards relevant to each individual; resulting adverse health events may, or may not, be vaccine preventable.

Comprehensive risk assessment, and an understanding of how to manage the risks identified, is essential in any travel health consultation. It requires the travel health professional to identify travel-related hazards relevant to each individual, to consider the likelihood of the traveller encountering the hazard and to estimate the probability (the risk) that this hazard will cause harm (in the context of this chapter, harm is considered as an adverse health event, which is vaccine preventable).

Having identified relevant travel-related hazards and determined what risk there may be, an appropriate risk management strategy must be shared with the traveller (Table 4.1). This needs to be evidence based where possible and acceptable to the traveller, who must be given enough information to enable as informed a decision as possible regarding planned interventions.

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Table 4.1 Examples of exposure to travel-related hazards, adverse health events and risk management strategies (interventions) exposure, travel-related hazards and risk management strategies (interventions)

Type of hazard	Example of resulting adverse health event	Possible risk management strategies – points for discussion (not exhaustive)
Accident	injury/infection	Supervision of children
		Road traffic awareness (driving culture, wearing motorcycle helmet, wearing safety belt)
		Avoidance of mind-/behaviour-altering substances
		Vaccination (*e.g. hepatitis B, tetanus*)
Animal	Infection	Avoidance of animal contact
		Avoidance of animal excreta/blood
		Avoidance of unpasteurised dairy products
		Knowledge of first aid and rapid medical intervention for animal bite
		Vaccination (*e.g. rabies, hepatitis B*)
Environment	Respiratory illness	Personal and cough hygiene measures
		Avoidance of crowded places
		Avoidance of source of infection (e.g. poultry, infected human)
		Vaccination (*e.g. diphtheria, influenza, meningococcal, tuberculosis*)
Food and water	Infection	Food and water hygiene
		Personal hand hygiene
		Access to safe water
		Vaccination (*e.g. cholera, hepatitis A, poliomyelitis, typhoid*)
Blood-borne or sexual contact	Infection	Universal precautions for health workers
		Medical care from reputable sources
		Safer sex (barrier protection)
		Vaccination (*e.g. hepatitis A, hepatitis B*)
Vector	Infection	Insect or tick bite avoidance measures
		Avoidance of unpasteurised dairy products
		Vaccination (*e.g. yellow fever, tick-borne encephalitis, Japanese encephalitis*)
FEW travel-related adverse health events are vaccine preventable		
All travellers should be up to date with their national vaccination schedule		
All travellers should have comprehensive travel insurance, including repatriation insurance and the means to pay for medical treatment at point of care		

How to Undertake Risk Assessment

Many factors impact on what the risk from travel-related hazards might be; these factors can be both traveller and journey related. As a baseline, the following factors should be explored during general risk assessment:

- Who is travelling?
- Why are they travelling?

- When are they leaving?
- Where are they going?
- What will they be doing?
- How are they getting there?

These factors are not terribly useful if considered individually, but cumulatively enable very specific information about the traveller and their journey to be gathered and allow risk management strategies (interventions) to be tailored to the individual. Management strategies include personal protection measures (e.g. insect bite avoidance, food/water precautions, personal and cough hygiene measures), vaccination or both.

When considering vaccination as a risk management strategy, a broad knowledge and understanding of the epidemiology of vaccine-preventable diseases including outbreak status, indications for vaccination (which may be routine, recommended or required; Table 4.2), vaccine schedules and vaccine side effect profile is essential. The risk of disease at the destination must be balanced with the potential for risk of vaccine adverse event. In addition, a health professional undertaking risk assessment and planning risk management strategies for travel should know where and how to access expert opinion should it be needed.

Who Is Travelling?

Age and Gender

- Young children are more vulnerable to travel-related adverse health events including injury, rabies (being low to the ground and less likely or able to report a lick, scratch or even bite from an animal) and other infections including diseases of close contact. Options for vaccination can be limited for very young children, and risk management strategy may have to focus on other preventative measures.
- Young adult travellers and particularly young males are more likely to indulge in risk-taking behaviour such as excess of alcohol or other mind-altering substances, driving at night or on motorcycles or unprotected sexual activity. Their risk of encountering adverse health events associated with such behaviours and activities (e.g. injury or sexually transmitted disease) may be increased, and they may fail to comply with complex vaccine scheduling.
- Senior travellers have a declining immune system (immunosenescence) and need to be considered potentially vulnerable to infection. Reduced immune function can also result in a less than optimum response to some vaccines or greater susceptibility to vaccine adverse events. In particular, yellow fever vaccine poses a risk for those over 65 years of age receiving the vaccine for the first time, and must be balanced with the risk of the disease at the destination.
- Travellers in their senior years may have missed or not completed primary vaccinations or may need boosting of previous vaccines.
- The travel health consultation is an ideal opportunity to ensure that travellers of all age groups, and those with special health needs (Fig. 4.1), are up to date with vaccines currently offered in the national vaccination schedule.

Table 4.2 Routine recommended and required vaccines

Routine	Vaccines given according to the national schedule	Diphtheria
		Haemophilus influenza B
		Hepatitis B
		Herpes (shingles)
		Human papillomavirus
		Influenza
		Meningococcal (usually single antigen)
		Measles, mumps, rubella
		Pertussis
		Pneumococcal
		Poliomyelitis
		Tetanus
		Tuberculosis
		Zoster (chicken pox)
Required	Vaccines given under:	Yellow fever
	International Health Regulations (2005)	Poliomyelitis
	An individual country requirement	Meningococcal
		In some circumstances, where there is a medical contraindication to vaccination, a medical waiver can be considered
Recommended	Vaccines advised for personal protection, according to individual risk assessment	*All travellers should be up to date with the vaccines recommended as routine in the national schedule. The vaccines may be boosted according to individual risk assessment*
		In addition specific vaccines may be recommended according to individual country risk:
		Cholera
		Hepatitis A
		Hepatitis B
		Japanese encephalitis
		Meningococcal (quadrivalent)
		Rabies
		Tick-borne encephalitis
		Typhoid
		Yellow fever

Medical History (Including Vaccination History)

A comprehensive medical history should be taken. By identifying special health needs, which could leave the traveller vulnerable to travel-related hazards and possible adverse health events, appropriate risk management strategies can be planned.

- In the context of vaccination, there may be medical contraindications or precautions to specific vaccine products; national guidance and a product's data sheet

Fig. 4.1 Examples of travellers with special health needs

should always be referred to and medical opinion sought where there is any doubt. In general, individuals with a compromised immune function either because of underlying disease process or treatment or both should never be given live vaccines because of the risk of an overwhelming and potentially life-threatening adverse systemic response. Inactivated vaccines can generally be safely given to those with a compromised immune system, though response to such vaccine may be suboptimal and alternative risk management strategies to prevent infectious disease (e.g. insect bite precautions, food/water/respiratory and personal hygiene measures) are essential (see also Chap. 13).

- Women may be planning to conceive during their trip and whilst inactivated vaccines do not pose a risk, caution should be taken with live vaccines. It is generally advised that conception be avoided for four weeks after live vaccine administration.
- Pregnant women will travel despite their vulnerability to travel-related hazards and travel related adverse health events such as infection, particularly malaria, and medical facilities and care may be of a less than desirable standard. Live vaccines can cross the placental barrier and should generally be avoided in the first trimester of pregnancy. Where the risk of vaccine-preventable disease at a destination is high, live vaccines can be considered with caution and expert opinion sought on an individual case basis.
- A history of allergy should be interpreted with care. History taking should differentiate between sensitivity to components of a vaccine (e.g. mild rash during systemic antibiotic treatment), which would indicate a precaution to vaccination, and anaphylaxis. Confirmed anaphylaxis to any component (Chap. 7) or to a previous dose is a contraindication.
- Vaccination history provides the health professional with essential information about previous vaccines received in any national programme or for travel. It is

recommended that an official written record is seen at initial pre-travel consultation. For travellers with an unknown or incomplete vaccination status, revaccination or completing a vaccination programme is appropriate and will not cause harm in a well person.

Travel Experience and Attitude to Risk

- Experienced travellers may be less inclined to seek pre-travel advice and/or may have a more relaxed attitude to risk. This should be respected, but does not preclude the need to undertake a systematic risk assessment, which may reveal hazards unrecognised by the traveller, or novel management strategies not previously considered or available, for example, new guidance on vaccine-preventable diseases or vaccine schedules.
- Conversely, where there has been a negative travel experience, even a well-travelled individual may become risk averse and seek vaccination where the risk of disease is remote.
- Travellers' attitudes to risk can only really be determined in the face-to-face consultation; health professionals should listen and watch for verbal and non-verbal clues that might indicate an area of concern for the traveller.
- Health professionals are advised to avoid making judgements based on their own attitudes to risk.
- Risk assessment should enable the health professional, and the traveller, to consider individual attitude to risk (thrill-seeker, risk-taker or risk averse) and acceptable and unacceptable hazards and to tailor risk management strategies accordingly (see also Risk Communication).

Why Are They Travelling?

Travel choice and the type of activities a traveller expects to undertake can be a good indicator of the likelihood of exposure to hazards. There are many variables relating to type of travel; examples include:

- Adventure – often undertaken by those actively seeking thrills and accepting of associated dangers. Standards of safety during adventure activities are variable; exposure to hazards may be greater due to poor supervision and/or sub-optimum equipment.
- Backpacking – associated with, but not exclusive to, young travellers, who may be on a tight budget and a relaxed itinerary in less developed countries.
- Budget travel – may be less inclined to spend on interventions to reduce risk such as vaccinations, malaria chemoprophylaxis or quality accommodation where access to safe food and water is more likely.

- Business travel – complex travel itineraries and little time for pre-travel health advice.
- Emigration – expatriates may have a greater potential for exposure to endemic disease, accident and culture shock.
- Leisure tourism – on a well-organised, short and set itinerary, e.g. the package tour, cruise or city break, less likelihood for exposure to hazards, but no trip is no risk.
- Luxury travel – travel in luxury may, but may not, equate to less likelihood of exposure to hazards.
- Medical tourism – potential for exposure to blood-borne disease during surgery overseas (e.g. dentistry, gender reassignment, orthopaedic procedure).
- Pilgrimage – greater potential for exposure to disease of close contact and injury.
- Sex tourism – exposure to sexually transmitted disease through sexual contact or assault.
- Visiting friends and relatives (VFR) – exposure to hazards may be exacerbated by underestimation of personal risks.

When Are They Leaving?

Ideally, risk assessment consultations should take place far in advance of the traveller departure date. This allows time to gather all the information needed to tailor the risk management strategy, including the planning and completion of vaccination schedules.

- For most, a number of consultations over a 4–6-week period should suffice.
- Late presenters pose a challenge; however, it is never too late to seek travel health advice. No opportunity to undertake risk assessment and discuss appropriate risk management strategies should be lost. In the context of vaccination, some protection is better than none, and vaccines may still be considered at the last minute. Because immune protection takes time to develop, the importance of scrupulous personal protective measures, such as food and water hygiene, animal avoidance or insect bite precautions, should be stressed.

Where Are They Going?

Destination hazards will vary, and a good baseline knowledge of the following destination specifics is essential in planning vaccination schedules and will guide risk assessment and the organising of risk management strategies:

- Epidemiology, e.g. a general knowledge of where a disease occurs in the world, the prevalence of disease or accident in a population and disease outbreak information – always use a reputable and ideally real-time source of information

- Geography, e.g. urban, rural, altitude, and remote
- Season, e.g. wet or dry, winter or summer; risk of exposure to disease or environmental hazards increases according to season, e.g. Japanese encephalitis is more likely to occur in the wet season, as are tick-borne encephalitis and meningitis
- Standards of medical care at a destination; potential risk of exposure to suboptimal treatments or infections where standards are low.

What Will They Be Doing?

The type of activities to be undertaken can be a key indicator for likelihood of exposure to travel-related hazards and adverse health events such as disease, accident and injury or even death (see also Why Are They Travelling?)

- Natural risk-takers are more likely to seek the thrills offered by activities such as bungee jumping, white water rafting, rock climbing or skiing. Relaxed inhibitions, a desire to try something new or different or pressure from peers may, result in even the risk averse exploring risky activities during travel.
- Accident, assault and sexually transmitted disease are more likely to happen where inhibition or reaction time has been blunted by mind- or behavioural-altering substances such as drugs or alcohol.
- Engaging in sexual activity can be risky and result in adverse health events such as sexually transmitted disease or assault.

How Are They Travelling?

Mode-capitalize mode of transport, can be hazardous whether this is by air, sea or land as can the style of travelling, e.g. cruise or pilgrimage.

- Long periods of inactivity in a cramped environment, such as during airline flights or coach journeys of more than 4 h, predispose to the development of venous thromboembolism (VTE). Travellers at greatest risk include those who have history of prothrombotic blood abnormalities or are obese, immune compromised or pregnant. Guidelines on VTE prevention such as regular mobilisation and the wearing of flight socks should be followed. Administration of low molecular weight heparin before travel may be indicated.
- Local transport systems can pose a hazard. Cyclists, motor vehicle passengers and pedestrians are at risk of road traffic accident (RTA). RTA is probably one of the greatest hazards that the global traveller will encounter, with more than 1 million people killed and 50 million injured each year. Raising the profile of RTA as a potential hazard and discussion of risk management strategies, including gaining some knowledge of the road and driving culture at a destination country, may minimise

risk of accident for some. Hepatitis B vaccine needs to be suggested for those using riskier transport options, e.g. local bus or taxi journeys in low-income countries.
- Infectious illness, and particularly respiratory infection, occurs where people live in a confined space and in close proximity. Influenza should be considered a potential travel-related adverse health event for those embarking on cruise travel or attending mass gathering events and pre-travel vaccination offered to those at greater risk (refer to national guidance).

Risk Communication

Communication about risk is necessarily a two-way process – a dialogue between the health professional and the traveller in which risk information is shared, discussed and understood, enabling appropriate risk management strategies to be developed. Communication about risk can be a challenge to do well; messages need to be clear, meaningful and tailored to the individual.

Effective risk communication can be enhanced by many things including:

- *Numeracy* – health professionals need to be confident in their ability to understand and describe the way health statistics are presented. Numerical values to express probability can be expressed differently but mean the same thing, e.g. 1/1000 or 0.001.
- *Clear and understandable explanation* – numerical expressions of risk can be difficult to comprehend; terms such as 'very common' or 'common' or 'rare' may be easier for some to understand but ideally should be used only where the term matches a numerical value of probability. For example, the frequencies of adverse drug reactions are usually expressed as ranging from 'common' (1 in 10) to 'very rare' (1 in 10,000).
- *Respect of the individual's attitude* to risk (that of both the traveller and the health professional).
- *Consideration of risk priorities*, which are likely to be different for each individual.
- *Provision of information*, evidence based where ever possible, which supports that an intervention is worth taking, i.e. there are more benefits from having a vaccine than there are risks from it.
- *Confidence to make the best decisions* depending on individual need.
- *Access to real-time, accurate information* regarding epidemiology of disease including outbreak information (see Fig. 4.2.). Knowing how to interpret that information in the context of making risk judgements is essential.
- *Use of decision-making aids or tools* –.
- *Traveller 'buy-in'* – in order for risk management strategies to be useful, the traveller has to acknowledge that a hazard poses a risk to them and be willing to change behaviours to reduce that risk.
- *Honesty* – sometimes giving an accurate estimation of risk versus benefit is just not possible. For example, whilst there is good data on the risk of severe adverse

Fig. 4.2 Real-time outbreak information and traveller alerts/notices

events following yellow fever vaccination for those aged over 60 years (60–69 years old = 2.6 per 100,000; 70 and over = 4.6 per 100,000), the risk of disease at a destination may not be known and so cannot be expressed in the same way statistically. Thus, making a clear judgement on whether to receive the vaccine or to travel unprotected can be challenging.

Skilled risk assessment, risk management and risk communication are fundamental to best practice in the travel health consultation. The health professional must consider the traveller as an individual and take into account their health status their experience of travel, attitude to risk and journey specific details. Understanding the potential for exposure to travel-related hazards, and the likelihood of harm that might result from such exposure, allows risk management strategies to be tailored appropriately to the individual.

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Chapter 5
Vaccines at a Glance

Marc Shaw

Key Points

- Chemicals are added to vaccines to inactivate either bacteria or viruses and stabilise a vaccine, helping to preserve it and prevent it from losing its potency over time.
- The amount of chemical additives found in vaccines is very small. They are needed to maximise a vaccine's effect.
- Whilst the ingredients may look unfamiliar, many of them are found naturally in the body.
- Millions of doses of vaccines are administered annually. Ensuring that those vaccines are potent, sterile and safe requires the addition of minute amounts of chemical ingredients.

Introduction

By far the majority of the over one billion doses of vaccines manufactured worldwide each year are given primarily to healthy infants and children and secondarily to adults. It is therefore essential that vaccines are demonstrated to be safe and effective. There are many types of vaccines each with its own active ingredient – the

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part that challenges the immune system to produce antibodies against disease. The information in this chapter is crafted from collated literature referred to from the variety of sources listed below.

Whilst vaccine ingredients can look unfamiliar, many of the substances used in vaccines are found naturally in the body, e.g. salts based on sodium and potassium and even formaldehyde. Each will have a specific purpose in a vaccine's production, depending on vaccine design and the need to maximise its effect.

There are many approaches to designing vaccines that will impact upon a micro-organism. Such selections tend to be based on variables such as the:

- Vaccine-preventable disease for which protection is required.
- Microbe causing it. This may include how it infects cells and how a person's immunity responds to it.
- Nature of the organism to be prevented. This may demand the creation, for example, of a chimeric vaccine, created by cloning pieces of one virus into another virus and deriving a single organism composed of genetically distinct cells.
- Need for a vaccine. This is proportional to the virulence of any disease to be protected against, and the harm it does to the affected population.
- Regions of the world where the vaccine is to be used.
- Politics of the population to be immunised.

There are currently seven types of vaccines described, with five being commercially available:

Live, Attenuated Vaccines

Live, attenuated vaccines use a live, though weakened (attenuated), form of a living microbe. A live vaccine is the closest thing to a natural infection, and so they elicit strong cellular and antibody responses and often confer lifelong immunity with only one or two doses.

Whilst the advantages of attenuated vaccines are apparent, there are some shortcomings. This is because it is the nature of organisms used in live, attenuated vaccines to mutate. Thus, there is always the remote possibility that an attenuated microbe in a vaccine may transform into virulence and cause disease. Furthermore, those who are immunocompromised cannot be given live vaccines for fear of initiating the disease for which protection is sought.

Attenuated viral vaccines are relatively easy to create as viruses are simple microbes with a small number of genes. Their characteristics can thus be more readily controlled. Live, attenuated bacterial vaccines are more difficult to create as bacteria have many more genes that are difficult to control. This is where recombinant DNA technology to remove several key genes is beneficial.

Examples Measles, mumps, rubella, chickenpox, yellow fever and oral typhoid.

Inactivated Vaccines

Inactivated vaccines are not alive, cannot replicate and are produced by growing bacteria or viruses in culture media. They are then inactivated with heat, radiation or chemicals (usually formalin). Such vaccines are safer and more stable than live vaccines, as the dead microbes are unable to mutate back into any disease-causing state. 'Fractional vaccines' are also inactivated, and with them the organism is further treated to purify only those components to be included in the vaccine (e.g. the polysaccharide capsule of typhoid Vi).

Although these vaccines cannot cause disease, even in an immune-compromised person, they stimulate a weaker immune system response than do live vaccines. Inactivated vaccines always require multiple doses to maintain a person's immunity: viz. the first dose will not develop a protective immunity but will only 'prime' the immune system for a second or more dose that will produce an ongoing protective immune response. Nevertheless, antibody titres against inactivated antigens diminish with time, and so inactivated vaccines may require periodic 'boosting' to supplement antibody titres.

The immune response to an inactivated vaccine is mostly humoral immunity, in that it is an acquired immunity where the role of circulating antibodies predominates. There is little or no cellular immunity. This contrasts with live vaccines, where the immune response simulates a natural infection.

Examples (i) inactivated whole viral vaccines, e.g. hepatitis A, influenza, polio and rabies; (ii) inactivated whole bacterial vaccines, e.g. pertussis and cholera; and (iii) 'fractional' vaccines include subunits (hepatitis B, acellular pertussis) and toxoids (diphtheria, tetanus).

Subunit Vaccines

Subunit vaccines include only antigens that stimulate the immune system. They do not use the entire microbe. In some instances these vaccines use very specific parts of an antigen that either antibodies or T cells recognise, and they bind to them. Adverse reactions to subunit vaccines are much lower than with other types of vaccines, because subunit vaccines contain only essential antigens and not other molecules that make up the microbe.

'Recombinant subunit vaccines' have been manufactured from a microorganism using recombinant DNA technology, in which the genetic material produced when segments of DNA from different sources are joined to produce recombinant (or recombined) DNA.

Example Hepatitis B virus vaccine.

Toxoid Vaccines

Toxoid vaccines consist of a toxin-chemical made by either bacteria or viruses. They are used when a toxin is the prime agent of illness. Toxoid vaccines inactivated by formaldehyde promote immunity to the harmful effects of infection rather than to the infection per se.

Examples Diphtheria and tetanus toxoid vaccines.

Conjugate Vaccines

Most polysaccharide-based vaccines are composed of pure cell-wall polysaccharide from bacteria. A conjugate vaccine is created by covalently attaching a poor (polysaccharide organism) antigen to a carrier protein (preferably from the same microorganism), thereby conferring the immunological attributes of the carrier on the attached antigen. Such an association makes the polysaccharide a more effective vaccine.

Example *Haemophilus influenzae* type B

DNA Vaccines

DNA vaccines dispense with both the whole organism and its parts and get right down to the essentials: the microorganism's genetic material. In particular, DNA vaccines use the genes that code for antigens. When these genes are introduced into the human body, some cells will take up the DNA which then instructs these cells to produce antigen. Thus, the body creates the antigens that stimulate the immune system.

An advantage of DNA vaccines is that they could not cause the disease as they do not contain the microorganism. They just have copies of some of its genes, the ones that code for the antigen.

Recombinant Vector Vaccines

Recombinant vector (either the virus or the bacterium used as the carrier) vaccines are similar to DNA vaccines, but they use an attenuated virus or bacterium to introduce microbial DNA to cells of the body. Viruses inject their genetic material into cells that they come in contact with. The recombinant vaccine is created by taking the genome of harmless viruses and inserting portions of genetic material from

other microbes into them. This carrier virus then transfers the microbial DNA into cells. Recombinant vector vaccines simulate a natural infection, thus adequately stimulate the immune system.

Vaccine Ingredients

Apart from any active ingredient, the main constituent in vaccines is water, approximately 0.5 ml of it. All other ingredients in any vaccine weigh, at most, a few thousandths of a gram. Many of the substances used in vaccines are found naturally in the body. For those that are not, there is no evidence that any of them cause harm in the small amounts that the vaccines contain.

- *Active ingredients***.** This is the antigenic component that challenges the immune system to produce antibodies against disease. Some vaccines are formulated using recombination (recombinant) DNA technology. Hepatitis B is an example of this; to make the vaccine, a segment of DNA from the hepatitis B virus (HBV) is inserted into the DNA of yeast cells. These cells are then able to produce one of the surface proteins from the HBV, which is then purified and used as the active ingredient in the hepatitis B vaccine.
- *Genetically modified organisms (GMOs)*. A live vaccine for Japanese encephalitis, available in Australia and Singapore, contains GMOs as the active ingredient.
- *Human cell lines*. Some vaccines need to have the active ingredient grown on cultures containing human cell lines. This is because the microbe is specific to humans, e.g. chickenpox, MMR and shingles vaccines. The cell lines are then removed, and (in the examples above) the resultant virus strain is pure. Two main human cell strains have been used to develop currently available vaccines, in each case with the original fetal cells in question obtained in the 1960s using small quantities of lung cells taken from two legally aborted fetuses. The WI-38 cell strain was developed in 1961 in the United States, and the MRC-5 cell strain was developed in 1965 in the United Kingdom.

The Vatican's position on the matter (Statement by the Pontifical Academy for Life, 2005) is that it is acceptable to use vaccines developed from abortions that were carried out decades ago, as immunisation plays an essential role in protecting life by preventing illness and death.

Examples Hepatitis A vaccines (Vaqta, Havrix, part of Twinrix), rubella vaccine (part of MMR II), varicella (chickenpox) vaccine (Varivax), zoster (shingles) vaccine (Zostavax) and rabies vaccine (Imovax)

- *Animal cell lines*. Viruses for some vaccines are grown in cultures containing animal cell lines, as they also will only grow on animal cells, e.g. vero cells, which are a cell line started in the 1960s using a few kidney cells from an African green monkey.

Examples Verorab rabies vaccine, Infanrix-IPV and Boostrix-IPV

- *Aluminium salts* act as adjuvants, strengthening and lengthening the immune response to a vaccine. These salts slow down the release of the active ingredient from the vaccine after it is injected, thus giving the immune system greater time to sero-react to the vaccine.
- Although the amount of aluminium present in vaccines is very small (less than a milligram of actual aluminium), in postvaccination there is a transient increase in aluminium in the body, though this is not lasting and there is no evidence that this causes risk to infants and children.
- *Thimerosal (thiomersal)* is an organic mercury compound that had been traditionally used in vaccines as a preservative. It is now infrequently used because of the concerns about mercury, though it still may be added to other consumer products such as cosmetics, skin test antigens, immunoglobulin preparations, antivenoms, ophthalmic and nasal products and tattoo inks.
- First introduced in the 1930s, because of its established antibacterial and antifungal properties, thimerosal prevents contamination of those products that contain it. It is particularly effective as a preservative in multi-dose vials.
- Thimerosal is metabolised to ethylmercury (and thiosalicylate) containing 49.6 % mercury by weight. In the final preparation of vaccines, however, the concentration of thimerosal is minute, and a person being immunised with a vaccine containing thimerosal has further reduction of metabolised ethylmercury as the body dilutes it still further.
- Vaccines, like other injectable products, need to be free of any microbial contamination. Single-dose vials of vaccines do not generally contain preservative if the sterilisation process during manufacture is effective. However, vaccines in multi-dose vials need protection against any unintended bacterial or fungal contamination caused by multiple penetrations of the stopper. The risk of contagion is real; as in 1928, during a diphtheria immunisation campaign, staphylococcal contamination of a multi-dose vial led to the septic deaths of 12 of 42 immunised children.
- In 1999, following a review of mercury-containing food and drugs, the US Centers for Disease Control and Prevention (CDC) and the American Academy of Pediatrics asked vaccine manufacturers to remove thimerosal from vaccines as a precautionary health measure. Even though it was phased out of most US and European vaccines, some parents considered the move to eliminate the preservative – in the then climate of a supposed increasing rate of autism – as indicating that it was the cause of autism. There is no scientific evidence to support this claim.
- *Preservatives* stop unwanted contamination of a vaccine. The most commonly used preservative is 2-phenoxyethanol. Whilst this product is also used in baby-care cosmetics, there is little toxicity in humans and some toxicity (irritation) with high doses in animals.
- *Vaccine stabilisers*, e.g. gelatin, stop chemical reactions from occurring in the vaccine so preventing the components from separating from each other. Note that

the gelatin in vaccines is different from that used in foods in that it is highly purified and hydrolysed, acting as a stabiliser to protect live viruses against the effects of temperature.

- Members of Muslim or Jewish religious communities may be concerned about using vaccines that contain gelatin from pigs. Leaders from both faiths have ruled there is no problem with gelatin or any other animal substance if it is used in a product that does not go into the mouth. Nevertheless, there may be variance in opinion of this that may need to be clarified before vaccination of porcine gelatin-containing vaccines.
- Other examples of stabilisers include: lactose, mannitol, sorbitol, sucrose and Medium 199 (a solution containing amino acids, vitamins and mineral salts).
- *Antibiotics* such as neomycin, streptomycin, gentamicin and polymyxin B prevent contamination, usually during the manufacture process. They can be allergenic, and such an allergy needs to be enquired about from travellers' pre-vaccination.
- *Formaldehyde* derivatives are organic compounds found naturally. Formaldehyde is used in the production of some vaccines to inactivate toxins from bacteria and viruses (e.g. diphtheria and tetanus toxins).
- *Acidity regulators* keep the pH balance right whilst vaccines are being manufactured.
- *Buffer solutions* are those that resist changes in pH. They tend to keep a vaccine at a similar pH to the body. Buffers are likely to be a salt. Salts, such as sodium chloride, are also often added to vaccines to keep them isotonic in order to reduce local reactions.
- *Emulsifiers* hold the ingredients of a vaccine together, e.g. polysorbate 80 (made from sorbitol and oleic acid, an omega fatty acid). There are minimal non-toxic amounts in vaccines.

Residual Substances in Vaccines

Occasionally traces of ingredients used during the manufacturing process are present in vaccines. These are not part of the final formulation but can be measured, usually in parts per million or billion (ppm, ppb). Such components may include:

- *Egg proteins*. These are used as a medium for growth of a number of vaccines. Egg allergies occur in approximately 0.5 % of the population and 5 % of atopic children. Because influenza and yellow fever vaccines both are propagated in the allantoic sacs of chick embryos (eggs), egg proteins (primarily ovalbumin) are present in the final product. Residual quantities of egg proteins found in these vaccines are sufficient to induce severe and rarely fatal hypersensitivity reactions. In contrast to influenza vaccine, measles and mumps vaccines are propagated in chick embryo fibroblast cells in culture. The quantity of residual egg proteins found in measles- and mumps-containing vaccines is at a quantity at least 500-fold less than those found for influenza vaccines. The quantity of egg

proteins found in measles- and mumps-containing vaccines is not sufficient to induce immediate-type hypersensitivity reactions, and those with severe egg allergies can receive these vaccines safely.

- *Yeast proteins*. Hepatitis B vaccines are made by transfecting cells of *Saccharomyces cerevisiae* (baker's yeast) with the gene that encodes hepatitis B surface antigen. Residual quantities of yeast proteins are contained in the final product. However, whilst immediate-type hypersensitivity reactions have been observed rarely after receipt of hepatitis B vaccine (approximately 1 case per 600,000 doses), yeast-specific IgE has neither been detected in anyone with such hypersensitivity nor in non-allergic patients after receipt of hepatitis B vaccine. Thus, the risk of anaphylaxis after receipt of hepatitis B vaccine because of allergy to baker's yeast is theoretical.
- *Latex* (natural rubber) is used in the packaging of some vaccines. Latex is the sap from rubber trees, and it contains naturally occurring impurities (e.g. plant proteins and peptides) that can cause allergic reactions. Latex is processed to form natural rubber latex and dry, natural rubber. Natural rubber latex is used to produce medical gloves, catheters and other products including the tips of syringe plungers, prefilled syringe tips, vial stoppers and injection ports on intravascular tubing. Synthetic derivatives are also used in syringe plungers, vial stoppers and medical gloves. However, they do not contain impurities linked to allergic reactions.

- Prevalence of natural-rubber-latex (NRL) allergic sensitisation in the general population is low, less than 1 %. After occupational exposure, rates of sensitisation and NRL-induced asthma rise dramatically in individuals using powdered NRL gloves, but not in individuals using powder-free gloves.

- The commonest clinical presentation of latex allergy is a non-immunologic irritant dermatitis of the hand, whilst contact dermatitis (type IV delayed hypersensitivity reactions to rubber additives) is the most common immunologic manifestation of NRL allergy.

- Allergic reactions (including anaphylaxis) after vaccinations are rare. A review of reports to US vaccine adverse event reporting system (VAERS) identified only 28 cases of possible immediate-type anaphylactic reactions among more than 160,000 vaccine adverse event reports.

- If a person reports an anaphylactic allergy to latex, vaccines supplied in vials or syringes that contain natural rubber latex should not be administered unless the benefit of vaccination clearly outweighs the risk for a potential allergic reaction. For latex allergies other than anaphylactic allergies (e.g. a history of contact allergy to latex gloves), vaccines supplied in vials or syringes that contain dry, natural rubber or natural rubber latex may be administered. Latex or dry, natural rubber used in vaccine packaging generally is noted in the manufacturers' package inserts.

Further Reading

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Chapter 6
Vaccine Summary Table

Marc Shaw, David Smith, and Brigid O'Brien

Key Points
- Vaccines are available as single vaccine or multi-dose schedules.
- Administration of vaccines is best given in consultation with intending travellers based on their itineraries.
- Vaccine administration is supportive of the health of those travelling, and knowledge about their affects and adverse reactions is a requirement for those giving them.
- Travel health professionals need to make sound risk assessments and recommendations on individualised vaccine schedule for intending travellers.

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Introduction

A major role of the travel health practitioner is to make sound risk assessments and recommend an individualised vaccine schedule for travellers. As technology develops, the range of available vaccines is continually increasing. A sound working knowledge of available vaccines is of paramount importance.

The following Table 6.1 provides the travel health practitioner with an overview of travel vaccines. It is recommended that practitioners consult the approved data sheet for further specific guidance on the use of any vaccine and to be familiar with national immunisation procedures and guidelines for the country they are practicing in.

Table 6.1 Comparison of private vaccines commonly used in travel health

Vaccine type	Main indications	Main contraindications	Main adverse effects	Schedule and no. of doses	Efficacy	Time to immunity	Use in pregnancy (category)	Duration of cover
Cholera (*inactivated*) Killed whole-cell-recombinant B subunit vaccine *Dukoral* Enterotoxic *Escherichia coli* (ETEC)	Adults and children from 2 yrs of age who are travelling to a cholera area	Hypersensitivity shown to previous cholera vaccinations	Mild GI upset	Adults and children >6 yrs of age 2 doses orally, 1–6 weeks apart	80–85 % against cholera for the 1st 6 mths and 63 % at 3 yrs 60 % against ETEC for 3 mths	7 days after last schedule dose (cholera)	Category B2	*Booster*: every 2 yrs Children 2–6 years of age: 3 doses *Booster*: every 6 mths *ETEC*: *3 mths*
Diphtheria Inactivated toxoid and *tetanus* (*ADT*)	Vaccination of children (≥5 yrs of age) and adults who have completed primary immunisation	Previous hypersensitivity reactions to ADT vaccination	Malaise, fever ≥ 38 °C Redness and swelling at the injection site	*Booster*: every 10 years for travellers	97 % after primary course	1–2 weeks after the 3rd dose	ADT – category A	*10 yrs*
Diphtheria, *tetanus and pertussis* (*DTaP*) *Inactivated vaccine Adacel Boostrix*	Consider DTaP for adolescents or adults who are due an ADT booster	Previous adverse reaction to either diphtheria, tetanus or pertussis toxoids	*Include* local pain, myalgia, swelling, redness at injection site, headache, lethargy, anorexia and irritability	*Booster*: every 10 years	1 mth post-vaccination: 92–100 % immune response	1 mth after booster dose >99 % seropositivity	Adacel – category B2 Boostrix – category B1	*10 yrs*

(continued)

Table 6.1 (continued)

Vaccine type	Main indications	Main contraindications	Main adverse effects	Schedule and no. of doses	Efficacy	Time to immunity	Use in pregnancy (category)	Duration of cover
Hepatitis A Inactivated *Havrix* adult (≥16 yrs) *Havrix* junior (1–15 yrs) *Avaxim* ≥2 yrs	All nonimmune travellers >12 months + going to intermediate and high endemicity (all developing countries)	Age <12 months Previous adverse reaction to hepatitis A vaccines	Include local pain at injection site, fatigue, headache, drowsiness, irritability and fever (>37.5 °C)	Havrix Adult dose: 1 mL IM Paediatric dose: 0.5 mL IM Havrix 1 primary and booster between 6 and 24 mths Avaxim *Booster*: 2nd dose between 6 and 36 months	2 weeks post-primary vaccination 86–95 % protection	15–30 days	Havrix – category B2	*30+ yrs after second dose*
Hep A immunoglobulin	Pretravel: in those > 40 yrs or immuno-compromised and who are departing in <2 weeks *Postexposure*: especially if >40 yrs or chronic disease or if immuno-compromised	Short duration passive immunity	Local pain	0.02 mL/kg IM	90 %	Days		*3 mths*

Hepatitis B recombinant DNA *Engerix HBvaxPRO*	Hepatitis B vaccine is indicated for active immunisation against hepatitis B virus infection	Known hypersensitivity to any component of the vaccine, previous hypersensitivity to hepatitis B vaccination administration	Local pain, mild to moderate fever, appetite loss, irritability, headache, pain and redness at injection site and fatigue	Engerix-B Dose 20 mcg 1 mL IM *Adults and adolescents* >15+yrs of age 1 dose at 0, 1 and 6 mths *Accelerated schedule*, *either* 1 dose at 0, 1 and 2 mths or 1 dose at d0, d7 and d21 and *booster* at 12 mths	89–90 % of vaccinees reach seroprotective levels *Accelerated schedule*: 65.2 and 76 % seroprotective within 1 and 5 weeks Following the booster: antibodies rises to 98.6 %	1 mth after the 3rd dose	No studies – use only if the benefit justifies the potential risk to the foetus	At least 20 yrs in immuno-competent For life, if seroconversion occurs

(continued)

Table 6.1 (continued)

Vaccine type	Main indications	Main contraindications	Main adverse effects	Schedule and no. of doses	Efficacy	Time to immunity	Use in pregnancy (category)	Duration of cover
Hepatitis A and *B* combined Inactivated *Twinrix Twinrix Junior*	Active immunisation against hepatitis A and hepatitis B virus	Age < 12 mths	Headache, diarrhoea, nausea, vomiting, pain and redness at the injection site, fatigue, irritability and loss of appetite	1 mL IM Adults 16+yrs of age: standard primary series 0, 1 and 6 mths *Adult rapid schedule*: at d0, d7 and d21 Booster recommended at 12 months *Children* 1–15 yrs: either 0.5 mL IM at day 0, 1 mth and 6 mths or 0.5 mL IM at d0 and 6–12 mths	Hepatitis A 94 % seroprotective levels after 1 mth. 100 % 1 mth after 3rd dose (mth 7) Hepatitis B 70 % seroprotective level after 1 mth and 99 % after third dose Rapid schedule Hepatitis A 82 % seroprotective levels after 1 week. 85 % 5 weeks after 3rd dose (mth 7) and 100 % seroprotective level 1 mth after fourth dose Hepatitis B 92 % seroprotective level at mth 7 and 57 % at 48 mths	Protection develops 2–4 weeks after 1st dose	No studies – use only if the benefit justifies the potential risk to the foetus	Hep A: 20–30 yrs Hep B: 15 yrs to life

Influenza Inactivated *Fluvax* *Vaxigrip* *Fluarix* *Influvac* *Intanza* FluQuadri	Prophylaxis against influenza in adults and children >6 mths of age *Travellers*: all those travelling to the tropics or to the northern hemisphere during season (Dec to March) or those who travel in large groups or on cruise ships at any time of the year Pregnancy	*Fluxax* (not to be used in children <5 yrs and not recommended for children 5–9 yrs) Hypersensitivity to previous dose	Redness or swelling at vaccination site, fever, headaches, fatigue and aches Rarely: Guillain-Barré syndrome (GBS)	Children 6–35 mths : 0.25 mL SC Adults and children 3+ yrs: 0.5 mL IM or deep SC In previously unvaccinated children <9 yrs of age, two doses separated by at least 4 weeks	70–90 % in healthy people <65 yrs 60 % in people >65 yrs	2–4 weeks	Category B2	6–12 mths

(continued)

Table 6.1 (continued)

Vaccine type	Main indications	Main contraindications	Main adverse effects	Schedule and no. of doses	Efficacy	Time to immunity	Use in pregnancy (category)	Duration of cover
Japanese encephalitis Inactivated *Jespect* Live attenuated Recombinant DNA *IMOJEV*	Active immunisation against Japanese encephalitis (JE) virus for persons 18 yrs of age and older IMOJEV is indicated for prophylaxis of JE caused by the Japanese encephalitis virus in individuals 12 mths of age and over	Hypersensitivity to thimerosal or proteins of neural or rodent origin Previous adverse reactions after receiving JEV <1 year of age Contraindicated in pregnancy or breastfeeding Previous severe allergic reaction to any component of the vaccine	Local pain/ inflammation, fatigue, malaise, injection site pain, headache and myalgia	*Adults*: 2 vaccinations (d0 and d28) *Children*: 2 mths – 2 yrs, each dose is 0.25 mL Individuals 12 mths of age and above: 0.5 mL single injection	95 % (both accelerated and standard) 80 % seroconversion after 1st 2 doses 14 days after single dose, there is a seroprotection level of 99.16 %	10 days A seroprotective level of antibodies is generally reached 14 days after vaccination	Not to be used during pregnancy	Jespect 3 years Imojev 5 years
Measles, mumps and rubella Live attenuated *MMR*	MMR is indicated for simultaneous vaccination against measles, mumps and rubella in individuals 12 mths of age+	Pregnancy, anaphylactic reaction to neomycin, active untreated TB and patients with immune deficiency conditions		0.5 mL SC 2 doses after 12 mths of age separated by at least 1 mth If dose given < 12 mths of age, requires 2 doses after 12 mths of age	90–95 % seroconvert to measles after 1st dose if given at > 12 mths; 2nd dose to cover initial non-seroconverters	2 weeks	No	Life

Meningitis ACYW135 Inactivated polysaccharide *Mencevax* *Menomune* Conjugated *Menactra* *Menveo*	Active immunisation of adults and children >2 yrs against meningococcal meningitis caused by serogroups A, C, W-135 and Y meningococci Menactra vaccine is indicated 9 mths–55 yrs of age Menveo is indicated for children <2 yrs of age, adolescents and adults	<2 yrs (poorly immunogenic) Hypersensitivity to any component	Local pain and inflammation at injection site, fever, headaches, irritability, drowsiness, nausea, vomiting, diarrhoea and malaise	0.5 mL SC Single 0.5 mL dose (IM)	Mencevax Seroconversion 1 mth after vaccination in people aged ≥ 6 yrs A 100 %, C 99 %, W135 100 % and Y 100 % *Menactra* In the 11–18 yrs, hsBA ≥1:8 1 mth post-vaccination (95%CI) A 92 %,C 91.7 %, Y 81.8 % and 96.7 % *Menveo* In the 11–18 year group reaching hsBA ≥1:8 1 mth post-vaccination (95%CI) A 81 %, C 84 %, W135 91 %, Y 95 %	10–14 days 1 mth	No studies – use only if the benefit justifies the potential risk to the foetus	Polysac-charide vaccine 2–3 yrs Conjugated at least 5 yrs

(continued)

Table 6.1 (continued)

Vaccine type	Main indications	Main contraindications	Main adverse effects	Schedule and no. of doses	Efficacy	Time to immunity	Use in pregnancy (category)	Duration of cover
Pertussis	Consider DTaP for adolescents and adults who are due for tetanus/ diphtheria booster	Hypersensitivity to any of the components including diphtheria, tetanus or pertussis toxoids	Pain, swelling, redness at the injection site, headache, decreased energy, generalised body ache, anorexia, irritability	A single 0.5 mL dose	1 mth post-vaccination: 92–100 % immune response	1 mth after booster dose >99 % seropositivity	Adacel – category B2 Boostrix – category B1	
Polio Inactivated (Vero) *Ipol* *Imovax*	Active immunisation of infants, children and adults for the prevention of poliomyelitis	Hypersensitivity to any of the components in the vaccine Vaccination should be postponed in cases of febrile or acute disease	Local pain and inflammation at injection site and fever	Primary immunisation: 3 doses of 0.5 mL SC administered at intervals of 8 weeks	1 mth post-vaccination	After series and after booster	IPOL category B2	A single booster dose of 0.5 mL every 10 yrs or if travelling to risk environments

Pneumococcal Polysaccharide Inactivated *Pneumo 23* *Pneumovax 23* Conjugated *Prevenar* (*PCV13*)	High-risk subjects ≥ 2 yrs of age to prevent pneumococcal pneumonia and systemic pneumococcal infections caused by the serotypes included in the vaccine. Active immunisation for the prevention of pneumococcal disease caused by *Streptococcus pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7 F, 9 V, 14, 18C, 19A, 19 F and 23 F in adults aged 50 yrs and older	Known systemic hypersensitivity reaction to any component of the vaccine Hypersensitivity to the active substances or to any of the excipients or to diphtheria toxoid	Headache, febrile convulsion, lymphade-nopathy, rash, urticarial myalgia, arthralgia, injection site pain/ tenderness, rash, diarrhoea, vomiting, decreased appetite and irritability	Single 0.5 mL dose IM or SC injection Prevenar 13, 0.5 mL given IM only	2–3 weeks after immunisation	The conferred immunity appears from 2 to 3 weeks after immunisation and lasts about 5 yrs 1 mth post-vaccination	Pneumo 23 Category B2 Category B2	

(continued)

Table 6.1 (continued)

Vaccine type	Main indications	Main contraindications	Main adverse effects	Schedule and no. of doses	Efficacy	Time to immunity	Use in pregnancy (category)	Duration of cover
Q fever Inactivated *Q-VAX*	Q-VAX® vaccine is indicated for the immunisation of susceptible adults at risk of infection It is essential to test for sensitisation to Q fever antigens using Q-VAX® skin test in every individual prior to immunisation	Q-VAX® should not be administered to: · Persons with history of Q fever · Persons who have a history of likely exposure followed by an illness strongly suggestive of Q fever Those who have a confirmed positive antibody test or a positive skin reaction must not be given Q-VAX®	Tenderness, erythema, headache and delayed skin reaction	The dose of Q-VAX® vaccine is 0.5 mL given by SC injection *Revaccination must never be undertaken*	Seroconversion rate is low (50–80 %) and antibody levels are transient Cell-mediated immunity develops The duration of protective immunity following immunisation is unknown		Category B2	Immunity in excess of 5 yrs
Rabies (pre-exposure) *Purified inactivated rabies vaccine* *Verorab* *Rabipur* *HDCV*	Rabies vaccine is indicated for the prevention of rabies prior to exposure	Hypersensitivity to the active substances or to any of the excipients	Pain, erythema, oedema, pruritus and induration at the injection site	Verorab and Rabipur 0.1 mL ID 1 mL IM Primary vaccination: 3 injections at d0, d7 and d21 or d28	1 mth after completing primary dose	Protective antibody titre (≥0.5 IU/mL) by day 28 of a primary series of three injections		First booster: 1 year later Subsequent boosters: every 5 yrs

Rabies postexposure prophylaxis	Rabies vaccine is indicated for the prevention following proven or suspected exposure	Hypersensitivity to the active substances or excipients	Pain, erythema, oedema, pruritus and induration at the injection site, moderate fever, shivering, malaise, fatigue, headache, dizziness, arthralgia, myalgia and gastrointestinal disorders (nausea, abdominal pain)	*Adults and children*: 4 or 5 0.5 mL injections at d0, d3, d7, d14 and d28 Complementary passive immunisation at d0 is necessary using: HRIG 20 IU/kg body weight or ERIG 40 IU/kg body weight The vaccine should be injected contralaterally to the sites of immunoglobulin administration *Vaccination of subjects that have completed PEP* 2 injections at d0 and d3 *Vaccination more than 5 yrs previously*: *give PEP at d0 and d3* *If incomplete vaccination*: 4/5 injections at d0, d3, d7, d14 and d28 with the administration of immunoglobulin, if necessary		Neutralising antibodies (≥0.5 IU/mL) in 98 % of patients within 14 days and in 99–100 % of patients by day 28–38 when administered according to the WHO recommended schedule of five IM injections of 1 mL, one each on days 0, 3, 7, 14 and 28	Verorab category B2 Rabipur may be administered to pregnant and breast-feeding women when postexposure prophylaxis is required	In practice, if the last booster was administered more than 5 yrs previously or if vaccination is incomplete, the subject should not be considered to be completely immunised

(continued)

Table 6.1 (continued)

Vaccine type	Main indications	Main contraindications	Main adverse effects	Schedule and no. of doses	Efficacy	Time to immunity	Use in pregnancy (category)	Duration of cover
Diphtheria Inactivated toxoid and *tetanus* ADT (booster)	Vaccination of children (≥5 yrs of age) and adults who have previously received at least 3 doses of a vaccine for primary immunisation against diphtheria and tetanus	Previous hypersensitivity reactions to ADT vaccination	Malaise, fever ≥ 38 °C, redness/ swelling at the injection site	A single 0.5 mL dose	97 % after primary course	1–2 weeks after the 3rd dose	ADT – category A	*10 yrs*
Tick-borne encephalitis Whole virus inactivated *TicoVac TicoVac Junior Encepur*	TicoVac 0.5 mL is indicated for the active immunisation of persons ≥16 + yrs of age TicoVac Junior 0.25 mL is indicated for the active immunisation of children aged 1 to 15 yrs of age	Hypersensitivity to the active substance and severe hypersensitivity to egg or chick proteins	Headache, nausea, vomiting, pyrexia, arthralgia, fatigue and malaise	0.5 mL *IM* 3 doses: D 0, 4–12 weeks and 5–12 mths Rapid schedule d0, d14, mth 5–12 after 2nd injection	A protection rate >90 % 14 days after the second vaccination and > 97 % 7 days after completion of the third vaccination	After 1 dose 50 % seroconvert after dose 1 and 90 % 2 weeks after dose 2	There are no data from the use of TicoVac 0.5 mL in pregnant women	Booster <3 yrs

Tuberculosis Live attenuated *BCG vaccine SSI*	Active immunisation against tuberculosis	No to be used in individuals taking systemic corticosteroids or immuno-suppressive treatment	Headache and fever	Adults and children >12 mths A dose of 0.1 mL injected strictly by the ID route Infants <12 mths A dose of 0.05 mL injected strictly by the ID route		Tuberculin positive after 6 weeks	Not recom-mended during pregnancy	Waning immunity after 10 yrs
Typhoid fever Live, attenuated bacterial *Vivotif Oral*	Vivotif Oral is indicated for active immunisation against typhoid in adults and children above 6 yrs of age	Primary and acquired immuno-deficiency, antimitotic drugs and hypersensitivity to the vaccine or to any components	Constipation, abdominal cramps, diarrhoea, nausea, fever, vomiting, anorexia, headache and urticarial exanthema	Ingestion of 1 capsule taken approximately 1 h before a meal, with cold or lukewarm drink, on d1, d3 and d5	Between 70 and 95 % protection from typhoid	Effective 7 days after last dose	Vivotif category B2	*Booster doses on days 1, 3 and 5 every 3 yrs*
Typhoid fever Vi Inactivated purified polysaccharide *Typherix* *Typhim Vi*	Active immunisation against typhoid fever in subjects 2+ yrs of age	Hypersensitivity to the vaccine or any component of the vaccine	Pain, swelling and erythema	A single dose of 0.5 mL IM or SC injection	28 days after single dose – seroconversion in over 90 % of recipients	7 days after injection	Typhim Vi category B2	*3 yrs*
Varicella Live attenuated *Varilrix* *Varivax*	Varilrix active immunisation in individuals >9 mths Varivax vaccination use in individuals 12 mths of age and older	Contraindicated in subjects with a lack of cellular immune competence	Pain, rash and swelling at injection site	Varilrix: children from the age of 9 mths up, two doses administered at least 6 weeks apart Varivax dosage Children 12 mths	6 weeks after 2nd vaccination 100 % seroconversion rate Overall seroconversion rate in high-risk patients was ≥80 %	6 weeks after 2nd vaccination	Contrain-dicated during pregnancy	

(continued)

Table 6.1 (continued)

Vaccine type	Main indications	Main contraindications	Main adverse effects	Schedule and no. of doses	Efficacy	Time to immunity	Use in pregnancy (category)	Duration of cover
Yellow fever Live attenuated	Every individual over 9 mths of age living or travelling through an endemic area	Not to be used in pregnancy or children <6 mths of age and with allergy to any components of the vaccine Not be administered to immuno-compromised individuals	Local reactions (including pain, redness, haematoma, induration, swelling), pyrexia, asthenia, headache, nausea, diarrhoea and myalgia	A single 0.5 mL dose given by IM or SC injection		10 days	Not to be used in pregnancy or children <6 mths of age	In order to be officially recognised, the yellow fever vaccination must be administered in an approved vaccination centre and registered on an international certificate This certificate is valid from the 10th day after vaccination for 10 yrs A single 0.5 mL dose provides protection for at least 10 yrs

The information presented is not comprehensive; please review the current data sheet for more information and prescribing information
The FDA-assigned pregnancy categories as used in the drug formulary are as follows:
Category A
Adequate and well-controlled studies have failed to demonstrate a risk to the foetus in the first trimester of pregnancy (and there is no evidence of risk in later trimesters)

Category B

Animal reproduction studies have failed to demonstrate a risk to the foetus, and there are no adequate and well-controlled studies in pregnant women

B1: Limited experience in the vaccine in pregnant women. No increase in the frequency of malformation or other harmful effects on the human foetus. Animal studies have not shown evidence of an increased occurrence of foetal damage

B2: Limited experience in the vaccine in pregnant women. No increase in the frequency of malformation or other harmful effects on the human foetus. Animal studies are lacking, but available data shows no evidence of an increased occurrence of foetal damage

Category C

Animal reproduction studies have shown an adverse effect on the foetus, and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks

IM intramuscularly, *SC* subcutaneously, *ID* intradermally, *d* day, *mth* month, *yrs* years, *GI* gastrointestinal, *PEP* postexposure prophylaxis, *HRIG* human rabies immunoglobulin, *ERIG* equine rabies immunoglobulin

Chapter 7
Vaccines and Their Contents

Marc Shaw, Tonia Buzzolini, Poh Lian Lim, and Smriti Pathak

Key Points
- The contents of vaccines available in Australia, New Zealand and Singapore are listed below.
- All attempts have been made to make this list conclusive, yet it is not necessarily definitive.
- This chart will assist the travel health practitioner in determining the potential risk of an allergic reaction to any vaccine.
- It is advised that a risk assessment be undertaken before the administration of any vaccine.

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Vaccine and manufacturer	Availability			Contents (*As listed by the company manufacturing the vaccine in consumer medicine information*)
	AU	NZ	SG	
Adacel				
Tetanus, diphtheria, pertussis *Sanofi Pasteur*	Yes	Yes	Yes	Active ingredients:
				Diphtheria toxoid, adsorbed
				Tetanus toxoid, adsorbed
				Pertussis toxoid
				Pertussis filamentous haemagglutinin
				Pertussis fimbriae types 2 and 3
				Pertussis pertactin
				Adjuvants:
				Aluminium phosphate
				Excipients:
				Formaldehyde
				Phenolxyethanol
				Glutaraldehyde
				Water for injection
Adacel-Polio				
Tetanus, diphtheria, pertussis, polio *Sanofi Pasteur*	Yes	Yes		
				Active ingredients:
				Diphtheria toxoid, adsorbed
				Tetanus toxoid, adsorbed
				Pertussis toxoid
				Pertussis filamentous haemagglutinin
				Pertussis fimbriae types 2 and 3
				Pertussis Pertactin
				Poliovirus inactivated types 1, 2, and 3
				Adjuvants:
				0.33 mg aluminium phosphate
				Excipients:
				Formaldehyde
				Glutaraldehyde
				Neomycin
				Phenolxyethanol
				Polysorbate 80
				Polymyxin B sulphate
				Streptomycin
				Water for injection
				(*Manufacture of this product includes exposure to bovine-derived materials*)

Vaccine and manufacturer	Availability			Contents (*As listed by the company manufacturing the vaccine in consumer medicine information*)
	AU	NZ	SG	
ADT				
Adsorbed diphtheria and tetanus *bioCSL*	Yes	Yes	Yes	Active ingredients:
				Purified diphtheria toxoid
				Purified tetanus toxoid
				Adjuvants:
				Aluminium hydroxide
				Excipients
				Sodium chloride
				Sodium hydroxide
				Water for injection
				(*Manufacture of this product includes exposure to bovine-derived materials*)
Agrippal				
Influenza vaccine *Novartis*	Yes		Yes	Active ingredients:
				Antigens representative of current viruses in hemispheric influenza
				Excipients:
				Sodium chloride
				Sodium phosphate (dibasic)
				Potassium chloride
				Potassium dihydrogen phosphate
				Magnesium chloride
				Calcium chloride
				The following are present in each 0.5 ml dose: *eggs*, *chicken proteins*, *kanamycin sulphate*, *neomycin sulphate*, *sodium citrate*, *barium sulphate*, *formaldehyde*, *sucrose*, *cetrimonium bromide* (*CTAB*), *polysorbate and less than 0.2 μg of ovalbumin per 0.5 ml dose*
				Water for injection
				EGG vaccine

Vaccine and manufacturer	Availability			Contents (*As listed by the company manufacturing the vaccine in consumer medicine information*)
	AU	NZ	SG	
Avaxim				
Hepatitis A Sanofi Pasteur	Yes	Yes	Yes	Active ingredients:
				Hepatitis A virus inactivated
				Adjuvants:
				Aluminium hydroxide
				Excipients:
				Phenoxyethanol
				Formaldehyde (preservative)
				Medium 199 (Hanks)
				(Medium 199 *is a complex mixture of amino acids including phenylalanine*, *mineral salts*, *vitamins and other components* (*e.g. glucose*) *supplemented with polysorbate 80. Hydrochloride acid or sodium hydroxide is added for pH adjustment*)
				Neomycin and bovine serum albumin may be present as residual traces
				(*Manufacture of this product includes exposure to bovine-derived materials*)
BCG				*Live bacterial vaccine*
Tuberculosis				Active ingredients:
				Mycobacterium bovis BCG (bacillus Calmette-Guerin), live attenuated
				List of excipients
				Powder:
				Sodium glutamate
				Solvent:
				Magnesium sulphate heptahydrate
				Dipotassium phosphate
				Citric acid, monohydrate
				l-asparagine monohydrate
				Ferric ammonium citrate
				Glycerol 85 %
				Water for injection
Berirab P				Human blood product
Human rabies immunoglobulin *CSL Behring*		Yes		Active ingredients:
				Human proteins
				Human rabies immunoglobulins
				Excipients:
				Aminoacetic acid (glycine)
				Sodium chloride
				Sodium hydroxide or hydrochloric acid *in small amounts to adjust pH*
				Contains no preservative

Vaccine and manufacturer	Availability			Contents (*As listed by the company manufacturing the vaccine in consumer medicine information*)
	AU	NZ	SG	
Bexsero				
Meningococcal Group B *Novartis*	Yes			Active ingredients:
				Recombinant meningococcal protein antigens
				Adjuvants:
				Aluminium hydroxide
				Excipients:
				Sodium chloride
				Histidine
				Sucrose
				There may be traces (<0.01 μg per dose) of residual kanamycin
				Water for injection
Boostrix				
Tetanus, diphtheria, pertussis *GSK*	Yes	Yes	Yes	Active ingredients:
				Diphtheria toxoid, adsorbed
				Tetanus toxoid, adsorbed
				Pertussis toxoid, adsorbed
				Filamentous haemagglutinin, adsorbed
				Pertactin
				Adjuvants:
				Aluminium hydroxide, aluminium phosphate
				Excipients:
				Formaldehyde
				Sodium chloride
				Polysorbate 80
				Glycine
				Water for injection
Boostrix-IPV				
Tetanus, diphtheria, pertussis *GSK*	Yes			Active ingredients:
				Diphtheria toxoid, adsorbed
				Tetanus toxoid, adsorbed
				Pertussis toxoid, adsorbed
				Filamentous haemagglutinin, adsorbed
				Pertactin
				Poliovirus inactivated types 1, 2, 3
				Adjuvants:
				Aluminium
				0.5 mg as aluminium hydroxide and aluminium phosphate
				Excipients:
				Traces of formaldehyde
				Polysorbate 80
				Polymyxin
				Neomycin
				Water for injection

Vaccine and manufacturer	Availability			Contents (*As listed by the company manufacturing the vaccine in consumer medicine information*)
	AU	NZ	SG	
Dukoral				
Cholera (*also licensed for traveller's diarrhoea in NZ*)				Active ingredients:
bioCSL	Yes	Yes		Vibrio cholerae 01 Inaba classic strain – HI
Johnson and Johnson			Yes	Vibrio cholerae I 01 El Tor strain – FI
				Vibrio cholerae 01 Ogawa classic strain – HI
				Vibrio cholerae 01 Ogawa classic strain – FI
				HI, *heat inactivated*; *FI*, *formalin inactivated*
				Excipients – vaccine:
				Sodium phosphate, monobasic monohydrate
				Sodium phosphate, dibasic dehydrate
				Sodium chloride
				Effervescent granules:
				Sodium carbonate – anhydrous
				Anhydrous citric acid
				Raspberry flavour
				Sodium bicarbonate
				Sodium citrate
				Saccharine sodium
				Water for injection
Engerix B adult *Engerix B paed*				
Hepatitis B GSK	Yes	Yes	Yes	Active ingredients:
				Hepatitis B surface antigen
				Adjuvants:
				Aluminium hydroxide
				Yeast cells (*Saccharomyces cerevisiae*)
				Excipients:
				Sodium chloride
				Sodium phosphate dehydrate
				Sodium dihydrogen phosphate
				Polysorbate 80
				Water for injection
				No substances of human origin in this product

Vaccine and manufacturer	Availability			Contents (*As listed by the company manufacturing the vaccine in consumer medicine information*)
	AU	NZ	SG	
Fluarix				
Influenza *GSK*	Yes	Yes	Yes	Active ingredients:
				Antigens representative of current viruses in hemispheric influenza
				Excipients:
				Haemagglutinin of each of strains
				Saccharose
				Sodium chloride
				d-alpha-tocopheryl acid succinate
				Formaldehyde
				Gentamicin sulphate
				EGG vaccine
Fluvax				
Influenza				Active ingredients:
bioCSL	Yes	Yes		Antigens representative of current viruses in hemispheric influenza
United Italian Corporation Ltd			Yes	Excipients:
				Sodium chloride
				Sodium phosphate (dibasic + monobasic)
				Potassium chloride
				Potassium phosphate – monobasic
				Calcium chloride
				Sodium taurodeoxycholate
				Ovalbumin
				Sucrose
				Neomycin
				Polymyxin B sulphate
				β-propiolactone
				Water for injection
				EGG vaccine

Vaccine and manufacturer	Availability			Contents (*As listed by the company manufacturing the vaccine in consumer medicine information*)
	AU	NZ	SG	
Havrix 1440, *Havrix Junior*				
Hepatitis A *GSK*	Yes	Yes	Yes	Active ingredients:
				Inactivated HA virus
				Adjuvants:
				Aluminium hydroxide
				Excipients:
				Neomycin
				Sodium chloride
				2-phenoxyethanol
				Neomycin sulphate
				Formaldehyde
				Polysorbate 20
				Amino acid supplement in a phosphate-buffered sodium chloride
				Water for injection
				Hep A on MRC5 human diploid cells
H-B-VAX II adult *H-B-VAX paed* *H-B-VAX dialysis formulation*				
Hepatitis B *Merck Sharp and Dohme*	Yes		Yes	Active ingredients:
				Subunit viral vaccine derived from surface antigen of hepatitis B virus
				Adjuvants:
				Aluminium hydroxide
				Excipients:
				May contain up to 1 % yeast protein
				Water for injection
				Preservative-free
				No substances of human origin in this product
H-B-VAX Pro				
Hepatitis B *Merck Sharp and Dohme*		Yes		Active ingredients:
				Subunit viral vaccine derived from surface antigen of hepatitis B virus
				Adjuvants:
				Aluminium hydroxyphosphate sulphate
				Excipients:
				May contain up to 1 % yeast protein
				Phosphate buffer
				Formaldehyde
				Water for injection
				Preservative-free
				No substances of human origin in this product

Vaccine and manufacturer	Availability			Contents (*As listed by the company manufacturing the vaccine in consumer medicine information*)
	AU	NZ	SG	
Imogam Rabies				Human blood product
Rabies immunoglobulin *Sanofi Pasteur*	Yes	Yes	Yes	Active ingredients:
				Human proteins
				Human rabies immunoglobulins
				Excipients:
				Glycine
				Sodium chloride
				Sodium hydroxide or hydrochloric acid *in small amounts to adjust pH*
				Contains no preservative
Imojev				*Live virus vaccine*
Japanese encephalitis – live virus vaccine *Sanofi Pasteur*	*Yes*		*Yes*	Active ingredients:
				Live, attenuated, recombinant Japanese encephalitis virus
				Adjuvants:
				No adjuvants or antibiotic preservative added
				Excipients:
				Mannitol
				Lactose
				Glutamic acid
				Potassium hydroxide
				Histidine
				Human serum albumin
				Sodium chloride
				Water for injection
				Imojev must be reconstituted by adding the entire contents of the diluent to the vial and shaking it until dissolved completely. Reconstituted vaccine must be used within 1 h

Vaccine and manufacturer	Availability			Contents (*As listed by the company manufacturing the vaccine in consumer medicine information*)
	AU	NZ	SG	
Imovax Polio				
Polio Sanofi Pasteur			Yes	Active ingredients:
				Inactive polio virus type 1
				Inactive polio virus type 2
				Inactive Polio virus type 3
				Excipients:
				Ethanol
				2-phenolxyethanol
				Formaldehyde
				Polymyxin B, streptomycin, neomycin and bovine serum albumin may be present
				Medium 199 Hanks (*without phenol red*, *is a complex mixture of amino acids including phenylalanine*, *mineral salts*, *vitamins and other components* (*e.g. glucose*) *supplemented with polysorbate 80. Hydrochloride acid or sodium hydroxide is added for pH adjustment*)
				(*Manufacture of this product includes exposure to bovine-derived materials*)
Influvac *Influvac Junior*				
Influenza vaccine *Abbott Laboratories*	Yes	Yes	Yes	Active ingredients:
				Antigens representative of current viruses in hemispheric influenza
				Excipients:
				Sodium chloride
				Sodium phosphate (dibasic) dihydrate
				Potassium chloride
				Potassium phosphate monobasic
				Magnesium chloride
				Calcium chloride
				The following are present in each 0.5 ml dose: egg protein, formaldehyde, cetrimonium bromide (CTAB), polysorbate 80 and gentamicin
				Water for injection
				EGG vaccine

Vaccine and manufacturer	Availability			Contents (*As listed by the company manufacturing the vaccine in consumer medicine information*)
	AU	NZ	SG	
IPOL				
Polio – inactivated Vero Sanofi Pasteur	Yes	Yes	Yes	Active ingredients:
				Inactive polio virus type 1
				Inactive polio virus type 2
				Inactive polio virus type 3
				Excipients:
				2-phenolxyethanol
				Formaldehyde
				Medium 199 Hanks (*without phenol red, is a complex mixture of amino acids including phenylalanine, mineral salts, vitamins and other components* (*e.g. glucose*) *supplemented with polysorbate 80. Hydrochloride acid or sodium hydroxide is added for pH adjustment*)
				Traces:
				Polymyxin B, streptomycin, neomycin and bovine serum albumin may be present
				(*Manufacture of this product includes exposure to bovine-derived materials*)
Ixiaro				
Japanese encephalitis *Novartis*			Yes	Active ingredients:
				Inactivated Japanese encephalitis virus
				Excipients: aluminium hydroxide
				Phosphate-buffered saline
				Water for injection
Japanese encephalitis vaccine – GCC inj				
Japanese encephalitis *Green Cross*			Yes	Active ingredients:
				Inactivated Japanese encephalitis suspension
				Excipients:
				Sodium chloride
				Potassium phosphate, monobasic
				Sodium phosphate, dibasic
				Gelatin
				Polysorbate 80
				Thimerosal
				Water for injection
Jespect				
Japanese encephalitis *bioCSL*	Yes	Yes		Active ingredients:
				Inactivated Japanese encephalitis virus
				Excipients:
				Aluminium hydroxide
				Phosphate-buffered saline
				Water for injection
				No preservative or antibiotics added

Vaccine and manufacturer	Availability			Contents (*As listed by the company manufacturing the vaccine in consumer medicine information*)
	AU	NZ	SG	
Menactra				
Meningitis – ACWY conjugated *Sanofi Pasteur*	Yes	Yes	Yes	Active ingredients:
				Meningococcal polysaccharide Group A
				Meningococcal polysaccharide Group C
				Meningococcal polysaccharide Group Y
				Meningococcal polysaccharide Gp W-135
				Diphtheria toxoid protein
				Excipients:
				Sodium chloride
				Sodium phosphate – dibasic anhydrous
				Sodium phosphate – monobasic
				Water for injection
				No preservative or adjuvant added
Mencevax				
Meningitis – ACWY polysaccharide *GSK*	Yes	Yes	Yes	Active ingredients:
				Lyophilised prep of polysaccharides from:
				Meningococcal polysaccharide Group A
				Meningococcal polysaccharide Group C
				Meningococcal polysaccharide Group Y
				Meningococcal polysaccharide Gp W-135
				Excipients
				Powder:
				Sucrose
				Trometamol
				Diluent:
				Sodium chloride
				Water for injection
				No preservative added
Menomune				
Meningitis – ACWY polysaccharide *Sanofi Pasteur*	Yes	Yes	Yes	Active ingredients:
				Meningococcal polysaccharide Group A
				Meningococcal polysaccharide Group C
				Meningococcal polysaccharide Group Y
				Meningococcal polysaccharide Gp W-135
				Diphtheria toxoid protein
				Excipients:
				Lactose
				Sodium chloride
				Water for injection
				No preservative added
				The manufacture of this product includes exposure to bovine-derived materials

Vaccine and manufacturer	Availability			Contents (*As listed by the company manufacturing the vaccine in consumer medicine information*)
	AU	NZ	SG	
Menveo				
Meningitis – ACWY conjugated *bioCSL*	Yes			Active ingredients:
				Lyophilised MenA conjugate component and one syringe/vial containing liquid MenACWY conjugate
				Diphtheria toxoid protein
				Excipients:
				Sucrose
				Potassium dihydrogen phosphate
				Sodium phosphate monobasic monohydrate
				Sodium phosphate dibasic dihydrate
				Sodium chloride
				Water for injections
				No preservative or adjuvant added
				Caution with hypersensitivity to latex. The vial has a butyl rubber stopper
Merieux Human diploid cell vaccine				
Rabies Sanofi Pasteur	Yes		Yes	Active ingredients:
				Inactivated rabies virus
				Excipients:
				Neomycin
				Human serum albumin
				Trace phenol red
				Trace bovine gelatin
				Trace propiolactone
				Does not contain stabiliser or preservative

Vaccine and manufacturer	Availability			Contents (*As listed by the company manufacturing the vaccine in consumer medicine information*)
	AU	NZ	SG	
MMR II				*Live virus vaccine*
Measles, mumps, rubella *Merck Sharp and Dohme*	Yes	Yes	Yes	Active ingredients:
				Measles, mumps, rubella viruses
				Adjuvants:
				Nil
				Excipients:
				Sorbitol
				Sucrose
				Sodium phosphate
				Sodium chloride
				Hydrolysed gelatin
				Human albumin
				Foetal bovine serum
				Neomycin
				Other residuals: dibasic potassium phosphate, Eagle's minimum essential medium, Medium 199, monobasic potassium phosphate, monosodium glutamate, phenolsulfonphthalein, sodium bicarbonate
				Sterile lyophilised preparation
				Sterile water for injection
				The product contains no preservative
				(*Manufacture of this product includes exposure to bovine-derived materials*)
Nimenrix				
Meningitis – ACWY conjugated *GSK*	Yes			Meningococcal polysaccharide Group A
				Meningococcal polysaccharide Group C
				Meningococcal polysaccharide Group Y
				Meningococcal polysaccharide Gp W-135
				Diphtheria toxoid protein
				Excipients:
				Powder:
				Sucrose
				Trometamol
				Solvent:
				Sodium chloride
				Water for injection
				No preservative or adjuvant added
				Butyl rubber stopper for vial and in a prefilled syringe

Vaccine and manufacturer	Availability			Contents (*As listed by the company manufacturing the vaccine in consumer medicine information*)
	AU	NZ	SG	
Pneumo 23				
Pneumococcus Sanofi Pasteur		Yes	Yes	Active ingredients:
				23 polysaccharides of *Streptococcus pneumococcus*
				Excipients:
				Phenol
				Sodium chloride
				Dihydrated disodium phosphate
				Dihydrated monosodium phosphate
				Water for injection
Pneumovax 23				
Pneumococcus				Active ingredients:
Merck Sharp and Dohme	Yes	Yes	Yes	23 polysaccharides of *Streptococcus pneumococcus*
Prevenar 13	Yes	Yes	Yes	Excipients:
				Sodium chloride
				Phenol
				Water for injection
				(*Manufacture of this product includes exposure to bovine-derived materials*)
				Active ingredients:
				Pneumococcal purified capsular polysaccharides for serotypes 1, 3, 4, 5, 6A, 7 F, 9 V, 14, 18C, 19A, 19 F and 23 F
				Pneumococcal purified capsular polysaccharides for serotype 6B
				Non-toxic diphtheria CRM197 protein
				Adjuvant:
				Aluminium phosphate
				Excipients:
				Succinic acid
				Polysorbate 80
				Sodium chloride
				Sterile water for injection

Vaccine and manufacturer	Availability			Contents (*As listed by the company manufacturing the vaccine in consumer medicine information*)
	AU	NZ	SG	
Priorix				*Live virus vaccine*
Measles, mumps, rubella *GSK*	*Yes*		*Yes*	Active ingredients:
				Attenuated measles, mumps, rubella viruses
				(*Attenuated Schwarz measles virus strain, the RIT 4385 strain of mumps virus and the Wistar RA 27/3 rubella virus strain – each separately obtained by propagation in either chick embryo tissue cultures* (*mumps and measles*) *or MRC5 human diploid cells* (*rubella*)
				Adjuvants:
				Nil
				Excipients:
				Sorbitol
				Lactose
				Neomycin
				Mannitol
				Exposure to bovine-derived materials
				Sterile lyophilised preparation
				Sterile water for injection
				(*Manufacture of this product includes exposure to bovine-derived materials*)
Q-Vax				
Q fever *bioCSL*	Yes	Yes		Active ingredients:
				Formalin-inactivated Coxiella burnetii
				Excipients:
				Sodium chloride
				Sodium phosphate – dihydrate
				Sodium phosphate monohydrate thimerosal
				Water for injection
				May contain egg protein

Vaccine and manufacturer	Availability			Contents (*As listed by the company manufacturing the vaccine in consumer medicine information*)
	AU	NZ	SG	
Rabipur PCEC – purified chick embryo cell				
Rabies				Active ingredients:
bioCSL	Yes	Yes	Yes	Rabies virus, Flury LEP strain (inactivated)
Novartis (*Singapore*)				Produced on primary chicken fibroblast
				Cell cultures
				Excipients:
				Trometerol
				Sodium chloride
				Disodium edetate
				Monopotassium glutamate
				Sucrose
				Polygeline
				Possible trace amounts: neomycin, chlortetracycline, amphotericin B
				Water for injection
				Lyophilised preparation
				Virus propagated in pathogen-free chick embryos
				(*Manufacture of this product includes exposure to bovine-derived materials*)
Rimevax				*Live virus vaccine*
Measles *GSK*	Yes	Yes	Yes	Active ingredients:
				Attenuated Schwarz measles virus strain
				Excipients: neomycin
				Lyophilised preparation
				Water for injection
				Virus propagated in pathogen-free chick embryos

Vaccine and manufacturer	Availability			Contents (*As listed by the company manufacturing the vaccine in consumer medicine information*)
	AU	NZ	SG	
Stamaril				*Live virus vaccine*
Yellow fever Sanofi Pasteur	*Yes*	*Yes*	*Yes*	Active ingredients:
				17-day yellow fever virus
				Free from avian leucosis virus
				Adjuvants:
				Aluminium hydroxide
				Aluminium phosphate
				Excipients:
				Lactose
				l-histidine hydrochloride
				l-alanine
				Sorbitol
				Calcium chloride
				Magnesium sulphate
				Potassium chloride
				Potassium phosphate – monobasic
				Sodium chloride
				Sodium phosphate – dibasic dihydrate
				Water for injection
				(*Manufacture of this product includes exposure to bovine-derived materials*)
				EGG vaccine: *virus propagated in pathogen-free chick embryos*
TicoVac adult *TicoVac junior*				
Tick-borne encephalitis *Baxter*	Yes	Yes		Active ingredients:
				Tick-borne encephalitis virus (strain Neudörfl)
				Adjuvants:
				Aluminium hydroxide
				Excipients:
				Human albumin
				Sodium chloride
				Disodium phosphate-dihydrate
				Potassium dihydrogen phosphate
				Trace amounts:
				Formaldehyde
				Neomycin
				Gentamicin
				Protamine sulphate
				Water for injection
				EGG vaccine: *virus propagated in pathogen-free chick embryos*

Vaccine and manufacturer	Availability			Contents (*As listed by the company manufacturing the vaccine in consumer medicine information*)
	AU	NZ	SG	
Typhim Vi				
Typhoid fever *Sanofi Pasteur*	Yes	Yes	Yes	Active ingredients:
				Purified polysaccharide capsule of salmonella (*S. typhi*)
				Excipients:
				Isotonic buffer solution (contains sodium chloride, sodium phosphate dibasic dehydrate, sodium phosphate monobasic)
				Phenol preservative
				Water for injection
				(*Manufacture of this product includes exposure to bovine-derived materials*)
Typherix				
Typhoid fever *GSK*	Yes	Yes	Yes	Active ingredients:
				Purified Vi polysaccharide of *Salmonella typhi* Ty2 strain
				Excipients:
				Sodium chloride
				Dibasic sodium phosphate
				Monobasic sodium phosphate
				Phenol preservative
				Water for injection
				(*Manufacture of this product includes exposure to bovine-derived materials*)
Twinrix (*adult and junior*)				
Combination hep A/B *GSK*	Yes	Yes	Yes	Active ingredients:
				Inactivated HA virus
				Recombinant HBsAg protein
				Hep B on genetically engineered yeast cells
				Hep A on MRC5 human diploid cells
				Adjuvants: aluminium hydroxide, aluminium phosphate
				Excipients: amino acids for injection
				Formaldehyde
				Neomycin sulphate
				Polysorbate 20
				Sodium chloride
				Trometamol
				Water for injection

Vaccine and manufacturer	Availability			Contents (*As listed by the company manufacturing the vaccine in consumer medicine information*)
	AU	NZ	SG	
Vaqta				
Adult and paediatric Hepatitis A				Active ingredients:
				Hepatitis A virus inactivated formaldehyde
				Adjuvants:
				Aluminium hydroxide
				Excipients:
				Borax
				Traces of formaldehyde
				Neomycin
				Sodium chloride
				(*Manufacture of this product includes exposure to bovine-derived materials*)
Varilrix				*Live virus vaccine*
Chicken pox *GSK*	*Yes*	*Yes*	*Yes*	Active ingredients:
				Lyophilised preparation of live attenuated
				Oka strain of varicella-zoster virus
				Excipients:
				Amino acids
				Human albumin
				Lactose
				Neomycin sulphate
				Polyalcohols (sorbitol, mannitol)
				May contain yeast protein
				Water for injection
				(*Manufacture of this product includes exposure to bovine-derived materials*)
				No preservatives
Varivax				*Live virus vaccine*
Chicken pox *Merck Sharp and Dohme*	Yes	Yes	Yes	Active ingredients
				Lyophilised preparation of live attenuated Oka/ Merck strain of varicella-zoster virus
				Excipients:
				Sucrose
				Gelatin
				Urea
				Sodium chloride
				Monosodium l-glutamate
				Sodium phosphate dibasic
				Potassium phosphate monobasic
				Potassium chloride
				Trace: MRC-5 cells and trace quantities of neomycin and bovine calf serum
				(*Manufacture of this product includes exposure to bovine-derived materials*)
				The product contains no preservative

Vaccine and manufacturer	Availability			Contents (*As listed by the company manufacturing the vaccine in consumer medicine information*)
	AU	NZ	SG	
Vaxigrip				
Influenza *Sanofi Pasteur*	Yes	Yes	Yes	Active ingredients:
				Inactivated flu vaccine – each prefilled syringe contains 15 mcg haemagglutinin of each of the 3 strains in a buffered saline solution
				Excipients:
				Sodium chloride
				Potassium chloride
				Sodium phosphate – dibasic dehydrate
				Potassium phosphate – monobasic
				May have traces of:
				Neomycin
				Formaldehyde
				Octoxinol 9
				Ovalbumin
				Water for injection
				EGG vaccine: *virus propagated in pathogen-free chick embryos*
				Contains no preservatives
Verorab				
Rabies *Sanofi Pasteur*		Yes	Yes	Active ingredients:
				Rabies virus, Wistar strain (inactivated)
				Produced on Vero cells
				Excipients:
				Maltose
				Human albumin
				NaCl
				Water for injection
				Lyophilised preparation

Vaccine and manufacturer	Availability			Contents (*As listed by the company manufacturing the vaccine in consumer medicine information*)
	AU	NZ	SG	
Vivaxim				
Combination (hepatitis A/typhoid) Sanofi Pasteur	Yes	Yes	Yes	Active ingredients:
				Salmonella typhi Vi polysaccharide
				Hepatitis A virus antigen
				Adjuvants:
				Aluminium
				0.3 mg as aluminium hydroxide
				Excipients:
				Salmonella typhi Vi polysaccharide components:
				Sodium chloride
				Sodium phosphate (dibasic + monobasic)
				Inactivated hepatitis A virus vaccine components:
				Phenoxyethanol
				Formaldehyde
				Medium 199 (*a complex mixture of amino acids including phenylalanine*, *mineral salts*, *vitamins and other components* (*e.g. glucose*) *supplemented with polysorbate 80. Hydrochloride acid or sodium hydroxide is added for pH adjustment*)
				Neomycin
				Hydrochloric acid/sodium hydroxide
				Water for injection
				(*Manufacture of this product includes exposure to bovine-derived materials*)
Vivotif				*Live bacterium vaccine*
Typhoid fever (*oral vaccine*)				Active ingredients:
bioCSL				Salmonella typhi Ty21a bacteria
Johnson and Johnson	*Yes*	*Yes*	*Yes*	Excipients:
				Ethylene glycol
				Sucrose
				Ascorbic acid
				Protein hydrolysate
				Lactose
				Magnesium stearate
				Hydroxypropyl methylcellulose phthalate
				Gelatin
				Titanium dioxide
				Erythrosine
				Iron oxide yellow
				Iron oxide red
				Dibutyl phthalate
				Diethyl phthalate

AU Australia, *NZ* New Zealand, *SG* Singapore

Chapter 8
Vaccine Administration

Claire Wong

Key Points
- Explain the procedure to the traveller allowing the opportunity to ask questions and gain informed consent.
- Follow the manufacturer's instructions to prepare and reconstitute the vaccine. Note the expiry date and batch number.
- Select the correct site and appropriate route of administration using the correct needle gauge and length.
- Position the traveller and administer the vaccine.
- Dispose of used needles and syringes safely and document the vaccine according to practice protocol.

Vaccine administration is a process that involves explanation of the procedure, gaining informed consent and then the administration of vaccines using the appropriate route, needle size and site. Familiarity with the recommended route, and site of administration of vaccines, ensures local reactions are minimised and that the vaccine is effective.

Immunisation training, including the recognition and treatment of anaphylaxis and other adverse events, is essential. Consultation before vaccine administration provides each traveller with the opportunity to discuss any concerns and ensures appropriate informed consent.

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Pre-vaccination Screening

Pre-vaccination screening is required to:

- Identify any potential risks
- Assess any medical contraindications
- Eliminate or minimise the risk of adverse events
- Identify any previous reactions to vaccinations
- Check the correct time intervals of previous vaccine/s
- Check whether or not the traveller has had any recent medical procedures or blood transfusions which could preclude vaccination

The process of screening travellers prior to administering vaccines is similar to that of screening children and adults prior to administering vaccines in a national immunisation schedule. It is, however, imperative to seek further information pertaining to the travel itinerary, medical history, past vaccination history and other special considerations as noted in Chapter 5 risk assessment in the travel health consultation.

Vaccine Preparation

- Prepare vaccines out of sight of the traveller to minimise anxiety.
- Refer to the vaccine data sheet for specific guidance on the preparation and reconstitution of vaccines.
- Prepare vaccines immediately prior to administration to avoid errors in preparation and ensure vaccine efficacy.
- Check the vaccine expiry date and record the batch number according to local practice policy.
- Freeze-dried vaccines must be reconstituted with the correct volume of diluent. This is usually supplied with the vaccine and needs to be used within the recommended timeframe.
- Once reconstituted, visually inspect the vaccine to ensure it conforms to the description given in the data sheet.

Needle Gauge and Length

Unless supplied with a prefilled syringe and integral needle, always use a new needle of the appropriate gauge (width) to administer the vaccine. This can involve discarding any needles supplied with the vaccine, as they are sometimes of inadequate length for intramuscular administration. For intramuscular (IM) and subcutaneous (SC) injections, the needle needs to be sufficiently long to ensure the vaccine is deposited into the muscle (IM) or deep into the subcutaneous tissue (SC). This

Table 8.1 Recommended needle gauge and length by age and site

Age	Site	Needle gauge and length	Angle of needle insertion
Intramuscular injection			
Newborn	Vastus lateralis	23–25G × 16 mm	90°
6 weeks	Vastus lateralis	23–25G × 16 or 25 mm, dependent on muscle mass	90°
3–12 months	Vastus lateralis	23–25G × 25 mm	90°
13 months–2 years	Deltoid	23–25G × 16 mm	90°
	Vastus lateralis	23–25G × 25 mm	
3 years to adult	Deltoid	23–25G × 16 or 25 mm, dependent on muscle mass	90°
	Vastus lateralis	21–22G × 25 or 38 mm, dependent on muscle mass	
Subcutaneous injection			
All ages	Deltoid	25–26G × 16 mm	45°

ensures minimal discomfort following immunisation. Poor immunisation technique can lead to pain, nodules or abscesses at the vaccine site.

The needle gauge is determined by the age and weight of the individual and the proposed site of vaccination. The use of a larger bore needle reduces the pain of vaccination as the fluid is injected under less pressure. See Table 8.1 for recommended needle gauge and lengths.

The precise intradermal (ID) injection route required for BCG vaccine, Mantoux and Q fever skin tests requires specialist training using a 26–27G × 10 mm needle. Observing two ID injections and administering ten under supervision is appropriate training for most health professionals.

In some countries, the rabies vaccine is administered via the ID route in order to reduce the cost to travellers. As this route of administration is not registered by the vaccine manufacturer, the health professional takes responsibility if they choose to administer the vaccine ID.

ID influenza vaccine (Intanza) is administered in a specifically designed needle and syringe with a microinjection system to deliver the vaccine into the dermal layer of the skin without the need for special training.

Vaccine Administration

Adopt a confident and unhurried approach, particularly when dealing with children or anxious travellers, as this will have a calming effect. Travellers with a history of fainting following injections may choose to lie down.

The skin does not need to be cleansed prior to vaccination unless visibly dirty. Alcohol skin wipes can inactivate live viral vaccines and if tracked in to the muscle can lead to local irritation.

Injection Sites

As a general guide, the vastus lateralis (anterolateral thigh) muscle is the preferred site for IM and SC immunisation of infants under 1 year of age as it provides a large muscle mass (see Fig. 8.1). The deltoid is the preferred site in children from 1 year of age and adults (see Fig. 8.2), although the vastus lateralis is an alternate site for IM administration, particularly in children under 2 years who may not have an adequately developed deltoid muscle mass.

The buttock is not an appropriate injection site due the risk of sciatic nerve damage and the possibility of injecting vaccine in to the fatty layers rather than the muscle. Injecting vaccines in to the fatty tissue will reduce the efficacy of the vaccine.

ID BCG vaccine is administered at the insertion of the deltoid muscle. Administering the vaccine any higher can result in the formation of significant keloid scarring.

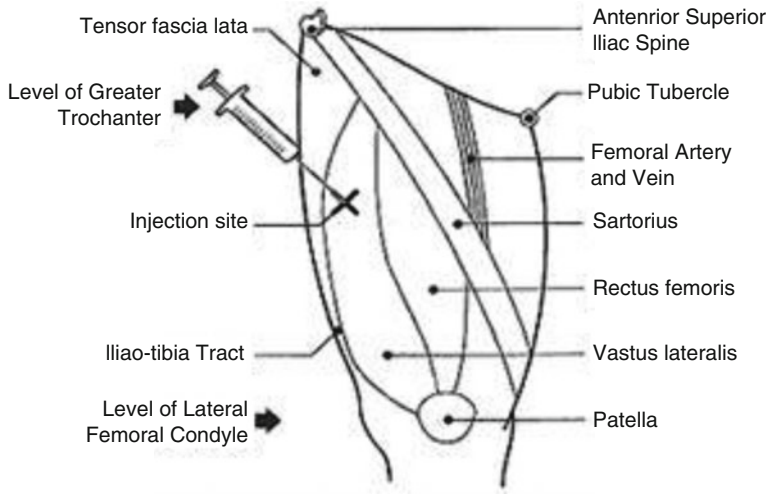


Fig. 8.1 Vastus lateralis injection site on the anterolateral thigh (Courtesy of the *Australian Immunisation Handbook* 2014)

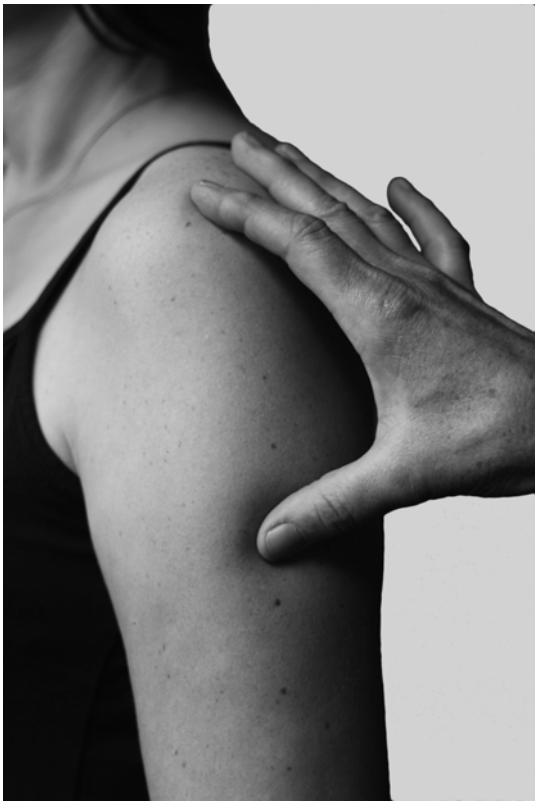


Fig. 8.2 Deltoid injection site (Photography by Clare Shaw)

Positioning

The appropriate limb for immunisation should be fully exposed to ensure the vaccine is given at the correct site. This can necessitate removing clothing, for a tightly rolled sleeve can increase the risk of bleeding and subsequent bruising following immunisation. Travellers should be in a sitting position with the arm relaxed, either hanging by the side or with the hand resting on the lap or hip. Those prone to fainting often request to lie down during immunisation, but should be observed either sitting or lying down for 15 min following immunisation.

Positioning of Infants and Children

Instruct the infant's parent or carer how to hold the child on their lap, ensuring that they understand the imminent procedure and the importance of keeping the limb still. Infants under 6 months of age do not need to be tightly restrained as this may cause increased anxiety.

Fig. 8.3 Cuddle position for vaccinating infants (Photography by Clare Shaw)

With the child sitting sideways, the free arm can be tucked behind the parent in a cuddle. The child's legs can be held firmly between those of the parent (see Fig. 8.3).

Older children may prefer to sit on their own; however, the parent may still be required to offer reassurance and help to hold the limb still.

Injection Technique

Intramuscular Injection

With the skin stretched gently with the finger and thumb of the nondominant hand, the needle is inserted dart-like at a 90° angle. Aspiration is no longer considered necessary. The vaccine is administered slowly and the plunger fully depressed before the syringe is smoothly removed. Gentle pressure can be applied with a cotton wool or gauze swab for a few seconds if bleeding occurs.

Subcutaneous Injection

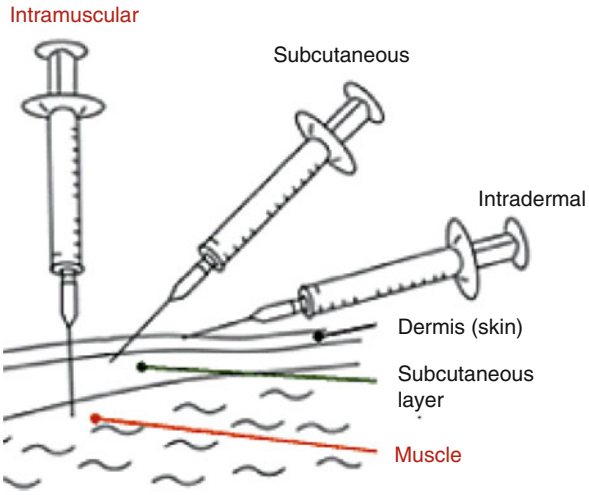
The skin is bunched between the thumb and forefinger of the nondominant hand to lift the adipose tissue from the underlying muscle. The needle is then inserted at a 45° angle; aspiration is unnecessary. The vaccine is injected slowly, the plunger fully depressed and the needle removed smoothly. Gentle pressure can then be applied for a few seconds if needed.

Intradermal Injection

The ID route requires some practice to ensure the vaccine is deposited in the correct location; the vaccine will be ineffective if given too deeply. In the case of BCG vaccine, incorrect administration can result in local reactions and keloid scarring.

The skin is stretched taunt with the thumb and forefinger of the nondominant hand. With the bevel uppermost, the needle is inserted almost parallel to the skin, until the bevel just disappears into the skin. As the vaccine is injected slowly, resistance should be felt as a bleb appears. If a bleb does not immediately appear, the needle should be removed and the procedure restarted. The vaccine can be administered again if necessary.

Intramuscular, Subcutaneous and Intradermal Injection Technique



Postvaccination Procedures

Discard vaccines, ampoules, vials and sharps immediately following vaccination into a sharps disposal bin.

Record all vaccinations in the traveller's notes according to clinic protocol. Most clinics also provide a personal vaccination document to travellers. Legally, all persons receiving yellow fever vaccine must be issued with an International Certificate of Vaccination or Prophylaxis.

Following vaccination, it is advised that travellers remain in the clinic for 15–20 min in case of reaction. The travel health professional should provide written information on the most common adverse events and how to manage them, including who to contact for advice or questions should concerns arise.

Further Reading

1. Chapter 2 Identifying injection sites. In: Australian immunisation handbook 2014. Available at: www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/handbook10-2-2. Accessed 7 Dec 2014.
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Chapter 9
Routine Vaccinations for the Traveller

Peter A. Leggat

Key Points
- Vaccination is one of the population health interventions that have had the greatest impact on global health.
- Millions of deaths and serious illnesses have been avoided every year through the implementation of routine population-based vaccination programmes and targeting improved vaccination coverage.
- If overall immunisation levels are high enough, epidemics can be prevented – thus providing social and individual protection.

Introduction

Vaccination is one of the population health interventions that have had the greatest impact on global health. Since the ground-breaking development of vaccines by scientists such as Jenner and Pasteur, millions of deaths and serious illnesses have been avoided every year through the implementation of routine population-based vaccination programmes and targeting improved vaccination coverage. The approximate timeline of early vaccine development is given in Table 9.1. Following the success of the smallpox eradication programme, the World Health Organization (WHO) and the United Nations Children's Fund (UNICEF) have introduced various initiatives to

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Table 9.1 Approximate timeline of early development of human vaccines

1798	Smallpox
1885	Rabies
1897	Plague
1923	Diphtheria
1926	Pertussis
1927	Tuberculosis (BCG)
1927	Tetanus
1935	Yellow fever
1955	Injectable polio vaccine (IPV)
1962	Oral polio vaccine (OPV)
1964	Measles
1967	Mumps
1970	Rubella
1981	Hepatitis B

After Plotkin et al.

maximise routine vaccination coverage, including the Expanded Programme on Immunisation and the WHO Global Immunisation Vision and Strategy.

The travel health consultation presents an excellent opportunity to update routine immunisations, as well as provide mandatory and other destination-specific travel-related vaccines. Routine vaccinations tend to be part of the national immunisation schedule of many countries, because of their prevalence, consequences of the disease and/or the need to eradicate a disease. Such schedules are administered mainly during childhood and adolescence and often need to be boosted or updated throughout life. The WHO provides a generic list of these routine vaccinations, which may, of course, differ slightly from country to country (see Table 9.2).

Benefits of Reviewing Routine Vaccination

There are a number of benefits in reviewing and updating travellers' routine vaccinations during the pretravel health consultation and considering the completion of these vaccine schedules on return. These include:

- Protecting travellers against infectious disease whilst abroad
- Protecting travellers against infectious diseases when they come back home
- Protecting host populations against carriage of infectious diseases during travel
- Improving the herd immunity of the travellers' home countries against infectious diseases

One of the issues of concern over the past few decades has been a variable rate of routine vaccination among children and adults for national schedule vac-

Table 9.2 Routine vaccinations to be reviewed in the pretravel health consultation

Vaccine-preventable disease	Type of vaccine
Diphtheria/tetanus/acellular pertussis (dTaP)	
Diphtheria	Toxoid vaccine
Tetanus	Toxoid vaccine
Acellular pertussis	Protein subunit vaccine
Hepatitis B (Hep B)	Protein subunit vaccine
Haemophilus influenzae type b (Hib)	Conjugate vaccine
Human papillomavirus	Protein subunit vaccine[a]
Influenza	Protein subunit vaccine
Measles, mumps, rubella (MMR)	
Measles	Attenuated (or live) vaccine
Mumps	Attenuated vaccine
Rubella	Attenuated vaccine
Pneumococcal disease	Conjugate and polysaccharide vaccines
Poliomyelitis	
Oral poliomyelitis vaccine (OPV)	Attenuated vaccine
Inactivated poliomyelitis vaccine (IPV)	Inactivated vaccine
Rotavirus	Attenuated vaccine
Tuberculosis (BCG)	Heterotypic (attenuated) vaccine
Varicella	Attenuated vaccine

After WHO

[a]Based on hollow virus-like particles (VLPs) assembled from recombinant HPV coat proteins

cines. Certainly vaccination rates for some routine immunisations remain well under 90 % for about half of the world's countries and in some cases even well under 50 %.

Risk Assessment

A detailed risk assessment needs to be undertaken to determine which routine vaccinations are indicated. This is described in detail in Chap. 5 and is dependent on several factors which include:

- The itinerary of the traveller, including the epidemiology of the potential infectious diseases and other hazards at the destination
- The medical profile and history of the traveller
- The time available before trip departure and personal circumstances of the traveller
- The adverse events and contraindications associated with each vaccine, particularly in the light of the medical profile and history of the traveller

Routine Vaccines and the Diseases They Prevent

Diphtheria

Diphtheria is a disease caused by toxigenic strains of *Corynebacterium diphtheria*, and humans are the only known reservoir. The disease remains endemic in various developing countries in Africa, Latin America and Asia, as well as parts of Albania and Russia. It is easily spread by close contact via respiratory droplets and discharge from wound lesions. As demonstrated by a large epidemic in the former Soviet Union in 1990–1997, diphtheria may flare up under specific circumstances. This epidemic resulted in dozens of importations to Western Europe and North America. The far less serious form of cutaneous diphtheria is occasionally imported, mainly from developing countries. Diphtheria is not manufactured as a monovalent vaccine and is given in combination with tetanus. Vaccines also containing pertussis and polio are also available.

Haemophilus Influenzae *Type B (Hib)*

Haemophilus influenzae type B (Hib) is a common cause of bacterial meningitis and other potentially life-threatening conditions. Hardly any data exist on the incidence of Hib in travellers, but it would be considered a risk for unprotected children who may be travelling, particularly those under five years of age. The first conjugate Hib vaccine is usually administered at 6 weeks of age, although the ACIP recommends 2 months of age.

Hepatitis B Virus

Hepatitis B virus (HBV) infection is a vaccine-preventable disease; however, HBV remains an important problem for travellers. The estimated monthly incidence of HBV is 25/100,000 for symptomatic infections and 80–420/100,000 for all infections in travellers. Transmission requires only a relatively small number of HBV particles. HBV is now a routine immunisation for children in many industrialised and developing countries including Australia, New Zealand and Singapore. However, there will be a number of adult travellers who may never have been immunised. The WHO recommends that hepatitis B vaccine be considered for all nonimmune travellers to moderate- and high-risk countries. The vaccine can be administered from birth.

Principal risky activities for HBV in travellers are given in Table 9.3.

HBV and other viruses can be transmitted in a number of developing country settings for travellers, including through casual sex and nosocomial transmission. Whilst expatriates and others living close to the local population are probably most

Table 9.3 Principal risky activities for Hepatitis B virus for travellers

Unprotected sexual intercourse with an infected person
Health-care interventions (medical, dental, laboratory or other) that entail direct exposure to human blood or body fluids
Receipt of a transfusion of blood that has not been tested for HBV
Exposure to needles (e.g. acupuncture, piercing, tattooing or injecting drug use) that have not been appropriately sterilised
Transmission from HBV-positive to HBV-susceptible individuals may occur through direct contact between open skin lesions following a penetrating bite or scratch

After WHO

at risk, surveys have suggested that between 10 and 15 % of travellers voluntarily or involuntarily expose themselves to blood and body fluids whilst abroad in high-risk countries. An Australian study of travellers, in 2009, who had returned from Southeast and East Asia, nearly half had indicated that they had participated in at least one activity with HBV risk during their last overseas trip.

Travel health professionals need to ensure that HBV vaccination does not engender complacency to the risks of other similarly transmitted disease causing viruses such as human immunodeficiency virus and hepatitis C virus, against which there is no vaccination at present.

Monovalent and combination hepatitis A and B vaccines are available. HBV vaccination is generally safe in pregnancy and can be administered to travellers at risk. Testing for HBV antigen should be performed in all pregnant women.

Influenza

Influenza has rapidly overtaken hepatitis A virus as the most common vaccine-preventable disease of travellers. In addition to the special groups that are considered for the pneumococcal vaccine, the influenza vaccine can be considered in all international travellers during influenza season. Influenza usually peaks during the months of November to March in the northern hemisphere and from April until September in the southern hemisphere. Travellers are advised to receive the most current vaccine available, and this could involve seeking vaccination on arrival at the destination.

Human Papillomavirus (HPV)

Genital human papillomavirus (HPV) is transmitted primarily by sexual contact and is highly transmissible. HPV can cause lesions and other genital diseases, and persistent infection with certain viral genotypes can lead to anogenital cancers. A

vaccine has been available since 2006 and has become routine in many countries for girls aged 10–14 years (or earlier). HPV transmission is a risk for travellers who engage in sexual activity abroad.

Measles, Mumps, Rubella

The viral communicable diseases, measles, mumps and rubella (MMR), remain global health problems and are a particularly risk for unvaccinated travellers. Measles is endemic in many developing nations. There has been an overlap between historical natural immunity in Australia, New Zealand and Singapore and the implementation of national immunisation guidelines of the aforementioned countries. This has resulted in a group that has not gained immunity. As such a booster of MMR vaccine is warranted for those who do not have either documentation of two doses of the vaccine or immunity by serum antibody testing.

The vaccine is routinely recommended in infants from 12 months of age but can be given from 6 months if travelling to highly endemic areas. Under these circumstances, infants must still receive two doses of the vaccine after 12 months of age to be considered fully immunised.

Pertussis

Pertussis or "whooping cough" is a highly infectious vaccine-preventable disease generally transmitted through respiratory droplets. Pertussis is a serious, potentially fatal disease in children and can be a cause of prolonged cough in adults. It has a global distribution and is therefore an important consideration for nonimmune travellers. In general, immunisation against pertussis with acellular pertussis vaccine is recommended in adult risk groups, such as health-care workers as well as adults in close contact with children under 3 months of age. It is considered with the routine vaccinations for travellers as it is a component of a number of multivalent vaccinations, although there is little specific data on the risk for travellers. Contacts, however, should be offered and given prophylactic vaccination.

Poliomyelitis

Poliomyelitis is an acute infectious viral disease, which is acquired through faecal-oral or oral transmission. A global eradication programme against poliomyelitis has existed for some time, and although significant progress has been made in most parts of the world, polio remains endemic in three countries: Afghanistan, Nigeria and Pakistan. Outbreaks of wild poliovirus still continue to be reported in a number

of countries. Therefore, travellers to these countries are advised to receive a single booster of inactivated polio vaccine (IPV) if the primary doses have already been administered.

Pneumococcus

Streptococcus pneumoniae or pneumococcus remains a leading cause of serious illness, including bacteraemia, meningitis and pneumonia among children and adults worldwide. The pneumococcal vaccine needs to be considered for travellers aged 65 years and older, as well as younger adults with chronic diseases such as chronic cardiopulmonary disease, asplenia, cirrhosis or diabetes. A national recommendation exists in a number of countries for routine vaccination of all infants as well as adults over 65 years of age.

Rotavirus

Rotavirus is a worldwide communicable infectious disease, spread by the faecal-oral route, directly from person to person or indirectly through contaminated fomites. It is a cause of acute gastroenteritis in infants and young children and can be fatal. It is low risk for adult travellers, usually due to acquisition of immunity. It is, however, a concern for children under the age of five years, and vaccination may be considered beneficial for this group, although there is no safety or efficacy data in infants over the age of 32 weeks.

Tetanus

Tetanus is a disease caused by a neurotoxin produced by *Clostridium tetani* generally grown in contaminated wounds. It is widespread and persists in the environment; hence tetanus is a risk to all travellers who sustain wounds contaminated by dirt, faeces or saliva. Although tetanus has not been specifically reported in travellers, it may be hidden in national surveillance data. A vaccination exists against tetanus which is generally regarded as safe; however, tetanus vaccination coverage remains extremely variable in travellers from many countries. Tetanus boosters are recommended 10 yearly for all adult travellers regardless of destination and duration. The tetanus and diphtheria combined vaccine (Td) or the tetanus, diphtheria, pertussis vaccine (Tdap) is generally recommended for primary immunisation and booster doses in adults and children aged over seven years. The diphtheria toxoid content in Td and Tdap vaccine is lower to decrease the likelihood of a local reaction.

Tuberculosis (TB)

Tuberculosis (TB) is a globally distributed bacterial disease transmitted in most cases through inhalation of *Mycobacterium tuberculosis* (MT). Most travellers are at low risk of TB, although there are a number of higher-risk settings and activities. There is a vaccine, the Bacillus Calmette-Guérin (BCG), which being a live vaccine is contra-indicated for individuals with severely impaired immune systems or those who have HIV infection. BCG has limited application in travel, although in some countries, BCG is given soon after birth, as when given in the first year of life appears to provide good protection against severe forms of MT, such as miliary TB and meningitis.

Varicella

Varicella or chickenpox is a contagious, acute, viral infectious disease caused by the varicella zoster virus (VZV) and is transmitted mainly through respiratory droplet spread. There is little published literature concerning VZV in travellers. The travel consultation is an opportunity to review a traveller's immune status. The manufacturers of varicella vaccine now recommend two dose given at least 6 weeks apart for all adults and children from 9 months of age (Varilrix vaccine) or 12 months of age (Varivax vaccine) to ensure optimal immunity. In particular, this vaccine should be considered for women of childbearing age who do not have documented varicella disease or immunity.

Conclusions

Travel health professionals ought to use the pretravel health consultation as an opportunity to review the status of travellers' routine vaccinations, according to their national schedule and/or accepted international recommendations, such as the WHO. The need for vaccination should be based on a thorough risk assessment, and it is important that each routine vaccination given be documented according to national policy. In addition, travel health professionals need to make travellers aware of other general measures to reduce their exposure to these preventable diseases.

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Chapter 10
The Last-Minute Traveller

Claire Wong and Lisa Scotland

Key Points
- Risks and benefits of vaccines at the last minute need to be considered on an individual basis, after consultation.
- Accelerated vaccine schedules are appropriate for some vaccines.
- Schedules of vaccines need to be started as soon as possible and can sometimes be completed, if necessary, overseas.
- Booster dose can be given at any time before travel.

Overview

In an ideal world, intending travellers would seek medical and vaccines advice for their upcoming travels at least 4–6 weeks before departure. Unfortunately, travel health professionals are frequently consulted to provide 'vaccines that I need to have' at short notice, sometimes within days or even hours. The traveller presenting at 'the last minute' is thus a challenge to any clinician, for there may be little time to adequately prepare either a group or single traveller.

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Vaccine administration often takes a lower priority for the last-minute traveller due to lack of time to complete vaccine schedules or mount an adequate immune response. Therefore, education regarding prevention behaviours to avoid illness and disease is paramount.

In the travel medicine environment, an imminent departure can be linked to a variety of factors including:

- An urgent business venture
- Those needing to visit friends and relatives (VFR)
- A bereavement or accident to a loved one overseas
- Deployment to an overseas disaster
- The unprepared traveller unaware of the need for travel health interventions

Travellers who are visiting friends and relatives (VFRs) have been shown to be less likely to seek a consultation prior to travel. VFRs often travel at short notice into regions considered high risk and where there is a higher incidence of certain diseases including malaria, typhoid and hepatitis A. VFRs are often at greater risk due to a false belief in their natural immunity to diseases they or their families were exposed to previously (e.g. malaria). Thus, there is a different perception of risk. In addition, VFRs tend to travel for extended periods of time, to rural areas, staying in family villages, and they may do so with their children, some very young.

The Consultation

Although the focus of many travel health consultations is vaccine-preventable disease, approximately only 5% of travel related ill-health is vaccine preventable and that it is lifestyle choices of the individual rather than the destination that will be the biggest risk to the traveller's health. Providing advice on behavioural measures to reduce the risk of illness and injury is particularly important for the last-minute traveller who cannot be adequately protected by vaccination.

The risk assessment process for the last-minute traveller should follow that of any traveller and includes asking questions about the individual and their intended travel; see also Chapter 5.

The 'Last-Minute Traveller' Check List

- Where is the traveller going?
- Why is the traveller going abroad?
- Who is the traveller going with, or are they travelling alone?
- What is the traveller going to do whilst abroad?
- When is the traveller going and returning?

Focused Consultation

The information obtained will guide the travel health professional in assessing appropriate advice to be provided, which vaccines will be beneficial at the last minute, and what other additional information needs to be discussed at this 'one-off' consultation:

- A medical history will ascertain any specific cautions, for example, immunosuppression.
- The age of the traveller will determine the use of some vaccines and not others.
- The need for comprehensive travel and health insurance is a must. If travellers cannot afford this, then they cannot afford to travel.
- Travelling without adequate preparation is harmful, especially if it is the intention of the traveller to, for example, assist in a natural disaster; thus good knowledge about the location and the health services can be a life-saver.
- Informing the traveller of country or disease alerts or hazards to personal safety and advising on appropriate precautions. Websites which provide this information include:
  - Australian Department of Foreign Affairs and Trade: www.smarttravel.gov.au
  - New Zealand Ministry of Foreign Affairs and Trade: www.safetravel.govt.nz
  - Ministry of Foreign Affairs Singapore: www.mfa.gov.sg

Vaccination

When recommending vaccinations, consideration should be given to how the infection is spread and the epidemiology of the disease at the destination. The traveller will need to know that immunity generally takes approximately 5–10 days to develop after vaccination, so for the traveller who comes in at the last minute, they are unlikely to be adequately protected if vaccinated immediately before travel. The immune response for a vaccine can be delayed further with a suboptimal response due to traveller immunosuppression or age. Appropriate pretravel counselling will determine this.

Routine Vaccines

Any travel health consultation is an ideal opportunity to ensure the childhood schedule vaccines are complete, including measles, mumps and rubella. Boosters for tetanus, diphtheria, pertussis and polio are to be advised and can be given at any time before departure.

Recommended Vaccines

Even if there is limited time before travel, certain single-dose vaccines will initiate protection, e.g. hepatitis A, polio and typhoid injectable and quadrivalent meningococcal meningitis. The commencement of multi-dose vaccines such as hepatitis B, rabies, Japanese encephalitis and cholera will be dependent on the time available before departure. Accelerated schedules for hepatitis B, Japanese encephalitis and rabies are available and detailed in Table 10.1.

Particular mention needs to be made of rabies, a fatal disease about which every traveller to risk areas needs to receive information, particularly regarding post-bite care and the need for postexposure vaccine. As multiple immunisations are required to complete a primary rabies vaccination series, it is often difficult for last-minute travellers to complete the series before departure. Therefore, a person starting, but not completing, a primary series, who is potentially exposed to the disease, should receive the same postexposure prophylaxis as a completely unimmunized person. Providing postexposure information in written format ensures the traveller can refer to it in the case of an emergency.

Required Vaccines

Yellow fever vaccination can be a requirement for travel to certain countries in sub-Saharan Africa, Central and South America and the Caribbean. The International Certificate of Vaccination or Prophylaxis becomes valid 10 days after vaccine administration. Travellers may be refused entry, quarantined or vaccinated at the port of entry if they travel without a valid certificate.

Meningococcal meningitis ACYW135 is required for pilgrims aged over 2 years performing the Hajj or Umrah in Saudi Arabia. This vaccine is required to be given not less than 10 days before arrival, and Hajj visas cannot be issued without proof that applicants received meningococcal vaccine $\geq$10 days and $\leq$3 years before arriving in Saudi Arabia. Further information on this and other vaccine requirements can be found on the Ministry of Health of the Kingdom of Saudi Arabia website at www.moh.gov.sa/en/Pages/Default.aspx.

Live Vaccines

Live parenteral vaccines such as yellow fever; measles, mumps and rubella; and varicella are ideally administered either on the same day or 1 month apart. For the last-minute traveller, this could mean a number of vaccines on the same day. See Chap. 22, frequently asked questions for further guidance on administering more than one live vaccine.

Table 10.1 Guide to vaccinations for the last-minute traveller

Vaccine	Accelerated schedule	Details
Hepatitis A	None – single dose prior to travel	A single dose will provide protection however close to departure date
Hepatitis B	Day 0, 7 and 21, 4th dose at 12 months	Most children are vaccinated as part of childhood schedule
	0, 1, 2 months, 4th dose at 12 months	Day 0,7,21 schedule approved for Engerix B® vaccine only
Combined hepatitis A and B	Day 0, 7, 21, 4th dose at 12 months	Accelerated schedule approved for adult dose age 16 years and older
Typhoid	None – single dose prior to travel	Approximately 70 % protection after 14 days. Consider length of stay in endemic area as may be of benefit to long-term or frequent travellers
Tetanus/ diphtheria/ pertussis	None – single booster dose prior to travel if no history of vaccine in last 10 years	Boosts childhood vaccination
Polio	None – single dose prior to travel	Recommended for high-risk destinations. One-time booster for adults
Yellow fever	None – single dose prior to travel	Effective 10 days after vaccination
		One dose thought to provide lifelong protection; currently certificate is valid for 10 years
Japanese encephalitis	Jespect®/Ixiaro®: day 0, 14 days	Accelerated schedule not approved by manufacturer
	Imojev®: none – single dose	
Rabies	Day 0, 7, 21	Importance of accessing urgent postexposure management should be emphasised
	No rapid course universally accepted	
Influenza	None – single dose annually	May take up to 2 weeks to fully protect
Meningococcal A,C,Y,W-135	None – single dose	Conjugate vaccine provides longer-lasting immunity than polysaccharide and prevents nasal carriage of disease
Cholera	None	Two doses 1–6 weeks apart. Expected immunity 2 weeks after last dose
		Consider for ETEC diarrhoea if time allows
Tick-borne encephalitis	Day 0, 14 days, 3rd dose 5–12 months after second dose	May be a delay in accessing this vaccine from Europe

Vaccination for the last-minute traveller needs to take these issues into consideration with decisions based on international requirements of the intending countries of travel and subsequent risk of infection whilst travelling there. Knowledge of the vaccines and their expected immune response should be foremost in the vaccinator's mind.

General Vaccine Considerations for the Last-Minute Traveller

Consideration of the risks and benefits of vaccine administration will need to be given to each traveller on an individual basis. Factors to take into account include the:

- Time necessary to mount an immune response
- Risk of adverse events
- Length of trip
- Risk of disease at the destination

In addition to the imminent trip, it may also be an appropriate opportunity to administer vaccines to protect for future travel plans. This is particularly so if a traveller regularly departs overseas at short notice. Those travelling long term will also still benefit from vaccines given shortly before departure.

Unless there is an accelerated schedule available, shortening intervals between vaccines can result in a suboptimal response and shorter duration of protection and should be avoided.

Some travellers request taking vaccines abroad with them, so that they may complete a prescribed course at their destination. Due to issues in maintaining the cold chain whilst travelling, this is not recommended. However, it may be possible to complete vaccine courses at a clinic at the destination. The International Society of Travel Medicine (ISTM) has a searchable Global Travel Clinic Directory available on their website: www.istm.org. If travellers are going to use this service, they should be encouraged to contact the relevant overseas clinic in advance to ensure vaccines are available in-country.

There is no limit to the number of vaccines that can be administered at one time. However, it may be difficult to determine the cause of any adverse event if multiple vaccinations are given. The amount of time before a traveller leaves the country may thus have a significant impact on a vaccine decision and risk to that traveller of a reaction during travel to an intended destination.

The Traveller Leaving in a Few Hours

If there is extremely limited opportunity to schedule an appointment, the clinician can still provide general prevention messages by telephone or e-mail.

Conclusion

The last-minute traveller is often a challenge. However, information and guidance from the travel health practitioner can reduce the incidence of disease. The importance of other measures to reduce the risk of illness or injury is paramount when

counselling the last-minute traveller. Although travellers should still be advised to seek advice 6–8 weeks prior to travel, it is never too late to offer travel health and safety advice, and the last-minute traveller should never be discouraged from attending a pretravel consultation.

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Chapter 11
Vaccinations in Pregnancy

I. Dale Carroll and Jenny Visser

Key Points

- Pregnant women are relatively immune-suppressed, so:
  - Live vaccines are generally contraindicated.
  - Vaccines may have suboptimal effects.
- Inactivated viruses and bacterial vaccines and toxoid vaccines are considered safe.
- Pregnant women should receive influenza- and pertussis-containing vaccines.
- Delay vaccinations until the second or third trimester when possible.
- Make an individualised risk assessment based on safety and efficacy of vaccine and the actual risk of exposure.

General Considerations

One of the goals of maternal vaccination is the protection of the infant against infectious diseases. Many times, the most effective way of protecting the unborn and newly born infant is to immunise the mother. Many antibodies can be passed transplacentally to the infant and thus provide a level of protection prior to and

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Table 11.1 Immunisations in pregnancy

Vaccine	Type of vaccine	Maternal risk from disease	Fetal risk from disease	Maternal risk of vaccine	Fetal risk of vaccine	Comment
Anthrax	Bacterial particles	May be more severe in pregnancy	Increased risk of miscarriage or preterm birth	None known	None known	
BCG	Live bacterial	Course of disease not affected by pregnancy	Congenital tuberculosis occurs	None known	Possible disseminated infection (theoretical)	Not effective enough to be felt useful
Brucellosis	Live bacterial	Not affected by pregnancy	Miscarriage and preterm birth	No data	No data	Prophylactic antibiotics are preferred to vaccination
Cholera/diarrhoea Oral	Live bacterial	Diarrhoea more severe, dehydration, acidosis	Increased risk of abortion or premature birth	No data available	No data available	Oral antibiotic prophylaxis for cholera felt to be preferred due to poor efficacy of vaccine
Hepatitis A	Inactivated virus	Possibly increased severity in third trimester	Increased risk of miscarriage or preterm birth	None known	None known	
Hepatitis B	Purified surface antigen	Possibly increased severity in third trimester	Miscarriage or preterm birth. Transmission to newborn	None known	None known	Use in pregnancy recommended in nonimmune women
Herpes zoster	Live virus	Not affected by pregnancy	Possible congenital varicella syndrome	No data available	No data available	Dose of live virus is greater than in varicella vaccine
Human papilloma virus (HPV)	Inactivated virus	Rapid growth of condylomata in pregnant	Viral transmission to fetus	None known	None known	Use of other methods of STD prevention is preferred

Immune globulins	Immune globulin			None known	Single report of congenital anomaly	Use usually limited to postexposure prophylaxis
Influenza	Inactivated virus	Increased morbidity and mortality	Increased risk of miscarriage	None known	None known	Use in all trimesters is advised
						Use of live virus not recommended
Japanese encephalitis	Inactivated virus	Animal data suggests adverse pregnancy outcome	Embryo-fetal death common in animals. No human data	None reported	None known	Preferred over the use of live vaccine in pregnancy
Measles	Live virus	Not affected by pregnancy	Increased miscarriage. Possible congenital anomalies	None known	None confirmed	Use only if exposure is likely and unavoidable
Meningitis	Conjugate/ polysaccharide	Not affected by pregnancy	Depending on severity of maternal illness	None known	None known	Registry exists for reporting conjugate use in pregnancy
Mumps	Live virus	Not affected by pregnancy	Possible increased rate of miscarriage	None known	None confirmed	Use only if exposure is likely and unavoidable
Pneumococcal	Polysaccharide	Disease may be more severe in pregnancy	Premature delivery, fetal death	None known	None known	Consider in splenectomised, immunosuppressed or those with sickle cell anaemia
Polio (eIPV)	Inactivated virus	Possibly increased disease severity in pregnancy	High mortality rate in neonatal disease	None known	None known	Use of live oral vaccine not recommended
Rabies	Killed virus	100 % fatality	Fatal to fetus if mother dies	None known	None known	Pre- and postexposure schedule same as in non-pregnant

(continued)

Table 11.1 (continued)

Vaccine	Type of vaccine	Maternal risk from disease	Fetal risk from disease	Maternal risk of vaccine	Fetal risk of vaccine	Comment
Rabies immune globulin	Immune globulin	100 % fatality	Potentially fatal to fetus	None known	None known	Dosage schedule same as in non-pregnant
Smallpox	Live virus	Not affected by pregnancy	Not affected by pregnancy	None known	Vaccinia virus may be transmitted to fetus	Use limited to instances of high risk of exposure
Rubella	Live virus	Not affected by pregnancy	High rate of miscarriage and multiple congenital anomalies	None known	None confirmed	Use only if exposure is likely and unavoidable. Registry exists for reporting use in pregnancy
Tetanus, diphtheria, pertussis (Tdap)	Toxoid	Not affected by pregnancy	Neonatal pertussis	None known	None known	Update during each pregnancy. Delay administration until third trimester if convenient
						(Malaria prophylaxis may interfere with immune response)
Tick-borne encephalitis	Inactivated virus	Not affected by pregnancy	Viral transmission to fetus	None known	None known	
Tuberculin skin test	Toxoid	Course of tuberculosis not affected by pregnancy	Congenital tuberculosis	None known	None known	Reaction to test appears unaltered by pregnancy
Typhoid Vi	Polysaccharide	Increased risk of diarrhoea, GI bleeding, perforation	Increased risk of abortion, fetal death	None known	None known	

Typhoid oral	Live bacterial	Increased risk of diarrhoea, GI bleeding, perforation	Increased risk of abortion, fetal death	Nausea, vomiting, diarrhoea	None known	Theoretical risk of mutation into pathogenic form. Inconvenient side effects of nausea and vomiting
Varicella	Live virus	Increase in severe pneumonia	Congenital varicella in second and third trimesters	None known	None confirmed	Use only if exposure is likely and unavoidable. Registry exists for reporting use in pregnancy
Yellow fever	Live virus	Not affected by pregnancy	Depending on severity of maternal illness	Possibly diminished immune response in pregnancy	Vaccine virus may be transmitted to newborn	Use only if exposure is likely and unavoidable. Immune response may be diminished. Postvaccination titres encouraged

immediately after birth. The primary goal of vaccination during pregnancy is, of course, to protect the mother (Table 11.1).

Because controlled studies are not carried out on pregnant women, data is not available regarding individual vaccines in pregnancy. However, there are no known significant risks involved in vaccinating pregnant women with inactivated virus or bacterial vaccines or toxoids. Live vaccines may pose a theoretical risk to the fetus. The benefits of vaccinating pregnant women usually outweigh potential risks when the likelihood of disease exposure is high and unavoidable and when infection would pose a risk to the mother or fetus. When feasible, the itinerary may need to be modified to avoid the risk of exposure to the disease.

Immunologic changes that occur during pregnancy, however, may in some cases dampen the immune response that one wishes to obtain by these vaccines. This has been seen to some extent with yellow fever vaccination and perhaps also with hepatitis B vaccination.

If possible, vaccination should be delayed until the second or third trimester, to avoid possible teratogenic febrile effects during the first trimester.

Toxoids

Tetanus, Diphtheria and Pertussis Vaccines (Tdap) Tetanus, diphtheria and pertussis vaccines are ones that are recommended for all pregnant women if they are not already immune. It is generally recommended that the combined vaccine be given during the third trimester of pregnancy to provide maximum benefit to both the mother and infant. There has been some concern that malnutrition, vitamin A deficiency or malaria chemoprophylaxis might interfere with an adequate immune response; therefore, the vaccine should be given whenever possible before the initiation of malaria chemoprophylaxis.

Tuberculin Skin Testing Mantoux testing, if indicated, is safe in pregnancy and interpreted according to the same criteria as in the non-pregnant.

Polysaccharide, Killed Bacterial and Conjugate Vaccines

Pneumococcal Morbidity from pneumonia is increased in pregnancy, largely due to respiratory and cardiovascular changes. Premature labour and fetal death may result from this. Thus, any recommendation for the use of pneumococcal vaccine is not altered by pregnancy. Patients and travellers, who might be considered for this vaccine, would include those who are immunosuppressed, have had a splenectomy or have sickle cell disease. Maternal vaccination has been shown to increase milk concentrations of IgA antibodies, so there is benefit to the newborn as well.

Meningococcal Studies of polysaccharide vaccine (MPSV4: quadrivalent meningococcal polysaccharide vaccine) use during pregnancy have not demonstrated adverse effects among either pregnant women or newborns. The available data regarding the use of the conjugate (MCV4: quadrivalent meningococcal) vaccine during pregnancy have shown no vaccine-related ill effects.

Typhoid Typhoid may be a more serious disease in pregnancy, with a higher incidence of complications such as bleeding intestinal ulcers. There is also an increased risk of abortion and fetal death. Transplacental infection of the fetus may also occur. Typhoid vaccination is recommended whenever it might otherwise be indicated. Both the injectable and the oral forms of vaccine are considered acceptable during pregnancy, but due to the slowing of gastrointestinal function and resulting side effects, the injectable form might be preferred. With either vaccine, no more than 70 % efficacy can be expected; thus, food and water precautions remain important.

Inactivated Virus Vaccines

Hepatitis A Hepatitis A infection during pregnancy may result in serious maternal consequences with fetal loss or vertical transmission to the fetus; therefore, vaccination during pregnancy is recommended.

Hepatitis B In the case of hepatitis B, the danger of the disease lies in the risk of transmission to the infant. While there is some evidence of a lower antibody response in pregnancy, vaccination of pregnant women with this vaccine has been shown to be safe and effective and is recommended in nonimmune women.

Influenza Influenza results in increased morbidity and mortality during pregnancy. Vaccination with the inactivated influenza vaccine is now recommended for all pregnant women at any stage of pregnancy.

Polio This disease, should it occur during pregnancy, may result in as high as a 40 % neonatal mortality, and there is an increased risk of maternal paralytic disease in pregnancy. The enhanced inactivated polio vaccine (eIPV) is preferred for its safety both in the pregnant patient and in the community. The live oral polio vaccine (OPV) is no longer available in most countries and is considered contraindicated in pregnancy, but there are reports of pregnant women having received it with no evidence of fetal or maternal harm.

Japanese Encephalitis The Japanese encephalitis virus causes embryo-fetal death in experimental animals and has been known to be passed transplacentally. The cell-derived, inactivated Jespect®/Ixiaro® vaccine would theoretically be safe in pregnancy. The live vaccine is contraindicated. Despite the lack of available data, due to severe consequences of the disease, it would seem prudent to vaccinate pregnant

women for whom exposure is likely. Mosquito avoidance should, however, remain the mainstay of prevention.

Rabies Because rabies is almost universally fatal, the consensus has long been that postexposure rabies vaccination should be used during pregnancy when indicated. There is presumptive evidence of transplacental passage of antibodies. This supports the use of pre-exposure vaccination when there is a substantial risk of maternal exposure to the disease.

Human Papilloma Virus (HPV) Recent data hint that there may be an association between high-risk HPV and pre-eclampsia. This plus the fact that many travellers become exposed to sexually transmitted diseases makes us consider this vaccine in counselling pregnant travellers. The HPV vaccine contains inactivated virus and thus is considered safe in pregnancy. Another consideration recommending the use of this vaccine during pregnancy is the vertical transmission of the virus to the fetus at the time of birth.

Tick-Borne Encephalitis The virus may be transmitted transplacentally, but there is little data on the consequences of this. There have been reports of high fever after the administration of the vaccine to young children, but this does not seem to be as common in adults. The manufacturers recommend its use in pregnancy only after careful, individual consideration.

Live Virus Vaccines

It is primarily the viral illnesses such as rubella and varicella that have shown the propensity to cause recognisable patterns of fetal damage if they occur during pregnancy. Thus, there is added reason to protect against these viruses during pregnancy. But the vaccines available for such protection are live viruses, altered from their original teratogenic form but with the theoretical potential nonetheless of causing the very pattern of birth defects that they are designed to prevent. Several decades of available data on inadvertently administered vaccine are somewhat reassuring, but these vaccines should be avoided during pregnancy wherever possible.

Mumps Some spontaneous abortions and other fetal anomalies have been reported when this disease occurs in the first trimester. In the rare event that exposure to this disease is likely to occur in a nonimmune pregnant woman, administration of the vaccine would be considered preferable to contracting the disease.

Measles Available data would seem to indicate an increased rate of abortion as well as a perinatal mortality rate of 10 % and possibly fetal anomalies if the disease is contracted during pregnancy. There is also the risk of serious maternal complications, particularly pneumonia and fetal loss, if this disease occurs during pregnancy. As with the mumps vaccine, no adverse maternal or fetal events have been reported following the inadvertent administration of this vaccine during pregnancy.

Rubella This is probably the most feared viral infection during pregnancy. Pre-vaccine statistics showed an almost 100 % incidence of congenital rubella syndrome (CRS) if the disease is contracted in the first trimester and up to 60 % in the second trimester.

Despite careful observation, no such syndrome has been seen to occur with vaccination, even though there is evidence of passage of the vaccine virus to the fetus. If there is risk of rubella infection in a nonimmune pregnant woman, use of the vaccine is felt to be preferable to contracting rubella during the pregnancy. It should be noted that about 2 % of women do not respond with sufficient antibody production to develop immunity. Rubella immune globulin may be considered as an alternative postexposure prophylaxis, but there is very little data to support its efficacy.

Varicella As with rubella, there is a risk of a syndrome of congenital defects associated with maternal varicella infection, and this disease can have serious maternal and fetal consequences if contracted late in pregnancy. For susceptible pregnant individuals with unavoidable likely exposure to this virus, the vaccine would be considered preferable to the disease. As with rubella, one may consider the use of postexposure varicella immune globulin, but its efficacy remains unproven.

Herpes Zoster Herpes zoster (shingles) is not known to be more common or more severe during pregnancy, but it may have serious fetal effects. Because the zoster vaccine contains a significantly larger dose of virus than the routine varicella vaccine, however, its use in pregnancy is not advised.

Yellow Fever Yellow fever is a very serious disease with up to 50 % mortality rate in native populations and thus needs to be avoided during pregnancy. There is reassuring data from several sources regarding the safety of this vaccine during pregnancy.

Meanwhile, the efficacy data is conflicting, with some data showing a lower antibody titre when this vaccine is given during pregnancy. The relative immune suppression that occurs with pregnancy or a difference in nutritional status might explain this difference. Even the lower titres, however, were not correlated with any diminished protectiveness of the vaccine. The consensus remains that if yellow fever exposure is likely and unavoidable during the travel, the vaccine should be given. Under these circumstances, however, it might be wise to obtain a titre to test for immunity. If travel requirements and no disease exposure are the only reason to vaccinate, then it would be preferable to provide the pregnant traveller with an appropriate waiver.

Live Oral and Bacterial Vaccines

BCG Tuberculosis is a serious disease even in pregnancy. The BCG vaccine, however, is of limited value in adulthood. Although no harmful effects to the fetus have been associated with BCG vaccine, disseminated infections with other mycobacteria have been reported in the infants of infected mothers, and so its use, being a live bacterium, is not recommended during pregnancy.

Typhoid When speaking of typhoid vaccine, some recommend the preferential use of live, oral vaccine. There is at least a theoretical risk, however, that the vaccine strains might replicate and cross the placental barrier, causing fetal harm similar to that seen with *Salmonella typhi.* In addition, decreased gastrointestinal motility along with increased exposure to gastric acid might either decrease the vaccine's effectiveness or enhance the risk of gastroenteritis. Also, one of the more common side effects of this vaccine is nausea and vomiting, a problem already frequent in pregnancy. These considerations might make the use of the Typhim Vi® vaccine preferable during pregnancy.

Cholera and Traveller's Diarrhoea Recent studies point out the severe risk that cholera presents during pregnancy. Traveller's diarrhoea is also likely to be more frequent and more severe in pregnancy. To date, the benefit from the available vaccines has been found to be short-lived and incomplete, and they are not usually recommended except when the traveller will be working in high-risk areas such as refugee camps. Dukoral® as an inactivated vaccine is probably safe to use in pregnancy, but as with the oral typhoid vaccine, the side effects of nausea and vomiting may reduce its benefit in an already nauseated pregnant patient.

Immune Globulin

Generally, the immune globulins are felt to be safe in pregnancy, but because the immune globulins are a human blood product, the possibility of inadvertent disease transmission remains. There remain conditions, however, such as varicella and rabies where postexposure use of these products is highly recommended, even in pregnancy.

Unusual Vaccines

These are vaccines of various types which are not in common use but the need for which might arise under special circumstances.

Anthrax At least one review estimates that this disease predisposes to miscarriage and preterm delivery. Most experts primarily recommend various medications for postexposure prophylaxis. In a study of women who became pregnant shortly after receiving the vaccine, there was no increased incidence of adverse pregnancy outcomes.

Smallpox The vaccine is prepared from vaccinia virus, a virus that occurs only in the laboratory. Infection with this virus has been reported in the fetus after maternal immunisation. Thus, the administration of smallpox vaccine is not recommended during pregnancy.

Brucellosis Brucellosis is known to cause abortion and preterm delivery in domestic animals and to a lesser degree in humans. Vaccination against this disease is usually limited to persons in high-risk occupations. Prophylactic or treatment doses of co-trimoxazole or rifampin are recommended instead of the vaccine.

Further Reading

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Chapter 12
Vaccine Considerations for Children and Breastfeeding Women

Marc Shaw and Jenny Visser

Key Points

- Children that travel need to be up to date with routine childhood vaccinations.
- Pretravel vaccination indications approximate those of adults.
- Polysaccharide vaccines are poorly immunogenic in children under 2–3 years.
- When children remain overseas, they should adhere to one set on national guidelines.
- Breastfeeding benefits babies and infants and should not be stopped/interrupted during maternal vaccination.
- Most vaccines can be given safely to breastfeeding mothers, but vaccination of a mother will not protect the breastfed baby.

The Child Traveller and Vaccines

Children pose a particular challenge to the travel health professional, for children travel overseas for many reasons including for family holidays and school or sports trips or to visit friends and family.

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The role of the travel health professional in guiding advice for children travelling is to:

- Raise awareness of the risks of travel and any vaccine-preventable disease
- Discuss strategies to minimise risks and perhaps suggest alternative destinations
- Guide advice that considers breastfeeding women and their infants

Pretravel Consultation: The pretravel consultation is the perfect opportunity to review the immunisation status of any child, for all children travelling overseas should first be up to date with routine childhood vaccinations. National immunisation schedules vary from country to country, and it is essential that all travel medicine professional be familiar with the national immunisation schedule in which they are working. Further details on the national schedules for Australia, New Zealand (NZ) and Singapore can be found in Chaps. 16, 17 and 18, respectively.

For the expatriate child, it is also important to be familiar with the vaccination schedule in the country to which they are travelling, for they may need to complete routine vaccinations in-country. Quick links to National immunisation schedules of the above countries and the United Kingdom, USA and Europe can be found in Table 12.1. A table of travel vaccines, including children, is found in Chap. 7.

The Acceleration of Primary Vaccination Schedules: Wherever possible, parents and guardians are to be encouraged to delay travel plans until a baby's primary vaccination series has been completed. However, there may be circumstances where travel is felt to be unavoidable although reducing the minimum time between doses in a primary series can affect vaccine efficacy. National health authorities will vary on guidelines as to the absolute minimum time interval between doses of vaccines. These guidelines are largely determined for children resident in their home country and therefore are naturally conservative. It is generally recommended that vaccines should not be given more than 5 days early.

For the young child travelling internationally, a balance needs to be struck between the benefits of an accelerated schedule and the risks of travelling with an incomplete primary series. An individual risk assessment will need to be made for each child and discussed with parents. If, for example, a young child is accompanying parents to a remote, low-income country where access to routine vaccinations may be difficult and/or exposure high, then a case could be made to shorten the optimal interval between doses.

Table 12.1 National immunisation schedules links

Australia	http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/nips-ctn
European schedules	http://vaccine-schedule.ecdc.europa.eu/Pages/Scheduler.aspx
New Zealand	http://www.health.govt.nz/our-work/preventative-health-wellness/immunisation/new-zealand-immunisation-schedule
Singapore	http://www.hpb.gov.sg/HOPPortal/gamesandtools-article/3216
United Kingdom	http://www.nhs.uk/Conditions/vaccinations/Pages/vaccination-schedule-age-checklist.aspx
USA	http://www.cdc.gov/vaccines/schedules/easy-to-read/child.html

The Lower Age Limit for Commencing the Childhood Vaccinations: While a few vaccines can be given from birth (BCG, hepatitis B), the generally accepted lower age limit for commencing most childhood vaccinations is 6 weeks. In countries where vaccinations are routinely commenced later than 6 weeks, consideration could be given to moving this to 6 weeks in the travelling child. Travelling to high-risk countries before a child is 6 weeks of age (and therefore unvaccinated) should be strongly discouraged.

Vaccines Not on a National Schedule: Not all countries include all the vaccines on the World Health Organization's (WHO) list of vaccines on the Expanded Programme of Immunisation (EPI) in their national programmes. Travelling children may benefit from these vaccinations, especially if they are going to travel or live in countries with limited health infrastructure. As an example, in New Zealand BCG vaccine is targeted just to certain high-risk resident children, but a New Zealand child going to live in a country with high tuberculosis prevalence could indeed benefit from the vaccine.

Specific Vaccines

Cholera

As discussed in Chap. 4, cholera is a rare disease of travellers, and vaccination is not commonly indicated for travel. Child travellers are unlikely to be exposed to cholera, although information should be shed about the disease if travel to a less developed country is planned, for cholera does have high case fatality rates in children in impoverished regions.

Dukoral (the only cholera vaccine licensed in Australia, NZ and Singapore) can provide a degree of cross protection against a certain type of *Escherichia coli*, a prominent etiological agent of travellers' diarrhoea, due to the structural similarity between the toxins of both cholera and enterotoxic *Escherichia coli* bacteria. Cross protection for the vaccine against travellers' diarrhoea has been claimed to be anywhere between 0 and 45 %; however, a recent study from Steffen and others found a level of protection of only approximately 10 %.

Vaccine Recommendation Dukoral is a two-dose oral vaccine in children over the age of 6 years but licensed as a three-dose oral vaccine from age 2–6 years.

BCG (Bacillus Calmette-Guerin)

Infection with *Mycobacterium tuberculosis* can result in tuberculosis (TB) disease. The risk of infection is greatest in countries with high prevalence of TB in the local population. The burden of TB disease is higher in impoverished countries, with

South Asia, Southeast Asia and Africa having particularly high rates. An excellent resource for country prevalence rates can be found at http://data.worldbank.org/indicator/SH.TBS.INCD.

In most developed countries, prevalence rates are such that routine use of BCG is not recommended. Children travelling to high prevalence areas, especially expatriate children however, may still benefit from BCG vaccination. There is evidence of BCG protecting children (especially those less than 5 years of age) from disseminated TB disease including miliary TB and TB meningitis.

Vaccine Recommendation National guidelines vary, but they would in general recommend BCG vaccination pretravel to children going to reside for over 6 months in a country with a TB prevalence of 40/100,000 or more. BCG is a live vaccine, contraindicated in certain conditions and should be given only after a screening tuberculin skin test or a Quantiferon Gold blood test, unless given within the first 6 months of birth.

Hepatitis A

Hepatitis A virus is endemic throughout the world and is associated with poor sanitation. Infection contracted in the first few years of life is often asymptomatic or mild, but it can occasionally cause significant illness in children. The main objective in vaccinating travelling children is to reduce carrier status and prevent the travelling child introducing the disease into pre-school or school on return.

There are a number of hepatitis A vaccines available as either monovalent vaccines or in combination with either hepatitis B or typhoid. All hepatitis A vaccines are inactivated vaccines and licensed from 12 months of age. While one dose will give excellent short-term protection, completion of the primary series with a second dose more than 6 months after the first confers long-term, possibly lifelong, protection. While all the inactivated vaccines are licensed in children 12 months and older, there is some evidence that they are immunogenic down to 9 months and possibly 6 months of age.

Vaccine Recommendation A standard vaccine recommendation for travel to all but developed or industrialised countries.

Hepatitis B

If travelling children are not already vaccinated as part of their routine childhood vaccinations, then travelling to countries with high prevalence of hepatitis B carriage will put them at risk, and they are advised to be fully vaccinated against hepatitis B virus. Children who contract hepatitis B are at high risk of becoming chronic carriers with increased lifetime risk of both cirrhosis and hepatocellular carcinoma.

Hepatitis B vaccination has been introduced into the national vaccination schedules of many developed countries including Australia, NZ and Singapore.

In the immunocompetent with documented complete primary series, proof of seroconversion is not required. Protection from disease appears long lasting, and currently there is no data to support the need for booster doses.

Unvaccinated children can be offered hepatitis B vaccination from birth. Younger children require a minimum of three doses 1 month apart. A two-dose adolescent schedule (between the ages of 14 and 16 years) is licensed in some countries.

Vaccine Recommendation A standard vaccine recommendation for children travelling internationally.

Combined Hepatitis A and B Vaccine

A combined hepatitis A and B vaccine, Twinrix Junior is available for use in children from 12 months of age. However, hepatitis B is part of the routine childhood schedule in Australia, NZ and Singapore, so all children born and raised in these countries should be vaccinated against the disease, and further re-vaccination is not usually necessary. Thus the combined vaccine is not frequently used.

Vaccine Recommendation
Generally recommended for children who are travelling but have missed out on hepatitis B series in childhood.

Influenza

Influenza disease can be devastating in children, and the viral infection is often quoted as the most common vaccine-preventable disease of international travel. For this reason, it is a vaccine worth discussing in pretravel consultation. The lower age limit for influenza vaccine is 6 months, and children who receive their first dose under 9 years of age require two doses to ensure maximum sero-response.

Many countries recommend targeted influenza vaccination, for example, to those with pre-existing respiratory disease. Others, including the USA, recommend universal influenza vaccination including all children over 6 months of age.

In 2010 an excess of febrile convulsions in children receiving influenza vaccine was noted; for this reason, some brands of influenza vaccines have age limits for use in children. This can be determined by referring to vaccine packet inserts or national guidelines.

Vaccine recommendation A standard vaccine recommendation for children travelling internationally.

Japanese Encephalitis

Japanese encephalitis, a viral infection transmitted via mosquitoes, occurs throughout parts of South and Southeast Asia. While the majority of infections are asymptomatic, approximately 1:300 are symptomatic, a third of which will die and a third will be left with permanent neurological deficit. In endemic countries the burden of this disease falls on children, predominantly in the form of permanent neurological sequelae. The risk to short-term travellers and those who confine their travel to urban regions is low; the decision to vaccinate children is dependent on the same variables as adults. Those children who plan to travel for more than a month or who plan to take up residence in endemic areas are strongly advised to be vaccinated against the disease. Such is the importance of the disease that children at high risk who will be residing in endemic areas who do not have time to complete their primary series prior to travel will need to seek options for vaccination on arrival.

Vaccine Recommendation New vaccines have largely replaced the use of the old mouse brain-derived vaccines, JE-Vax, which is only available in Singapore. This vaccine requires a three-dose regime but has been linked to delayed hypersensitivity reactions, hence tends to be used with caution. Jespect is licensed in both NZ and Australia for those 18 years and older. Prescription of Jespect to those less than 18 years of age is unlicensed, and off-licence use needs to be considered only after a risk assessment with informed parental consent. Ixiaro, in Singapore, North America and much of Europe, is licensed from 2 months of age. Both Jespect and Ixiaro are given in a two-dose (28 days apart) primary series. Australia and Singapore carry the single-dose live attenuated vaccine Imojev, not permitted at this stage into NZ.

Meningococcal Vaccines

Meningococcal disease caused by *Neisseria meningitidis* is often a devastating disease of children, with high case fatality rates and permanent disability. The consequences of meningococcal infection contracted while travelling in an impoverished country with poor health care facilities is even greater. Vaccination against meningococcal disease needs to be discussed at pretravel consultations.

A number of meningococcal vaccines (both polysaccharide and conjugated) are available, and some national schedules routinely include one or more of them. Others only recommend and/or fund targeted use. Many strains circulate worldwide, most commonly A, B, C, W, Y and X. In many developed countries, the predominant strain is C and vaccines effective against C strain may be included in various national schedules; however polyvalent vaccines may be of greater benefit to the travelling child as predicting exactly what strain they may encounter at their destination is unlikely.

Vaccine Recommendation A standard vaccine recommendation for children travelling internationally and particularly to those going to the 'meningitis belt' (a popular term for the region of sub-Saharan Africa which has hosted large epidemics of meningococcal meningitis for over a century). The conjugated vaccines induce good immune memory (so that subsequent doses boost immune memory), improve herd immunity via reduction of nasopharyngeal carriage and provide longer coverage. As such, they are preferred over polysaccharide vaccines for children when available.

Rabies

Rabies virus is most commonly contracted by humans via exposure to the saliva of infected mammals, principally dogs in less developed countries. Once the rabies virus has invaded neural tissue, it is protected from the immune system, and progression to fatal encephalitis is virtually inevitable. Children may be at greater risk of rabies in that they are easier "prey" to dogs being smaller than adults, suffer more intense bites, are less able to defend themselves against dog attacks and may be less animal-aware and less likely to report less obvious exposures.

Vaccine Recommendation There is no minimum age for administration of rabies vaccine. The decision as to whether to offer pre-exposure vaccine comes after assessing the individual risk of an exposure. The primary series consists of three doses at day 0, 7 and 28 days, though this can be brought forward to 21 days for those travelling soonest. The vaccine is recommended for all children to endemic regions.

Rotavirus

Rotavirus is the commonest cause of severe gastroenteritis in infants and young children worldwide. In developing countries, rotavirus gastroenteritis is responsible for approximately 500,000 deaths per year among children aged under 5 years.

Vaccine Recommendation Routine rotavirus vaccination beginning at age 6 weeks to 2 months is recommended for infants. The first dose of three doses to be administered at 6–12 weeks of age; the subsequent doses should be administered at a minimum interval of 4 weeks between each dose. The vaccination course should be completed by 32 weeks of age. Vaccination is not advised to be initiated for infants aged ≥15 weeks, because of insufficient data on the safety of the first dose of rotavirus vaccine in older infants. The minimum interval between doses of rotavirus vaccine is 4 weeks. All doses should be administered before age 8 months, 0 days.

Typhoid

Infection with *Salmonella* typhi and *Salmonella* paratyphi can result in enteric fever. Current vaccines only protect against *Salmonella typhi*. The course of illness in most children is much the same as adults, although they may be at increased risk of severe disease outcomes. Children who are visiting friends and relatives (VFR travellers) are at significant increased risk. All travelling children over the age of 2 years should be assessed for risk and vaccinated as indicated.

Vaccine Recommendation Children accompanying their parents to visit friends and relatives, particularly to the Indian Subcontinent, should be vaccinated with either the oral typhoid vaccine (if over 6 years) or the polysaccharide intramuscular one.

Varicella

Varicella infection (chicken pox) occurs worldwide. In temperate countries, in an unvaccinated population, natural infection is almost universal during childhood. In tropical countries, it is more often a disease of adolescents and adults. While in many children infection results in mild and self-limiting disease, it can result in severe illness (including encephalitis, pneumonia and sepsis) and, uncommonly, in fatalities. Children who have had neither natural infection nor previous vaccination will be at risk of disease.

Vaccine Recommendation Pretravel vaccination presents an opportunity to protect the child both during travel and on return. Licensing will vary between countries. Varicella vaccines can be given from 9 to 12 months of age. It is recommended that two doses given 6–8 weeks apart will provide better coverage than a single dose, for all age groups.

Yellow Fever

Yellow fever vaccination may be either recommended or required by travellers to parts of the world endemic for the yellow fever virus. The guidelines for vaccine use equally apply to children and adult travellers. The course of natural infections and the high case fatality rates are similar in children to those seen in adults, although the former may be more vulnerable to neurological pathology.

Vaccine recommendation: The yellow fever vaccine Stamaril is a live vaccine. In most countries it is licensed from 9 to 12 months of age, though it can be used with caution, if justified by risk, in those aged 6–9 months. It must not, however, be given to children less than 6 months of age due to an unacceptable risk of neurological adverse events.

The Breastfeeding Traveller and Vaccines

The medical preparation of a traveller who is breastfeeding differs only slightly from that of other travellers and depends in part on whether the mother and child will be separated or together during travel. It is accepted that mothers be advised to continue breastfeeding their infants throughout travel, for other risks of international travel (e.g. food and waterborne disease) will often be prevented.

Immunisations

As a rule, travel health professionals can safely advise that immunisations for breastfeeding mothers and their children be administered. Most are compatible with breastfeeding, and counselling mothers on either weaning before vaccine administration or on withholding vaccination is inappropriate.

There is a concern that antibody transferred via human milk may interfere with an infant's response to childhood immunisation, especially oral vaccines such as polio, though noting that this oral vaccine is not recommended in Australia, NZ and Singapore. While this is correct, and the newborns' seroconversion following polio immunisation is inhibited, the effect is transient, and there is no need to withhold breastfeeding with polio vaccine administration.

Breastfeeding and lactation do not affect maternal or infant dosage guidelines for any immunisation or medication, and children will need to be considered independently for their own vaccines.

Breastfeeding mothers and children will need to be vaccinated according to respective routine, recommended schedules for their intended travel. This includes the MMR vaccine, though the attenuated rubella strain is transmitted via breast milk, but infants are usually not affected by the vaccine strain. Only preventive vaccinia (smallpox) vaccine is contraindicated for use in breastfeeding mothers, but this vaccine certainly is neither universally available nor routinely advised. Administration of most live and inactivated vaccines does not affect breastfeeding, breast milk or the process of lactation.

Yellow Fever Vaccination

It is unknown whether this vaccine is excreted in human milk, although at least three cases of yellow fever vaccine-associated neurologic disease have been documented in infants. While it is presumed that this neurologic disease was caused by the breastfeeding transmission of yellow fever vaccine virus, no testing was done to determine if there was any vaccine virus in breast milk.

Breastfeeding is a precaution to yellow fever vaccination, and women travelling will need to be cautioned to avoid both this vaccination and travel to yellow fever

endemic regions while breastfeeding unless there is a genuine requirement to travel. Nevertheless, if travel to a risk region cannot be avoided or postponed, then vaccination may be carried out with appropriate informed consent.

An option for some could be to pump and discard breast milk and switch to formula for the duration of the vaccine viraemia in the mother (approximately 10 days); however, this need to be weighed against the potential consequences of stopping breastfeeding. This choice would generally only apply to mothers breastfeeding infants too young to receive yellow fever vaccine themselves.

Where yellow fever vaccine has been administered during breastfeeding, in all cases the children survived without sequelae. Thus, the overall risk is likely to be very low. There are no special precautions for vaccinating both a breastfeeding mother and an infant aged 9 months or older.

Incipients

Preservatives and other compounds of vaccines have caused concern over their potential effects on infants. However, all scientific data refutes such an association. This relates especially to thimerosal.

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Chapter 13
The Immune-Affected Traveller

Marc Shaw

Key Points

- Many of those wanting to travel live with immunocompromised health.
- Preparing an immunocompromised patient for travel is a challenge because of the risk of infectious disease.
- Careful consideration of the cause and degree of immunocompromise will mitigate the risk of vaccine preventable disease.
- Vaccinations tend to be less safe or effective than in the immunocompetent traveller, so pretravel consultation is fundamental for safe travel.
- Patients with leukaemia, lymphoma or other malignancies whose disease is in remission, who have restored immunocompetence and who completed chemo- or radiotherapy at least 3 months previously can receive live attenuated vaccines.
- Some specific malignancies, particularly Hodgkin's, may be associated with significant deficits in cell-mediated immunity that can persist even after cure. For these travellers, pretravel counselling is essential.

An increasing number of those wanting to travel overseas live with health conditions that cause reduced immunocompetence. Preparing an immunocompromised patient for travel can be a challenge because of the risk for infectious diseases. Nonetheless, careful consideration of the cause and degree of immune and

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well-being compromise, potential for drug interactions and health hazards at the destination will mitigate this risk.

Intending travellers with reduced immunocompetence include those with:

- Medical conditions such as:
  - Alcoholism, diabetes, HIV, renal failure, Crohn's disease, ulcerative colitis and cirrhosis
  - Rheumatoid arthritis and connective tissue disorders
- Medical conditions being treated with high-dose corticosteroid or cytotoxic medications
- Normal senescence
- Malignancies being treated with immunosuppressive therapies either continuous or intermittent
- An organ transplantation
- Stem cell transplantation
- Chronic immunosuppressive conditions
- Chronic conditions requiring on/off immunosuppression
- HIV, AIDS, and congenital immunodeficiencies
- Asplenia/hyposplenia

More and more of these individuals are travelling to tropical and low-income countries, potentially putting themselves at increased health risk due to their immunocompromised state. They have a greater risk of becoming ill with travel-related infections and an increased risk of complications. In addition, vaccinations tend to be less safe or effective than in the immunocompetent traveller. For all this, with careful and clear instruction, subsequent recommendations and accepted management, most travel can be undertaken safely as there are few absolute contraindications to travel.

The main concerns between immunosuppression and travel vaccine advice are:

- Possible increased susceptibilities to infection
- Concerns regarding vaccine use:
  - Live vaccines tend to be less safe than in the non-compromised traveller
  - Safety of live vaccines needs to be balanced with risk of travel
  - Possible decreased vaccine efficacy

Recommendations for Travellers

- Travel health professionals advising immunocompromised individuals need to emphasise the importance for expert travel advice, especially for a review of vaccination status, prior to travel to tropical and low-income countries.

The Traveller Without Significant Immunosuppression

Travellers whose health status places them in one of the following groups are not considered significantly immunocompromised and need to have vaccines discussed

as for any other traveller, albeit with deference to any issues that the traveller may have with respect to their health condition:

1. *Autoimmune disease*. Travellers with autoimmune disease (such as systemic lupus erythematosus, inflammatory bowel disease or rheumatoid arthritis) who are not being treated with immunosuppressive or immunomodulatory drugs, although definitive data are lacking
2. *Cancer.* Travellers with a history of cancer who received their last chemotherapy treatment 3 months or more previously and whose malignancy is in remission
3. *Corticosteroids.* Travellers receiving corticosteroid therapy under any of the following circumstances:
   - Short- or long-term daily or alternate-day therapy with less than 20 mg of prednisone or equivalent or with short-acting preparations
   - Maintenance physiologic doses, as in replacement therapy
   - Topical steroids, for eyes, ears or skin
   - Steroid inhalers
   - Intra-articular, bursal or tendon injection of steroids
   - If more than 1 month has passed since high-dose steroids (20 mg per day or more of prednisone or equivalent for greater than 2 weeks) have been used. However, after short-term (less than 2 weeks) therapy with daily or alternate-day dosing of greater than or equal to 20 mg of prednisone or equivalent, it is suggested that a patient wait at least 2 weeks before administering live vaccines
4. *HIV.* HIV patients with greater than 500/mm^3 CD4 T lymphocytes
5. *Multiple sclerosis.* Travellers with multiple sclerosis (MS) who are not on immunosuppressive or immunomodulatory agents and those who are not experiencing an exacerbation of disease
6. *Transplant.* Bone marrow transplant recipients who are more than 2 years post-transplant, not on immunosuppressive drugs and without graft-versus-host disease

Recommendations for Travellers

- Vaccinations for travel as per appropriate region or country recommendations, following liaison with the specialist healthcare and travel healthcare provider

Specific Immune Suppressing Conditions

The Traveller with Cancer

The immunological impact of cancer has a broad spectrum of effect, dependent upon the particular cancer and any consequent treatment. For most malignancies, the main period of immunosuppression is either during or immediately following chemo- or radiotherapy for at these times injury at a cellular level is most likely, neutropenia and mucosal injury being most common. Patients of such therapy are

generally unlikely to travel at these times because of side effects of their various therapies. Therefore, for those anticipating travel, response to vaccination is best if given either prior to chemotherapy or radiotherapy or some months after they are completed.

Patients with leukaemia, lymphoma or other malignancies whose disease is in remission, who have restored immunocompetence and who completed chemo- or radiotherapy at least 3 months ago can receive live attenuated vaccines, including yellow fever and MMR. Nevertheless, some specific malignancies, particularly Hodgkin's and, to a lesser degree, non-Hodgkin's lymphomas, may be associated with significant deficits in cell-mediated immunity that can persist even after cure. Caution is therefore urged, as this group of travellers may be accompanied by ongoing risk of reactive infections to both a malignancy and its management.

Revaccination with common childhood vaccines after chemotherapy for acute lymphoblastic leukaemia is indicated for travellers; however, patients with chronic lymphocytic leukaemia (CLL) rarely respond to vaccines. Such patients should also be completely revaccinated, including standard childhood vaccines, after bone marrow transplantation. If the patient is immunocompetent, the MMR vaccine can be administered 24 months after transplantation; however, it is generally recognised that patients with CLL are immunodeficient as far as vaccination with live attenuated vaccines is concerned, and these are to be avoided.

Some chronic cancer therapies are hormonal (tamoxifen, gonadotropin release inhibitors) and have no significant immunologic effects.

Recommendations for Travellers

- Cancer patients are advised not to travel during the immediate post-chemotherapy or post-radiotherapy period – they need to wait at least until the treatment course is complete, neutrophil counts have normalised, and they do not require transfusions.
- Travel plans need to be discussed in conjunction with the oncology team before any decisions are made.
- Cancer patients in full remission for at least 3 months, or who are taking only hormonally based therapies, generally do not require special measures.
- Live vaccines are contraindicated in patients with CLL.
- Specific patients identified by their oncologists as being likely to have relatively profound immunosuppression due to their disease or treatment should be offered advice similar to that provided to HIV-infected individuals with a CD4 cell count < 200 cells/mm^3 (see below).
- Hormonal therapies (e.g. tamoxifen) are not a contraindication to vaccination.

The Traveller with HIV/AIDS

The first issue faced by HIV-infected travellers is the risk of exclusion or discrimination on the basis of their infected status. Travellers can determine the legal requirements of specific countries from the website http://www.hivtravel.org.

The degree of immunosuppression, which particularly affects cell-mediated immunity, varies widely among HIV-infected individuals, reflecting disease stage and response to antiretroviral therapy, and is approximately predicted by a recent CD4 cell count. Vaccine recommendations differ according to the extent of immunocompromise, as determined by CD4 counts increased by antiretroviral drugs (reconstitution) rather than by nadir counts. The exact time at which reconstituted lymphocytes are fully functional is not well defined. To achieve a maximal vaccine response with minimal risk, a delay of 3 months after reconstitution with medication before immunisations are administered is advised.

Transient increases in HIV viral load, which return quickly to baseline, have been observed after administration of several different vaccines to HIV-infected people. The clinical significance of these increases is not known, but they do not preclude the use of any vaccine.

CD4 count > 500 cells/mm^3 (relatively normal). The patient is not significantly compromised; prepare as for any other traveller but inactivated rather than live virus vaccines are advised whenever possible.

CD4 count 200–500 cells/mm^3 and no history of HIV-related symptoms (mild to moderate immunosuppression). Although seroconversion rates and geometric mean titres of antibody in response to vaccines may be less than those measured in healthy controls, most vaccines elicit seroprotective levels of antibody in most HIV-infected patients in this category.

CD4 count < 200 cells/mm^3, history of AIDS-defining illness, or manifestations of symptomatic HIV or in the newly diagnosed patient (relatively severe immunosuppression). Patients should delay travel pending reconstitution. This delay will minimise risk of infection and avoid immune reconstitution illness during the travel. Live attenuated viral or bacterial vaccines are contraindicated. Inactivated vaccines will produce a suboptimal response; any that are received while CD4 count is < 200 cells/mm^3 should be re-administered at least 3 months after reconstitution.

CD4 count < 50 cells/mm^3 (profound immunosuppression). No vaccinations by primary healthcare providers are advised.

Recommendations for Travellers

- HIV-infected travellers should take the opportunity of preparing for travel to ensure they are up to date with their routine vaccinations including pneumococcus and hepatitis A and B.
- HIV-infected travellers need to discuss upcoming travel plans with their HIV specialist.
- Live oral and parenteral vaccines are contraindicated in CD4 counts less than 200 cells/mm^3.
- Transient increases in HIV viral load, which return quickly to baseline, have been observed after administration of several different vaccines to HIV-infected people. The clinical significance of these increases is not known, but they do not preclude the use of any vaccine.

The Traveller with Multiple Sclerosis (MS)

It is advisable that travel plans and interventions be discussed with an MS specialist; however, inactivated vaccines are generally considered safe for people with the disease. However, vaccination should be delayed during clinically significant relapses, until patients have stabilised or begun to improve from the relapse. This is classically 4–6 weeks after the beginning. The administration of tetanus, hepatitis B, or influenza vaccines does not appear to increase the short-term risk of relapses in MS travellers; however, published studies are lacking on the safety and efficacy of other vaccines.

Current MS management includes aggressive and early immunomodulatory therapy for almost all MS patients, even those with stable disease. A few published studies suggest that measles, rubella, varicella, and zoster vaccines may be safe in people with stable MS if administered 1 month before starting or 1 month after discontinuing immunosuppressive therapy. Live virus vaccines should not be given to people with MS during therapy with immunosuppressants, with immunomodulating therapies or during chronic corticosteroid therapy.

Yellow fever vaccine has not been well studied in people with MS and is only advised if there is a compelling reason, e.g. unavoidable direct exposure to yellow fever, and the risks of potential adverse events are balanced against the likelihood of exposure to the disease.

Recommendations for Travellers

- Inactive vaccines are considered safe for travellers with MS, although they ought not to be given during any relapse of their condition.
- Avoid live vaccines if a patient is experiencing a current exacerbation and for 6 weeks after the exacerbation resolves.
- Avoid live virus vaccine administration to those with MS during immunosuppression therapy.

The Traveller Who Has Had Transplantation

People who have had bone marrow transplantation are more immunosuppressed than those who have had solid organ transplants. After bone marrow transplantation, the highest risk period for acquiring an infectious disease is in the first 3 months. Hence high-risk travel to low-income or remote regions is not advised during this time. Two years after their transplant, haematopoietic stem cell transplant recipients are presumed immunocompetent if they are free of immunosuppressant therapy, and they are without graft-host disease.

Solid organ transplant recipients need not routinely repeat vaccinations given 2 weeks or more prior to transplantation, though it is advised to defer travel to high-risk destinations for 1 year after a transplant. Vaccines received during

immunosuppressive therapy are not valid and should be re-administered 3 months after therapy is discontinued.

Because of likely low immune efficacy in the first 6 months post-solid organ transplant, vaccination is best carried out before transplantation or at least 6 months after solid organ transplantation when immunosuppression has been reduced and the immune response capacity is optimally recovered.

Recommendations for Travellers

- In general, live vaccines should be avoided for:
  - Post-solid organ transplant or
  - Stem cell transplant recipients
- In the first 2 years post-transplant or in those who continue to take immunosuppressant drugs, the risks of exposure to the disease must be balanced against the risks of vaccination and the individual's degree of immunosuppression.
- Stem cell transplant recipients should repeat all vaccinations including any appropriate travel-related vaccines, post-transplant – when immune reconstitution is likely to have taken place and the patient is off immunosuppressive medications and does not have any 'graft-versus-host' disease. This is usually around 2 years post-transplant.

The Traveller with Asplenia/Hyposplenia

Patients without spleens, or with hyposplenia, are susceptible to overwhelming sepsis with encapsulated bacterial pathogens, and pretravel consultation with these patients needs to be focused on protection against such bacteria and malaria. There is limited data that shows a vaccine response in people who have had a splenectomy was more impaired if splenectomy was performed because of hematologic malignancy rather than for splenic trauma.

Recommendations for Travellers

- The meningococcal ACYW135 conjugate vaccine is indicated for both adults and children with asplenia.
- The polysaccharide-protein conjugate vaccine against disease due to *H. influenzae* type b (Hib conjugate vaccine) appears to elicit an increased immune response and duration of protection in vaccine recipients. A single dose is recommended for splenectomised patients.
- *Streptococcus pneumoniae* vaccine is recommended for asplenic patients.
- There is no evidence that live vaccines pose any risk to asplenic individuals; therefore, they can be administered.
- A 'standby' course of a broad-spectrum antibiotic therapy such as a fluoroquinolone or amoxicillin/clavulanate can be advised for travellers who may have limited access to emergency medical care during their travel.

The Traveller with Chronic Disease

Continuing medical conditions that may be associated with varying degrees of immune deficit include chronic renal disease, chronic liver disease (including hepatitis C), diabetes mellitus and complement deficiencies. Because no information is available regarding possible increased adverse events or decreased vaccine efficacy following administration of live, attenuated viral or bacterial antigen vaccines to patients with these diseases, caution should be used when considering vaccinating such patients. Factors to consider in assessing the general level of immunocompetence include disease severity, duration, clinical stability, complications and comorbidities.

A blunted response to hepatitis B vaccine has been reported in patients with chronic liver disease; a decreased response to hepatitis B vaccine has also been observed in patients with diabetes. Additional doses of hepatitis B vaccine beyond the primary three-dose series may be necessary. Double-dose hepatitis B vaccine preparations are used to promote optimal immunisation of people with chronic renal failure and other patients with absent or suboptimal response to standard hepatitis B vaccine doses.

Recommendations for Travellers

- The meningococcal ACYW135 conjugate vaccine is indicated for both paediatric and adult populations at risk.
- Hepatitis A and B vaccines are recommended for those with liver disease.
- People with terminal complement deficiencies appear to have increased susceptibility to meningococcal infections and should be immunised against meningococcal disease.
- The most immunogenic regimen should be used. This can include a double dose of the usual hepatitis B vaccine and intramuscular rather than intradermal administration of rabies vaccine.

The Patient on Immunosuppressive Medication

Vaccines administered to patients while they are concurrently receiving immunosuppressive therapy or during the 2 weeks prior to starting therapy are not considered valid. A wait of at least 3 months after therapy is discontinued is indicated, and then patients need to be revaccinated with all vaccines that are still indicated.

People taking any of the following categories of medications are considered severely immunocompromised, and live vaccination is contraindicated (after CDC):

- *Alkylating agents: e.g.* cyclophosphamide
- *Antimetabolites: e.g.* azathioprine and 6-mercaptopurine

- *Cancer chemotherapeutic agents: e.g.* methotrexate but excluding tamoxifen. Methotrexate is classified as severely immunosuppressive, as evidenced by increased rates of opportunistic infections and blunting of responses to certain vaccines among patient groups. Limited studies show that methotrexate monotherapy had no effect on the response to influenza vaccine, but it did impair the response to pneumococcal vaccine.
- *High-dose corticosteroids*: doses of corticosteroids of either >2 mg/kg of body weight or ≥20 mg per day of prednisone or equivalent in people who weigh >10 kg, when administered for ≥2 weeks, as sufficiently immunosuppressive to raise concern about the safety of vaccination with live virus vaccines. Furthermore, the immune response to vaccines may be impaired.
  - Live attenuated vaccines may be contraindicated for patients on corticosteroid therapy, which can impair the immune response to vaccines.
  - Live virus vaccines are contraindicated during therapy. Vaccination providers must defer live virus vaccination for at least 1 month after discontinuation of high-dose systemically absorbed corticosteroid therapy administered for >14 days.
  - All other corticosteroids, including replacement therapy, inhalers, and topical steroids, present no significant compromise. Vaccine advice is the same as for any other traveller.
- *Transplant-related immunosuppressive drugs: e.g.* cyclosporine, tacrolimus, sirolimus, mycophenolate mofetil and mitozantrone.
- *Tumour necrosis factor (TNF) blockers***:** *e.g.* etanercept, adalimumab, certolizumab pegol, golimumab and infliximab blunt the immune response to certain vaccines and certain chronic infections.
  - Despite measurable impairment of the immune response, post-vaccination antibody titres are often sufficient to provide protection for most people; therefore, treatment with TNF blockers does not exclude immunisation against influenza and pneumococcal disease.
  - The use of live vaccines is contraindicated, and in general, the recommendations for high-dose corticosteroids should be followed, i.e. delay until 1 month after discontinuing treatment.

Recommendations for Travellers

- Live vaccine administration is contraindicated.
- Additional doses of vaccine may be required for immunocompromised travellers.
- If vaccines need to be given during immunosuppressive medication for travel (including the 2 weeks prior to treatment), such persons need to be revaccinated 3 months or more after discontinuing therapy with all indicated vaccines.
- Influenza vaccine is indicated in these travellers.

Recommendations for Timing of Vaccination

A difficult question for clinicians about to start immunosuppressive medication on a patient is 'when should vaccines be administered to immunocompetent patients in whom initiation of immunosuppressive medications is planned'?

Recommendations for Travellers

- Vaccines should be administered prior to planned immunosuppression wherever feasible.
- Live vaccines should be administered ≥ 4 weeks prior to immunosuppression and should be avoided within 2 weeks of initiation of immunosuppression.
- Inactivated vaccines should be administered ≥ 2 weeks prior to immunosuppression.

Special Vaccine Considerations for Immunocompromised Travellers

The pretravel assessment often provides an opportunity to update routine vaccinations in all travellers.

Recommendations

- Except in specific circumstances as discussed below, live vaccines should be avoided in immunocompromised hosts.

Bacillus Calmette-Guérin (BCG) has variable and limited efficacy in immunocompetent hosts, unknown benefit in immunocompromised hosts and a very limited role at most, in TB protection for travellers. Although it is uncommon, there is a well-documented risk of dissemination in HIV-infected individuals and in patients with some types of congenital immune deficiency.

Recommendations for Travellers

- BCG is not recommended for any immunocompromised patient.

Cholera vaccination is rarely indicated for travellers, and occasions where its use is optimal (such as with humanitarian aid workers) are improbable destinations for immunocompromised travellers. Dukoral has been shown to be effective against cholera even in a population with high HIV prevalence. It may result in a temporary increase in HIV viral load, which is generally inconsequential. Because of its limited benefit in the prevention of travel-associated diarrhoea, Dukoral is not routinely recommended as a priority for travellers but may be considered in those for whom diarrhoea would be associated with increased risk.

Recommendations for Travellers

- Dukoral may be considered for immunocompromised travellers or those with compromised renal function, as an adjunctive measure in the prevention of travellers' diarrhoea.

Hepatitis A. Risk and disease severity of hepatitis A are similar in immunocompromised and immunocompetent individuals. Failure of serological response after vaccination is much more common in some groups of immunocompromised patients.

Recommendations for Travellers

- Hepatitis A vaccine is advised for travellers with mild to moderate degrees of immunosuppression, as for all travellers to tropical or low-income countries.
- Immune globulin is recommended for travellers who have moderate to severe degrees of immunosuppression, who lack serologic or historical evidence of immunity from natural infection and who are travelling to low-income countries.

Hepatitis B can be more severe, and vaccine efficacy is decreased in the immunocompromised. High-dose hepatitis B vaccination has been shown to increase seroconversion rates in groups who have higher rates of vaccine failure such as dialysis and HIV-infected patients. Immunity may wane even after successful vaccination, in immune suppressed hosts.

Recommendations for Travellers

- Immunocompromised adults who lack antibodies to hepatitis B surface antigen (HBsAb), and who are hepatitis B surface antigen (HBsAg) negative, should receive an increased dose (40 micrograms) of hepatitis vaccine at 0, 1 and 6 months and checked serologically at completion.

Influenza or its complications may be more severe in immune suppressed patients.

Recommendations for Travellers

- Inactive influenza vaccine is specifically recommended for immunocompromised individuals regardless of travel and should be included in pretravel vaccination, taking into account the influenza season at the destination.

Measles can be much more serious in the immune suppressed and HIV infected with reported case fatality rates of 40–70 %. Vaccine efficacy is markedly reduced in the immunocompromised. As with other diseases, measles immunity is commonly lost in recipients following allogeneic stem cell transplantation.

Recommendations for Travellers

- Stem cell (bone marrow) transplant recipients can receive two doses of measles, mumps and rubella (MMR) vaccination 6–12 months apart 24 months or more post-transplant provided they have finished immunosuppressive medications and are not suffering from graft-versus-host disease.
- MMR vaccine should be recommended to travellers who are believed to be non-immune to measles (no history of measles disease or vaccination, serology negative) who will be travelling in a low-income country with poorly controlled measles, unless they have clinical or laboratory indicators of very severe immunosuppression.

- Immune globulin should be considered for profoundly immune suppressed, measles non-immune travellers to high transmission areas.

Meningococcal disease risk does not clearly differ in most types of immunosuppression, the exception being specific complement disorders, but the vaccine is recommended for all splenectomised individuals regardless of travel. It is likely that the protective response may be decreased in relation to the degree of immunosuppression.

Recommendations for Travellers

- Quadrivalent ACYW135 conjugate meningococcal vaccine is indicated.

Pneumococcal disease is more common in some low-income country settings. Most immunosuppressed individuals are considered candidates for pneumococcal vaccine regardless of travel plans.

Recommendations for Travellers

- An initial dose of pneumococcal vaccine, with a booster dose 5 years after the initial dose, should be offered to immunocompromised patients.

Polio vaccine (live) can rarely cause vaccine-associated poliomyelitis. The risk may be higher in the immunocompromised, but very few cases have been identified in Africa where millions of HIV-infected children have received the vaccine. Spread of vaccine virus between close contacts is common.

Recommendations for Travellers

- Immunosuppressed travellers to endemic regions are advised to be vaccinated with: Inactivated polio vaccine
- Immunocompromised people should avoid contact with people who were vaccinated with oral polio vaccine (OPV) in the previous 6 weeks, as they may shed live polio virus.

Tetanus, Diphtheria and Pertussis (Tdap). There is no significant increased risk of the disease in the immunocompromised.

Recommendations for Travellers

- All travellers, including the immunocompromised, are advised to ensure their Tdap is up to date prior to travel.

Tuberculosis Screening and Skin Test Reactivity. Illnesses that compromise immunity, such as measles, severe acute or chronic infections, HIV infection and immune disorders, can create a relatively low, or lack of, immunity to an antigen during which the tuberculin skin test (TST) could produce a false-negative reaction. Although any live, attenuated measles vaccine hypothetically can suppress TST reactivity, the degree of suppression is likely to be less than that from an acute infection from wild-type measles virus.

No data exists regarding the potential degree of TST suppression that might be associated with live, attenuated virus vaccines (e.g. varicella or yellow fever) other

than measles. Therefore, in the absence of such data, following guidelines for measles vaccine when scheduling TST screening and administering other live, attenuated virus vaccines is practical.

The preferred option is for TST and measles (and other live) vaccine to be administered at the same visit. By administering the TST and measles vaccine simultaneously, there is no interference with reading the TST result 48–72 h later.

If the measles vaccine has been recently injected, then it is advised that TST screening be delayed for at least 4 weeks after vaccination. A delay in performing the TST removes the concern of any theoretical but transient suppression of TST reactivity from the vaccine. TST screening can be performed and read before administration of the measles-containing vaccine.

TST reactivity in the absence of tuberculosis disease is not a contraindication to administration of any vaccine, including live, attenuated virus vaccines; unless the patient is moderately or severely ill.

Recommendations for Travellers

- In a general screening situation in which tuberculosis is not suspected, a TST may be administered simultaneously with live vaccines or should be deferred for 28 days after vaccination. This does not apply to live oral vaccines.
- If a live vaccine has been administered, the first dose of a two-step TST should be delayed for 4 weeks, and if additional doses of live vaccines are indicated thereafter, they should be delayed until the second TST.

Typhoid vaccine response may be reduced in immunocompromised patients.

Recommendations for Travellers

- The injectable Vi capsular polysaccharide vaccine, rather than the live oral vaccine, is advised for immunocompromised travellers at risk for typhoid.

Yellow fever vaccination is required in some countries of sub-Saharan Africa, South America and the Caribbean. Yellow fever has a high mortality rate even in the immunocompetent. Limited experience suggests that yellow fever vaccine can be given safely and produce protective levels of antibody in HIV-infected individuals with CD4 cell counts > 200 cells/mm3.

Recommendations for Travellers

- Immunocompromised travellers should be made aware of the risk of visiting areas with active yellow fever transmission.
- In general, yellow fever vaccine should be avoided in immunosuppressed individuals.
- When the primary reason for vaccination in an immunosuppressed traveller is a country- specific vaccine requirement rather than significant epidemiologic risk of infection, a waiver letter can be provided.
- Travellers thought to have mild to moderate degrees of immunosuppression can be offered the vaccine after being first advised of the risks of the disease in the anticipated region of travel and of the vaccine.

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Chapter 14
Vaccines for Mass Travel

Claire Wong

Key Points

- Mass gatherings pose special risks for travellers, for there are a large number of people in small areas; thus, the spread of vaccine-preventable infectious diseases is more likely.
- Masses that travel can seriously impact upon a destination putting infrastructure and facilities under strain, resulting in potential difficulty accessing medical care.
- The health infrastructure at a mass gathering determines the ability to respond to anticipated and unanticipated incidents and infections.
- Knowledge of the country or region being visited is essential.
- The travel health professional needs to guide such healthy practice as:
  - Safe food and water habits
  - Prevention of insect bites
  - Prevention of blood-borne viruses and sexually transmitted diseases
  - Avoidance of animals, especially dogs
  - Hygiene and regular handwashing
  - Advice on basic first aid and personal health care

Introduction

Mass overseas travel occurs for a variety of reasons including attendance at rock concerts or festivals, international sporting events or for religious events. The World Health Organization defines a mass gathering as an event where the number of

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people attending is sufficient to strain the planning and response resources of the community, state or nation hosting the event. Although there is no accepted definition in terms of numbers, a mass gathering is usually defined as a group of 25,000 or more people, but could equally refer to as little as 1,000 people.

Most mass gatherings are planned events, with some taking place regularly at different locations (e.g. Olympic Games) and others recurring in the same location (e.g. Hajj).

This chapter will also address considerations for those travelling in smaller groups. Typically this includes numerous individuals who are known to each other and are travelling together, for example, school groups or sports teams.

Risks Associated with Mass Travel

Risks that all mass travellers will have in common are related to the close proximity of attendees and the resulting crowding. Specific risks will be dependent on the purpose of the gathering and location.

The reason for the event will often determine the characteristics of the attendees. Rock concerts and festivals would be expected to be noisy and boisterous and attract younger risk takers.

Specific risks will be determined by the location of the event. Many religious gatherings are held outdoors over several days, exposing participants to extremes of temperature. Several pilgrimage sites in India and Nepal are at extreme altitude posing specific risks of altitude-associated illness. As an example, the Mt. Kailash pilgrimage in Tibet involves travel to over 5,600 m altitude – too high to allow rescue by helicopter.

Preparing the Mass Traveller

The travel health preparation of the mass traveller should follow the same principles for advising any other traveller. Chapter 5 evaluates the risk assessment process.

Inconsistencies in travel advice can be a significant issue with group travel if participants attend different travel health providers. For smaller groups based in the same locality, encouraging all participants to visit the same travel clinic, perhaps by offering a group consultation or arranging a pre-travel meeting at the school or club to discuss risks and preventative measures, ensures that all travellers receive consistent advice and recommendations. In some circumstances, participants may be encouraged to attend for vaccinations if an off-site service can be arranged.

In addition to personal preparation, thought must be given to the facilities and infrastructure at the destination and the impact the intended mass travel could have. In particular, travellers need to consider the availability of medical facilities and how these may be affected by the demands of so many people, particularly in

low-income countries. Travel insurance is therefore essential and needs to be stressed for all travellers. Sanitation and hygiene facilities can also be lacking and subject to the demands of so many people.

Group Travellers

As stated above, the pre-travel preparation of those travelling as a group is often more streamlined and consistent if participants are encouraged to attend the same travel medicine provider. The risk assessment process is the same as that of every traveller with vaccine recommendations and requirements guided by:

1. Destination
2. Current disease outbreaks
3. Planned activities

Specific consideration should be given to risks that could impact the trip for the whole group. Group travellers may benefit from the oral cholera vaccine, Dukoral, as it provides some protection against traveller's diarrhoea in those visiting higher-risk areas. Travelling in close proximity can increase the risk of gastrointestinal illness transmission amongst the group, particularly if hygiene facilities are lacking.

Influenza vaccine is recommended as respiratory illness is an increased risk for those in close contact. In addition to vaccination, practising 'cough hygiene' will decrease the transmission of influenza and other respiratory illnesses:

- Coughing and sneezing into a disposable tissue, or the crook of the elbow
- Discarding used tissues hygienically
- Washing hands regularly with soap and water, or using hand sanitiser
- Wearing a disposable face mask if suffering from a respiratory illness

A potential rabies exposure can have serious consequences for group travellers as it is likely that at least one leader will be required to escort the traveller to access postexposure treatment, potentially terminating the trip for all involved. For this reason, pre-exposure rabies vaccine should be considered by those travelling to rabies-endemic regions.

Religious Gatherings

Pilgrims performing Hajj or Umrah in Saudi Arabia are required to produce proof of vaccination against meningococcal meningitis serotypes A, C, W135 and Y. Meningococcal outbreaks have occurred amongst pilgrims and contacts during previous events. The conjugate meningococcal vaccine is preferred, if available, as it also prevents nasal carriage of meningococcal bacteria, thus reducing the risk of transmission to close contacts.

The Saudi Arabia Ministry of Health strongly suggests that all pilgrims receive seasonal influenza vaccine due to the increased risk of transmission in such crowded conditions.

Hajj and Umrah pilgrims arriving from countries with a risk of poliomyelitis are required to provide proof of polio vaccination on arrival in Saudi Arabia.

One of the rituals of Hajj is the requirement for male pilgrims to have their heads shaved. Licensed barbers are available, but many unlicensed barbers may be using unsterile razors. Blood-borne virus transmission is therefore a concern and hepatitis B vaccine should be discussed.

Pilgrimages can often be to remote and difficult to access regions. A lack of hygiene facilities contributes to the risk of faecal-oral transmitted illnesses such as hepatitis A and typhoid.

The travel health consultation is an ideal opportunity to ensure travellers are up to date with their routine vaccines. A tetanus-containing vaccine received within the previous 10 years avoids the need to obtain vaccine at the destination in the event of a tetanus-prone wound. It is prudent to offer tetanus, diphtheria and acellular pertussis vaccine to those requiring a tetanus booster given the current increased rates of pertussis in many countries.

Recent outbreaks of measles have been associated with overseas travel; all travellers should be offered measles, mumps and rubella vaccines if their vaccine status is uncertain. Those born between 1969 and 1981, in particular, may not have received the recommended two doses during childhood.

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Chapter 15
A Guide to Contraindications, Precautions and Adverse Events

Nick Zwar

Key Points
- The travel health professional needs to consider whether contraindications or precautions exist for any vaccination, prior to intended travel.
- A contraindication is a specific situation where a vaccine may not be used because it may be harmful to the patient. Usually, this situation applies to the administration of live attenuated vaccines.
- A precaution to vaccination occurs when there is a chance of an adverse event following immunisation or a condition or situation may compromise the ability of the vaccine to produce immunity.
- Immunisation practice methods or procedures can avoid or reduce the risk of adverse outcomes or decreased immunisation effectiveness.

Contraindications and Precautions: What Is the Difference?

Prior to administering any vaccination, the travel health professional needs to consider whether contraindications or precautions exist for the particular vaccination. In medical practice, a contraindication is a specific situation in which a drug, procedure, or surgery should not be used because it may be harmful to the patient. The term absolute contraindication is used to describe a situation where a medical intervention is likely to result in serious harm or even death. There are only a small number of contraindications to vaccination, and these will be described.

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A precaution is a condition or situation that may increase the chance of an adverse event following immunisation or may compromise the ability of the vaccine to produce immunity. In immunisation practice, there are often methods or procedures that can avoid or reduce the risk of adverse outcomes or decrease immunisation effectiveness. An example is timing of live attenuated vaccines (given simultaneously or separated by 4 weeks) to ensure that efficacy of vaccination is not compromised.

Contraindications to Vaccination

There are only two situations that constitute an absolute contraindication for all vaccines. These are:

- Anaphylaxis following a previous dose of the vaccine
- Anaphylaxis following any component of the vaccine

Overall, the risk of anaphylaxis from a single vaccine dose has been estimated at less than 1 in 1 million, but this does vary by vaccine type. An antigen associated with anaphylactic reactions in some patients is egg protein. This is present in a number of vaccines which are grown in chicken eggs such as influenza, yellow fever and Q fever vaccines. There is also a rabies vaccine cultured in purified chick embryos. Measles/mumps/rubella (MMR) vaccine is not grown in eggs, and the recommendation from most medical authorities is that it can be safely given to patients with severe egg allergies. Many people with severe egg allergy can also be safely vaccinated for influenza. This is because the amount of residual egg ovalbumin is very low (less than 1 μg per dose). To maximise safety, administration in a hospital environment should be considered for those with a severe egg allergy. Yellow fever and Q fever vaccines contain larger quantities of egg ovalbumin. If vaccination is required, then these patients should be referred for specialist assessment such as to a hospital allergy or vaccination clinic. For egg-allergic patients needing rabies vaccination, the purified chick embryo cell vaccine should not be used, and an alternative, such as the human diploid cell or the Vero cell, vaccine used. Besides egg protein, antibiotics and gelatin are the vaccine components most often provoking an allergic reaction. Latex proteins can occasionally be present in some prefilled syringes and in vaccine vial bungs and syringe plungers. If the patient has a history of allergy to latex, these products need to be avoided.

Contraindications to Live Vaccines

The other two situations where vaccination may be contraindicated are applicable to live (both parenteral and oral) vaccines. The first situation is where the patient is significantly immunocompromised for any reason. This can be due to diseases such

as HIV or to immunosuppressive treatment such as following tissue or organ transplantation. Increasingly, it is also associated with the use of biologicals such as tumour necrosis factor-alpha antagonists in rheumatology and gastroenterology. Assessment of the degree of immunocompromise is needed and may require consultation with other health professionals treating the patient (see Chap. 13).

The second situation is the use of live vaccines in pregnancy. In general, live vaccines should not be used in pregnancy, and women should be advised to avoid conception within 28 days of receiving a live vaccine. The basis of the contraindication is the hypothetical risk of harm related to viral replication in the fetus. Nevertheless, inadvertent administration of a live vaccine in pregnancy is not a reason to consider termination of pregnancy as this occurrence has not been associated with any observed increase in congenital abnormalities. In some instances, such as yellow fever vaccination, following risk assessment and discussion of other options, it may be decided that administering the vaccine is safer than travelling unvaccinated.

It is important that travel health professionals providing immunisation services are also aware of the range of conditions and clinical situations that are not contraindications to vaccination. Common examples include:

- Minor illness without significant fever (temperature less than 38.5°C)
- Family history of an adverse event following immunisation
- Past history of convulsions
- Current treatment with antibiotics
- Treatment with inhaled or low-dose topical steroids
- Treatment with replacement corticosteroids, e.g. for Addison's disease
- Asthma, eczema and allergic rhinitis
- Neurological conditions

Precautions

There is a wide range of situations where the chance of an adverse event related to immunisation is increased, where there is the risk of decreased effectiveness or where special care is needed. Some of these are generic and apply to all or a number of vaccines, and some are vaccine specific. Examples of generic precautions are:

- Febrile illness at the time of vaccination. In general, vaccination is postponed if there is a significant febrile illness (temperature > 38°C). This is not because the rate of adverse events has been shown to be higher but because the intercurrent illness makes it difficult to discern a vaccine adverse effect.
- Injected live vaccines should be given on the same day or separated by at least 4 weeks. The live oral Ty21a typhoid vaccine can be given at any time in relation to injectable live vaccines.
- Administration of blood or immunoglobulin products can interfere with the immune response to MMR and varicella live vaccines. This does not apply to rotavirus vaccine which does not act parenterally or to yellow fever or zoster

vaccines. It is therefore necessary to administer MMR and varicella vaccines at least 3 weeks before or defer for a variable period up to 11 months after blood or immunoglobulin products have been used. The deferment period depends on the particular blood or immunoglobulin product used. The most common situation is normal human immunoglobulin where the deferment period is at least 3 months. Both the Australian and New Zealand immunisation handbooks have a table covering the deferment periods for specific blood and immunoglobulin products.

- Patients with thrombocytopenia or bleeding disorders. A haematoma following intramuscular vaccination is more common in such patients. The risk can be minimised by use of a 23-gauge needle and applying firm pressure at the injection site for at least 2 min. An alternative is to use subcutaneous injection, but this is not applicable to hepatitis B vaccination as efficacy is likely to be compromised. Specialist advice may be needed if the immunisation provider is not familiar with the patients' bleeding risk.
- Patients who have had axillary node dissection. This occurs most commonly in treatment for breast cancer. The limb is at risk for lymphoedema, and injection into that arm should be avoided.

Adverse Events Following Immunisation

Adverse events following immunisation (AEFI) are defined as any untoward medical event following immunisation. Some of these will be causally related to the immunisation, and some are coincidental. It is important that AEFIs are notified to health authorities using the local monitoring systems. Establishing with certainty that a vaccination caused an event is often impossible but is more likely if the reaction is typical or where there is no other plausible explanation.

The term adverse reaction is commonly used when an event is considered to be causally related to the vaccination. Overall vaccine adverse reactions fall into two broad categories: local and systemic. Local reactions are the most common and occur at the injection site. Typical local reactions are pain, swelling and redness. Another common reaction is injection site nodules. These are firm lumps at the injection site, typically following an intramuscular vaccination. They are due to a fibrous reaction to vaccine components, typically to an adjuvant. They can persist for weeks after a vaccination but do not require treatment and eventually resolve. Systemic adverse reactions include fever, headache and lethargy. Typically, these last a few days.

Another reasonably common adverse event after vaccination in adults and older children is fainting (vasovagal episode). This is rare in infants and younger children. Typically, fainting occurs at the time of, or soon after, vaccination. Features include pallor and sweatiness. The patient may slump to the ground and partially or completely lose consciousness. Once in a prone position, the patient typically regains consciousness within 1–2 min. It is helpful to ask patients if they have a history of fainting in association with vaccination and if so have them lying down for the

administration of the vaccine and for a period afterwards. In children, faints need to be distinguished from hypotonic-hyporesponsive episode which typically occurs one to 48 h after vaccination. These episodes involve sudden onset of pallor or cyanosis, muscle hypotonia and reduced responsiveness. The episode can last from a few minutes to 36 h.

Febrile convulsions can occur in children in response to fever from any cause. They are most common in children aged <3 years. Febrile convulsions are rare following vaccination. The vaccine most often associated with febrile convulsions is the first dose of MMR or MMRV.

As previously mentioned, allergic reactions also occur, but these are rare (0.01 to <0.1% in clinical trials). Allergic reactions can take a range of forms including pruritus, a serum sickness-type reaction and anaphylaxis. Immediate recognition and early treatment of anaphylaxis is very important, as it has a number of features which assist diagnosis. Onset is usually within 15 min after the injection but occasionally can be more than 1 h. Early symptoms and signs include the patient feeling hot and itchy, skin redness, urticaria or angioedema. Gastrointestinal symptoms can also occur such as abdominal cramps, nausea, vomiting and diarrhoea. Cardiovascular features are tachycardia, hypotension (which does not improve when lying flat) and occasionally circulatory arrest. Respiratory signs are airway narrowing resulting in wheeze or stridor and upper airway swelling. The patient may complain of anxiety. Loss of consciousness may occur which does not improve in a supine or head-down position.

Management of Adverse Reactions to Vaccines

Table 15.1 describes the various adverse reactions and their management.

Anticipating Adverse Reactions

Adverse reactions to vaccination are not entirely predictable, but it is possible to reduce the risk by pre-vaccination assessment and careful postvaccination observation and care. A pre-vaccination screening checklist can be used to help identify contraindications and precautions for vaccination. Items for a checklist include asking if the person about to be vaccinated:

- Is unwell today
- Has a disease which lowers immunity (e.g. leukaemia, cancer, HIV/AIDS) or is having treatment which lowers immunity (e.g. oral steroid medicines such as cortisone and prednisone, radiotherapy, chemotherapy)
- Has had a severe reaction following any vaccine
- Has any severe allergies (to anything)

Table 15.1 Adverse reactions and their management

Adverse reaction	Management
Local reactions – pain, swelling or redness at injection site	Explanation and reassurance, simple analgesia such as paracetamol or non-steroidal anti-inflammatory drugs
	Choice of analgesia will depend on individual factors such as age
Injection site nodules	Explanation and reassurance. No other treatments needed
Systemic adverse reactions – fever, headache and therapy	Explanation and reassurance
	Encourage increased fluid intake
	If fever is prominent (e.g. over 38.50°C), then an antipyretic such as paracetamol can be advised
	Aspirin should be avoided in children
Vasovagal episode	Assess airway, breathing and circulation
	Lay the patient down and elevate lower limbs
Hypotonic-hyporesponsive episode	Initial management as for shock (airway, breathing, circulation)
	Transfer to hospital for assessment
	Follow-up of children experiencing these episodes has not found any adverse effects
	Studies of children who have continued routine vaccination schedules have not shown a recurrence
Febrile convulsion	Assessment for other possible causes of fever and for neurological disease
Brachial neuritis	Has been reported after administration of tetanus toxoid-containing vaccines
	Referral for neurological assessment
Guillain-Barré syndrome	Assessment and neurology specialist referral
	People with a history of Guillain-Barré syndrome may be at risk of recurrence if given influenza vaccine
Allergic reactions	Management depends on the nature of the reaction
	See Chap. 21 for management of anaphylaxis

- Has had any vaccine in the last month
- Has had an injection of immunoglobulin or received any blood products or a whole blood transfusion within the past year
- Is pregnant
- Has a past history of Guillain-Barré syndrome
- Was a preterm infant
- Has a chronic illness
- Has a bleeding disorder

Positive answers to any of these questions require further assessment and may result in a decision not to administer the vaccine, to defer vaccination or to seek specialist advice.

It is good immunisation practice to ask the patient to remain in the clinic for at least 15 min after vaccination. This is because the majority of serious adverse effects such as anaphylaxis will occur within this time period.

The Management of Emergencies

The most serious and life-threatening emergency associated with vaccination is anaphylaxis. Management of emergencies starts before they happen with clinic equipment, organisation and staff training. Emergency equipment includes:

- Adrenaline 1:1000 ampoules, injection equipment and instructions for anaphylaxis management in very room where vaccines are administered
- Resuscitation equipment – oxygen supply, adult and paediatric airways, adult and paediatric masks and a suitable resuscitation bag and a variety of sizes of oxygen masks

Travel health professionals who are providing immunisation services need to be trained in cardiopulmonary resuscitation and to update their skills regularly. Vaccinating whilst alone is not recommended as more than one health professional is needed if an emergency occurs. The clinic staff needs to review practice policy and practice emergency procedures regularly, including the need to check that adrenaline supplies are in date.

Managing Anaphylaxis

Chapter 21 discusses the management of emergencies in a practice; however, the important points of this are:

- If anaphylaxis is suspected, the first action is to call for help. This will mean assistance from other clinic staff and an ambulance.
- Early administration of IM adrenaline is a key step of management of anaphylaxis. If there is doubt about the need for adrenaline, it is generally recommended to give the drug as no serious or permanent harm is likely to result, but progression of anaphylaxis can be fatal.
- Assessment involves laying the person in the recovery position and following the ABC process (check airway, breathing and circulation). The clinical staff should assess the patient for the symptoms and signs of anaphylaxis as described earlier.
- If any respiratory and/or cardiovascular features are present, adrenaline should be administered at the appropriate dose for age or weight by deep IM injection into the anterolateral thigh. The dose is 0.01 ml/kg body weight, but in an emergency situation, selecting the dose by age is usually necessary (see Table 15.2). Further doses should be given at 5 min intervals until the patient's condition has improved.
- Oxygen should be administered at a high flow rate using an age-/size-appropriate mask.
- If cardiopulmonary arrest occurs, then age-appropriate cardiopulmonary resuscitation should be administered in accordance with national guidelines.

Table 15.2 Dosing guide: intramuscular adrenaline 1:1000 by weight for anaphylaxis

Age	Adrenaline dose (ml)
Infants aged < 1 year	0.05–0.1
1–2 years	0.1
2–3 years	0.15
4–6 years	0.2
7–10 years	0.4
10–12 years	0.5
>12 years and adults	0.5

- In all cases, the patient should be transferred to the hospital for observation and further treatment if needed.
- Document the event as fully as possible, including noting the times and doses of adrenaline.

Waiving of Immunisation Requirements

A small number of immunisations can be required for travel. Vaccination requirements can be under the International Health Regulations (IHR), or they may be mandated by an individual country. IHR are an international legal instrument that is binding 196 countries across the globe, including all the member states of the World Health Organization. Their aim is to help the international community prevent and respond to acute public health risks that have the potential to cross borders and threaten people worldwide. One of the more contentious issues in the practice of immunisation for travel is what constitutes a legitimate reason for a waiver from these regulations. The IHR originally come into force in 1969, but following the outbreak in 2003 of Severe Acute Respiratory Syndrome, their scope was widened in recognition of the need to collect information and respond to emerging international disease threats. In 2014, the IHR have been important in the international response to the spread of wild polio virus.

Yellow fever vaccination has long been a requirement for entry to many countries under the IHR. The purpose of this is twofold. One is to protect travellers from the disease if visiting yellow fever-endemic areas. The other purpose is to reduce the risk of spread of yellow fever across international borders. Many countries have the mosquito vectors that can spread yellow fever, but the disease has either never been present or has been eliminated.

In some circumstances, yellow fever vaccination is contraindicated. The contraindications are:

- Anaphylaxis following a previous dose of the vaccine or any vaccine component. As previously mentioned, yellow fever vaccine is contraindicated in people with known anaphylaxis with eggs.

- Age <9 months. This is due to a higher rate of neurological reactions in infants. The age cut-off varies between different guidelines. The US CDC and UK National Travel Health Network and Centre cut-off is <6 months.
- Immunocompromise due to congenital condition, disease processes or medical treatment
- Thymus disorder of any kind, as this is associated with greater risk of viscerotropic adverse reactions.

If patients with one of these contraindications decide to travel to a yellow fever-endemic area, then they can be issued with a medical waiver. This needs to be written on the doctor's letterhead and should provide the reason for the waiver. The traveller needs to be informed that the destination country has discretion about whether they accept the waiver and allow entry. These travellers also need to be aware that they are at risk of yellow fever infection and to protect themselves against mosquito bites.

The area of contention is whether precautions for yellow fever vaccination also constitute reasonable grounds for providing a medical exemption. One precaution is pregnancy, and the other is age over 60 years which is associated with a substantially higher incidence of severe adverse reactions. This risk is particularly the case in older patients receiving the vaccine for the first time. Some authorities such as the UK National Travel Health Network and Centre have regarded these precautions as reasonable grounds for providing a medical exemption if it is considered that the risk from vaccination outweighs the risk of yellow fever at the destination. Other authorities such as the Australian Immunisation Handbook state that exemption letters should only be issued to travellers with true contraindications.

The Kingdom of Saudi Arabia government requires evidence of ACW135Y meningococcal vaccination for travellers applying for a visa for the Hajj or Umrah pilgrimages. The vaccination must have been given not more than 3 years and not less than 10 days before arrival in the Kingdom of Saudi Arabia. Where there is a contraindication to meningococcal vaccination, a medical exemption letter can be sent with the visa application. It will be at the embassies' discretion whether such visa applications are approved.

University colleges in the United States commonly require evidence of vaccination for enrolment. Meningococcal vaccination is the most common requirement, but other vaccinations may also be required. Colleges will generally accept a medical waiver letter if there is a contraindication to vaccination.

Further Reading

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Chapter 16
Myths Surrounding Vaccines

Helen Petousis-Harris

Key Points
- Repeating a myth can serve to reinforce it so start communications with facts.
- Provide an alternative explanation that also explains where the myth came from.
- Misinformation is untrue or a myth: discuss the science and discuss the facts.

Myths about vaccines and vaccination have been in wide circulation since the earliest smallpox vaccinations in the eighteenth century. While there is plenty of science to provide rebuttals to false claims, the debunking of myths is more difficult. Debunking incorrect information can sometimes result in reinforcement of the myth rather than correcting misinformation. Research suggests the most effective approach requires three key elements: (1) focus on central facts and not the myth so as false information is not reinforced; (2) the mention of the myth should be framed in the context of a myth, warning that it is a myth (this is a myth or false); and (3) include an alternative explanation that accounts for core tenets of the myth – replace the myth with solid facts.

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Myth	Fact	Reasoning
Measles, mumps and rubella (MMR) vaccine causes autism	No, this is incorrect	This claim is based on fraudulent data and stories that appeared in the mass media in 1998. Since then many very large well-conducted epidemiological studies, including millions of subjects across many counties, have consistently found no association
		The original publication that sparked the controversy has been withdrawn from the medical literature due to the horrific breaches of human ethics, fraud and undisclosed conflicts of interest
		The reduction in vaccine coverage that resulted from the controversy has resulted in measles epidemics and associated morbidity and mortality
		Measles, mumps and rubella vaccine has an excellent safety record, and serious adverse events causally related to MMR vaccine, though rare, are:
		Idiopathic thrombocytopaenia (around 1/30,000)
		Anaphylaxis (around 1 per million)
		Febrile convulsions (around 1 per 1,000)
		Other vaccine-associated events are generally mild and of short duration and occur 7–14 days after vaccination
Vaccines cause autoimmune disease	Generally no – with some exceptions	While there are a range of infectious agents that are known to cause autoimmunity, including influenza, routinely used vaccines have not been found to trigger autoimmune diseases
		A notable exception was a swine flu vaccine in the 1970s which caused an increase in Guillain-Barre syndrome and an association between a 2010 adjuvant pandemic influenza vaccine used in some northern hemisphere countries and onset of narcolepsy
		Many well-controlled epidemiologic studies do not support the hypothesis that vaccines cause autoimmunity
		It is biologically plausible that vaccines could trigger an autoimmune response, and safety surveillance systems monitor for these closely
		Vaccines have an excellent safety record in terms of autoimmunity and also prevent some infections, such as influenza, implicated in autoimmune disease

Myth	Fact	Reasoning
Vaccines contain aborted fetus	No, this is incorrect	There is a view that vaccines are grown on aborted foetuses. This is not the case. The vaccine strain of rubella was derived from an aborted fetus infected with rubella in the 1960s, as was also the case with a rabies cell-derived vaccine. These viruses require human cells to replicate; therefore the virus is grown in a foetal cell line that was established in the 1960s from a single aborted fetus. There has been no further foetal tissue used in the production of either rubella or rabies vaccine since this time, and there are no cells or human tissue in either vaccine
		Vaccine formulation includes ingredients essential for effectiveness and safety
		Viruses require cells to replicate in. Cell lines used in vaccine manufacture undergo rigorous evaluation before they can be used in human vaccines
Multiple vaccines overload the immune system	No, this is incorrect	Some believe that multivalent vaccines (vaccines containing protection against several diseases) may overwhelm the immune system. There is no biological reason why this should happen, and extensive scientific research supports this. Vaccines are much gentler on the immune system than the diseases they serve to prevent
		From birth infants are exposed and make immune responses to hundreds of microbial species and billions of antigens. Vaccines contain as few as a single antigen to as many as a few hundred. Vaccines on most childhood immunisation schedules contain around 60 antigens if given all together. This has a minimal effect upon the immune system
Aluminium in vaccines is a neurotoxin	No, this is incorrect	Many vaccines contain a tiny amount of aluminium to assist as an adjuvant to the immune response. There is no evidence that aluminium in vaccines causes neurological problems. Exposure to aluminium from vaccines constitutes an extremely small proportion of the overall exposure that occurs every day in food, water and environment. The amount of aluminium in vaccines is less than a day's worth of infant formula
		Aluminium is the most abundant metallic element on earth and present in the human body from birth. Throughout life, exposure is mainly via food and water
		Most aluminium in the body is excreted via kidneys. In renal failure, high levels of aluminium can become toxic

Myth	Fact	Reasoning
Formaldehyde in vaccines is toxic	No, this is incorrect	Some vaccines use formaldehyde during the manufacturing process. It is not a vaccine ingredient per se but is often present to inactivate toxins from bacteria and viruses (e.g. poliovirus, hepatitis B antigen and diphtheria and tetanus toxins)
		There is 60 times more formaldehyde in a pear than any vaccine
		Formaldehyde is essential for DNA synthesis but toxic in large amounts
		Environmental exposure occurs via a variety of sources from cheese and soft furnishings to road traffic pollution
Vaccines are not tested for long-term safety	No, this is incorrect	Vaccine safety is followed in clinical studies, and once the vaccine is used, there are a range of methods used to monitor its ongoing safety in the population. These methods include passive monitoring systems and active safety studies where vaccinated people are compared with unvaccinated people. Follow-up can be over many years
		Vaccines are more rigorously tested and followed up for safety than any other medicine. The approval process can take up to 10 years
Vaccines cause cot death	No, this is incorrect	Although some cases of cot death (unexplained sudden infant death) occur by chance after vaccination, this is unrelated to receiving vaccines. Academic data shows that infants who received their vaccines on time are slightly less likely to die from sudden infant death syndrome
		Cot death usually occurs in the first 3 months of life, at a time vaccines are administered. Every country will experience some cases of cot death that occur shortly after vaccination, simply by chance. This does not mean the event was caused by a vaccine
Injecting vaccines bypasses the body's natural defences	No, this is incorrect	Some people think that by injecting a vaccine, the body's natural defences are bypassed. This is not true. Vaccines stimulate a specific immune response within the lymph nodes, as do natural infections
		Vaccines stimulate a protective immune response without causing the illness

Myth	Fact	Reasoning
Vaccines do not work. Most people who get the disease have already been vaccinated	Vaccines are immunostimulants and protect most people who receive them	While some vaccines protect over 98 % of the people who get them for life, others are less effective with shorter duration of protection
		Some field examples of vaccine failure as proof that they do not work. This is called 'cherry picking'. Because vaccines are not 100 % protective for a population, sometimes those vaccinated get the disease. Overall, however, vaccines protect most who receives them for at least a few years to sometimes for life
Government, scientists and health professionals are all in the pockets of big pharma	No, this is incorrect	While generally it is the industry that has the money to fund the large-scale clinical trials required to get a vaccine licensed, the process of vaccine manufacturing and clinical trials are very tightly regulated
		The decision to license vaccines is made by regulatory agencies such as the US FDA, the European EMA, Australian TGA and the NZ MedSafe
		In many countries the decision to recommend and buy vaccines is made by other groups such as expert technical groups who are not allowed to engage with the pharmaceutical industry, and purchasing of vaccines and choice of provider may be made by yet another group. Pharmaceutical companies found trying to bribe health providers are likely to be fined
		Every country in the world has an immunisation programme to help protect the health of its citizens
		Pharmaceutical companies are businesses and are required by their shareholders to make a profit

Further Reading

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Chapter 17
Australian Immunisation Practice

Tonia Buzzolini

Key Points
- A knowledge of immunisation procedures in the country of practice is essential.
- Travel Health Professionals need to ensure they have appropriate training.
- Required protocols for practice should be in place, reviewed and updated as appropriate.

Introduction

The Australian Immunisation Handbook provides clinical guidelines for healthcare practitioners on the most effective, best-practice usage of vaccines based on available international scientific evidence. The guidelines are based on recommendations developed by the Australian Technical Advisory Group on Immunisation (ATAGI) and approved by the National Health and Medical Research Council (NHMRC).

The role of ATAGI is to provide advice to the Minister for Health on the Immunise Australia Program and related subjects. ATAGI is made up of technical experts, as well as general practitioner and consumer representatives.

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The Immunise Australia Program was set up to increase immunisation rates nationally by funding free vaccination programmes for vaccines included in the National Immunisation Program (NIP).

There are two registers which support the documentation of immunisation records in Australia:

1. The Childhood Immunisation Register (ACIR)
2. The National Human Papillomavirus Vaccination Program Register (HPV Register)

Vaccine Administration

Vaccinations in Australia are primarily undertaken in general practice; however, they may also be administered through local council clinics, community centres, school-based vaccination programmes, travel medicine clinics, public hospitals, pharmacies, staff occupational health clinics and aged care facilities. It is also possible for private companies to administer vaccinations off-site (workplace). There are legislative requirements governing the administration of vaccines, which vary between the states and territories. The types of vaccines authorised for administration under the NIP, as well as the requirements and processes for administration, are subject to jurisdictional variations.

To learn more about these variations and the individual state/territory requirements, companies are advised to contact the relevant department of health for further information (see Table 17.1).

Pre-vaccination Preparations

Various steps and procedures will need to be followed prior to administering vaccinations. They are the following.

Anaphylaxis Kit

It is imperative that prior to administering vaccines clinicians ensure that they have the necessary protocols in place to manage an emergency, with equipment and medications readily available.

Preparing an anaphylaxis kit is an important first step.

The kit needs to contain the following:

- Adrenaline 1:1,000 (minimum of three ampoules – check expiry dates regularly)

Table 17.1 State or territory health department contact information

Australian government health authorities	
Department of Health and Ageing	Central office in Canberra
	Free call: 1800 020 103
	Website: http://www.health.gov.au
Australian Childhood Immunisation Register (ACIR) or national register which records vaccinations given to children <7 years of age)	Free call: 1800 653 809
	Vaccination providers can also use this number to obtain information on the vaccination history of individuals
	Email: acir@medicareaustralia.gov.au
	Website: www.humanservices.org.au/customer/services/medicare/australian-childhood-immunisation-register
State and territory government health authorities	
Australian Capital Territory (ACT) Immunisation	Immunisation information line: (02) 6205 2300
	Website: www.health.act.gov.au/health-services/a-z-health-information/immunisation-and-vaccination
NSW Immunisation Program	Contact via the state-wide public health access line: 1300 066 055
	Website: http://www.health.nsw.gov.au/publichealth/immunisation/index.asp
Northern Territory (NT) Department of Health Centre for Disease Control	Phone: 08 8922 8044
	Website: http://www.health.nt.gov.au/Centre_for_Disease_Control/Immunisation/index.aspx
Queensland (Qld) Immunisation Program	Phone: 13432584
	Website: www.health.qld.gov.au/immunisation
South Australian (SA) Communicable Disease Control Branch – Immunisation	Phone: 1300 232272
	Website: http://www.health.sa.gov.au/pehs/immunisation-index.htm
Tasmania (TAS) Department of Health and Human Services	Public health hotline: 1800 671 738
	Website: http://www.dhhs.tas.gov.au/peh/immunisation
Victoria (VIC) Department of Health Immunisation Section	Ph: 1300 882 008
	Website: http://www.health.vic.gov.au/immunisation
Western Australian (WA) Department of Health – Public Health	Ph: (08) 9321 1312
	Website: http://www.public.health.wa.gov.au/1/51/2/immunisation.pm

- Minimum of three 1 ml syringes and 25 mm-length needles for intramuscular (IM) injection
- Cotton wool swabs
- Pen and paper to record the time adrenaline was administered
- Laminated copy of adrenaline doses for adults and children
- Laminated card with signs and management of anaphylaxis, which is available on the back cover of the Australian Immunisation Handbook (10th edition)

Vaccine Storage

To ensure peak potency and efficacy, vaccines must remain at a temperature range of +2 °C to +8 °C from the place of manufacture to the time they are administered. If vaccines are purchased via prescription from a pharmacy, then travelling individuals must be informed by both the doctor and the pharmacist of the imperative for vaccines to remain within this temperature range and how best to ensure this.

In Australia, all immunisation providers must adhere to the national vaccine storage guidelines, *Strive for 5* (www.health.gov.au/internet/immunise/publishing.nsf/Content/IMM77-cnt). This document provides information on the necessary infrastructure required for a vaccination service, including information on how to safely store vaccines, the types of refrigerators that can be used, recommendations on effective vaccine storage, and which monitors should be used to maintain the cold chain. Maintaining the cold chain off-site, how to pack vaccine storage coolers and the steps to take in the event of a power outage are also covered.

Poor storage practices can result in vaccines being made partially or completely ineffective. Clinicians are advised to adhere to the following guidelines to ensure vaccines are stored effectively for optimal performance:

- Vaccines ideally should be stored in a purpose-built vaccine refrigerator (see following section).
- An appropriate member of the staff needs to be responsible for the management of vaccines.
- Clear procedures and protocols are essential for the management of vaccines.
- Vaccine refrigerator temperatures need to be monitored twice a day.
- Plans must be in place to respond to cold chain breaches and power failures.
- Temperature failures outside of the +2 °C to+8 °C have to be reported to the state or territory health department or the supplier/manufacturer of privately purchased vaccines.

Purpose-Built Refrigerators

Storing vaccines in a purpose-built refrigerator rather than a domestic type is preferable for a number of reasons. These include it being:

- Easier to manage
- Specifically designed to store vaccines at the optimum temperature range
- Equipped with an alarm that alerts to temperature fluctuations

Some models have inbuilt data loggers/monitors so nearly the entire internal space can be used for the storage of vaccines.

In Australia, vaccine refrigerators can be purchased through medical equipment wholesalers or directly through medical refrigeration manufacturers such as Quirks

(quirksaustralia.com.au/medisafe-vaccine-fridges.html) or Rollex Medical (www.rollexmedical.com.au).

If a domestic refrigerator is to be used for vaccine storage, a bar or cyclic defrost refrigerator should not be considered due to the significant temperature changes which occur within these refrigerators. Refer to the *Strive for 5* national vaccine storage guidelines for further information on how to store and monitor vaccines using a domestic refrigerator or access the advice online.

Different Types of Monitors

In order to be alerted to cold chain breaches, it is important to record minimum/maximum temperatures on a temperature chart – even if a fridge monitor is being used.

Data Loggers

Data loggers are small electronic devices fitted with an alarm which can be set to measure temperatures in cold storage units at preset time intervals and record the results over a period of time. They are preprogrammed via a computer and placed in the refrigerator near the temperature probe or vaccines. The device will continue to record on its own battery until the collected data is downloaded to the computer. This needs to be undertaken weekly. Some refrigerators contain inbuilt data loggers. Twice daily minimum/maximum temperatures must still be recorded manually in order to alert clinicians/staff to any breach in the cold chain.

Thermometers

The use of a minimum/maximum digital thermometer is essential for temperature monitoring in domestic refrigerators, during power failures and off-site or community/school vaccination programmes.

It is important to use a minimum/maximum thermometer even if using a purpose-built vaccine refrigerator as some types do not have a battery back-up for their temperature monitoring system.

Thermometers will need to be reset every time the temperature is recorded on a graph or in a logbook. They should also be checked annually to ensure that they are functioning properly and for faulty or damaged probes and cables which can affect measurements. Batteries should be checked regularly and changed every 12 months.

It is further recommended to check the accuracy of every thermometer after the battery is changed, at least every 12 months, and following a cold chain problem.

The *Strive for 5* national vaccine storage guidelines outline how to check the accuracy of a thermometer. The guidelines can also be accessed online at www.health.gov.au/internet/immunise/publishing.nsf/Content/IMM77-cnt.

Vaccine fridge thermometers can be purchased online through a private company, ENLAKE
(www.enlake.com.au/min-max-thermometers/).

Vaccine fridge temperature charts can be ordered online through the Australian Department of Health Immunise Australia website at www.immunise.health.gov.au/.

Cold Chain Monitors

All vaccine deliveries come with a cold chain monitor (CCM) which indicates if there has been a cold chain breach during delivery.

If the CCM indicates a breach, it is important to immediately isolate these vaccines in the refrigerator and to contact the relevant state or territory health department or vaccine supplier in the case of private vaccines for further advice.

Consent

Before a vaccine is administered, the recipient's consent must be obtained and documented or scanned into their medical records in the case of paperless medical records.

In order for a person to be able to give consent, they must be provided with information pertaining to the procedure and any potential risks and benefits associated with specific vaccines. Furthermore, they must be advised of potential adverse events, how common these are and what can be done to minimise any possible side effects.

There are various resources available to healthcare professionals for providing further information and advice to patients on the risks and benefits of vaccination. These include the summary table 'Comparison of the effects of diseases and the side effects of National Immunisation Program (NIP) vaccines' on the inside back cover of the current Immunisation Handbook as well as the booklet *Understanding Childhood Immunisation,* which can be accessed online at the National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases (NCIRS) website at www.ncirs.edu.au/. Here, consumers can access fact sheets related to specific vaccines and diseases.

Consent is preferably obtained in a written format for it to be legally valid, and it needs to be given:

- By a person with the legal capacity and satisfactory intellectual capacity to comprehend the implications of being vaccinated
- Voluntarily and without excessive pressure, force or manipulation

- Particular to the procedure that is being performed
- Only after the possible risks and benefits for the relevant vaccine, the risks of not having it and any alternate options have been explained

It is imperative that travel healthcare professionals give the intending traveller sufficient opportunity to seek clarification about the vaccine/s and how it is/they are administered. The information should be provided in a language understood by the individual. Otherwise, an interpreter or support person will need to be involved.

Moreover, it is crucial to ensure that there are no medical or other contraindications prior to giving the vaccine/s. Further information on how to obtain consent can be sought from local state or territory health authorities. See Table 17.1 in 'Vaccine practices' above for contact details.

Consent for Children or Adolescents

The authority to give consent on behalf of a child as a parent/guardian varies with the different state/territory authorities, and it is important to check if any doubt exists. In general, an individual is considered a child if under the age of 18 years in Tasmania, Victoria and Western Australia, under the age of 14 years in NSW and under the age of 16 years in the Australian Capital Territory, South Australia and the Northern Territory. Queensland adheres to common law principles.

If a child or an adolescent refuses a vaccination for which a parent/guardian has given consent, then the child or adolescent's requests should be respected and the parent/guardian informed accordingly.

Consent on Behalf of an Adult Lacking the Intellectual Ability

In order to obtain consent for an adult whose capacity to give consent is impaired, practitioners should refer to the relevant state/territory legislation regarding enduring guardianship for further guidance and advice.

School-Based Vaccination Programmes and Consent

As with consent for children and adolescents above, consent for school vaccination or other community-based programmes needs to be obtained prior to administering vaccines. If for some reason written consent cannot be attained prior to the day of vaccination, verbal consent can be given by the parent or guardian over the phone. This needs to be clearly documented on the child or adolescent's consent form.

Consent for Off-Site Vaccinations

The procedure for obtaining consent off-site will be discussed below.

Postvaccination Practices

Adverse Event Reporting

All immunisation providers must report adverse events following immunisation (AEFI) in order to identify any vaccine safety issues as soon as possible. Anyone is able to report an adverse event, including the individual receiving the vaccine or a provider who did not administer the vaccine.

In most states and territories in Australia, AEFI need to be reported directly to the relevant state/territory health authority (ACT, NSW, NT, QLD, SA, VIC and WA); these are then forwarded onto the Therapeutic Goods Administration (TGA) who manages the Adverse Drug Reactions System (ADRS) database. AEFI can also be reported directly to the TGA using the 'blue card' adverse reaction reporting form available from the TGA or online at www.tga.gov.au/safety/problem-medicines-forms-bluecard.htm, or they can be completed and submitted online on the TGA website at www.ebs.tga.gov.au/ebs/ADRS/ADRSRepo.nsf?OpenDatabase.

Furthermore, immunisation providers must advise these individuals on how to manage future vaccinations, including referring them to experts, such as specialist immunisation clinics.

Documentation

Australian Childhood Immunisation Register (ACIR)

Details of all vaccines administered must be documented in the individual's medical records and in the case of children, in their state/territory child health record. The record should include type of vaccine, dose, site of administration, batch number, date of expiry and a boosting reminder if required.

The ACIR is a national database established in 1996 to record the details of vaccinations given to children under the age of 7 years. This register is used to measure vaccination coverage nationally, as well as at state/territory and local levels, and for determining whether families are entitled to tax benefit supplements (that are only payable if a child is fully immunised or has an approved exemption). It is for these

reasons that immunisation providers must report all vaccination encounters promptly. Data can be sent electronically via Medicare online, the ACIR secure Internet site or official vouchers (except for QLD and the NT where the information is submitted directly to their state/territory health departments).

In the case of medical contraindications to vaccines or 'conscientious objectors', forms are also forwarded to the ACIR. Immunisation history statements are available from the ACIR including details of those vaccines administered and when they are next due.

National Human Papillomavirus (HPV) Vaccination Program Register

This national register details HPV vaccinations given in the community by immunisation providers. Details are submitted electronically, via data uploads or direct entry using the secure website, except for QLD and the NT where records are submitted to their state/territory health department. In order to submit vaccination information electronically or in hard copy, general practitioners must be registered with the HPV Register.

The HPV Register is also used to provide immunisation providers with details of missed or overdue vaccines for their patients.

Other Immunisation Registers in Australia

Q Fever Register

The Meat and Livestock Australia (MLA) established the Q Fever Register to keep individual records of vaccinations for its workers who are occupationally exposed to *Coxiella burnetii* bacteria.

School-Based Vaccination Records

Records of all vaccines administered through school-based vaccination programmes are kept by state/territory health departments.

Queensland health authorities maintain a database for vaccines administered to children up to the age of 10 years, adolescents and some adults through the Vaccine Information and Vaccination Administration System (VIVAS).

In the NT, an immunisation register records details of all vaccines administered in the territory.

Table 17.2 State and territory drugs and poisons legislation

ACT	*Medicines, Poisons and Therapeutic Goods Act 2008.* At: http://www.legislation.act.gov.au/a/2008-26/default.asp
	Medicines, Poisons and Therapeutic Goods Regulation 2008. At: http://www.legislation.act.gov.au/sl/2008-42/default.asp
NSW	*Poisons and Therapeutic Goods Act 1966.* At: http://www.legislation.nsw.gov.au/maintop/view/inforce/act+31+1966+cd+0+N
	Poisons and Therapeutic Goods Regulation 2008. At: http://www.legislation.nsw.gov.au/fullhtml/inforce/subordleg+392+2008+FIRST+0+N
NT	*Poisons and Therapeutic Goods Act 2014.* At: http://www.health.nt.gov.au/Environmental_Health/Poisons_Control/index.aspx
	Poisons and Dangerous Drugs Regulations. At: http://notes.nt.gov.au/dcm/legislat/legislat.nsf/linkreference/medicines, poisons and therapeutic goods regulations?opendocument
QLD	*Health Act 1937.* At: https://www.legislation.qld.gov.au/LEGISLTN/CURRENT/H/HealA37.pdf
	Health (Drugs and Poisons) Regulations 1996. At: http://www.legislation.qld.gov.au/LEGISLTN/CURRENT/H/HealDrAPoR96.pdf
SA	*Controlled Substances Act 1984.* At: http://www.legislation.sa.gov.au/lz/c/a/controlled substances act 1984.aspx
	Controlled Substances (Poisons) Regulations 2011. At: http://www.legislation.sa.gov.au/LZ/C/R/CONTROLLED%20SUBSTANCES%20(POISONS)%20REGULATIONS%202011/CURRENT/2011.140.UN.PDF
TAS	*Poisons Act 1971.* At: http://www.thelaw.tas.gov.au/tocview/index.w3p;cond=all;doc_id=81++1971+AT@EN+20050124000000
	Poisons Regulations 2008. At: http://www.austlii.edu.au/au/legis/tas/consol_reg/pr2008230/
VIC	*Drugs, Poisons and Controlled Substances Act 1981.* At: http://www.austlii.edu.au/au/legis/vic/consol_act/dpacsa1981422/
	Drugs, Poisons and Controlled Substances Regulations 2006. At: http://www.austlii.edu.au/au/legis/vic/consol_reg/dpacsr2006531/
WA	*Poisons Act 1964.* At: www.austlii.edu.au/au/legis/wa/consol_act/pa1964121/
	Poisons Regulations 1965. At: http://www.austlii.edu.au/au/legis/wa/consol_reg/pr1965230/

Off-Site Vaccine Administration

There are particular legislative requirements governing the administration of drugs and poisons in the different states/territories of Australia. A poison is defined as any substance that is included in the Schedules of the Poisons Act (see Table 17.2 below for the different drug and poison legislations). In some states and territories, organisations must be in possession of a poisons' license or permit to be able to purchase, distribute or use schedule 2, 3, 4, 7 or 8 poisons, such as vaccines.

In Australia, authorised immunisers are either registered medical practitioners or appropriately qualified, competent and authorised registered nurses. Registered

medical practitioners and registered nurses are listed in the Australian Health Practitioner Regulation Agency (AHPRA) register and need to provide proof of indemnity insurance.

Registered nurses (nurse immunisers) who have completed an approved study programme, who hold a current statement of proficiency in cardiopulmonary resuscitation and who are currently listed as registered by APHRA are permitted under state/territory legislation to administer specified vaccines under defined conditions within the state or territory where the study was undertaken (if they move interstate, further training must be undertaken or approval obtained through 'recognition of prior learning'). The vaccine/s must be administered as part of an immunisation programme, delivered by an approved organisation and in accordance with the current Australian Immunisation Handbook guidelines.

In some states/territories, nurses are able to administer vaccines without a medical order in accordance with the authorisation above; in others, medical approval of completed consent forms or a standing order is required. There is no endorsement for nurse immunisers on the Nursing and Midwifery Board of Australia's National Register of Practitioners.

If healthcare organisations wish to use a nurse immuniser to provide vaccinations in the workplace (such as influenza, hepatitis A and B, tetanus, diphtheria and whooping cough), they must contact the relevant state and territory department for further information. Organisations must not proceed with administering vaccines without satisfying these legislative requirements.

Policy and Procedures

Healthcare organisations need to develop a policy and procedure manual for immunisation services off-site in partnership with the service provider, a registered medical practitioner and an authorised nurse immuniser and, in some states, a pharmacist.

The manual must include:

- A checklist or flow chart of the equipment, documentation, medical consumables and anaphylaxis kit required to go off-site
- A clearly defined description of the roles and responsibilities of everyone involved in the service
- Guidelines and procedures for the set-up and care of the consultation area on-site, including screening of employees (consent), furniture needed, equipment for storing and administering vaccines, information pamphlets on vaccines to be administered as well as possible side effects
- A process for sharps and medical waste disposal
- A vaccine management policy for safeguarding cold chain, including transportation, storage while off-site and monitoring requirements

- A protocol for responding to medical emergencies following the administration of vaccines, including the management of anaphylaxis and the roles and responsibilities of authorised immunisers in this scenario
- Contact details for the on-call medical practitioner who needs to be contactable during periods when immunisations are being administered, if required by state or territory legislation
- Protocols with reference to needlestick injury, exposure to blood and bodily fluids, including a process for postexposure prophylaxis, as well as documents for incident and investigation reporting
- A policy for documentation and storage of employee records ensuring confidentiality is maintained
- A policy for reporting adverse events to the vaccine, as per the Immunisation Handbook direct to the Therapeutic Goods Administration (TGA) or as mandated by the relevant state or territory departments

How to Pack a Cooler for Off-Site Vaccinations

While transporting vaccines off-site, they need to continue to be stored between +2 °C and + 8 °C as per the national vaccine storage guidelines, *Strive for 5*. They can be stored in a small insulated container such as an Esky® or similar, which contains an ice/gel pack. In order to maintain the temperature inside, it must be solid-walled with a tight-fitting lid. Vaccine temperature monitoring should occur using a minimum/ maximum thermometer with the probe placed into the cooler.

When using a cooler as per the national vaccine storage guidelines, *Strive for 5*:

- Vaccines need to remain in their original packaging and must not come in contact with the ice or gel to minimise the risk of freezing.
- The cooler needs to be pre-chilled before use.
- Vaccines need to be insulated using shredded paper, polystyrene chips or other such insulation materials.
- Temperature must be monitored hourly.
- Contents need to be packed securely.
- Vaccines must be kept out of direct sunlight.
- Vaccines should only be removed when about to be administered.
- Ice/gel packs should be 'conditioned'* before use as their temperature when removed from the freezer can be as low as −18 °C.

*Ice packs are to be removed from the freezer and should be laid out in rows leaving 5 cm in between until they begin to 'sweat', which will take up to 1 h. They are considered to be conditioned as soon as water begins to 'slosh' inside the ice pack. Gel packs usually take longer.

The national vaccine storage guidelines *Strive for 5* have images on how to pack a cooler.

Further Reading

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Chapter 18
New Zealand Immunisation Practice

Claire Wong

Key Points
- A knowledge of immunisation procedures in the country of practice is essential.
- Travel health professionals need to ensure they have appropriate training.
- Required protocols for practice should be in place, reviewed and updated as appropriate.

Introduction

Clinical guidance on the administration of vaccines in New Zealand is provided by the Ministry of Health and published in the *Immunisation Handbook*. Although the specific guidance relates to the publicly funded vaccines that form part of the National Immunisation Schedule (the Schedule) and targeted programmes, the immunisation standards relate equally to travel vaccinations.

Vaccines administered as part of the Schedule, and those that form targeted vaccination programmes for specific groups, are funded and effectively free of charge. Funding is provided by each District Health Board. There is no funding for travel vaccines in New Zealand which are administered in general practice, or at specialist centres.

Currently there are no national guidelines for the administration of travel vaccines in New Zealand, with the exception of yellow fever.

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Vaccine Administration

Vaccines in New Zealand can only be administered by medical practitioners, registered midwives, designated prescribers or practitioners authorised to do so in accordance with a standing order. Registered nurses, and to some degree pharmacists, having attended a vaccinator training course and gaining Independent Vaccinator status, can administer vaccines without a prescription or standing order as part of an approved immunisation programme. This includes the Schedule vaccines, but not necessarily travel vaccines. Travel vaccines may be approved as an immunisation programme by a Medical Officer of Health; however, this is at the discretion of each individual District Health Board and not at a national level.

For Independent Vaccinators practising in districts where travel vaccines are not part of an approved programme, these vaccines must be administered under a standing order. A standing order allows non-prescribers, including nurses, to administer vaccines to a defined group, for example, travellers. Guidelines for writing standing orders are published by the Ministry of Health.

Applying to be an Independent Vaccinator involves attending an approved training course, passing a written exam and undergoing a clinical assessment. This initial approval is valid for 2 years after which attendance of an update course and self-assessment of vaccination practice is required.

Further information on the Independent Vaccinator authorisation process is available in Appendix 4 of the *Immunisation Handbook*: www.health.govt.nz/publication/immunisation-handbook-2014.

Specific Vaccine Policies

Approval of Yellow Fever Vaccination Centres and Vaccinators

Administration of yellow fever vaccine, provision of International Certificates of Vaccination or Prophylaxis and letters of medical exemption are responsibilities devolved by the World Health Organization to national health authorities. In New Zealand, the Ministry of Health holds this responsibility and requires practitioners to apply for Yellow Fever Vaccinator (YFV) approval, as well as Yellow Fever Vaccination Centre (YFVC) approval.

Applications are initially made through the local Medical Officer for Health for the health district the practitioner is in practice and the medical centre is located. If the Medical Officer for Health recommends approval, the application is forwarded to the Ministry of Health which decides whether to grant approval.

The Ministry of Health has stipulated conditions for approval as a YFV which must be met prior to application. These conditions include:

- New Zealand registered medical practitioner
- Must hold a postgraduate qualification in travel medicine

- The demonstration of continuing medical education in travel medicine and specific education in yellow fever

Approval as both a YFV and YFVC is renewable every 3 years, and a record of all vaccines administered and medical exemptions issued must be maintained. Yellow fever vaccine can only be ordered by approved YFV and YFVC.

Although YFV approval is limited to medical practitioners, the responsibility for administering the vaccine can be delegated to a nurse on the provision that the doctor conducts the consultation and prescribes the vaccine.

Further information on the requirements for YFVC and YFV approval can be found on the Ministry of Health website: www.health.govt.nz/our-work/diseases-and-conditions/yellow-fever

BCG Vaccination

Under the Tuberculosis Regulations 1951, BCG vaccine can only be administered in New Zealand by gazetted BCG vaccinators. The majority of BCG vaccines are administered by Public Health Nurses to babies considered at high risk of exposure, but occasionally the vaccine is given for international travel. In order to be added to the BCG gazette, a practitioner must undergo a period of supervised practice in placing and reading Mantoux tests and administering BCG vaccines. Application is then made via the Director General of Health.

Other Specialist Vaccines

Vaccines which are unregistered in New Zealand include Q fever and tick-borne encephalitis.

Q fever vaccine is given at specialist centres for those at occupational risk. Such individuals are required to undergo Q fever serology and skin testing prior to vaccination and receive counselling on potential adverse events as well as advice on other protective measures.

Supplies of unregistered vaccines can be arranged by the vaccine manufacturer under Section 29 of the Medicines Act 1981.

There are a number of immunoglobulin products available in New Zealand including specific preparations for tetanus, hepatitis B, varicella and rabies. These are accessed via the New Zealand Blood Service which operates a 24 hour on-call service for medical advice.

Rabies immunoglobulin is the most commonly used preparation in a travel health setting. Travellers requiring this must be referred to a specialist centre as it is imperative that as much as possible of the recommended dose is infiltrated into the wound.

Rabies immunoglobulin is available free of charge to New Zealand citizens and permanent residents; however, postexposure rabies vaccines are not funded. Travel insurance policies may cover these costs but increasingly are declining claims as

only treatment received overseas is covered. In these circumstances, the Accident Compensation Corporation (ACC) may make some financial contribution towards the cost of rabies vaccines and other treatment as the result of the exposure.

Pre-vaccination Preparations

Anaphylaxis Kit

All vaccinators must ensure they are prepared and trained to recognise and treat anaphylaxis. Life support training is required every 2 years for vaccinators at a standard equivalent to that of New Zealand Resuscitation Council (NZRC) Rescuer Level 4.

Every room where vaccinations are given needs an emergency kit containing:

- Adrenaline 1: 1,000, three ampoules plus dosing chart
- Syringes: 1.0 ml × 3 (not insulin syringes)
- Needles: a range of lengths and gauges
- Airways: a range of sizes, including paediatric sizes if vaccinating children

Also available in the clinic should be:

- Oxygen, tubing and a range of masks
- A bag valve mask resuscitator (Ambu bag)
- Access to a telephone

Optional equipment includes:

- Intravenous fluids
- Hydrocortisone injection
- Antihistamine injection
- Sodium bicarbonate solution

Further specific guidance on anaphylaxis is available in Chapter 2 of the *Immunisation Handbook,* available online at: www.health.govt.nz/publication/immunisation-handbook-2014

Vaccine Storage

All vaccines are stored between a temperature of +2 °C to +8 °C, and the cold chain ensures that vaccines are maintained at this temperature range from the place of manufacturer to the point of vaccine administration. Privately funded vaccines, including travel vaccines, are distributed to immunisation providers by Healthcare Logistics who store vaccines according to manufacturer's specifications.

The *Immunisation Handbook*, the *National Guidelines for Vaccine Storage and Distribution* and the *Annual Cold Chain Management Guide and Record* set the standards for ensuring vaccines delivered within New Zealand are stored correctly.

All practices are required to demonstrate their cold chain management through self-assessment and review by an approved Cold Chain Accreditation (CCA) reviewer. CCA is currently valid for 3 years.

In order to meet the cold chain requirements, each immunisation provider must have a written policy detailing the action to be taken in the event of a power failure and a designated staff member responsible for cold chain issues. The cold chain policy must be dated and reviewed on an annual basis.

Vaccine Refrigerator

The Medicines Act 1981 requires all vaccines to be stored in a pharmaceutical fridge placed in a reasonably sized well-ventilated room against an internal wall. There are other parameters too:

- Food must never be stored in the vaccine fridge.
- Vaccine preparation must not take place on surfaces used for food storage or consumption.
- The fridge should not be over stocked – there should be enough room within the fridge for air to circulate around the vaccines. Door seals must be in good condition and an engineer should check the fridge function annually.
- Insulated containers and ice packs must be available for vaccine storage or transport in the event of a power failure.

Guidelines on the preparation of insulated boxes including the placement of ice packs and packaging material is provided in the *National Guidelines for Vaccine Storage and Distribution.* When packed correctly, vaccines can be maintained at a temperature of +2 °C to 8 °C for up to 5 hours in an insulated box.

Vaccine Refrigerator Monitoring

Vaccine fridges must be fitted with an electronic temperature recording device (e.g. data logger or temperature logger) in order to meet the requirement of CCA. The device measures the current temperature and the minimum and maximum temperatures reached since the device was last reset. It should also be able to record and download temperature data from the previous month.

It is still a requirement to record the minimum and maximum temperatures at least daily on a temperature recording chart, such as the one provided in the *Annual Cold Chain Management Guide*. Temperature charts are required to be kept for 10 years under the Health (Retention of Health Information) Regulations 1996.

Each district of New Zealand has an immunisation coordinator who is the first point of contact for guidance on vaccine storage and cold chain issues. Contact details of immunisation coordinators can be found on the Immunisation Advisory Centre (IMAC) website: www.immune.org.nz/education-and-training

Informed Consent

Informed consent is a fundamental part of immunisation practice in New Zealand and is based on ethical obligations supported by legal provisions such as the Health and Disability Act 1994, the Code of Health and Disability Services Consumer's Rights 1996 and the Health Information Privacy Act 1993.

The informed consent process is regarded as having three elements:

1. The right to effective communication
2. The right to be fully informed
3. The right to make an informed choice and therefore give informed consent

Health professionals have a legal obligation to obtain informed consent prior to any procedure, including immunisation.

In a travel health setting, a fundamental aspect of the pretravel health consultation and risk assessment includes discussion of potential adverse events and the risks of not being vaccinated. There is no obligation to seek written consent but is considered good practice to document that consent was obtained. Attending for immunisations does not imply consent – the individual has the right to withdraw consent at any time, so it is advisable to obtain consent prior to administering each vaccine dose.

Consent requirements are different in mass immunisation campaigns, such as schools. Immunisation information must be provided to parents or guardians of children before proceeding with immunisation. Written consent is required prior to immunising children under 16 years of age in a school setting.

In New Zealand, there is no particular age at which all children are regarded as being able to give their consent. Although there is a presumption that consent is required from parents/guardians on behalf of children under 16 years of age, this is inconsistent with common law.

A child under 16 years of age has the right to give consent providing they understand fully the risks and benefits.

Vaccine Administration

Needlestick Injuries

Reduce the risk of needlestick injuries occurring by making sure the sharps container is easily accessible, disposing sharps immediately after vaccine administrations, and not removing needles from syringes prior to disposal.

The risk of blood-borne virus transmission following needlestick injury is low; however, all vaccinators should be immunised against hepatitis B and each practice should have a policy for dealing with needlestick injury.

In summary:

- Wounds must be washed immediately with soap and water.
  The incident reported to the manager or medical advisor.
- Blood drawn from the vaccinator within a few days to test for hepatitis B and C and HIV.
- Serology arranged from the source individual.
- Depending on circumstances, it may be appropriate to start postexposure HIV medications and/or hepatitis B immunoglobulin.

Further specific guidance on the action to be taken in the event of a needlestick injury is available in Appendix 7 of the *Immunisation Handbook:* www.health.govt.nz/publication/immunisation-handbook-2014.

Postvaccination Practices

Vaccine Disposal

Disposal of vaccines (e.g. expired stock or those subjected to a breach in cold chain) is arranged through ProPharma for any funded vaccines and Healthcare Logistics in the case of privately funded travel vaccines.

Quarantine vaccines awaiting disposal in an appropriate container and mark them clearly with a 'Vaccines for Destruction' label together with the reason for disposal. Contact ProPharma or Healthcare Logistics to arrange return.

Adverse Event Reporting

New Zealand health professionals are considered to have a professional and ethical responsibility to report any unexpected adverse events following immunisation (AEFI). Adverse event reporting is part of the immunisation procedure, and as such the informed consent process should also include the reporting of adverse events.

Adverse event reporting is managed nationally by the Centre for Adverse Reactions Monitoring (CARM). Some practice management systems allow the reporting of adverse events directly to CARM. Otherwise reports can be completed online or by post using the form provided on the CARM website. Although CARM prefers reports to be made by health professionals, consumers are also able to report adverse events.

Example of adverse events to be reported to CARM can be found in Chap. 2 of the *Immunisation Handbook*: www.health.govt.nz/publication/immunisation-handbook-2014.

Documentation

National Immunisation Register

Since 2005, immunisation information has been recorded for New Zealand children on the National Immunisation Register (NIR). The NIR is a national, computerised system which facilitates immunisation delivery and provides a record of an individual's immunisation history. In 2014 the system began recording some adult immunisation information.

The NIR includes information on the New Zealand Schedule vaccinations, human papilloma virus (HPV) immunisations and some targeted programmes such as BCG, pneumococcal, meningococcal and influenza vaccines, but not travel vaccinations.

Authorised health personnel including GPs and vaccinators using an electronic patient management system are able to access the NIR through and enter immunisation information directly. For other practices, a paper-based system is used.

School-Based Vaccination System

The School-Based Vaccination System (SBVS) collects and manages data on vaccines given as part of a school immunisation programme, e.g. the year 7 and 8 vaccines. This data is then transferred to the NIR.

Clinical Notes

Keeping timely and accurate patient records is part of the vaccination process and ensures there is a record of the encounter in the case of legal scrutiny.

Confirmation of the following is required in the clinical notes:

- Informed consent obtained.
- The individual observed for 20 min following vaccination.
- No adverse events occurred.

If an adverse event does occur, action taken is to be documented and the event reported to CARM.

Schedule vaccines are then recorded in the child's *Well Child Tamariki Ora Health Book* ('Plunket Book'). For travellers it is good practice to provide a personal vaccination record; the Government printers provide free vaccine record books, and many travel medicine clinics and vaccine manufacturers produce their own vaccine record books and provide them to vaccinators.

It is a legal requirement for yellow fever vaccination to be recorded on an International Certificate of Vaccination or Prophylaxis, provided by the Ministry

of Health and distributed by Wickliffe to approved Yellow Fever Vaccination Centres.

Off-Site Vaccinations

In order to administer vaccines off-site, application must be made for approval of an immunisation programme via the Medical Officer for Health at the District Health Board's public health unit.

Consideration of the following must be made, and supporting documentation provided where required:

- Staff: At least two people must be present for an off-site programme, one of whom must be an Independent Vaccinator. The other must be a competent adult who is able to summon help and provide support in the event of an emergency.
- Location: Thought must be given to the venue to ensure it provides privacy, a resting place and a waiting space.
- Equipment: Emergency equipment including adrenaline, oxygen, adult and paediatric masks and airways must be available together with access to a telephone or cell phone.
- Documentation: Processes for pre- and postvaccination information to be provided for patients together with the recording of vaccines administered must be in place.

A checklist detailing the specific requirements and supporting documentation for an immunisation service is available in appendix 4.4 of the *Immunisation Handbook:* www.health.govt.nz/publication/immunisation-handbook-2014.

Application forms for approval of an off-site immunisation programme are available from the public health unit of the District Health Board.

Further Reading

General Immunisation Practices

1. Immunisation Handbook. 2014. Available at: www.health.govt.nz/publication/immunisation-handbook-2014. Accessed 15 Dec 2014.
2. Immunisation Advisory Centre for health professionals. Available at: www.immune.org.nz/health-professionals/vaccine-administration. Accessed 19 Dec 2014.
3. Immunisation Advisory Centre: Successful strategies towards best practice for svaccination. Available at: www.immune.org.nz/sites/default/files/resources/SuccessfulStrategiesBestPracticeforVaccination25014%20FINAL.pdf. Accessed 19 Dec 2014.
4. Ministry of Health Standing Order guidelines. Available at: www.health.govt.nz/publication/standing-order-guidelines. Accessed 19 Dec 2014.
5. ProPharma. Available at: www.fundedvaccines.co.nz. Accessed 19 Dec 2014.
6. Healthcare Logistics. Available at: www.hconline.co.nz. Accessed 19 Dec 2014.

Specific Vaccine Policies

7. Ministry of Health Requirements for approval as a Yellow Fever Vaccination Centre and a Yellow Fever Vaccinator. www.health.govt.nz/our-work/diseases-and-conditions/yellow-fever.
8. New Zealand Blood Service. www.nzblood.co.nz.
9. Tuberculosis Regulations. www.legislation.govt.nz/regulation/public/1951/0290/7.0/whole.html.

Vaccine Storage

10. Annual Cold Chain Management Guide and Record. www.health.govt.nz/publication/annual-cold-chain-management-guide-and-record.
11. National Guidelines for Vaccine Storage and Distribution. www.health.govt.nz/publication/national-guidelines-vaccine-storage-and-distribution-2012.

Adverse Event Reporting

12. Centre for Adverse Event Monitoring (CARM). https://nzphvc.otago.ac.nz/carm/.

Needle Stick Injuries

13. Starship Hospital Needlestick injuries guidelines. http://adhb.govt.nz/starshipclinicalguidelines/Needlestick%20Injuries.htm.

Chapter 19
Singaporean Immunisation Practice

Poh-Lian Lim and Smriti Pathak

Key Points
- Singapore has a good, comprehensive national childhood vaccination system.
- A wide range of travel vaccinations are available in Singapore, including yellow fever, rabies, meningococcal, Japanese encephalitis vaccines.
- High standards exist in Singapore for vaccine supply and administration, including good cold chain management.

Vaccination Policy in Singapore

Vaccinations in Singapore are considered prescription-only medications (POM) and can only be administered by registered medical practitioners or by registered nurses working under the direction of medical practitioners. This can be done through authorised medically approved protocols and standing orders. Registered nurses can attend vaccination training courses with regular follow-up competency assessments.

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This allows them to administer vaccinations to defined low-risk groups of patients according to approved protocols.

Clinical guidance regarding immunisation recommendations is provided by the Ministry of Health Singapore (MOH) through regular circulars to medical doctors, hospitals and clinics. The Expert Committee on Immunization (ECI) comprising adult and paediatric experts, travel medicine practitioners and other stakeholders advises MOH on routine and travel-related vaccination policy and practices.

The Health Promotion Board (HPB) is the government agency that works closely with MOH to implement immunisations through the School Health Service. HPB also maintains the National Immunization Registry (NIR) and conducts public education campaigns and other targeted initiatives. The NIR is a computerised database of patient vaccination records. Uploading patient vaccine records by providers is done voluntarily and is not mandated. The NIR is fairly complete and reliable for childhood and adolescent immunisations, but NIR records for adult vaccines are incomplete and patchy.

National Childhood Immunisation Schedule

The National Childhood Immunisation Schedule (NCIS) is provided by the MOH. Infant immunisations are provided through a network of publicly funded polyclinics and private general practitioners (GPs) and paediatricians. Vaccines are subsidised and the use of Medisave is permitted for specific vaccines in the NCIS. Medisave is a medical savings programme within the Central Provident Fund (CPF) which is administered by the Singapore government. Every Singaporean citizen and permanent resident who works is required to contribute to CPF through automatic payroll deductions, with the employer providing matching funds. CPF savings go towards retirement, purchase of a first home and medical expenses.

Childhood vaccines are recorded in each child's health booklet. Polyclinics and private doctors upload their patients' vaccine records onto the NIR.

Immunisations from Birth to 6 Years

Bacille Calmette-Guerin (BCG) vaccine is given at birth, together with the first dose of hepatitis B vaccine, with a second dose of hepatitis B at 1 month of age. Tetanus, diphtheria, pertussis, polio and *Haemophilus influenzae* B vaccine are typically given at ages 3–5 months. Pneumococcal conjugate vaccine (PCV) is administered at 3, 5 and 12 months of age.

The first dose of measles, mumps and rubella (MMR) vaccine is given at 12 months of age. One of the differences in the Singapore schedule is that the second dose of MMR is given relatively early at age 15–18 months.

Measles and diphtheria vaccination are compulsory for all Singaporean children by law. Varicella and rotavirus vaccines are considered optional and are not included in the NCIS, but are routinely available and used.

School and Adolescent Immunisations

Children are required to show vaccination records to register for school in Singapore. During the primary school years (ages 6–12 years), the HPB provides immunisations through the School Health Service. School Health Service nurses make regular visits to schools to check vaccine records and conduct catch-up immunisations for students.

The second booster doses for tetanus, diphtheria, pertussis (Tdap) and polio are routinely administered at age 10–11 years (Primary 5). Human papillomavirus (HPV) vaccination is recommended for females aged 9–26 years, and the cost of HPV vaccine can be covered using Medisave.

All males who are Singaporean citizens and second-generation permanent residents are required to do National Service (NS) at approximately 18 years of age. All NS men will generally receive a tetanus-diphtheria (Td) and oral polio vaccine (OPV) booster at age 18 years.

Adult Immunisations

MOH provides vaccine recommendations for adults with medical co-morbidities and older individuals (over 65 years of age) to receive influenza and pneumococcal vaccine through regular circulars. MOH also recommends HPV vaccination for females 9–26 years of age.

Travel Immunisations

MOH makes vaccination recommendations for Singaporean Muslim pilgrims travelling for the Hajj and Umrah pilgrimages in Saudi Arabia. These generally include meningococcal vaccine and influenza and pneumococcal vaccine if indicated, due to medical co-morbidities or age.

Singapore also requires yellow fever vaccination for travellers going to and coming from countries with yellow fever (YF) transmission. Yellow fever vaccinations can only be administered in approved YF vaccination centres, which are also authorised to issue YF vaccination certificates and waivers on the basis of medical exemptions. Consistent with other routine and travel vaccines, yellow fever vaccination is limited to medical practitioners and nurses working according to standing-order protocols.

Clinic Vaccination Policies and Procedures

Vaccine Storage

Maintaining the cold chain from manufacture to vaccine administration is an integral part of providing effective vaccination. All vaccines must be stored correctly at the temperature ranges recommended by the manufacturer. For refrigerated vaccines, this temperature range is generally +2 to +8 °C.

Clinics should have a written policy in place to address disruptions in the cold chain due to failures in power supply or equipment. Designated clinic staff should be responsible for monitoring and responding to cold chain incidents.

Vaccine Refrigerator

Vaccines should be stored in a pharmaceutical fridge, fitted with an electronic temperature recording device, to monitor minimum and maximum temperatures. Fridge temperature records should be checked daily by clinic staff.

It is given that refrigerators used for medications and vaccines should never be used to store food. Ice packs and insulated containers need to be available to maintain temperatures for off-site vaccination visits and in the event of a power failure.

Vaccine Supply Management

Vaccines that look alike or sound alike should be clearly marked to avoid mistakes in administration.

Vaccine supplies received should be recorded in a log with expiry dates monitored. Clinic staff should conduct regular checks of vaccine supplies, and vaccine supplies should be used on a first-in, first-out basis.

Vaccines that expire before the next check should be marked clearly for priority use before the expiry date. Expired vaccines should be quarantined promptly and removed for appropriate disposal.

Adverse Event Reporting

The Health Sciences Authority (HSA) in Singapore is the government agency which regulates registration of medications and vaccines. Medical practitioners may report adverse events associated with vaccines to HSA using the specified form.

Infection Prevention and Control with Vaccinations

Current guidelines recommend standard precautions for staff providing immunisations. These include hand hygiene (alcohol hand rub or handwashing). Gloves are not required for administering vaccinations. If bleeding occurs, contact precautions for blood and body fluids are recommended.

Good practices to minimise the risk of needle-stick injuries include:

- Not recapping needles
- Disposing of needles immediately after use
- Making sure sharps containers are accessible and not over-filled

Healthcare workers giving vaccinations should be immunised for hepatitis B, according to employee health policy for the hospital or clinic. Needle-stick injuries should be reported and managed according to infectious exposure management policy.

Informed Consent for Vaccinations

Informed consent is required for medical procedures, including vaccinations. This includes:

- Providing the patient with information about the risks of the disease
- Advising on the benefits of receiving vaccination
- Informing about the potential adverse events of the vaccine
- Providing advice on alternatives to vaccination

Informed consent can be provided verbally and needs to be documented. For children under 18 years, parental consent is generally required for vaccinations.

Specific Vaccine Issues

Rabies Post-exposure Prophylaxis

Rabies post-exposure prophylaxis (RPEP) requires the use of rabies immunoglobulin (RIG) as well as rabies vaccine for individuals not immunised before exposure. All travellers who require post-exposure prophylaxis should be evaluated by a travel medicine doctor to carefully assess history of vaccination and risk of the exposure and to prescribe the RIG and vaccine. RIG is typically given in the Emergency Department because of the need for monitoring after administration.

Travellers requiring rabies pre-exposure vaccination are also recommended to see a travel medicine doctor for the assessment of need for this vaccine.

Japanese Encephalitis Vaccine

Travellers requiring Japanese encephalitis (JE) vaccination are required to see the travel medicine doctor in Singaporean practice. This arose out of the risk of hypersensitivity reactions with the JE mouse brain vaccine (JE-MB) but has continued because of the complexities with changes in JE vaccine regimens available and for a careful assessment of risk with long-term travel.

Yellow Fever Vaccine

Travellers who require yellow fever vaccination (YFV) and who have potentially increased risk for serious adverse effects (SAE) are required to see the travel medicine doctor in our practice. Travellers who may be at increased risk of YFV-associated SAE include:

- Older individuals (>60 years of age)
- Persons who are immunocompromised due to malignancy, chemotherapy, solid organ transplant or on immunosuppressive treatment
- Persons with thymus disorders
- Pregnant women
- Infants under 9 months of age
- Individuals reporting egg allergy or hypersensitivity reactions to YFV

A careful medical and vaccination history and discussion of the proposed travel is required to assess risk for the patient. Clinical risk-benefit assessment should take into account the patient's travel plans, risk of acquiring disease as well as Singapore's public health regulations.

Further Reading

The following are useful resources for vaccination issues described above:

Ministry of Health (MOH)

Subsidies for childhood vaccines. www.moh.gov.sg/content/moh_web/home/pressRoom/Parliamentary_QA/2013/national-childhood-and-adolescent-immunisation-schedule-subsidie.html

Use of WHO approved yellow fever vaccines. www.moh.gov.sg/content/moh_web/healthprofessionalsportal/allhealthcareprofessionals/guidelines/use_of_who_approved_yellow_fever_vaccines.html

Immigration & Checkpoints Authority

Requirements for entry into Singapore (including yellow fever vaccination status). www.ica.gov.sg/page.aspx?pageid=95

Health Promotion Board (HPB)

Childhood immunisation chart based on age: www.hpb.gov.sg/HOPPortal/gamesandtools-article/3216
Immunisation for primary school. www.hpb.gov.sg/HOPPortal/health-article/630

Travellers Health & Vaccination Clinic (THVC) at Tan Tock Seng Hospital (TTSH)

Rabies post-exposure prophylaxis. www.ttsh.com.sg/patient-guide/medical-departments/page.aspx?id=831

THVC website. www.ttsh.com.sg/travellershealth/

Chapter 20
Regional Vaccinations: A Global Guide

Marc Shaw

Please Note
The following regional guide for vaccinations is a generalization of what may be required for vaccine-preventable disease travel to the region only. Each vaccination should be recommended by the travel health professional only after a full risk assessment as to its actual need for an individual traveller. It is important to note that not all vaccinations suggested in the regions will necessarily be advised or required.

Europe

Countries: Albania, Andorra, Austria, Belgium, Bosnia and Herzegovina, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Finland, France, Germany, Gibraltar, Greece, Holland, Hungary, Iceland, Ireland, Italy, Luxembourg, Macedonia, Malta, Monaco, Norway, Poland, Portugal, Romania, San Marino, Slovakia, Slovenia, Sweden, Switzerland, Spain, Turkey, United Kingdom and Yugoslavia

Vaccine	Route	No. of doses	Time to immunity	Duration of cover/ boosting
Hepatitis A	1 ml IM	2 primary series, 6–18 mths apart	80 % protection after 14 days, first vaccination	30 years – life

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Vaccine	Route	No. of doses	Time to immunity	Duration of cover/ boosting
Hepatitis B	1 ml IM	Standard series: 2–3 primary series at 0,1,6 mths, Rapid series: 0,7,21 day and 1 yr	After primaries and after booster	10+ years – life
Hepatitis A and B comb.	1 ml IM	Standard series: 2–3 primary series at 0,1,6 mths, Rapid series: 0,7,21 day and 1 yr	>80 % protection one month after first 2 vacc.	As for A and B
Rabies (pre-exposure)	0.1 ml ID	0, 7, 21/28 days	ID: 30 days after full series	5–10 years
	0.5/1 ml IM		IM: 10–14 days after full series	
Tetanus/ diphtheria	0.5 ml IM	3 vaccinations in childhood	Allow 2 weeks after booster dose	Boost @ age: 11, 45 and 65 yrs and 10 yrly, if travelling to 'at-risk' countries
Tetanus/ diphtheria/ pertussis [whooping cough]	3 vaccinations in childhood	3 vaccinations in childhood	Allow 2 weeks after booster dose	Boost @ age: 11, 45 and 65 yrs and 10 yrly, if travelling to 'at-risk' countries
Tick-borne encephalitis	0.5 ml IM	*3 doses*: day 1, 1–3 mths, 5–12 mths	50 % seroconvert after dose 1, 98 % after dose 2	3–5 years

IM intramuscular, *SC* subcutaneous, *ID* intradermal

Eastern Europe, Central Asia

Countries: Armenia, Azerbaijan, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Moldova, Russia, Tajikistan, Turkmenistan, Ukraine, Uzbekistan, Estonia, Latvia and Lithuania

Vaccine	Route	No. of doses	Time to immunity	Duration of cover/boosting
Cholera (inactivated) *(may be indicated in preventing ETEC diarrhoea)*	1 vaccine dose + 1 sach sod. Hydrog. carbonate oral	2 doses, 1 wk apart, for all over age 6 years	7 days	Approx. 3 years
Hepatitis A	1 ml IM	2 primary series, 6–18 mths apart	80 % protection after 14 days, first vaccination	30 years – life

Vaccine	Route	No. of doses	Time to immunity	Duration of cover/boosting
Hepatitis B	1 ml IM	Standard series: 2–3 primary series at 0,1,6 mths, Rapid series: 0,7,21 day and 1 yr	After primaries and after booster	10+ years – life
Hepatitis A and B comb.	1 ml IM	Standard series: 2–3 primary series at 0,1,6 mths, Rapid series: 0,7,21 day and 1 yr	>80 % protection one month after first 2 vacc.	As for A and B
Meningococcus ACYW *polysaccharide*	0.5 ml SC	One	10 days	2–3 years
Meningococcus ACYW *conjugated*	0.5 ml IM	One	14 days	5–10 years
Rabies (pre-exposure)	0.1 ml ID	0, 7, 21/28 days	ID: 30 days after full series	5–10 years
	0.5/1 ml IM	0, 7, 21/28 days	IM: 10–14 days after full series	
Tetanus/diphtheria	0.5 ml IM	3 vaccinations in childhood	Allow 2 weeks after booster dose	Boost @ age: 11, 45 and 65 yrs and 10 yrly, if travelling to 'at-risk' countries
Tetanus/diphtheria/ pertussis [whooping cough]	3 vaccinations in childhood	3 vaccinations in childhood	Allow 2 weeks after booster dose	Boost @ age: 11, 45 and 65 yrs and 10 yrly, if travelling to 'at-risk' countries
Tick-borne encephalitis	0.5 ml IM	*3 doses*: day 1, 1–3 mths, 5–12 mths	50 % seroconvert after dose 1, 98 % after dose 2	3–5 years
Typhoid fever	Oral	3 capsules on days 0, 2, 4	Effective 7 days after last dose	1 year
Typhoid fever Vi	0.5 ml IM	1 primary, booster 2–3 yrly (not <2 yrs age)	7 days after injection	2–3 years

IM intramuscular, *SC* subcutaneous, *ID* intradermal, *sach* sachet, *ETEC* Enterotoxic Escherichia coli

Middle East

Countries: Arabian Gulf States (Bahrain, Kuwait, Oman, Qatar, United Arab Emirates), Iran, Iraq, Israel, Lebanon, Saudi Arabia, Syria, Turkey and Yemen

Vaccine	Route	No. of doses	Time to immunity	Duration of cover/boosting
Cholera (inactivated) *(may be indicated in preventing ETEC diarrhoea)*	1 vaccine dose + 1 sach sod. Hydrog. carbonate oral	2 doses, 1 wk apart, for all over age 6 years	7 days	Approx. 3 years
Hepatitis A	1 ml IM	2 primary series, 6–18 mths apart	80 % protection after 14 days, first vaccination	30 years – life
Hepatitis B	1 ml IM	Standard series: 2–3 primary series at 0,1,6 mths, Rapid series: 0,7,21 day and 1 yr	After primaries and after booster	10+ years – life
Hepatitis A and B comb.	1 ml IM	Standard series: 2–3 primary series at 0,1,6 mths, Rapid series: 0,7,21 day and 1 yr	>80 % protection one month after first 2 vacc.	As for A and B
Meningococcus ACYW *polysaccharide*	0.5 ml SC	One	10 days	2–3 years
Meningococcus ACYW *conjugated*	0.5 ml IM	One	14 days	5–10 years
Rabies (pre-exposure)	0.1 ml ID	0, 7, 21/28 days	ID: 30 days after full series	5–10 years
	0.5/1 ml IM	0, 7, 21/28 days	IM: 10–14 days after full series	
Tetanus/diphtheria	0.5 ml IM	3 vaccinations in childhood	Allow 2 weeks after booster dose	Boost @ age: 11, 45 and 65 yrs and 10 yrly, if travelling to 'at-risk' countries
Tetanus/diphtheria/ pertussis [whooping cough]	3 vaccinations in childhood	3 vaccinations in childhood	Allow 2 weeks after booster dose	Boost @ age: 11, 45 and 65 yrs and 10 yrly, if travelling to 'at-risk' countries

Vaccine	Route	No. of doses	Time to immunity	Duration of cover/boosting
Typhoid fever	Oral	3 capsules on days 0, 2, 4	Effective 7 days after last dose	1 year
Typhoid fever Vi	0.5 ml IM	1 primary, booster 2–3 yrly (not <2 yrs age)	7 days after injection	2–3 years

IM intramuscular, *SC* subcutaneous, *ID* intradermal, *sach* sachet, *ETEC* Enterotoxic Escherichia coli

Asia

Developing: Afghanistan, Bangladesh, Bhutan, Pakistan, India including Kashmir and the Andaman Islands, Myanmar, Nepal and Sri Lanka

Vaccine	Route	No. of doses	Time to immunity	Duration of cover/boosting
Cholera (inactivated) *(may be indicated in preventing ETEC diarrhoea)*	1 vaccine dose + 1 sach sod. Hydrog. carbonate oral	2 doses, 1 wk apart, for all over age 6 years	7 days	Approx. 3 years
Hepatitis A	1 ml IM	2 primary series, 6–18 mths apart	80 % protection after 14 days, first vaccination	30 years – life
Hepatitis B	1 ml IM	Standard series: 2–3 primary series at 0,1,6 mths, Rapid series: 0,7,21 day and 1 yr	After primaries and after booster	10+ years – life
Hepatitis A and B comb.	1 ml IM	Standard series: 2–3 primary series at 0,1,6 mths, Rapid series: 0,7,21 day and 1 yr	>80 % protection one month after first 2 vacc.	As for A and B
Japanese encephalitis vaccine *Inactive*	0.5 ml IM	2 vaccinations (0 and 28 days)	14 days	Approx 2 years
Japanese encephalitis vaccine *Live*	0.5 ml IM		14 days	Approx 4 years
Meningococcus ACYW *polysaccharide*	0.5 ml SC	One	10 days	2–3 years
Meningococcus ACYW *conjugated*	0.5 ml IM	One	14 days	5–10 years
Rabies (pre-exposure)	0.1 ml ID	0, 7, 21/28 days	ID: 30 days after full series	5–10 years

Vaccine	Route	No. of doses	Time to immunity	Duration of cover/boosting
	0.5/1 ml IM	0, 7, 21/28 days	IM: 10–14 days after full series	
Tetanus/diphtheria	0.5 ml IM	3 vaccinations in childhood	Allow 2 weeks after booster dose	Boost @ age: 11, 45 and 65 yrs and 10 yrly, if travelling to 'at-risk' countries
Tetanus/diphtheria/ pertussis [whooping cough]	3 vaccinations in childhood	3 vaccinations in childhood	Allow 2 weeks after booster dose	Boost @ age: 11, 45 and 65 yrs and 10 yrly, if travelling to 'at-risk' countries
Tick-borne encephalitis	0.5 ml IM	*3 doses*: day 1, 1–3 mths, 5–12 mths	50 % seroconvert after dose 1, 98 % after dose 2	3–5 years
Typhoid fever	Oral	3 capsules on days 0, 2, 4	Effective 7 days after last dose	1 year
Typhoid Fever Vi	0.5 ml IM	1 primary, booster 2–3 yrly (not <2 yrs age)	7 days after injection	2–3 years

IM intramuscular, *SC* subcutaneous, *ID* intradermal, *sach* sachet, *ETEC* Enterotoxic Escherichia coli

Far East Asia

Countries: Brunei, Cambodia, China, Hong Kong, Indonesia, Japan, Laos, Macao, Malaysia, Mongolia, Philippines, Singapore, South Korea, Taiwan, Thailand and Vietnam

Vaccine	Route	No. of doses	Time to immunity	Duration of cover/boosting
Cholera (inactivated) *(may be indicated in preventing ETEC diarrhoea)*	1 vaccine dose + 1 sach sod. Hydrog. carbonate oral	2 doses, 1 wk apart, for all over age 6 years	7 days	Approx. 3 years
Hepatitis A	1 ml IM	2 primary series, 6–18 mths apart	80 % protection after 14 days, first vaccination	30 years – life

Vaccine	Route	No. of doses	Time to immunity	Duration of cover/boosting
Hepatitis B	1 ml IM	Standard series: 2–3 primary series at 0,1,6 mths, Rapid series: 0,7,21 day and 1 yr	After primaries and after booster	10+ years – life
Hepatitis A and B comb.	1 ml IM	Standard series: 2–3 primary series at 0,1,6 mths, Rapid series: 0,7,21 day and 1 yr	>80 % protection one month after first 2 vacc.	As for A and B
Japanese encephalitis vaccine *Inactive*	0.5 ml IM	2 vaccinations (0 and 28 days)	14 days	Approx 2 years
Japanese encephalitis vaccine *Live*	0.5 mls IM		14 days	Approx 4 years
Rabies (pre-exposure)	0.1 ml ID	0, 7, 21/28 days	ID: 30 days after full series	5–10 years
	0.5/1 ml IM	0, 7, 21/28 days	IM: 10–14 days after full series	
Tetanus/diphtheria	0.5 ml IM	3 vaccinations in childhood	Allow 2 weeks after booster dose	Boost @ age: 11, 45 and 65 yrs and 10 yrly, if travelling to 'at-risk' countries
Tetanus/diphtheria/ pertussis [whooping cough]	3 vaccinations in childhood	3 vaccinations in childhood	Allow 2 weeks after booster dose	Boost @ age: 11, 45 and 65 yrs and 10 yrly, if travelling to 'at-risk' countries
Tick-borne encephalitis	0.5 ml IM	*3 doses*: day 1, 1–3 mths, 5–12 mths	50 % seroconvert after dose 1, 98 % after dose 2	3–5 years
Typhoid fever	Oral	3 capsules on days 0, 2, 4	Effective 7 days after last dose	1 year
Typhoid fever Vi	0.5 ml IM	1 primary, booster 2–3 yrly (not <2 yrs age)	7 days after injection	2–3 years

IM intramuscular, *SC* subcutaneous, ID intradermal, *sach* sachet, *ETEC* Enterotoxic Escherichia coli

Oceania

Countries: Australia, New Zealand, Papua New Guinea and Pacific Island Nations

Vaccine	Route	No. of doses	Time to immunity	Duration of cover/ boosting
Cholera (inactivated) *(may be indicated in preventing ETEC diarrhoea)*	1 vaccine dose + 1 sach sod. Hydrog. carbonate oral	2 doses, 1 wk apart, for all over age 6 years	7 days	Approx. 3 years
Hepatitis A	1 ml IM	2 primary series, 6–18 mths apart	80 % protection after 14 days, first vaccination	30 years – life
Hepatitis B	1 ml IM	Standard series: 2–3 primary series at 0,1,6 mths, Rapid series: 0,7,21 day and 1 yr	After primaries and after booster	10+ years – life
Hepatitis A and B comb.	1 ml IM	Standard series: 2–3 primary series at 0,1,6 mths, Rapid series: 0,7,21 day and 1 yr	>80 % protection one month after first 2 vacc.	As for A and B
Japanese encephalitis vaccine *Inactive*	0.5 ml IM	2 vaccinations (0 and 28 days)	14 days	Approx 2 years
Japanese encephalitis vaccine *Live*	0.5 mls IM		14 days	Approx 4 years
Q fever	0.5 ml SC	One	14 days	5 years
Tetanus/diphtheria	0.5 ml IM	3 vaccinations in childhood	Allow 2 weeks after booster dose	Boost @ age: 11, 45 and 65 yrs and 10 yrly, if travelling to 'at-risk' countries
Tetanus/diphtheria/ pertussis [whooping cough]	3 vaccinations in childhood	3 vaccinations in childhood	Allow 2 weeks after booster dose	Boost @ age: 11, 45 and 65 yrs and 10 yrly, if travelling to 'at-risk' countries
Typhoid fever	Oral	3 capsules on days 0, 2, 4	Effective 7 days after last dose	1 year
Typhoid fever Vi	0.5 ml IM	1 primary, booster 2–3 yrly (not <2 yrs age)	7 days after injection	2–3 years

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America (North)

Countries: Canada and United States (including Alaska)

Vaccine	Route	No. of doses	Time to immunity	Duration of cover/boosting
Hepatitis A	1 ml IM	2 primary series, 6–18 mths apart	80 % protection after 14 days, first vaccination	30 years – life
Hepatitis B	1 ml IM	Standard series: 2–3 primary series at 0,1,6 mths, Rapid series: 0,7,21 day and 1 yr	After primaries and after booster	10+ years – life
Hepatitis A and B comb.	1 ml IM	Standard series: 2–3 primary series at 0,1,6 mths, Rapid series: 0,7,21 day and 1 yr	>80 protection one month after first 2 vacc.	As for A and B
Rabies (pre-exposure)	0.1 ml ID	0, 7, 21/28 days	ID: 30 days after full series	5–10 years
	0.5/1 ml IM	0, 7, 21/28 days	IM: 10–14 days after full series	
Tetanus/diphtheria	*0.5 ml IM*	*3 vaccinations* in childhood	Allow 2 weeks after booster dose	Boost @ age: 11, 45 and 65 yrs and 10 yrly, if travelling to 'at-risk' countries
Tetanus/diphtheria/ pertussis [whooping cough]	*3 vaccinations* in childhood	*3 vaccinations* in childhood	Allow 2 weeks after booster dose	Boost @ age: 11, 45 and 65 yrs and 10 yrly, if travelling to 'at-risk' countries
Tick-borne encephalitis (Canada)	0.5 ml IM	*3 doses*: day 1, 1–3 mths, 5–12 mths	50 % seroconvert after dose 1, 98 % after dose 2	3–5 years

IM intramuscular, *SC* subcutaneous, *ID* intradermal

America (Central)

Central America: Bahamas, Belize, Bermuda, Costa Rica, Cuba, Caribbean Islands, Dominican Republic, El Salvador, Guatemala, Haiti, Honduras, Jamaica, Mexico, Nicaragua, Panama and Trinidad and Tobago

Vaccine	Route	No. of doses	Time to immunity	Duration of cover/boosting
Cholera (inactivated) *(may be indicated in preventing ETEC diarrhoea)*	1 vaccine dose + 1 sach sod. Hydrog. carbonate oral	2 doses, 1 wk apart, for all over age 6 years	7 days	Approx. 3 years
Hepatitis A	1 ml IM	2 primary series, 6–18 mths apart	80 % protection after 14 days, first vaccination	30 years – life
Hepatitis B	1 ml IM	Standard series: 2–3 primary series at 0,1,6 mths, Rapid series: 0,7,21 day and 1 yr	After primaries and after booster	10+ years – life
Hepatitis A and B comb.	1 ml IM	Standard series: 2–3 primary series at 0,1,6 mths, Rapid series: 0,7,21 day and 1 yr	>80 % protection one month after first 2 vacc.	As for A and B
Polio *(Haiti and Dominican Republic)*	0.5 ml SC	Primary series in childhood 1 booster as an adult	After series and after booster	For adults, available data indicated one booster for a lifetime
Rabies (pre-exposure)	0.1 ml ID	0, 7, 21/28 days	ID: 30 days after full series	5–10 years
	0.5/1 ml IM	0, 7, 21/28 days	IM: 10–14 days after full series	
Tetanus/diphtheria	0.5 ml IM	3 vaccinations in childhood	Allow 2 weeks after booster dose	Boost @ age: 11, 45 and 65 yrs and 10 yrly, if travelling to 'at-risk' countries
Tetanus/diphtheria/ pertussis [whooping cough]	3 vaccinations in childhood	3 vaccinations in childhood	Allow 2 weeks after booster dose	Boost @ age: 11, 45 and 65 yrs and 10 yrly, if travelling to 'at-risk' countries
Typhoid fever	Oral	3 capsules on days 0, 2, 4	Effective 7 days after last dose	1 year

Vaccine	Route	No. of doses	Time to immunity	Duration of cover/boosting
Typhoid fever Vi	0.5 ml IM	1 primary, booster 2–3 yrly (not <2 yrs age)	7 days after injection	2–3 years
Yellow fever *(East of Panama Canal, Trinidad)*	0.5 ml SC	One	6–10 days	10 years to life

IM intramuscular, *SC* subcutaneous, *ID* intradermal, *sach* sachet, *ETEC* Enterotoxic Escherichia coli

America (South)

South America: Argentina, Brazil, Bolivia, Chile, Columbia, Ecuador, French Guiana, Guyana, Paraguay, Peru, Surinam, Uruguay and Venezuela

Vaccine	Route	No. of doses	Time to immunity	Duration of cover/boosting
Cholera (inactivated) *(may be indicated in preventing ETEC diarrhoea)*	1 vaccine dose + 1 sach sod. Hydrog. carbonate oral	2 doses, 1 wk apart, for all over age 6 years	7 days	Approx. 3 years
Hepatitis A	1 ml IM	2 primary series, 6–18 mths apart	80 % protection after 14 days, first vaccination	30 years – life
Hepatitis B	1 ml IM	Standard series: 2–3 primary series at 0,1,6 mths, Rapid series: 0,7,21 day and 1 yr	After primaries and after booster	10+ years – life
Hepatitis A and B comb.	1 ml IM	Standard series: 2–3 primary series at 0,1,6 mths, Rapid series: 0,7,21 day and 1 yr	>80 protection one month after first 2 vacc.	As for A and B
Rabies (pre-exposure)	0.1 ml ID	0, 7, 21/28 days	ID: 30 days after full series	5–10 years
	0.5/1 ml IM	0, 7, 21/28 days	IM: 10–14 days after full series	
Tetanus/diphtheria	0.5 ml IM	3 vaccinations in childhood	Allow 2 weeks after booster dose	Boost @ age: 11, 45 and 65 yrs and 10 yrly, if travelling to 'at-risk' countries

Vaccine	Route	No. of doses	Time to immunity	Duration of cover/boosting
Tetanus/diphtheria/ pertussis [whooping cough]	3 vaccinations in childhood	3 vaccinations in childhood	Allow 2 weeks after booster dose	Boost @ age: 11, 45 and 65 yrs and 10 yrly, if travelling to 'at-risk' countries
Typhoid fever	Oral	3 capsules on days 0, 2, 4	Effective 7 days after last dose	1 year
Typhoid fever Vi	0.5 ml IM	1 primary, booster 2–3 yrly (not <2 yrs age)	7 days after injection	2–3 years
Yellow fever *(not Chile/Uruguay)*	0.5 ml SC	One	6–10 days	10 years to life

IM intramuscular, *SC* subcutaneous, *ID* intradermal, *sach* sachet, *ETEC* Enterotoxic Escherichia coli

Africa

North Africa: Algeria, Canary Islands, Ceuta, Libya, Madeira Islands, Melilla, Morocco and Tunisia

East and Northeast Africa: Burundi, Djibouti, Egypt, Eritrea, Ethiopia, Kenya, Rwanda, Seychelles, Somalia, Sudan, Tanzania and Uganda

Central and West Africa: Ascension Island, Benin, Burkina, Faso, Cameroon, Cape Verde, Islands, Central African Republic, Chad, Congo, Cote d'Ivoire, Equatorial Guinea, Gabon, Gambia, Guinea- Bissau, Liberia, Mali, Mauritania, Niger, Nigeria, Sao Tome and Principe, Senegal, Sierra Leone, Togo and Zaire

Southern Africa: Angola, Botswana, Comoros, La Reunion, Lesotho, Madagascar, Malawi, Mauritius, Mozambique, Namibia, St. Helena, Swaziland, Tristan da Cunha, Zambia and Zimbabwe

Vaccine	Route	No. of doses	Time to immunity	Duration of cover/ boosting
Cholera (inactivated) *(may be indicated in preventing ETEC diarrhoea)*	1 vaccine dose + 1 sach sod. Hydrog. carbonate oral	2 doses, 1 wk apart, for all over age 6 years	7 days	Approx. 3 years
Hepatitis A	1 ml IM	2 primary series, 6–18 mths apart	80 % protection after 14 days, first vaccination	30 years – life

Vaccine	Route	No. of doses	Time to immunity	Duration of cover/ boosting
Hepatitis B	1 ml IM	Standard series: 2–3 primary series at 0,1,6 mths, Rapid series: 0,7,21 day and 1 yr	After primaries and after booster	10+ years – life
Hepatitis A and B comb.	1 ml IM	Standard series: 2–3 primary series at 0,1,6 mths, Rapid series: 0,7,21 day and 1 yr	>80 protection one month after first 2 vacc.	As for A and B
Meningococcus ACYW *polysaccharide*	0.5 ml SC	One	10 days	2–3 years
Meningococcus ACYW *conjugated*	0.5 ml IM	One	14 days	5–10 years
Polio	0.5 ml IM	Primary series in childhood 1 booster as an adult	After series and after booster	For adults, available data indicated one booster for a lifetime
Rabies (pre-exposure)	0.1 ml ID	0, 7, 21/28 days	ID: 30 days after full series	5–10 years
	0.5/1 ml IM	0, 7, 21/28 days	IM: 10–14 days after full series	
Tetanus/diphtheria	0.5 ml IM	3 vaccinations in childhood	Allow 2 weeks after booster dose	Boost @ age: 11, 45 and 65 yrs and 10 yrly, if travelling to 'at-risk' countries
Tetanus/diphtheria/ pertussis [whooping cough]	3 vaccinations in childhood	3 vaccinations in childhood	Allow 2 weeks after booster dose	Boost @ age: 11, 45 and 65 yrs and 10 yrly, if travelling to 'at-risk' countries
Typhoid fever	Oral	3 capsules on days 0, 2, 4	Effective 7 days after last dose	1 year
Typhoid fever Vi	0.5 ml IM	1 primary, booster 2–3 yrly (not <2 yrs age)	7 days after injection	2–3 years
Yellow fever	0.5 ml SC	One	6–10 days	10 years to life

IM intramuscular, *SC* subcutaneous, *ID* intradermal, *sach* sachet, *ETEC* Enterotoxic Escherichia coli

Chapter 21
Emergencies and Managing Adverse Events: Emergency Medical Equipment

Marc Shaw and David Smith

Key Points
- Current licensed available vaccines are very safe and effective.
- Vaccine-associated side effects are emergencies and are rare.
- Anaphylaxis is defined as a serious reaction that is rapid in onset and may cause death.
- All centres practising travel medicine must have an emergency response policy that is re-evaluated annually.
- Rapid response in an emergency is essential, and all participants need to know their role in it.

Current licensed modern vaccines are effective and extremely safe. They need to undergo wide-ranging and exactingly controlled preclinical and clinical safety trials, together with considerable follow-up, before being licensed for routine community usage.

Nevertheless, vaccine-associated adverse events can occur, and their recommendations for travel must always be associated with a 'risk analysis' evaluating benefit versus disadvantage of a vaccine.

The authors are grateful to the New Zealand Resuscitation Council for their advice and contribution to this chapter. http://www.nzrc.org.nz

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Vaccine-associated side effects and emergencies are rare. Approximately 10 % of all vaccinees complain of mild side effects after vaccination. These are either local or systemic:

- Local: pain and redness at the injection site and swelling and pain of the limb vaccinated
- Systemic: fever, headaches, malaise and myalgia

An anaphylactic event involving cutaneous, cardiovascular, respiratory, gastrointestinal and genitourinary signs and symptoms is extremely rare and usually a very unexpected, though potentially fatal, reaction. It develops over several minutes, and in general, the more rapidly the symptoms emerge, the more severe the reaction, although a delay in diagnosis may occur if the symptoms are limited to one body system. Nevertheless, biphasic reactions have been reported, with symptoms recurring 8–12 h after the onset of the original attack and lasting up to 48 h.

Emergency Reactions to Vaccination

Most life-threatening adverse events begin within 10 min of vaccination. The intensity usually peaks around 1 h after onset.

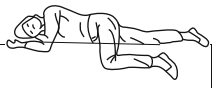
The most common reactions are:

1. Hyperventilation phenomenon
2. Vasovagal reaction
3. Acute anaphylaxis

For all intents and purposes, the immediate management will be the same.

Emergency Management

If the victim is unresponsive and not breathing normally, the rescuer should follow the guidelines of the Australian Resuscitation Council and New Zealand Resuscitation Council Basic Life Support Flowchart (Fig. 21.1).

Resuscitation Sequence	Accompanying Notes
The sequence of actions for Adult, Childhood and Infant basic life support. **Early recognition** is a key step in initiating early management of an emergency situation.	**RECOGNITION:** Before loss of consciousness, the victim may experience yawning, dizziness, sweating, change from normal skin colour, blurred or changed vision, urination or nausea.
In all emergencies, a rescuer must **remember the acronym: DRS ABCD** • **D** **Dangers:** Check for dangers. *Ensure personal safety and that of others before attending to the patient. Ensure the patient is out of further danger (consider moving the patient).*	In an emergency, **COLLAPSE** is often the first sign of an impending problem. The travel health professional, or rescuer, needs to assess the collapsed victim'sresponse to verbal and tactile stimuli ('talk and touch'), ensuring that this does not cause or aggravate any injury. A person who fails to respond or shows only a minor response, such as groaning without eye opening, should be managed as if unconscious.
• **R** **Responsiveness:** Check responsiveness of the patient and if unresponsive then • **S** **Send for Help:** ask a bystander to call Emergency Services **(000 in Australia, 111 in NZ, 995 in Singapore)** … or *activate the emergency response* • Ask any bystander to return immediately to confirm the call has been made. *Use a directed, specific and acknowledged communication technique.*	**UNCONSCIOUSNESS** is a state of unarousable unresponsiveness, where the victim is unaware of their surroundings and no purposeful response can be obtained. Should this occur, then the **KEY DECISION IS:** A. Is the patient **unconscious and breathing normally**, in which case they may be put into the recovery position (below) for monitoring. B. Is the patient **unconscious and not breathing normally**, in which the travel health professional needs to proceed to **DRS ABCD**.
• **A** **Airway:** Open the airway by applying head tilt and chin lift (jaw thrust). Remove obvious causes of airway obstruction.	 **Recovery position** 1. Patient to be put on their side. 2. Unconscious persons who are breathing normally must remain on their side. 3. It is reasonable to roll a face-down unresponsive victim onto their back to assess airway and breathing and initiate resuscitation.
• **B** **Breathing:** Taking no more than 10 seconds, check for the presence of normal breathing. Look for movement of the chest and upper abdomen, listen and feel forthe escape of air from the nose and mouth. If normal breathing is present: place the patient in the recovery position if they are unconscious. If normal breathing is absent, or there is uncertainty, start Cardio-Pulmonary Resuscitation (CPR)	**Managing the victim's airway** Airway management is required to provide an open airway when the victim: • Is unconscious • Has an obstructed airway • Needs rescue breathing. **For unresponsive adults and children:** 1. The airway may be opened by using the **HEAD TILT/CHIN LIFT MANOEUVER** • One hand is placed on the forehead or the top of the head. • Other hand is used to provide Chin Lift. • The head (NOT the neck) is tilted backwards. • When the victim is in a lateral position, the head will usually remain in this position when the rescuer's hands are withdrawn. • Chin lift is commonly used in conjunction with **BACKWARD HEAD TILT.** • Chin is held up by the rescuer's thumb and fingers to open the mouth and pull the tongue and soft tissues away from the back of the throat. *(e.g. placing thumb over the chin below the lip and supporting the tip of the jaw with the middle finger and the index finger lying along the jaw line)*
• **C** **Circulation:** If the unconscious patient is unresponsive and not breathing normally after the airway has been opened and cleared, CPR to be commenced:	

- **30 compressions followed by 2 breaths for adults** -almost two compressions/second followed by two breaths. *The music of the Bee Gees song 'Staying Alive' is the rhythm to remember!*
- **2 rescue breaths followed by 15 compressions followed by 2 breaths for for infants and children.**
- If rescuers are unable or strongly opposed to performing rescue breathing, they should do chest compressions only.
- If chest compressions only are given, they should be continuous at a rate of approximately 100/min.
- Attach an AED (Automated External Defibrillator) if available and follow the prompts.

• **D** **Defibrillation:** As soon as a defibrillator becomes available it should be connected to the casualty and used if an AED is available, turn on the power, and follow the instructions on the device.

NOTE: **Minimise interruptions to chest compressions** and CPR should not be discontinued to check for breathing or responsiveness.

- Care is required to prevent the ring finger from squashing the soft tissues of the neck.
- The jaw is held open slightly and pulled away from the chest.

2. Administer **oxygen** by mask, if possible, at a rate of 4 litres a minute.

Cardio-Pulmonary Resuscitation (CPR): should continue until:

- The patient responds or begins to breath normally
- It is impossible to continue (e.g. exhaustion), or
- Someone trained in advanced life support techniques either takes over or directs that CPR should be discontinued

CPR: *This guideline is applicable to adults, children and infants.*

CPR is the technique of chest compressions combined with rescue breathing. The purpose is to temporarily maintain a circulation sufficient to preserve brain function until specialised treatment is available.
A rescuer:

- Must start CPR if the victim is unresponsive and not breathing normally
- Should start CPR, even if the victim takes occasional gasps
- Can enlist the help of bystanders or colleagues. *In victims who need resuscitation, bystander CPR dramatically increases the chance of survival.* Bystander CPR rarely leads to harm in victims who are eventually found not to have suffered cardiac arrest: so bystander CPR should be encouraged.

Interruptions of Chest Compressions: During CPR take care to minimise interruptions of chest compressions unless the victim responds or begins breathing normally. Interruption of chest compressions is associated with lower survival rates.

Risks of disease transmission during CPR: The risk of disease transmission whilst carrying out CPR performance is very low. A systematic review found no reports of transmission of hepatitis B, hepatitis C, human deficiency virus (HIV) or cytomegalovirus during either training or actual CPR when high-risk activities, such as intravenous cannulation were not performed. Use of a barrier device during rescue breathing can be considered to reduce this risk.

Anaphylaxis

Anaphylaxis is defined as a 'serious allergic reaction that is rapid in onset and may cause death'. The prevalence of anaphylaxis is estimated to be as high as 2 % and seems to be rising, particularly in the younger age group.

Anaphylaxis is frequently under-recognised and so is likely to be treated inadequately. Furthermore, diagnosis and management of the syndrome are challenging since reactions are often immediate and unexpected, for the more rapidly the condition develops, the more likely it is to be severe and life threatening. To this end, both speedy recognition and management of anaphylaxis are imperative.

Symptoms and Signs

Symptoms and signs of anaphylaxis may occur within seconds of exposure to a vaccine allergen and can *include* any combination of the following (*after Kim H, Fischer D. Anaphylaxis*):

- Mouth: Itching and swelling of lips/tongue
- Throat: Itching, tightness, closure and hoarseness

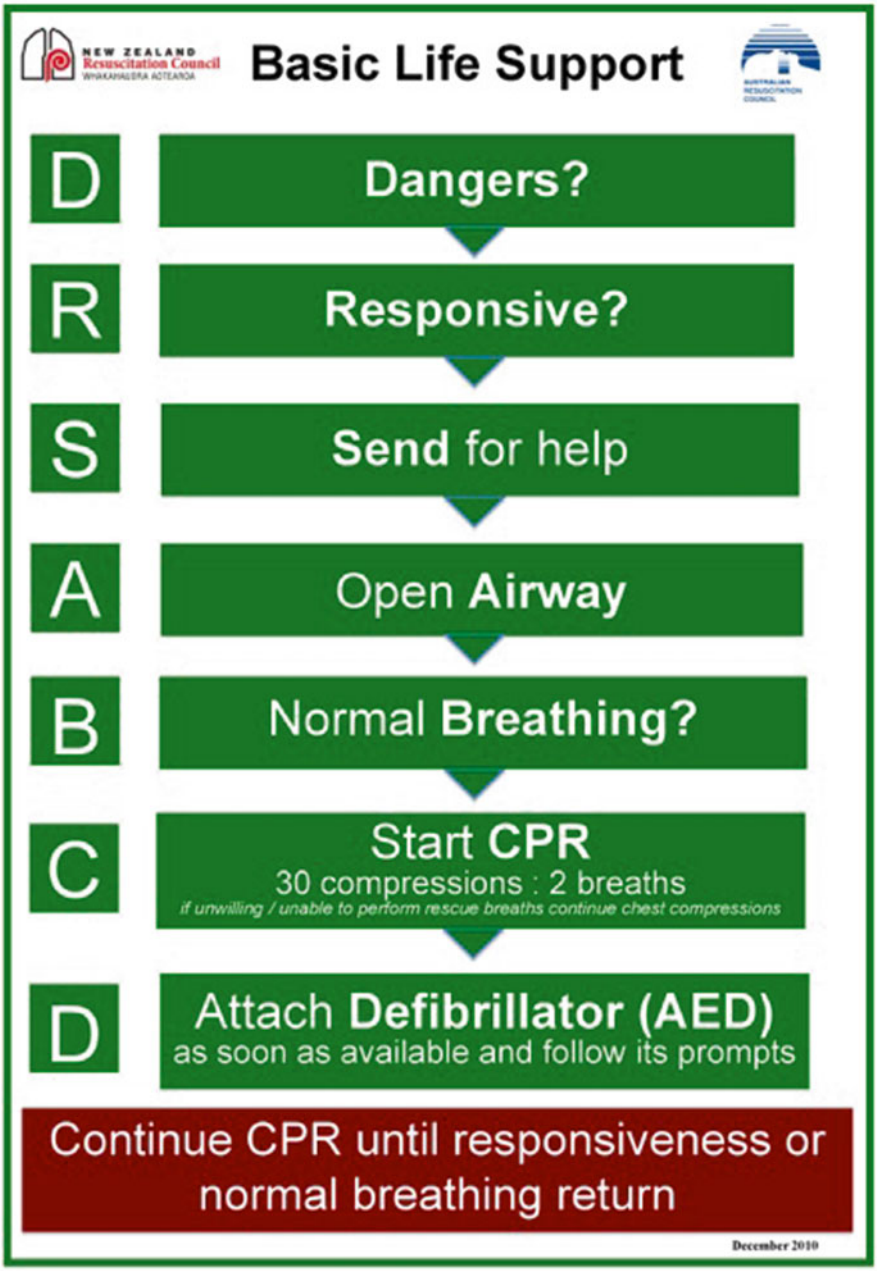


Fig. 21.1 BASIC LIFE SUPPORT CHART

- Skin: Itching, hives, eczema, swelling and flushing
- Gut: Difficult swallowing, vomiting, diarrhoea and abdominal pain
- Lung: Shortness of breath, cough and wheeze

- Heart: Hypotension, dizziness, syncope and tachycardia
- Neurological: Light-headedness
- Other: Feeling of impending doom and anxiety
  Collapse and unconsciousness
  Pallor and floppiness (in young children)

In some cases, anaphylaxis is preceded by less dangerous allergic symptoms, which can include:

- Collapse and unconsciousness
- Pallor and floppiness (in young children)
- Swelling of face, lips and eyes
- Hives or welts on the skin
- Stomach pain and vomiting

Several factors can influence the severity of anaphylaxis, including asthma, exercise, heat, alcohol and, in people with food allergies, the amount eaten and how it is prepared and consumed.

Presentation

There are two stages of the acute presentation of anaphylaxis

Mild-Moderate Reaction

This includes:

Skin rashes and itching
Not to be confused with a vasovagal attack or hyperventilation reaction

Management

- Patient is to remain in the clinic under observation.
- Treatment that can be authorised to be given, if necessary, is:

  (a) Oral antihistamines (e.g. promethazine) under medical orders
  (b) Steroid creams for topical application

If there is no worsening of the symptoms after 30 min, then the patient may be permitted to depart the clinic, with advice to seek medical attention should they continue to feel unwell.

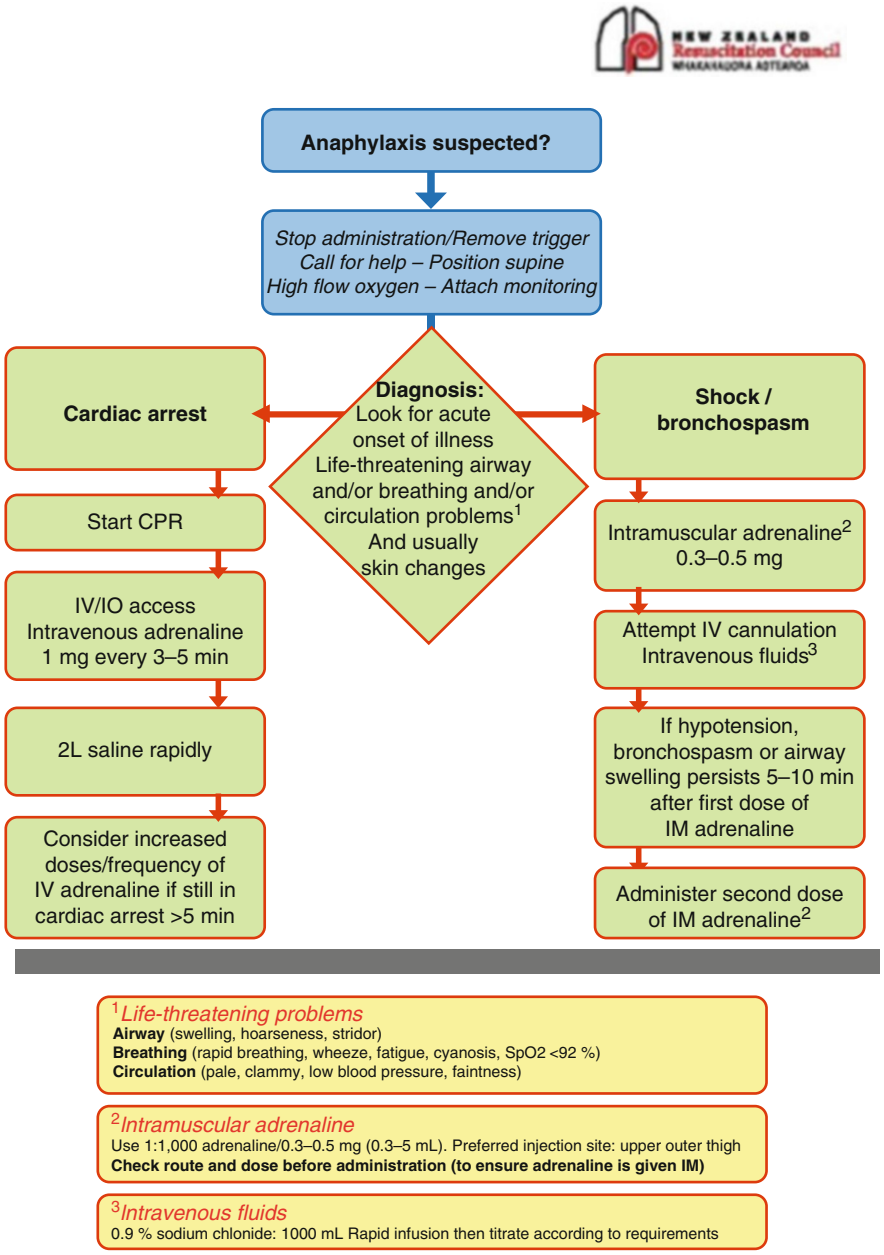


Fig. 21.2 Managing Anaphylaxis

Moderate-Severe Reaction

Shortness of breath and asthmatic attack and asthmatic attack
Skin swelling and reactive oedema
Blotching of the skin
Collapse

Management of Anaphylaxis

Refer immediately to the chart Fig. 21.2.

Airways and Body Placement Management

Oxygen	Administer oxygen at high flow rates where there is respiratory distress, stridor or wheeze
	If stridor is present, elevate head and chest
Circulation	Blood pressure – if hypotensive, then elevate the legs
	If there is *no strong pulse*, assume patient is having an anaphylactic reaction
	A *strong regular carotid pulse* in a 'collapsed' patient suggests a faint
	Young children are *unlikely* to faint
Follow-up	After resuscitation all victims should be reassessed and re-evaluated for resuscitation-related injuries

Equipment and Medication for Management of Emergencies

In the first-line treatment of anaphylaxis (Fig. 21.2), the following (Table 21.1) are the recommended medications and medical equipment for those surgeries where vaccinations for international travel are given.

Medication Administration

Should medication be required to additionally manage a case of acute anaphylaxis, then the following are appropriate to use, under medical supervision. Table 21.2 lists the appropriate medications that can be used, under medical supervision.

Table 21.1 Kit – medications and equipment for emergency management

Kit	Accompanying notes
Medications	
Adrenaline	1:1,000
Hydrocortisone	100 mgs vial
Promethazine	25 mgs/ml
Salbutamol	500 mcg/ml
Needles	
Assorted syringes	1, 3 and 5 ml
Needles	23, 25 and 27 gauge
Venous cannulae	21, 23qne 25 gauge
Butterfly needles	16, 18, 20, 22 gauge
Tape	
Tourniquet	
Luer	
Fluids	
Crystalline and colloid IV fluids	Normal saline
Giving sets	Hartmann's solution
Airways equipment	
Oxygen (check that it is filled)	
Airways including paediatric size	
Ambu bag face masks for both adults and children	
Intubation equipment	
Laryngeal mask airway (LMA)	

Table 21.2 Medication and routes of administration

Medication	Dosage
Adrenaline **Intramuscular**	**1:1000 = 1 mg/ml** Administration dosage (deep intramuscularly): **A) Body weight: 0.01 mL/kg to a maximum of 0.5mL** **B) If body weight is not known:** Infants aged under 1 year: 0.05–0.1 mL Infants aged under 2 years: 0.1 mL Children 2–4 years: 0.2 mL Children 5–10 years 0.3 mL Adolescents ≥11 years: 0.3–0.5 mL Adults: 0.5 mL **C)** Expect a response to the adrenaline within 1-2 minutes of administration. Adrenaline can be repeated at 5-15 minute intervals, to a maximum of 3 doses.
Hydrocortisone **Intramuscular or** **Intravenous over 10 minutes**	**Adults:** 100–200 mgs This dose can be repeated after 2, 4 or 6 hours **NOTE: This drug,*if given intravenously*, it should administered in the presence of a medical practitioner.** **Children: Hydrocortisone** 4 mg/kg (maximum100 mg) every 6 hours If weight unavailable, **child under 2 years** 25 mg, every 6 hours **child 2–5 years** 50 mg,every 6 hours **child 5–18 years** 100 mg, every 6 hours
Promethazine **Intramuscular or** **Slow Intravenous infusion**	**Adults: 25–50 mgs** **Children:** 6.25–12.5 mgs ***deep intramuscular injection*** *(Take 1 ampoule of **promethazine** injection and add 9 mL of water for injection to make up the solution to 10 mLs. This will give a 0.25% solution)*
SALBUTAMOL **Inhaled beta$_2$-agonists**	**Adult: 100 or 200 micrograms (mcg) when required to a maximum 200 mcg 4 times/day** **Children:** Inhaled **short-acting beta$_2$ agonis** using a pressurised metered-dose inhaler with a spacer device **Age up to 5 years:** **Give 6 puffs of salbutamol** (100 micrograms/metered inhalation), each puff inhaled separately (with 5 breaths between puffs) (**child over 5 years or adult** give 12 puffs). **Age 5 years to adulthood:** Give 12 puffs of salbutamol (100 micrograms/metered inhalation), each puff inhaled separately (with 5 breaths between puffs). • If oxygen cannot be safely interrupted to apply the spacer then use oxygen-driven nebulised salbutamol 2.5 mg; nebulised doses may be doubled for children over 5 years. • Repeat the dose every 20 minutes for 1–2 hours (3 doses per hour), then reduce the frequency on improvement to hourly, then weaning to 4 hourly according to progress. • If life threatening use continuous nebulised salbutamol.
Subcutaneous or Intramuscular	**Subcutaneous injection or intramuscular injection** **Adult** 500 micrograms, repeated every 4 hours if necessary **Slow intravenous injection** **Adult** 250 micrograms (diluted to a concentration of 50 micrograms/mL), repeated if necessary **Intravenous infusion** **Adult** initially 5 micrograms/minute, adjusted according to response and heart rate; usual rate–320 micrograms/minute

Surveillance

Record vital signs every 5–10 min. All observations and interventions should be recorded and clearly documented in the medical notes accompanying the patient to the hospital.

Arrange ambulance and hospital admission. All cases of anaphylaxis should be admitted to the hospital for observation. Rebound anaphylaxis can occur 12–24 h after the initial episode.

Further Reading

1. Koster RW, Sayre MR, Botha M, et al. Part 5: adult basic life support: 2010 international consensus on cardiopulmonary resuscitation and emergency cardiovascular care science with treatment recommendations. Resuscitation. 2010;81:e48–70.
2. de Caen AR, Kleinman ME, Chameides L, et al. Part 10: paediatric basic and advanced life support: 2010 international consensus on cardiopulmonary resuscitation and emergency cardiovascular care science with treatment recommendations. Resuscitation. 2010;81:e213–59.
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4. Consensus on Resuscitation Science & Treatment Recommendations. Part 2: adult basic life support. Resuscitation. 2005;67:187–201.
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7. Deakin CD, Morrison LJ, Morley PT, et al. Part 8: advanced life support: 2010 international consensus on cardio-pulmonary resuscitation and emergency cardiovascular care science with treatment recommendations. Resuscitation. 2010;81:e93–174.
8. Nolan JP, Hazinski MF, Billi JE, et al. 2010 international consensus on cardiopulmonary resuscitation and emergency cardiovascular care science with treatment recommendations. Resuscitation. 2010;81:e1–25.
9. Kim H, Fischer D. Anaphylaxis. Allergy, asthma & clinical immunology. 2011;7(Suppl 1):S6. Available at: www.aacijournal.com/content/7/S1/S6. Accessed 14 Dec 2014.
10. Ministry of Health. Immunisation handbook 2014. Wellington: Ministry of Health; 2014.
11. New Zealand Resuscitation Council. Advanced Resuscitation for Health Professionals 2012. Wellington: Wyatt and Wilson; 2012.
12. Soar J, Mancini ME, Bhanji F, et al. Part 12: education, implementation, and teams: 2010 International consensus on cardiopulmonary resuscitation and emergency cardiovascular care science with treatment recommendations. Resuscitation. 2010;81:e288–330.

Appendix: Frequently Asked Questions

There are questions that regularly come up as challenges for the travel health professional. Here are some of the more common ones and answers to them that have been garnered from international sources.

1. **How many vaccines can be given at one time?**

   Medically there is no limit to how many vaccines can be administered at one time, although in reality it is rarely necessary to give more than six. However, for last minute travellers, or those who have not completed childhood immunisations, it may be necessary to give many vaccines at one visit.

   There are no interactions between several inactivated vaccines administered at the same time, nor between live and inactivated vaccines. If a traveller requires more than one injected live vaccine, precautions are necessary – see below.

2. **How many vaccines can be given at one site?**

   Wherever possible, one vaccine per muscle mass should be used in infants. In reality this is not always possible and is less important in adults as the muscle is more developed. The vastus lateralis muscle is the preferred site for infants requiring several vaccines.

   It is recommended that vaccination sites are at least 2 cm apart, with up to three vaccinations per arm at the apices of a triangle. This is to ensure that local reactions, should they occur, do not overlap.

3. **What are the recommendations for giving more than one live vaccine?**

   Traditionally the guidance on administering more than one live vaccine has been to give them on the same day, or at an interval of 4 weeks. This guidance has been based on old studies with measles and smallpox vaccine. The theory behind this guidance was that the interferon produced in response to virus replication of the first vaccine could prevent replication of the second, resulting in a sub-optimal response to the second vaccine.

M. Shaw, C. Wong (eds.), *The Practical Compendium of Immunisations for International Travel*, DOI 10.1007/978-3-319-15922-5

A more recent review of the evidence suggests that this guidance is not applicable to all live vaccines as some immune mechanisms differ between vaccines. Therefore the following updated guidelines have recently been adopted by Public Health England and are supported by the editors of this book.

- *Measles*, *mumps and rubella* (*MMR*) *and yellow fever vaccines*: These vaccines, wherever possible, should be given at a 4-week interval and *not* administered on the same day.
  Administration on the same day can lead to a sub-optimal response to the mumps, rubella and yellow fever viruses.
  Where time is short and protection is required rapidly, these vaccines can be given at the same time, although an additional dose of MMR vaccine may be considered at a later stage.
- *Varicella*, *zoster and MMR*: These vaccines should either be given on the same day, or at an interval of at least 4 weeks. A significant increase in varicella infections has been observed when the vaccine was administered within 30 days of MMR vaccine. This was not observed when the vaccines were given on the same day.
  As the zoster vaccine contains the same virus at varicella, this advice is extrapolated to the administration of zoster and MMR. In practice, however, these two vaccines are rarely indicated in the same age group.
  If protection against these diseases is required rapidly, the vaccines can be given at any interval, with an additional dose of the vaccine given second being considered at a later stage.
- *All other live vaccines*: BCG, MMR, live influenza, oral typhoid, rotavirus, yellow fever, varicella and zoster. Apart from the combinations listed above, these vaccines can be administered either on the same day, or at any interval between each other.

4. **Can vaccine intervals be shortened?**

Although there is no harm in shortening intervals between vaccine courses, it should be avoided wherever possible.

Recommended vaccine intervals are made by vaccine manufacturers based on clinical trials and reflect the schedules required to ensure the majority of recipients mount the best immune response. Theoretically if an interval was shortened the response to the vaccine could be impaired. It is accepted that extending intervals between vaccines is preferable to shortening them.

Nevertheless, when time is short, it is accepted that intervals between vaccines can be shortened by a few days without major impact on efficacy.

An exception to this is rabies vaccine which should be given on the World Health Organization (WHO) recommended pre- or post-exposure regimen. In the case of pre-exposure vaccination (given on day 0, 7, 28, or day 21 if time is short), this is largely due to a consideration of the post-exposure management in the case of an animal bite or scratch. The questions that arise: 'Can we confidently reassure an individual that a standard post-exposure rabies course would be adequate if they have not followed a standard pre-exposure course?' Similarly,

if the post exposure course is shortened, 'can we confidently reassure an individual that they are protected against rabies, a disease we know is invariably fatal?'

In some cases, it may be preferable not to commence a pre-exposure course of rabies if there is no time to complete it on the recommended schedule. In this situation, travellers need to be advised of the importance of seeking urgent medical assessment in the event of a potential exposure. Alternatively, a traveller may be able to complete a vaccine course at the destination – see below

5. **The traveller hasn't got time to complete a vaccine course – can the vaccine be carried with them for administration overseas?**

The short answer: no.

The majority of vaccines need to be stored at a temperature of between 2 and 8° Celsius. This is difficult to achieve whilst travelling long distances. In addition, because of the current security climate, it may not be possible to carry pharmaceutical products containing liquids, powders and needles on aircraft. Also, one must consider professional colleagues overseas who will be put in the difficult position of being asked to administer a vaccine which an individual has carried, not knowing if the cold chain has been adequately maintained.

6. **Can I advise my traveller to complete their vaccine course overseas?**

Yes, in most circumstances this is entirely possible, with a few precautions.

Both the International Society of Travel Medicine (ISTM) and the International Association for Medical Assistance to Travellers (IAMAT) list contact details for global clinics and are a useful resource for travellers requiring completion of vaccine courses or medical assistance whilst travelling.

It is worth considering that vaccine availability is not the same throughout the world. In many situations this is not an issue. Different brands of modern cell cultured rabies vaccines and hepatitis A and B vaccines are considered to be interchangeable. Travel health practitioners using the intradermal route for rabies vaccine should consider whether this is available at the overseas destination, and consider initiating an intramuscular course instead.

The Japanese encephalitis vaccine Jespect (or Ixiaro) is not universally available globally. In many Asian Pacific countries either the live attenuated Imojev, or the Chengdu vaccine (in China or India especially), is in general use. In the case of long-term travellers requiring these vaccines, it may be preferable and cheaper for travellers to source these vaccines at the destination, rather than commence the course before departure.

Travellers considering completing vaccine courses overseas should endeavour to contact their chosen travel health clinic before departure to ensure availability of the vaccine, together with appointment times and costs. Travellers will need to be provided with an accurate record of vaccines administered, and advised that protection cannot be considered until the course is complete.

7. **Are there any travellers who should not be vaccinated?**

For a variety of reasons including medical conditions or treatments, certain vaccinations will be contraindicated, or it may be preferable to postpone vaccination. The travel health professional will need to consider the following:

- Anyone with a history of auto-immune disease, immunodeficiency, cancer or immunosuppressive treatments and medication should be evaluated before vaccination, especially live vaccines.
- Low platelet count, if the intending traveller has HIV or other blood dyscrasia.
- A recent blood transfusion.
- Any recent ill health or current febrile illness. It is recommended that vaccination be postponed if the traveller has a high fever so as to be able to differentiate between any reaction to the vaccine and the current illness. Note that a person with a mild, common ailment, such as a cold with a low-grade fever, may be vaccinated.
- Anyone who has had a serious allergic reaction to a previous dose of a vaccine about to be administered should not get another dose.
- Anyone who has a severe allergy to any vaccine component, including latex, should not get a dose.
- Anyone who has had Guillain Barré syndrome (GBS) needs further assessment before vaccination.
- Intended vaccination for childhood and pregnancy needs further assessment before being administered.
- Any child who suffered a brain or nervous system disease within 7 days after a dose of DTaP should not get another dose.

This list is not exhaustive, and a thorough risk assessment should be made before vaccinating any traveller. Under some circumstances it can be appropriate to discuss the advisability of travel and to liaise with any specialist medical professionals overseeing the care of the traveller.

Appendix: Resources

Resources For Travellers

Immunise Australia

Information from the Australian Government including booklets for parents with questions and answers about immunisation for children, vaccine preventable diseases, vaccines, vaccine side effects and eligibility for national vaccine programmes. Available at: www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/IMM52-cnt. Accessed 16 Dec 2014.

Australian National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases

Provides fact sheets related to specific vaccines, vaccine-preventable diseases and vaccine safety. The website also hosts online decision aids to assist patients in deciding whether to vaccinate or not. Available at: www.ncirs.edu.au. Accessed 16 Dec 2014.

Australian Travel Health Advisory Group

A joint initiative between travel industry and travel health practitioners providing travel health information and advice for travellers. Available at: www.welltogo.com.au/. Accessed 16 Dec 2014.

U.S. Centers for Disease Control and Prevention (CDC)

Official U.S. government health recommendations for traveling with information and advice for travellers. A link is also available to the CDC travel health book for health professionals: *Health Information for International Travel*. Available at: www.nc.cdc.gov/travel. Accessed 16 Dec 2014.

New Zealand Ministry of Health

Information on vaccination laws and practices in New Zealand, plus advice for parents/guardians and health professionals about the vaccines and the disease they protect against, immunisation coverage, and links to other reputable national and international websites. Available at: www.health.govt.nz/immunisation. Accessed 16 Dec 2014.

Immunisation Advisory Centre

A New Zealand national organisation providing factual advice on immunisation for parents and health professionals. They also run vaccination courses for health professionals and a telephone advice line. Available at: www.immune.org.nz. Accessed 16 Dec 2014.

Don't Assume You're Immune

New Zealand website providing immunisation information for young adults. Available at: www.getimmunised.org.nz. Accessed 16 Dec 2014.

International Society of Travel Medicine (ISTM)

Includes a Global Travel Clinic Directory – a searchable database of clinics around the world providing pre- and post-travel care, run by members of the ISTM. Available at: www.istm.org/AF_CstmClinicDirectory.asp. Accessed 16 Dec 2014.

International Association for Medical Assistance to Travellers (IAMAT)

IAMAT is an organisation providing health advice for overseas travel and a list of IAMAT approved English speaking doctors around the world. Available at: http://www.iamat.org. Accessed 16 Dec 2014.