

Vaccine-preventable diseases and vaccines

General considerations

Vaccination is the administration of a vaccine to stimulate a protective immune response that will prevent disease in the vaccinated person if contact with the corresponding infectious agent occurs subsequently. Thus vaccination, if successful, results in immunization: the vaccinated person has been rendered immune to disease caused by the infectious pathogen. In practice, the terms “vaccination” and “immunization” are often used interchangeably.

Disease prevention

Vaccination is a highly effective method of preventing certain infectious diseases. For the individual, and for society in terms of public health, prevention is better and more cost-effective than cure. Vaccines are generally very safe and serious adverse reactions are uncommon. Routine immunization programmes protect most of the world’s children from a number of infectious diseases that previously claimed millions of lives each year. For travellers, vaccination offers the possibility of avoiding a number of dangerous diseases that may be encountered abroad. Immunized travelers will also be less likely to contaminate other travelers or local population with a number of potentially serious diseases. However, vaccines have not yet been developed against several of the most life-threatening infections, including malaria and HIV/AIDS.

Vaccination and other precautions

Despite their success in preventing disease, vaccines do not always fully protect 100% of the recipients. The vaccinated traveller should not assume that there is no risk of contracting the disease(s) against which he/she has been vaccinated. All additional precautions against infection (see Chapter 5) should be followed carefully, regardless of any vaccines or other medication that have been administered. These same precautions are important in reducing the risk of acquiring diseases for which no vaccines exist and that represent health problems commonly faced by international travellers. It is also important to remember that immunization is not a substitute for avoiding potentially contaminated food and water.

Planning before travel

Before departure, travellers should be advised about the risk of disease in the country or countries they plan to visit and the steps to be taken to prevent illness. The risk to a traveller of acquiring a disease depends on the local prevalence of that disease and on several other factors such as: age, sex, immunization status and current state of health, travel itinerary, duration and style of travel (e.g. first class, adventure, hiking, relief work).

Based on the traveller's individual risk assessment, a health care professional can determine the need for immunizations and/or preventive medication (prophylaxis) and provide advice on precautions to avoid disease.

There is no single schedule for the administration of immunizing agents to all travellers. Each schedule must be personalized and tailored to the individual traveller's immunization history, the countries to be visited, the type and duration of travel, and the amount of time available before departure.

Travel is a good opportunity for the health care provider to review the immunization status of infants, children, adolescents and adults. Un-immunized or incompletely immunized travellers should be offered the routine vaccinations recommended in national immunization schedules, in addition to those needed for travel.

The protective effect of many vaccines takes some time to develop following vaccination. The immune response of the vaccinated individual will become fully effective within a period of time that varies with the vaccine, the number of doses required and whether the individual has previously been vaccinated against the same disease. For this reason, travellers are advised to consult a travel medicine practitioner or physician 4–8 weeks before departure in order to allow sufficient time for optimal immunization schedules to be completed. However, an imminent departure still provides the opportunity to provide both advice and possibly some immunizations.

Vaccine schedules and administration

The vaccines that may be recommended or considered for travellers are shown in Table 6.1. Further information on the schedule for administration of these vaccines can be found in the respective individual vaccines sections. Recommendations on time intervals for administration of vaccines requiring more than one dose are provided; some slight variation can be made to accommodate the needs of travellers who may not be able to complete the schedule exactly as recommended. In general, it is acceptable to lengthen the time intervals between doses, but significant shortening of the intervals is not recommended.

The route of administration differs for individual vaccines and is critical for induction of the protective immune response. For injectable vaccines, the route of injection – subcutaneous, intramuscular or intradermal – determines the gauge and length of the needle to be used. Intramuscular injections should be given in the anterolateral aspect of the thigh for infants and children under 2 years of age, and in the deltoid muscle for older children and adults; injection into the buttock is not recommended.

Safe injections

The same high standard of injection safety should be applied to the administration of vaccines as to any other injection. A sterile needle and syringe should be used for each injection and disposed of safely.

WHO recommends the use of single-use (“auto-disable”) syringes or disposable monodose preparations whenever possible. Syringes should not be recapped (to avoid needle-stick injuries) and should be disposed of in a way that is safe for the recipient, the provider and the community.

Multiple vaccines

Inactivated vaccines do not generally interfere with other inactivated or live vaccines and can be given simultaneously with, or at any time in relation to, other vaccines without prejudicing immune responses. Most live vaccines can be given simultaneously. However, if two injected live-virus vaccines are not administered on the same day, the two injections should be separated by an interval of at least 4 weeks. The Ty21a typhoid vaccine can be administered simultaneously with or at any interval before or after other live vaccines.

A number of combination vaccines are now available, providing protection against more than one disease, and new combinations are likely to become available in future years. For routine vaccination, the combined diphtheria/tetanus/pertussis (DTP) and measles/mumps/rubella (MMR) vaccines are in widespread use in children. Other examples of combination vaccines are hepatitis A+B and hepatitis A + typhoid, IPV+DTP, IPV+DTP+Hib, MMR+varicella, IPV+DTP+HepB+Hib.¹ In adults, the combined diphtheria–tetanus vaccine (with reduced diphtheria, Td) is generally used in preference to monovalent tetanus toxoid vaccine. Combina-

¹ DTP= diphtheria, tetanus, pertussis; IPV = inactivated poliomyelitis vaccine; Hib = Haemophilus influenzae type b [vaccine]; HepB = hepatitis B [vaccine]; MMR= measles, mumps, rubella

tion vaccines offer important advantages for travellers, by reducing the number of injections required and the amount of time involved, so aiding compliance. Combination vaccines are just as safe and effective as the individual single-disease vaccines.

Choice of vaccines for travel

Vaccines for travellers include: (1) those that are used routinely, particularly but not only in children; (2) others that may be advised before travel to disease-endemic countries; (3) those that, in some situations, are mandatory.

Most of the vaccines that are routinely administered in childhood require periodic booster doses throughout life to maintain an effective level of immunity. Adults in their country of residence often neglect to keep up the schedule of booster vaccinations, particularly if the risk of infection is low. Some older adults may never have been vaccinated at all. It is important to realize that diseases such as diphtheria and poliomyelitis, which no longer occur in most industrialized countries, may be present in those visited by travellers. Pre-travel precautions should include booster doses of routine vaccines if the regular schedule has not been followed, or a full course of primary immunization for people who have never been vaccinated.

Other vaccines will be advised on the basis of a travel risk assessment for the individual traveller (see also Chapter 1). In deciding which vaccines would be appropriate, the following factors are to be considered for each vaccine:

- risk of exposure to the disease
- age, health status, vaccination history
- reactions to previous vaccine doses, allergies
- risk of infecting others
- cost.

Mandatory vaccination, as authorized by the International Health Regulations, nowadays concerns only yellow fever. Yellow fever vaccination is carried out for two different reasons: (1) to protect the individual in areas where there is a risk of yellow fever infection; and (2) to protect vulnerable countries from importation of the yellow fever virus. Travellers should therefore be vaccinated if they visit a country where there is a risk of exposure to yellow fever. They must be vaccinated if they visit a country that requires yellow fever vaccination as a condition of entry; this condition applies to all travellers who arrive from (including airport transit) a yellow fever endemic country.

Vaccination against meningococcal disease is required by Saudi Arabia for pilgrims visiting Mecca annually (Hajj) or at any time (Umrah) and/or Medina.

Table 6.1 **Vaccines for travellers**

Category	Vaccine
1. Routine vaccination	Diphtheria, tetanus, and pertussis Hepatitis B <i>Haemophilus influenzae</i> type b Human papillomavirus ^a Influenza ^b Measles, mumps and rubella Pneumococcal disease Poliomyelitis Rotavirus ^a Tuberculosis (BCG) ^c Varicella
2. Selective use for travellers	Cholera Hepatitis A ^d Japanese encephalitis ^d Meningococcal disease ^d Rabies Tick-borne encephalitis Typhoid fever Yellow fever ^d
3. Mandatory vaccination	Yellow fever (see country list) Meningococcal disease and polio (required by Saudi Arabia for pilgrims; updates are available on http://www.who.int/wer)

^a These vaccines are currently being introduced in some countries.

^b Routine for certain age groups and risk factors, selective for general travellers.

^c No longer routine in most industrialized countries.

^d These vaccines are also included in the routine immunization programme in several countries.

Some polio-free countries may also require travellers from polio-endemic countries to be immunized against polio in order to obtain an entry visa, e.g. Saudi Arabia (proof of oral poliovirus vaccination is required 6 weeks prior to application for an entry visa for visitors arriving from countries reporting poliomyelitis cases). Updates are available on <http://www.who.int/wer>.

Travellers should be provided with a written record of all vaccines administered (patient-retained record), preferably using the international vaccination certificate (which is required in the case of yellow fever vaccination). The certificate can be ordered from WHO at <http://www.who.int/ith/en/>.

Vaccines for routine use

Recommendations on vaccines for routine use are provided by WHO in regularly updated vaccine position papers: http://www.who.int/immunization/documents/positionpapers_intro/en/index.html

Since the information provided in this chapter is limited, readers are encouraged to refer to the WHO vaccine position papers as well as to national guidelines on routine vaccinations. It is recommended that travellers ensure that all routine vaccinations are up to date. Information on safety of routine vaccines can be found at: http://www.who.int/vaccine_safety/en/

DIPHTHERIA/TETANUS/PERTUSSIS

DIPHTHERIA

Disease

Diphtheria is a bacterial disease caused by *Corynebacterium diphtheriae*. The infection commonly affects the throat and may lead to obstruction of the airways and death. Exotoxin-induced damage occurs to organs such as the heart. Nasal diphtheria may be mild, and chronic carriage of the organism frequently occurs; asymptomatic infections are common. Transmission is from person to person, through droplets and close physical contact, and is increased in overcrowded and poor socioeconomic conditions. A cutaneous form of diphtheria is common in tropical countries and may be important in transmission of the infection.

Occurrence

Diphtheria is found worldwide, although it is not common in industrialized countries because of long-standing routine use of DTP vaccine. Large epidemics occurred in several east European countries in the 1990s.

Risk for travellers

Potentially life-threatening illness and severe, lifelong complications are possible in incompletely immunized individuals. Diphtheria is more frequent in parts of the world where vaccination levels are low.

Vaccine

All travellers should be up to date with the vaccine, which is usually given as “triple vaccine” – DTP (diphtheria/tetanus/pertussis or diphtheria/tetanus/acellular pertussis). After the initial course of three doses, additional doses may be given

as DT until 7 years of age, after which a vaccine with reduced diphtheria content (Td) is given. Since both tetanus toxoid (see below) and diphtheria toxoid can reasonably be given on a booster basis about every 10 years, there is no reason to use monovalent diphtheria vaccine. In some countries, adult boosters that contain acellular pertussis (TdaP) are being introduced.

TETANUS

Disease

Tetanus is acquired through environmental exposure to the spores of *Clostridium tetani*, which are present in soil worldwide. The disease is caused by the action of a potent neurotoxin produced by the bacterium in dead tissue (e.g. dirty wounds). Clinical symptoms of tetanus are muscle spasms, initially of the muscles of mastication causing trismus or “lockjaw”, which results in a characteristic facial expression – risus sardonicus. Trismus can be followed by sustained spasm of the back muscles (opisthotonus) and by spasms of other muscles. Finally, mild external stimuli may trigger generalized, tetanic seizures, which contribute to the serious complications of tetanus (dysphagia, aspiration pneumonia) and lead to death unless intense supportive treatment is rapidly initiated.

Occurrence

Dirty wounds can become infected with the spores of *Clostridium tetani* anywhere in the world.

Risk for travellers

Every traveller should be fully protected against tetanus. Almost any form of injury, from a simple laceration to a motor-vehicle accident, can expose the individual to the spores.

Vaccine

Tetanus toxoid vaccine is available as single toxoid (TT), combined with diphtheria toxoid (DT) or low-dose diphtheria toxoid (Td), and combined with diphtheria and pertussis vaccines (whole pertussis wP or acellular pertussis aP) (DTwP, DTaP, or TdaP). In some countries, combination vaccines with *Haemophilus influenzae* type b and/or IPV exist. Vaccines containing DT are used for children under 7 years of age and dT-containing vaccines for those aged 7 years and over. Vaccine combinations containing diphtheria toxoid (D or d) and tetanus toxoid, rather than tetanus toxoid alone, should be used when immunization against tetanus is indicated.

A childhood immunization schedule of 5 doses is recommended. The primary series of 3 doses of DTP (DTwP or DTaP) should be given in infancy, with a booster dose of a tetanus toxoid-containing vaccine ideally at age 4–7 years and another booster in adolescence, e.g. at age 12–15 years. For adult travellers, an extra tetanus toxoid-containing dose will provide additional assurance of long-lasting, possibly lifelong, protection.

All travellers should be up to date with the vaccine before departure. The type of tetanus prophylaxis that is required following injury depends on the nature of the lesion and the history of previous immunizations. However, no booster is needed if the last dose of tetanus vaccine was given less than 5 (for dirty wounds) to 10 years (for clean wounds) previously.

PERTUSSIS

Disease

Pertussis (whooping cough) is a highly contagious acute bacterial disease involving the respiratory tract and caused by *Bordetella pertussis*. It is transmitted by direct contact with airborne discharges from the respiratory mucous membranes of infected persons. It causes a severe cough of several weeks' duration with a characteristic whoop, often with cyanosis and vomiting. In young infants, the cough may be absent and disease may manifest with spells of apnea. Although pertussis can occur at any age, most serious cases and fatalities are observed in early infancy and mainly in developing countries. Major complications include pneumonia, encephalitis and malnutrition (due to repeated vomiting). Vaccination is the most rational approach to pertussis control.

Occurrence

Recent estimates from WHO suggest that about 17.6 million cases of pertussis occurred worldwide in 2003, 90% of which were in developing countries, and that some 279 000 patients died from this disease.

Risk for travellers

Unprotected infants are at high risk, but all children and young adults are at risk if they are not fully immunized. Exposure to pertussis is greater in developing countries.

Vaccine

All travellers should be up to date with the vaccine. Both whole-cell (wP) and acellular (aP) pertussis vaccines provide excellent protection. For several decades, wP vaccines have been widely used in national childhood vaccination programmes; aP vaccines, which cause fewer adverse effects, have been developed and are now being licensed in several countries. Both wP and aP are usually administered in combination with diphtheria and tetanus toxoids (DTwP or DTaP). Three doses are required for initial protection. Protection declines with time and probably lasts only a few years. A booster dose administered 1–6 years after the primary series is warranted. Some countries now offer an adult/adolescent booster, in particular to health care workers and young parents. Only aP or dTaP vaccines are used for vaccination of older children and adults.

HAEMOPHILUS INFLUENZAE TYPE B**Disease**

Haemophilus influenzae type b (Hib) is a common cause of bacterial pneumonia and meningitis and of a number of other serious and potentially life-threatening conditions, including epiglottitis, osteomyelitis, septic arthritis and sepsis in infants and older children.

Occurrence

Hib is estimated to cause at least 3 million cases of serious disease and hundreds of thousands of deaths annually, worldwide. Rarely occurring in infants under 3 months or after the age of 6 years, the disease burden is highest between 4 and 18 months of age. Hib is the dominant cause of sporadic (non-epidemic) bacterial meningitis in this age group, and is frequently associated with severe neurological sequelae despite prompt and adequate antibiotic treatment. In developing countries, it is estimated that 2–3 million cases of Hib pneumonia occur each year. The disease has practically disappeared in countries where routine vaccination of children is carried out.

Risk for travellers

All unprotected children are at risk at least up to the age of 5 years.

Vaccine

All children who are not up to date with this vaccine should be offered it. Conjugate Hib vaccines have dramatically reduced the incidence of Hib meningitis in

infants and of nasopharyngeal colonization by Hib. The vaccine is often given as a combined preparation with DTP or poliomyelitis vaccine in routine immunization programmes but is available as a single antigen preparation for use in children who did not receive the vaccine as part of routine immunization. Hib vaccine is not yet used routinely in many developing countries where there is continuing high prevalence of the disease.

HEPATITIS B

Disease and occurrence

See Chapter 5.

Risk for travellers

The risk depends on (1) the prevalence of HBV infection in the country of destination, (2) the extent of direct contact with blood or body fluids or of sexual contact with potentially infected persons, and (3) the duration and type of travel. Principal risky activities include health care (medical, dental, laboratory or other) that entails direct exposure to human blood or body fluids; receipt of a transfusion of blood that has not been tested for HBV; and dental, medical or other exposure to needles (e.g. acupuncture, piercing, tattooing or injecting drug use) that have not been appropriately sterilized. In addition, in less developed countries, transmission from HBV-positive to HBV-susceptible individuals may occur through direct contact between open skin lesions following a penetrating bite or scratch.

The vaccine should be considered for virtually all non-immune individuals travelling to areas with moderate to high risk of infection. It can be administered to infants from birth.

Vaccine

Hepatitis B vaccine is produced by recombinant DNA technology, most commonly in yeast. Three doses of vaccine constitute the complete series; the first two doses are usually given 1 month apart, with the third dose 1–12 months later.

A complete series of immunization provide protection for at least 15 years and, according to current scientific evidence, probably for life. Boosters are not recommended.

Because of the prolonged incubation period of hepatitis B, some protection will be afforded to most travellers following the second dose given before travel. However, the final dose should always be given upon return.

A rapid schedule of administration of monovalent hepatitis B vaccine has been proposed by the manufacturer as follows: day 0; 1 month; 2 months. An additional dose is given 6-12 months after the first dose. A very rapid schedule of administration of hepatitis B vaccine has been proposed as follows: day 0; 7 days; 21 days. An additional dose is given at 12 months.

A combination vaccine that provides protection against both hepatitis A and hepatitis B should be considered for travellers potentially exposed to both organisms. This inactivated vaccine is administered as follows: day 0; 1 month; 6 months. A rapid schedule at day 0, 1 month and 2 months, with an additional dose at 12 months, as well as a very rapid schedule with administration at day 0, day 7 and day 21 with a booster dose at 12 months, have been proposed by the vaccine manufacturer and approved by national regulatory authorities in some countries.

HUMAN PAPILLOMAVIRUS

Disease

Human papillomavirus (HPV) is a family of viruses that are very common all over the world. Although most HPV infections cause no symptoms and are self-limited, persistent genital HPV infection can cause cervical cancer in women (as well as other types of anogenital cancers, head and neck cancers, and genital warts in both men and women).

Occurrence

HPV is common worldwide and estimated to cause more than half a million new cancers and 274 000 deaths every year (2002 estimate), most of which affect women in developing countries.

Risk for travellers

Travel itself does not increase the risk of exposure. Transmission of HPV occurs most commonly through sexual activity; condoms may not offer complete protection. Since 2006, two HPV vaccines have been licensed; one vaccine targeting four and the other two HPV genotypes. Both vaccines are designed to protect against about 70% of cervical cancer cases worldwide (the 4-valent vaccine also protects against genital warts). The vaccines are intended for use primarily in girls and young women. Over the next few years, HPV vaccination will be introduced into the immunization schedules of several countries. Travellers are advised to check with the relevant health authorities regarding national recommendations and the availability of HPV vaccination in their country.

INFLUENZA

Disease and occurrence

See Chapter 5.

Risk for travellers

In the tropics, seasonal influenza can occur throughout the year. However, in the southern hemisphere, peak activity occurs between April and September and in the northern hemisphere, between November and March. Influenza transmission may be enhanced in crowded conditions associated with air travel, cruise ships and tour groups. Elderly people and individuals with certain medical conditions such as respiratory and cardiac disease, diabetes mellitus or any immunosuppressive condition are particularly at risk of more severe disease.

Vaccine

Influenza viruses constantly evolve, with rapid changes in their characteristics. To be effective, influenza vaccines need to stimulate immunity that protects against the principal strains of virus circulating at the time. Every year, the composition of influenza vaccines is modified separately for the northern and southern hemispheres. Since the antigenic changes in circulating influenza viruses can occur abruptly and at different times of the year, there may be significant differences between prevailing influenza strains in the northern and southern hemispheres. The internationally available vaccines contain three inactivated viral strains, the composition of which is modified every 6 months to ensure protection against the strains prevailing in each influenza season. The composition of vaccines is therefore adjusted for the hemisphere in which the vaccine will be used. Thus, a vaccine obtainable in one hemisphere may offer only partial protection against influenza infection in the other hemisphere; although in some years, the viruses in the vaccine may be antigenically identical. Available influenza vaccines do not protect against avian influenza.

Travellers with conditions placing them at high risk for complications of influenza should be regularly vaccinated every year. In years in which the northern and southern hemisphere influenza vaccine strains differ, those high-risk individuals travelling from one hemisphere to the other shortly before or during the other hemisphere's influenza season should obtain vaccination for the opposite hemisphere in a travel clinic. Where this is not possible, the traveller should arrange vaccination as soon as possible after arriving at the travel destination. Otherwise, receiving a vaccination at least 2 weeks before travel is advisable.

One dose of vaccine is given by intramuscular injection for individuals aged over 9 years. Two doses are administered at least 4 weeks apart for immunocompromised people and for children aged 6 months – 9 years; those aged 3–36 months should receive half the dose of the adult vaccines injections. Mild local reactions such as pain or swelling at the injection site are common. Systemic reactions such as fever are less common. Vaccination is relatively contraindicated in case of egg allergy.

MEASLES

Disease

Measles is a highly contagious infection; before vaccines became available, this disease affected most people by the time of adolescence. In 2005, measles still affected nearly 21 million persons, and the number of global measles deaths was estimated to be 345 000. Common complications include middle-ear infection and pneumonia. Transmission, which is primarily by large respiratory droplets, increases during the late winter and early spring in temperate climates, and after the rainy season in tropical climates.

Occurrence

Measles occurs worldwide in a seasonal pattern. However, following the introduction of large-scale measles immunization, far fewer cases now occur in industrialized countries and indigenous transmission has virtually stopped in the Americas. Epidemics may still occur every 2 or 3 years in areas where there is low vaccine coverage. In countries where measles has been largely eliminated, cases imported from other countries remain an important continuing source of infection.

Risk for travellers

Travellers who are not fully immunized against measles are at risk when visiting countries or areas where vaccine coverage is incomplete.

Vaccine

The measles/mumps/rubella triple (MMR) or measles/rubella (MR) vaccine is given in many countries instead of monovalent measles vaccine. In industrialized countries, measles vaccination is usually given at the age of 12–15 months, when seroconversion rates in excess of 90% are expected. In most developing countries, high attack rates and serious disease among infants necessitate early vaccination,

usually at 9 months of age, despite the relatively low (80–85%) seroconversion rates following vaccination in this age group. To ensure optimum population immunity, all children should be given a second opportunity for measles immunization. Although generally administered at school entry (age 4–6 years), the second dose may be given as early as one month following the first dose, depending on the local programmatic and epidemiological situation.

Special attention must be paid to all children and adolescent/young adult travellers who have not been vaccinated against measles at the appropriate time. Measles is still common in many countries and travel in densely populated areas may favour transmission. For infants travelling to countries where measles is highly endemic, a dose of vaccine may be already given at 6 months of age. However, children who receive the first dose between 6 and 8 months should subsequently receive the two doses according to the national schedule. Older children or adults who did not receive the two lifetime doses should consider this before travel.

It is generally recommended that individuals with a moderate degree of immune deficiency receive the vaccine if there is even a low risk of contracting measles infection from the community. There is a low level of risk in using measles vaccine in immunocompromised HIV-infected individuals. Where the risk of contracting measles infection is negligible, physicians who are able to monitor immune status, for instance CD4 counts, may prefer to avoid the use of measles vaccine.

MUMPS

Disease

Mumps, or parotitis epidemica, is a viral infection that primarily affects the salivary glands. Although mumps is mostly a mild childhood disease, the virus may also affect adults, in whom complications such as meningitis and orchitis are relatively common. Encephalitis and permanent neurological sequelae are rare complications of mumps.

Occurrence

In most parts of the world, annual mumps incidence is in the range of 100–1000 per 100 000 population, with epidemic peaks every 2–5 years. Peak incidence is found among children aged 5–9 years. Natural infection with mumps virus is thought to confer lifelong protection.

Risk for travellers

Travellers who are not fully immunized against mumps are at risk when visiting endemic countries.

Vaccine

The mumps vaccine is usually given in combination with measles and rubella vaccine (MMR). Different attenuated strains of the mumps virus are used for the production of live mumps vaccines, all of which are considered safe and efficacious, except for the Rubini strain. In order to avoid possible interference with persistent maternal antibodies, the first of the two recommended doses of the vaccine is usually given at 12–18 months of age, the second after a minimum interval of one month. A single dose of mumps vaccine, either as single antigen or in combination, has a protective efficacy of 90–96%. The second dose given in some countries at age 4–6 years provides protection to most individuals who do not respond to the first.

RUBELLA**Disease**

Rubella occurs worldwide and is normally a mild childhood disease. However, infection during early pregnancy may cause fetal death or congenital rubella syndrome (CRS) which is characterized by multiple defects, particularly of the brain, heart, eyes and ears. CRS is an important cause of hearing and visual impairment and mental retardation in countries where acquired rubella infection has not been controlled or eliminated.

Occurrence

Although the worldwide burden of CRS is not well characterized, it is estimated that more than 100 000 cases occur each year in developing countries alone.

Risk for travellers

Travellers who are not immunized against rubella may be at risk when visiting countries where the vaccine coverage is suboptimal. Particular attention should be paid to ensuring protection of women who may become pregnant during the period of travel.

Vaccine

The internationally licensed rubella vaccines, based on live attenuated RA 27/3 strain of the rubella virus and propagated in human diploid cells, have proven safe and efficacious, achieving 95–100% protection, possibly life-long, after just one dose. Following well designed and implemented programmes using such vaccines, rubella and CRS have almost disappeared from many countries. Other attenuated vaccine strains are available in Japan and China.

Rubella vaccine is commercially available in a monovalent form, in a bivalent combination with either measles or mumps vaccine, and in the trivalent measles/mumps/rubella (MMR) vaccine. Rubella vaccination of pregnant women should be avoided, and pregnancy should be avoided within one month of receiving the vaccine.

PNEUMOCOCCAL DISEASE

Disease

The term “pneumococcal disease” refers to a group of clinical conditions caused by the bacterium *Streptococcus pneumoniae*. Invasive pneumococcal infections include pneumonia, meningitis and febrile bacteraemia; the common non-invasive conditions include otitis media, sinusitis and bronchitis. Infection is acquired by direct person-to-person contact via respiratory droplets or oral contact. There are many healthy, asymptomatic carriers of the bacteria, but there is no animal reservoir or insect vector.

Several chronic conditions predispose to serious pneumococcal disease (see below). Increasing pneumococcal resistance to antibiotics underlines the importance of vaccination.

Occurrence

Pneumococcal diseases are a worldwide public health problem. *S. pneumoniae* is the leading cause of severe pneumonia in children under 5 years of age, causing 0.7 – 1 million deaths each year, mainly in developing countries. In industrialized countries, most pneumococcal disease occurs in the elderly.

Risk for travellers

While travel itself does not increase the risk of acquiring pneumococcal infection, access to optimal health care may be limited during travel, increasing the risk of poor outcomes should disease occur. Certain conditions predispose to complica-

tions of pneumococcal infections, including sickle-cell disease, other haemoglobinopathies, chronic renal failure, chronic liver disease, immunosuppression after organ transplantation and other etiological factors, asplenia and dysfunctional spleen, leaks of cerebrospinal fluid, diabetes mellitus and HIV infection. Elderly individuals, especially those over 65 years of age, are also at increased risk for pneumococcal disease. Pneumococcal vaccine may be considered for travellers who belong to these high-risk groups.

Vaccine

The current 23-valent polysaccharide vaccine represents pneumococcal serotypes that are responsible for 90% of pneumococcal infections and is immunogenic in those over 2 years of age. Children under 2 years of age and immunocompromised individuals do not respond well to the vaccine. Vaccination provides a relative protection against invasive pneumococcal disease in healthy adults. Pneumococcal polysaccharide vaccine is often recommended for selected groups, over the age of 2 years, at increased risk of pneumococcal disease. In some countries, such as the United States, routine vaccination is recommended for everyone aged over 65 years.

A conjugate vaccine containing seven serotypes of the pneumococcus is now available and is safe and immunogenic also in infants and children under 2 years. This vaccine is recommended by WHO as part of routine immunization in infants and has been introduced in some countries. It is advisable that children be up to date with immunization, as per the national recommendations, before undertaking travel.

POLIOMYELITIS

Disease

Poliomyelitis is a disease of the central nervous system caused by three closely related enteroviruses, poliovirus types 1, 2 and 3. The virus is spread predominantly by the faecal–oral route, although rare outbreaks caused by contaminated food or water have occurred. After the virus enters the mouth, the primary site of infection is the intestine, although the virus can also be found in the pharynx. Poliomyelitis is also known as “infantile paralysis” because it most frequently caused paralysis in infants and young children in the pre-vaccine era in industrialized countries. In developing countries, 65–75% of cases currently 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. There is no cure.

Occurrence

Significant progress has been made towards global eradication of poliomyelitis. More than 125 countries were endemic for polio in 1988; as of 2008, there are only four countries where indigenous wild poliovirus transmission has never been interrupted: Afghanistan, India, Nigeria and Pakistan (see Map). Wild poliovirus importations from the four 'endemic' countries into previously polio-free countries continue to occur, with some resulting in new outbreaks. As of mid-2008, imported wild poliovirus was circulating in seven previously polio-free countries: Angola, Chad, Democratic Republic of the Congo, Ethiopia, Ghana, Niger and the Sudan. Until wild poliovirus transmission has been stopped globally, all polio-free countries and areas remain at risk of importation and of renewed outbreaks.

Risks associated with international travel

The consequences of polio infection are crippling and sometimes life-threatening. Infection and paralysis may occur in non-immune individuals of any age. Infected travellers are potential vectors for transmission and possible reintroduction of the virus into polio-free zones, now that worldwide eradication is near. Until the disease has been certified as eradicated globally, the risks of acquiring polio (for travellers to infected areas), and of reinfection of polio-free areas (by travellers from infected areas), remain. Travellers to and from endemic and reinfected countries should be fully protected by vaccination. Updates on countries with ongoing transmission of indigenous and imported wild poliovirus and countries with recent transmission of imported wild poliovirus can be found at <http://www.polioeradication.org/caseload.asp>.

Vaccine

All travellers to and from polio-infected areas should be up to date with vaccination against poliomyelitis according to national immunization policy. There are two types of vaccine: inactivated (IPV), which is given by injection, and oral (OPV). OPV is composed of the three types of live attenuated polioviruses. Because of the low cost and ease of administration of the vaccine and its superiority in conferring intestinal immunity, OPV has been the vaccine of choice for controlling endemic and epidemic poliomyelitis in many countries. On very rare occasions (2–4 cases per million births per year) OPV causes vaccine-associated paralytic poliomyelitis (VAPP). The risk of VAPP is higher with the first dose of OPV than with subsequent doses. VAPP is more common in individuals who are immunocompromised, for whom IPV is the vaccine of choice.

Most industrialized countries now use IPV, either as the sole vaccine against poliomyelitis or in schedules combined with OPV. Although IPV suppresses

pharyngeal excretion of wild poliovirus, this vaccine has only limited effects in reducing intestinal excretion of poliovirus. Following the first dose, previously unvaccinated older children and adults receive the second dose 1–2 months later, with the third dose after 6–12 months. An additional dose is recommended after 4–6 years. For adults who have received a primary series of vaccination in childhood, a one-time only additional dose is recommended in some countries. IPV is also the vaccine of choice to protect travellers to polio infected areas who have no history of OPV use, as well as for immunocompromised individuals and their contacts and family members.

Travellers to polio-infected countries and areas who have previously received three or more doses of OPV or IPV should be offered another dose of polio vaccine before departure. Non-immunized individuals intending to travel to polio-infected countries and areas require a complete course of vaccine. Countries recommend OPV or IPV in these circumstances, depending on national policy. OPV has the advantage of boosting intestinal mucosal immunity to poliovirus and reducing the risk of intestinal infection while travellers are in polio-infected areas as well as subsequent virus excretion by returning travellers. For frequent travellers to polio-infected areas for brief periods of time, a one-time-only additional dose of polio vaccine after the primary series should be sufficient to prevent disease.

Travellers who are resident in a polio-infected country or area should have a full course of vaccination against polio, preferably with OPV, before leaving their country of residence to reduce the risk of international spread of wild poliovirus to polio-free areas. To optimize intestinal mucosal immunity against poliovirus, and minimize the risk of inadvertent intestinal carriage, such travellers should receive an additional dose of OPV between 1 and 12 months prior to each international travel. In cases of urgent travel, a minimum of one dose of OPV should be given before departure.

Some polio-free countries (e.g. Saudi Arabia) may require travellers from polio-infected countries to be immunized against polio in order to obtain an entry visa and/or to receive an additional dose on arrival in the country.

ROTAVIRUS

Disease

Rotavirus causes an acute gastroenteritis in infants and young children and is associated with profuse watery diarrhoea, projectile vomiting and fever. Rapid dehydration can occur, especially in very young infants, requiring rehydration

therapy. The virus is transmitted via the faecal–oral route and by direct person-to-person spread, although a respiratory mode of transmission has been proposed also. It replicates in the enterocytes of the small intestine, causing extensive damage to the microvilli that results in malabsorption and loss of fluids and electrolytes.

Occurrence

Rotavirus is found worldwide. The virus is ubiquitous, infecting a large proportion of young children by their second or third birthday. Re-infection of older children and adults is common, although the infection is usually sub-clinical.

Risk for travellers

The potential risk for travellers is extremely limited since most individuals will have good immunity through repeated exposures early in life.

Vaccine

Two live, attenuated, oral rotavirus vaccines are internationally licensed and routine childhood vaccination has been initiated in a number of countries. To date, the clinical efficacy of the rotavirus vaccines has been demonstrated mainly in the Americas and in Europe. WHO recommends the inclusion of rotavirus vaccination into the national immunization programmes of regions where vaccine efficacy data suggest a significant public health impact. Vaccination is not currently recommended for travellers or older children outside the routine childhood immunization schedule.

TUBERCULOSIS

Disease and occurrence

See Chapter 5.

Risk for travellers

Most travellers are at low risk for tuberculosis (TB). The risk for long-term travellers (>3 months) in a country with a higher incidence of TB than their own may be comparable to the risk for local residents. Living conditions, as well as duration of travel and purpose of travel, e.g. emergency relief, are important in determining the risk of infection: high-risk settings include impoverished communities, areas experiencing civil unrest or war, refugee areas, health facilities, prisons and shelters for the homeless. Persons with HIV infection are at higher risk of TB.

Vaccine

All versions of the BCG vaccine are based on live, attenuated mycobacterial strains descended from the original, attenuated bacillus Calmette–Guérin. The vaccine is administered intradermally and can be given simultaneously with other childhood vaccines. BCG vaccine is contraindicated for persons with severely impaired immunity, including individuals with HIV infection.

BCG vaccine is of very limited use for travellers. In the first year of life it provides good protection against severe forms of TB (miliary TB and meningitis). In countries with high TB prevalence, infants are generally immunized with a single dose of BCG as soon after birth as possible. Children who are known to be HIV-infected, even if asymptomatic, should not be immunized with BCG vaccine. Other protective benefits of the vaccine are uncertain. One dose of BCG should be considered for unvaccinated infants travelling from an area of low incidence to one of high incidence.

Many industrialized countries with a low incidence of TB have ceased giving BCG routinely to neonates.

Booster doses of BCG are not recommended by WHO.

VARICELLA**Disease and occurrence**

The causative pathogen is the varicella zoster virus (VZV). Varicella (chickenpox) is an acute, highly contagious disease with worldwide distribution. In temperate climates most cases occur before the age of 10 years. The epidemiology is less well understood in tropical areas, where a relatively large proportion of adults in some countries are seronegative.

Transmission is via droplets, aerosol or direct contact, and patients are usually contagious from a few days before rash onset until the rash has crusted over. While mostly a mild disorder in childhood, varicella tends to be more severe in adults. It is characterized by an itchy, vesicular rash, usually starting on the scalp and face, and initially accompanied by fever and malaise. As the rash gradually spreads to the trunk and extremities, the first vesicles dry out. It normally takes about 7–10 days for all crusts to disappear. The disease may be fatal, especially in neonates and immunocompromised persons. Complications include VZV-induced pneumonitis or encephalitis and invasive group A streptococcal infections. Following infection, the virus remains latent in neural ganglia; upon subsequent reactivation, VZV may

cause zoster (shingles), a disease affecting mainly immunocompromised persons and the elderly.

Risk for travellers

In several industrialized countries, varicella vaccines have been introduced into the childhood immunization programmes. Most adult travellers from temperate climates are immune (as a result of either natural disease or immunization). Adult travellers without a history of varicella who travel from tropical countries to temperate climates may be at increased risk and should consider vaccination.

Vaccine

Various formulations of the live attenuated vaccine, based on the so-called Oka strain of VZV, are in use. Some formulations are approved for use at 9 months of age and older. Following a single dose, seroconversion occurs in about 95% of healthy children. From a logistic as well as an epidemiological point of view, the optimal age for varicella vaccination is 12–24 months. In Japan and several other countries, 1 dose of the vaccine is considered sufficient, regardless of age. In the United States, 2 doses, 4–8 weeks apart, are recommended for adolescents and adults. In a few cases (<5%) vaccinees experience a mild varicella-like disease with rash within 4 weeks. Contraindications to varicella vaccine are pregnancy (because of a theoretical risk to the fetus; pregnancy should be avoided for 4 weeks following vaccination), ongoing severe illness, a history of anaphylactic reactions to any component of the vaccine, and immunosuppression.

Vaccines for selective use

Vaccines in this section need be offered only to travellers who are going to certain specific destinations. The decision to recommend a vaccine will depend on a travel risk assessment for the individual.

CHOLERA

Disease and occurrence

See Chapter 5.

Risk for travellers

Travellers are not at significant risk from cholera provided that simple precautions are taken to avoid potentially contaminated food and water. Vaccination is

of questionable benefit to general tourist travellers, for whom the risk is very low, and is therefore recommended only for individuals at increased risk of exposure, particularly emergency relief and health workers in refugee situations.

Cholera vaccination is not required as a condition of entry to any country.

Vaccine

Although two new cholera vaccines (live and killed), given orally, are safe and effective and have been licensed in a limited number of countries, the live vaccine is currently no longer available commercially. The killed, oral vaccine is safe and efficacious for individuals over 2 years of age and confers high-grade (85–90%) protection for 6 months after the second dose, to be given at least 1 week after the first. Protection declines rapidly in young children after 6 months, but remains as high as 62% in adult vaccine recipients.

Precautions and contraindications

The vaccine is not intended for children under 2 years of age, and children between 2–6 years should receive half the adult dose only.

Type of vaccine:	Killed oral
Number of doses:	Two, at least 1 week apart
Contraindications:	Hypersensitivity to previous dose
Adverse reactions:	Mild gastrointestinal disturbances reported
Before departure:	3 weeks
Consider for:	Travellers at high risk (e.g. emergency or relief workers)
Special precautions:	None

HEPATITIS A

Disease and occurrence

Although hepatitis A is rarely fatal in children and young adults, most infected adults and some older children become ill and are unable to work for several weeks or months. The case-fatality rate exceeds 2% among those over 40 years of age and may be 4% for those aged 60 years or more. (See also Chapter 5.)

Risk for travellers

The vaccine should be considered for all travellers to areas with moderate to high risk of infection, and those at high risk of acquiring the disease should be strongly encouraged to be vaccinated regardless of where they travel.

People born and raised in developing countries, and those born before 1945 in industrialized countries, have often been infected in childhood and are likely to be immune. For such individuals, it may be cost-effective to test for antibodies to hepatitis A virus (anti-HAV) so that unnecessary vaccination can be avoided.

Vaccine

Current hepatitis A vaccines, all of which based on inactivated (killed) virus, are safe and highly effective. Anti-HAV antibodies are detectable by 2 weeks after administration of the first dose of vaccine. The second dose – given at least 6 months, and usually 6–24 months, after the first dose – is necessary to promote long-term protection. Results from mathematical models indicate that, after completion of the primary series, anti-HAV antibodies probably persist for 25 years or more. Booster doses are not recommended. Serological testing to assess antibody levels after vaccination is not indicated. Given the long incubation period of hepatitis A (average 2–4 weeks), the vaccine can be administered up to the day of departure and still protect travellers. The use of immune globulin is now virtually obsolete for the purposes of travel prophylaxis.

A combination hepatitis A/typhoid vaccine is available for those exposed to waterborne diseases. The vaccine is administered as a single dose and confers high levels of protection against both diseases. A second dose of hepatitis A vaccine is needed 6–24 months later and boosters of typhoid vaccine should be given at 3-yearly intervals.

A combination vaccine that provides protection against both hepatitis A and hepatitis B may be considered for travellers who may be exposed to both organisms. Primary immunization with the combined hepatitis A and B vaccine consist of three doses, given on a schedule of 0, 1 and 6 months. According to the manufacturer's instructions, this combination vaccine may also be administered on days 0, 7 and 21, with a booster dose at 12 months. Minor local and systemic reactions are fairly common. Minimum age is 1 year.

Precautions and contraindications

None.

Type of vaccine:	Inactivated, given i.m.
Number of doses:	Two
Schedule:	Second dose 6–24 months after the first
Booster:	May not be necessary
Contraindications:	Hypersensitivity to previous dose
Adverse reactions:	Mild local reaction of short duration, mild systemic reaction
Before departure:	Protection 2–4 weeks after first dose
Recommended for:	All non-immune travellers to endemic areas
Special precautions:	None

JAPANESE ENCEPHALITIS**Disease and occurrence**

See Chapter 5.

Risk for travellers

Japanese encephalitis (JE) is the leading cause of viral encephalitis in Asia and occurs in almost all Asian countries (see Map). Its incidence has been declining in Japan and the Korean peninsula and in some regions of China, but is increasing in Bangladesh, India, Nepal, Pakistan, northern Thailand and Viet Nam. Transmission occurs principally in rural agricultural locations where flooding irrigation is practised – some of which may be near or within urban centres. Transmission is seasonal and mainly related to the rainy season in south-east Asia, but all-year transmission occurs. In the temperate regions of China, Japan, the Korean peninsula and eastern parts of the Russian Federation, transmission occurs mainly during the summer and autumn. Vaccination is not recommended for all travellers to Asia because of the low incidence of the disease in travellers and potential (although rare) adverse events of current inactivated vaccine: it should be based on individual risk assessment, taking into account the season, the type of accommodation and the duration of exposure, as well as the travel itinerary. The risk to short-term travellers and those who travel mainly to urban areas is very low. Vaccination is recommended for travellers with extensive outdoor exposure (camping, hiking, bicycle tours, outdoor occupational activities, in particular in areas where flooding irrigation is practised) in rural areas of an endemic region during the transmission season. It is also recommended for expatriates living in endemic areas through a transmission season or longer.

Vaccine

Two types of JE vaccine are widely available: inactivated mouse-brain-derived vaccine (IMB) and cell-culture-derived live attenuated SA 14-14-2 vaccine. Until recently, the IMB vaccine was the most widely available commercially, but its production is being discontinued by several manufacturers. New vaccines including cell-culture derived, inactivated vaccines are in the process of being licensed or in the final stage of development.

Precautions and contraindications

A hypersensitivity reaction to a previous dose is a contraindication. The live attenuated vaccine should be avoided in pregnancy unless the likely risk favours its administration. Rare, but serious, neurological side-effects attributed to IMB vaccine have been reported from endemic as well as non-endemic regions. Allergic reactions to components of the vaccine occur occasionally. As such reactions may occur within 2 weeks of administration, it is advisable to ensure that the complete course of vaccine is administered well in advance of departure.

Type of vaccine:	Inactivated mouse-brain-derived or live attenuated
Schedule:	For the inactivated vaccine: 3 doses at days 0, 7 and 28; or 2 doses given preferably 4 weeks apart (0.5 or 1.0 ml for adults, 0.25 or 0.5 ml for children depending on the vaccines) For the live attenuated SA 14-14-2 vaccine equally good protection is achieved with a single dose followed, as required, with a single booster dose given at an interval of about 1 year
Booster:	After 1 year and then 3-yearly (for IMB only) when continued protection is required
Contraindications:	Hypersensitivity to a previous dose of vaccine, pregnancy and immunosuppression (live vaccine)
Adverse reactions:	Occasional mild local or systemic reaction; occasional severe reaction with generalized urticaria, hypotension and collapse
Before departure:	Inactivated vaccine, at least two doses before departure. Live attenuated vaccine, one dose is enough
^a The duration of immunity after serial booster doses in adult travellers has not been well established for the mouse-brain-derived vaccine. For children aged 1–3 years, the mouse-brain-derived vaccine provides adequate protection throughout childhood following two primary doses 4 weeks apart and boosters after 1 year and subsequently at 3-yearly intervals until the age of 10–15 years.	

MENINGOCOCCAL DISEASE

Disease and occurrence

See Chapter 5.

Risk for travellers

Vaccination should be considered for travellers to countries where outbreaks of meningococcal disease are known to occur.

- Travellers to industrialized countries are exposed to the possibility of sporadic cases. Outbreaks of meningococcal C disease occur in schools, colleges, military barracks and other places where large numbers of adolescents and young adults congregate.
- Travellers to the sub-Saharan meningitis belt may be exposed to outbreaks of serogroup A disease with comparatively very high incidence rates during the dry season (December–June). Long-term travellers living in close contact with the indigenous population may be at greater risk of infection. In recent years, outbreaks caused by serogroups W135 have also occurred.
- Pilgrims to Mecca are at risk. The tetravalent vaccine, (A, C, Y, W-135) is currently required by Saudi Arabia for pilgrims visiting Mecca for the Hajj (annual pilgrimage) or for the Umrah.

Vaccine

Polysaccharide vaccines

Internationally marketed meningococcal polysaccharide vaccines are either bivalent (A and C) or tetravalent (A, C, Y and W-135). The vaccines are purified, heat-stable, lyophilized capsular polysaccharides from meningococci of the respective serogroups.

Both group A and group C vaccines have documented short-term efficacy levels of 85–100% in older children and adults. However, group C vaccines do not prevent disease in children under 2 years of age, and the efficacy of group A vaccine in children under 1 year of age is unclear. Group Y and W-135 polysaccharides have been shown to be immunogenic only in children over 2 years of age.

A protective antibody response occurs within 10 days of vaccination. In school-children and adults, the bivalent and tetravalent polysaccharide vaccines appear to provide protection for at least 3 years, but in children under 4 years the levels of specific antibodies decline rapidly after 2–3 years.

The currently available bivalent and tetravalent meningococcal vaccines are recommended for immunization of specific risk groups as well as for large-scale immunization, as appropriate, for the control of meningococcal outbreaks caused by vaccine-preventable serogroups (A and C, or A, C, Y, W-135 respectively). Travellers who have access to the tetravalent polysaccharide vaccine (A, C, Y, W-135) should opt for this rather than the bivalent vaccine because of the additional protection against groups Y and W-135.

These vaccines do not provide any protection against group B meningococci, which are the leading cause of endemic meningococcal disease in some countries.

Conjugate vaccines

A T-cell-dependent immune response is achieved through conjugation of the polysaccharide to a protein carrier. Conjugate vaccines are therefore associated with an increased immunogenicity among infants and prolonged duration of protection.

Monovalent serogroup C conjugate vaccines were first licensed for use in 1999 and are now incorporated in national vaccination programmes in an increasing number of countries. In contrast to group C polysaccharide vaccines, the group C conjugate vaccine elicits adequate antibody responses and immunological memory even in infants who are vaccinated at 2, 3 and 4 months of age.

More recently, a tetravalent conjugate vaccine (A, C, Y, W-135) has been licensed in a limited number of countries.

Precautions and contraindications

The internationally available polysaccharide vaccines are safe, and significant systemic reactions have been extremely rare. The most common adverse reactions are erythema and slight pain at the site of injection for 1–2 days. Fever exceeding 38.5 °C occurs in up to 2% of vaccinees. No significant change in safety or reactogenicity has been observed when the different group-specific polysaccharides are combined into bivalent or tetravalent meningococcal vaccines. Cross-protection does not occur and travellers already immunized with conjugate vaccine against serogroup C are not protected against other serogroups.

Type of vaccine:	Purified bacterial capsular polysaccharide meningococcal vaccine (bivalent or tetravalent)
Number of doses:	One
Duration of protection:	3–5 years
Contraindications:	Serious adverse reaction to previous dose

Adverse reactions:	Occasional mild local reactions; rarely, fever
Before departure:	2 weeks
Consider for:	All travellers to countries in the sub-Saharan meningitis belt and to areas with current epidemics; college students at risk from endemic disease; Hajj and Umrah pilgrims (mandatory)
Special precautions:	Children under 2 years of age are not protected by the vaccine

RABIES

Disease and occurrence

See Chapter 5

Risk for travellers

The risk to travellers in areas endemic for rabies (see Map, or www.who.int/rabies/rabnet) is proportional to their contact with potentially rabid mammals. Dogs, both owned and ownerless, are very common, with an estimated 1:10 ratio of dogs to humans in most developing countries. An average of 100 suspected rabid dog bites per 100 000 inhabitants are reported in endemic countries. According to a recent survey conducted in India, 1.6% of the total population received a dog bite during a 12-month period. As rabies is a lethal disease, medical advice should be sought immediately at a competent medical centre, ideally in the rabies treatment centre of a major city hospital. First-aid measures should also be started immediately (see Post-exposure prophylaxis, below).

Travellers should avoid contact with free-roaming animals, especially dogs and cats, and with wild and captive animals. For travellers who participate in caving or spelunking, casual exposure to cave air is not a concern, but cavers should be warned not to handle bats. In most countries of the world, suspect contact with bats should be followed by post-exposure prophylaxis.

The map in Chapter 5 shows the WHO categories of risk: from no risk (rabies-free areas), to low, medium and high risk (areas with endemic dog rabies). Categorization is based primarily on the animal host species in which rabies virus(es) is/are maintained in a country, that is bats and/or other wildlife and/or dogs. Access to proper medical care and the availability of modern rabies vaccines have also been taken into consideration on a country basis. In countries belonging to categories 2–4, pre-exposure immunization against rabies is recommended for travellers with certain characteristics:

Category 1: no risk.

Category 2: low risk. In these countries travellers involved in activities that might bring them into direct contact with bats (for example, wildlife professionals, researchers, veterinarians and adventure travellers visiting areas where bats are commonly found) should receive pre-exposure prophylaxis.

Category 3: medium risk. In these countries, travellers involved in any activities that might bring them into direct contact with bats and other wild animals especially carnivores (for example, wildlife professionals, researchers, veterinarians and travellers visiting areas where bats and wildlife are commonly found) should receive pre-exposure prophylaxis.

Category 4: high risk. In these countries, travellers spending a lot of time in rural areas involved in activities such as running, bicycling, camping, or hiking should receive pre-exposure prophylaxis. It is also recommended for people with significant occupational risks, such as veterinarians, and expatriates living in areas with a significant risk of exposure to domestic animals, particularly dogs, and wild carnivores. Children should be immunized as they are at higher risk due to playing with animals, particularly with dogs and cats, may receive more severe bites or are more likely not to report contact with suspect rabies animals.

Vaccine

Vaccination against rabies is used in two distinct situations:

- to protect those who are at risk of exposure to rabies, i.e. pre-exposure vaccination;
- to prevent clinical rabies occurrence after exposure has occurred, usually following the bite of an animal suspected of having rabies, i.e. post-exposure prophylaxis.

The vaccines used for pre-exposure and post-exposure vaccination are the same, but the immunization schedule differs according to the type of application. Rabies immunoglobulin is used only for post-exposure prophylaxis. Modern vaccines of cell-culture or embryonated egg origin are safer and more effective than the older vaccines, which were produced in brain tissue. These modern rabies vaccines are now available in major urban centres of most countries of the developing world. Rabies immunoglobulin, on the other hand, is in short supply worldwide and may not be available even in major urban centres in many dog rabies-infected countries.

Pre-exposure vaccination

Pre-exposure vaccination should be offered to people at high risk of exposure to rabies, such as laboratory staff working with rabies virus, veterinarians, animal

handlers and wildlife officers, and other individuals living in or travelling to areas where rabies is endemic. Travellers with extensive outdoor exposure in rural areas – such as might occur while running, bicycling, hiking, camping, backpacking, etc. – may be at risk, even if the duration of travel is short. Pre-exposure vaccination is advisable for children living in or visiting rabies-endemic areas, where they provide an easy target for rabid animals. Pre-exposure vaccination is also recommended for persons travelling to isolated areas or to areas where immediate access to appropriate medical care is limited or to countries where biologicals are in short supply and locally available rabies vaccines might be unsafe and/or ineffective.

Pre-exposure vaccination consists of three full intramuscular doses of cell-culture or embryonated egg origin rabies vaccine given on days 0, 7 and 21 or 28 (a few days' variation in the timing is not important). For adults, the vaccine should always be administered in the deltoid area of the arm; for young children (under 2 years of age), the anterolateral area of the thigh is recommended. Rabies vaccine should never be administered in the gluteal area: administration in this manner will result in lower neutralizing antibody titres.

To reduce the cost of cell-derived vaccines for pre-exposure rabies vaccination, intradermal vaccination in 0.1-ml volumes on days 0, 7 and either 21 or 28 may be considered. This method of administration is an acceptable alternative to the standard intramuscular administration, but it is technically more demanding and requires appropriate staff training and qualified medical supervision. As an open vial should not be kept for more than 6 hours, wastage can be avoided by vaccinating several people during that period. Concurrent use of chloroquine can reduce the antibody response to intradermal application of cell-culture rabies vaccines. People who are currently receiving malaria prophylaxis or who are unable to complete the entire three-dose pre-exposure series before starting malarial prophylaxis should therefore receive pre-exposure vaccination by the intramuscular route.

Rabies vaccines will induce long-lasting memory cells, giving rise to an accelerated immune response when a booster dose of vaccine is administered. Periodic booster injections are therefore not recommended for general travellers. However, in the event of exposure through the bite or scratch of an animal known or suspected to be rabid, persons who have previously received a complete series of pre- or post-exposure rabies vaccine (with cell-culture or embryonated egg vaccine) should receive two booster doses of vaccine. Ideally, the first dose should be administered on the day of exposure and the second 3 days later. This should be combined with thorough wound treatment (see Post-exposure prophylaxis, below). Rabies immunoglobulin is not required for previously vaccinated patients (as mentioned above).

Periodic booster injections are recommended only for people whose occupations put them at continuous or frequent risk of rabies exposure, e.g. rabies researchers or staff in diagnostic laboratories where rabies virus is present. For more information on continuous or frequent risk, see *WHO Expert Consultation on Rabies*.¹ For persons at continuous or frequent risk of rabies exposure who have previously received pre-exposure rabies vaccination, a booster vaccination is administered if the serological titre of the person at risk falls below 0.5 IU/ml, the antibody level considered to be protective.

Precautions and contraindications

Modern rabies vaccines are well tolerated. The frequency of minor adverse reactions (local pain, erythema, swelling and pruritus) varies widely from one report to another. Occasional systemic reactions (malaise, generalized aches and headaches) have been noted after both intramuscular and intradermal injections.

Type of vaccine:	Modern cell-culture or embryonated egg vaccine
Number of doses:	Three, one on each of days 0, 7 and 21 or 28, given i.m. (1 ml/dose) or i.d. (0.1 ml/per inoculation site) ^a
Booster:	Not routinely needed for general travellers ^b
Adverse reactions:	Minor local or systemic reactions
Before departure:	Pre-exposure prophylaxis for those planning a visit to a rabies-endemic country, especially if the visited area is far from major urban centres where appropriate care, including the availability of post-exposure rabies prophylaxis, is not assured.
<p>^a For information on which vaccines are recommended for intradermal use, see: http://www.who.int/rabies/human/postexp/en/index.html</p> <p>^b In the event of exposure through the bite or scratch of an animal known or suspected to be rabid, persons who have previously received a complete series of pre-exposure or post-exposure cell-culture or embryonated egg rabies vaccine should receive two booster doses of vaccine, the first dose ideally on the day of exposure and the second 3 days later. Rabies immunoglobulin should not be administered.</p>	

Rabies post-exposure prophylaxis

In a rabies-endemic area, the circumstances of an animal bite or other contact with an animal suspected to be rabid may require post-exposure prophylaxis. In such situations, medical advice should be obtained immediately.

¹ *WHO Expert Consultation on Rabies: first report*. Geneva, World Health Organization, 2005 (WHO Technical Report Series, No. 931); available at www.who.int/rabies/Expert-ConsultationOnRabies.pdf

Post-exposure prophylaxis to prevent the establishment of rabies infection involves first-aid treatment of the wound followed by administration of rabies vaccine; in the case of category III exposure, rabies immunoglobulin should also be administered.

Strict adherence to the WHO-recommended guidelines for optimal post-exposure rabies prophylaxis virtually guarantees protection from the disease. The administration of vaccine, and immunoglobulin if required, must be conducted by, or under the direct supervision of, a physician.

Post-exposure prophylaxis depends on the type of contact with the confirmed or suspect rabid animal, as follows:

Type of contact, exposure and recommended post-exposure prophylaxis

<i>Category</i>	<i>Type of contact with a suspect or confirmed rabid domestic or wild^a animal, or animal unavailable for testing</i>	<i>Type of exposure</i>	<i>Recommended post-exposure prophylaxis</i>
I	Touching or feeding of animals Licks on intact skin	None	None, if reliable case history is available
II	Nibbling of uncovered skin Minor scratches or abrasions without bleeding	Minor	Administer vaccine immediately. ^b Stop treatment if animal remains healthy throughout an observation period of 10 days ^c or is proved to be negative for rabies by a reliable laboratory using appropriate diagnostic techniques
III	Single or multiple transdermal bites or scratches, licks on broken skin Contamination of mucous membrane with saliva (i.e. licks) Exposures to bats ^d	Severe	Administer rabies immunoglobulin and vaccine immediately. Stop treatment if animal remains healthy throughout an observation period of 10 days or is found to be negative for rabies by a reliable laboratory using appropriate diagnostic techniques

^a Exposure to rodents, rabbits and hares seldom, if ever, requires specific anti-rabies post-exposure prophylaxis.

^b If an apparently healthy dog or cat in or from a low-risk area is placed under observation, the situation may warrant delaying initiation of treatment.

^c This observation period applies only to dogs and cats. Except in the case of threatened or endangered species, other domestic and wild animals suspected to be rabid should be humanely killed and their tissues examined for the presence of rabies antigen using appropriate laboratory techniques.

^d Post-exposure prophylaxis should be considered when contact between a human and a bat has occurred unless the exposed person can rule out a bite or scratch or exposure to a mucous membrane.

(1) Local treatment of wounds (first aid treatment)

Elimination of the rabies virus at the site of bite or scratch by chemical or physical means is an effective mechanism to aid in the protection against infection. Immediate washing and flushing for a minimum of 15 minutes with soap or detergent and water, or water alone, is imperative. Following washing, ethanol (70%) or iodine or povidone iodine should be applied. Most severe bite wounds are best treated by daily dressing. Suturing should be avoided; if it cannot be avoided, the wound should first be infiltrated with passive rabies immunization products and suturing delayed for several hours. This will allow diffusion of the antibody through the tissues before suturing is performed. Antibiotics and tetanus prophylaxis should be administered as appropriate for other wounds.

(2) Rabies biologicals for passive immunization:

Rabies immunoglobulins (RIG) should be administered in all category III exposures (as well as in category II exposures when the patient is immunosuppressed). Human rabies immunoglobulin (HRIG) is mainly available in industrialized countries; both purified equine rabies immunoglobulin (ERIG) and human immunoglobulin are used in developing countries. F(ab')₂ products have recently been developed from equine immunoglobulins. Given that the clearance of F(ab')₂ fragments is more rapid than that of intact immunoglobulins, in case of multiple severe exposures, HRIG should preferably be used for passive immunization.

Dosage and administration: The dose for HRIG is 20 IU/kg body weight, and for ERIG and F(ab')₂ products 40 IU/kg body weight. The full dose of rabies immunoglobulin, or as much as is anatomically feasible, should be administered into and around the wound site. Any remainder should be injected i.m. at a site distant from the site of vaccine administration. Multiple needle injections into the wound should be avoided. If the dose of rabies immunoglobulin is too small to infiltrate all wounds, as might be true of a severely bitten individual, the correct dosage of rabies immunoglobulin can be diluted in physiological buffered saline to ensure greater wound coverage.

HRIG gives rise to virtually no serious adverse reactions. ERIG is now highly purified and the occurrence of adverse events has been significantly reduced (<1–2%, compared with 40% for the original unpurified rabies antisera). F(ab')₂ products were originally developed from equine immunoglobulins in order to reduce the severe adverse reactions initially described in association with the use of heterologous immunoglobulin products. Thus, they cause virtually no serious adverse reactions. Pregnancy, infancy, old age and concurrent illness are not contraindications for rabies post-exposure prophylaxis in the event of an exposure.

Rabies biologicals for passive immunization should not be administered later than 7 days after post-exposure vaccination with cell-culture or embryonated egg rabies vaccine has been initiated.

(3) Active immunization for post-exposure prophylaxis:

Highly purified and potent modern cell-culture or embryonated egg vaccines should be used. Cell-culture and embryonated egg vaccines can be administered either i.m. or i.d.

Intramuscular regimens: Two i.m. regimens are recommended for post-exposure vaccination; the five-dose regimen (Essen regimen) is the more commonly used:

- *Essen regimen:* this five-dose regimen is administered on days 0, 3, 7, 14 and 28 in the deltoid muscle.
- *Zagreb or '2-1-1' regimen:* administered as 2 doses on day 0 (one dose in the right and one in the left deltoid), and one dose on each of days 7 and 21 in the deltoid muscle.

Intradermal regimens: Intradermal administration of cell-culture and embryonated egg rabies vaccines has been successfully used in many developing countries that cannot afford the five-dose intramuscular schedule. Intradermal schedules have been evaluated and used extensively for post-exposure prophylaxis in some developing countries to replace nerve-tissue vaccines where intramuscular vaccination regimens are not an alternative from an economic viewpoint. Intradermal injections should be administered by staff well trained in the technique.

WHO recommends the following intradermal regimens and vaccines for use by the intradermal route:

- *8-site intradermal method (8-0-4-0-1-1):* one intradermal injection at 8 sites on day 0 (one in each upper arm, one in each lateral thigh, one on each side of the suprascapular region, and one on each side of the lower quadrant region of the abdomen); one injection at 4 sites on day 7 (one in each upper arm and in lateral thigh); and one injection at one site on days 30 and 90 (one upper arm).

For use with: human diploid cell vaccine (HDCV) (Imovax™) and purified chick embryo cell vaccine (PCECV) (Rabipur™). Both vaccines at 0.1 ml per intradermal site.

- *2-site intradermal method (2-2-2-0-2):* one intradermal injection at 2 sites on days 0, 3, 7 and 28.

For use with: 0.1 ml for purified vero cell rabies vaccine (PVRV) (Verorab™); 0.1 ml for PCECV (Rabipur™).

Post-exposure rabies prophylaxis

1. **Wound treatment:** Thorough washing of the wound with soap/detergent and water, followed by the application of ethanol or an aqueous solution of iodine or povidone.
2. **Passive immunization:** Human rabies immunoglobulin or equine rabies immunoglobulin or F(ab')₂ products for category III exposure (see table, above). Human rabies immunoglobulin should be used in case of multiple severe exposure. Passive immunization should be administered just before administration of the first dose of vaccine given in the post-exposure prophylaxis regimen. If it is not immediately available, passive immunization can be administered up until the seventh day after the primary series of post-exposure prophylaxis (with cell-culture or embryonated egg rabies vaccine) was initiated.
3. **Active immunization:** Cell-culture or embryonated egg rabies vaccines should always be used for post-exposure prophylaxis (see regimens above).^a

Post-exposure prophylaxis in previously vaccinated individuals: For persons who have previously received a full course of cell-culture or embryonated egg rabies vaccine, post-exposure prophylaxis consists of a series of two booster doses of vaccine given either intramuscularly or intradermally on days 0 and 3. It is not necessary to administer passive immunization products.

^a Post-exposure prophylaxis can be stopped if the suspect animal is proved by appropriate laboratory examination to be free of rabies or, in the case of domestic dogs and cats, if the animal remains healthy throughout a 10-day observation period.

TICK-BORNE ENCEPHALITIS**Disease and occurrence**

See Chapter 5.

Risk for travellers

Travellers who walk and camp in infested areas during the tick season (usually spring to early autumn) are at risk and should be vaccinated. Some degree of protection is afforded by clothing that covers as much skin as possible and by applying insect repellent.

Vaccine

The vaccine should be offered only to at risk travellers. Two vaccines are available in Europe, in adult and paediatric formulations. These are inactivated whole-cell vaccines containing a suspension of purified tick-borne encephalitis virus grown on chick embryo cells and inactivated with formaldehyde. Both provide safe and reliable protection. Immunity is induced against all variants of the tick-borne encephalitis virus including the European and Far Eastern subtypes. Two doses of 0.5 ml should be given i.m. 4–12 weeks apart. A third dose is given 9–12 months after the second dose and confers immunity for 3 years. Booster doses are required to maintain immunity and should be given every 3 years if the risk continues. Outside endemic countries, the vaccines may not be licensed and will have to be obtained by special request.

Precautions and contraindications

Occasional local reactions may occur, such as reddening and swelling around the injection site, swelling of the regional lymph nodes or general reactions (e.g. fatigue, pain in the limb, nausea and headache). Rarely, there may be fever above 38 °C for a short time, vomiting or transient rash. In very rare cases, neuritis of varying severity may be seen, although the etiological relationship to vaccination is uncertain. The vaccination has been suspected of aggravating autoimmune diseases such as multiple sclerosis and iridocyclitis, but this remains unproven. Hypersensitivity to thiomersal (a vaccine preservative) is a contraindication.

Type of vaccine:	Killed
Number of doses:	Two, given i.m. 4–12 weeks apart, plus booster
Booster:	9–12 months after second dose
Contraindications:	Hypersensitivity to the vaccine preservative thiomersal; adverse reaction to previous dose
Adverse reactions:	Local reactions occasionally; rarely fever
Before departure:	Second dose 2 weeks before departure
Recommended for:	High-risk individuals only
Special precautions:	Avoid ticks; remove ticks immediately if bitten

TYPHOID FEVER

Disease and occurrence

See Chapter 5.

Risk for travellers

All travellers to endemic areas are at potential risk of typhoid fever, although the risk is generally low in tourist and business centres where standards of accommodation, sanitation and food hygiene are high. The risk is particularly high in the Indian subcontinent. Even vaccinated individuals should take care to avoid consumption of potentially contaminated food and water as the vaccine does not confer 100% protection.

Vaccine

Travellers to countries where the risk of typhoid fever is high, where hygiene is poor, and where there is a high prevalence of antibiotic-resistant organisms, may be offered one of the following vaccines.

- Oral Ty21a. This live, attenuated mutant strain of *Salmonella typhi* Ty21a, supplied as enteric coated capsules, is given orally in three doses (four in North America) 2 days apart, and produces protection 7 days after the final dose. Seven years after the final dose the protective efficacy is 67% in residents of endemic areas but may be less for travellers. A liquid formulation is no longer available.
- Injectable Vi CPS. Capsular Vi polysaccharide vaccine (Vi CPS), containing 25 µg of polysaccharide per dose, is given i.m. in a single dose and produces protection 7 days after injection. In endemic areas, the protective efficacy after vaccination is 72% after 1.5 years and 50% after 3 years.

Both vaccines are safe and effective. However, their efficacy in children under 2 years of age has not been demonstrated.

A combined typhoid/hepatitis A vaccine is also available in some countries.

Precautions and contraindications

Proguanil, mefloquine and antibiotics should be stopped from 3 days before until 3 days after giving Ty21a.

No serious adverse effects have been reported following administration of Ty21a or Vi CPS.

These vaccines are not recommended for use in infant immunization programmes: there is insufficient information on their efficacy in children under 2 years of age.

Type of vaccine:	Oral Ty21a and injectable Vi CPS
Number of doses:	One of Vi CPS, i.m. Three or four of live Ty21a, given orally at 2-day intervals as enteric coated capsule
Booster:	Every 2 to 3 years for Vi CPS; for Ty21a see package inserta
Contraindications:	Proguanil, mefloquine and antibiotics 3 days before or after starting Ty21a
Adverse reactions:	None significant
Before departure:	1 week
Recommended for:	Travellers to high-risk areas and travellers staying longer than 1 month or likely to consume food or beverages away from the usual tourist routes in developing countries
Special precautions:	Vi CPS – not under 2 years of age; avoid proguanil, mefloquine and antibiotics with Ty21 ^a
<p>^a The duration of protection following Ty21a immunization is not well defined and may vary with vaccine dose and possibly with subsequent exposures to <i>Salmonella typhi</i> (natural booster). In Australia and Europe, 3 tablets are given on days 1, 3, and 5; this series is repeated every year for persons travelling from non-endemic to endemic countries, and every 3 years for persons living in endemic areas. In North America, 4 tablets are given on days 1, 3, 5, and 7 and revaccination is recommended only after 5 years (United States) or 7 years (Canada) for all, regardless of typhoid fever endemicity in the country of residence.</p>	

YELLOW FEVER

Disease and occurrence

See Chapter 5.

Risk for travellers

The normally low risk to travellers increases with travel to jungle areas in endemic countries and in or near cities during urban outbreaks. Areas where yellow fever virus is present far exceed those officially reported. The risk of exposure to infection can be reduced by taking measures to prevent mosquito bites (see Chapter 3). It should be noted that the mosquito vectors of yellow fever bite mostly during daylight hours. Although reported cases of human disease are the principal indicator of disease risk, some countries may have no reported cases, either because of a

high level of vaccine coverage against yellow fever in the population or because poor surveillance resulted in no cases being reported. However, the risk of yellow fever may still persist as the virus, the vector or the animal reservoir is still present.

Vaccine

The 17D vaccine, which is based on a live, attenuated viral strain, is the only commercially available yellow fever vaccine. It is given as a single subcutaneous (or intramuscular) injection. Yellow fever vaccine is highly effective (approaching 100%), while the disease may be fatal in adults who are not immune. With few exceptions (see below), vaccination is recommended for all travellers to countries or areas where there is a risk of yellow fever transmission (see country list and Annex 1).

Precautions and contraindications

Tolerance of the vaccine is generally excellent – only 2–5% of vaccine recipients have mild reactions, including myalgia and headache. Contraindications include true allergy to egg protein, cellular immunodeficiency (congenital or acquired, the latter sometimes being only temporary) and symptomatic HIV infection. Many industrialized countries administer yellow fever vaccine to persons with symptomatic HIV infection provided that the CD4 count is at least 200 cells/mm³. Asymptomatic HIV-positive individuals may have a reduced response to the vaccine. There is a theoretical risk of harm to the fetus if the vaccine is given during pregnancy, but this must be weighed against the risk to the mother of remaining unvaccinated and travelling to a high-risk zone. (However, pregnant women should be advised not to travel to areas where exposure to yellow fever may occur.) Encephalitis has been reported as a rare event following vaccination of infants under 9 months of age; as a result, the vaccine is contraindicated in children aged under 6 months and is not recommended for those aged 6–8 months.

There have been recent reports of a small number of serious adverse events (including deaths), of vaccine-associated viscerotropic disease, following immunization with the yellow fever 17DD vaccine. The evidence suggests that the incidence of adverse events may be different in regions where yellow fever is endemic (from 0 to 0.21 per 100 000 doses) and in regions with populations not exposed to the virus (from 0.09 to 0.4 per 100 000 doses). The risk of adverse events may be related to population differences (e.g. previous vaccination or exposure to wild yellow fever virus). This risk appears to be limited to the first immunization. Also recently identified as potential risk factors are a history of thymus disease (e.g. thymoma) and age over 60. Adverse events of vaccine-associated neurotropic disease have been reported (e.g. meningoencephalitis, acute disseminated encephalomyelitis and Guillain-Barré syndrome). The incidence rate reported in travellers from the United States and Europe ranges between 0.19 to 0.8 per 100 000 doses.

The risk to unvaccinated individuals who visit countries where there may be yellow fever transmission is far greater than the risk of a vaccine-related adverse event, and it remains important for all travellers at risk to be vaccinated. Nonetheless, great care should be exercised not to prescribe yellow fever vaccination to individuals who are not at risk of exposure to infection, based on an accurate assessment of the travel itinerary. Yellow fever vaccination should be encouraged as a key prevention strategy, but it is important to screen travel itineraries, particularly of older travellers, and carefully evaluate the potential risk of systemic illness after yellow fever vaccination.

Type of vaccine:	Live, attenuated
Number of doses:	One priming dose of 0.5 ml
Booster:	10-yearly (if re-certification is needed)
Contraindications:	Egg allergy; immunodeficiency from medication, disease or symptomatic HIV infection; hypersensitivity to a previous dose; pregnancy (see text above)
Adverse reactions:	Rarely, encephalitis or hepatic failure
Before departure:	International certificate of vaccination becomes valid 10 days after vaccination
Recommended for:	All travellers to areas with risk of yellow fever transmission and wherever mandatory
Special precautions:	Not for infants under 9 months of age; restrictions in pregnancy

Mandatory vaccination

Yellow fever

Mandatory vaccination against yellow fever is carried out to prevent the importation of yellow fever virus into vulnerable countries. These are countries where yellow fever does not occur but where the mosquito vector and non-human primate hosts are present. Importation of the virus by an infected traveller could potentially lead to the establishment of infection in mosquitoes and primates, with a consequent risk of infection for the local population. In such cases, vaccination is an entry requirement for all travellers arriving from countries, including airport transit, where there is a risk of yellow fever transmission.

If yellow fever vaccination is contraindicated for medical reasons, a medical certificate is required for exemption.

The international yellow fever vaccination certificate becomes valid 10 days after vaccination and remains valid for a period of 10 years.

For information on countries that require proof of yellow fever vaccination as a condition of entry, see country list.

Travelers should be aware that the absence of a requirement for vaccination does not imply that there is no risk of exposure to yellow fever in the country.

The international certificate of vaccination is reproduced with explanatory notes at the end of the chapter. A revision of the International Health Regulations was adopted on 23 May 2005 by the World Health Assembly, and these Regulations entered into force in June 2007 (see Annex 2). As from June 2007, the previous “International certificate of vaccination or revaccination against yellow fever” has been replaced by the “International certificate of vaccination or prophylaxis”. Clinicians who will issue the certificate should note that the main difference compared with the previous certificate is that they should specify in writing in the space provided that the disease for which the certificate is issued is “yellow fever”.

Meningococcal disease

Vaccination against meningococcal disease is required by Saudi Arabia for pilgrims visiting Mecca for the Hajj (annual pilgrimage) or for the Umrah.

Following the occurrence of cases of meningococcal disease associated with *N.meningitidis* W-135 among pilgrims in 2000 and 2001, the current requirement is for vaccination with tetravalent vaccine (A, C, Y and W-135). Vaccine requirements for Hajj pilgrims are issued each year and published in the *Weekly Epidemiological Record*.

Poliomyelitis

Some polio-free countries may require travellers from endemic countries to be immunized against polio in order to obtain an entry visa. Updates are published in the *Weekly Epidemiological Record*. For more information on Hajj visa requirements, see Chapter 9.

Special groups

Infants and young children

Because not all vaccines can be administered to the very young, it is especially important to ensure protection against health hazards such as foodborne illnesses and

mosquito bites by means other than vaccination. Some vaccines can be administered in the first few days of life (BCG, oral poliomyelitis vaccine, hepatitis B). Other vaccines cannot be given before a certain time, e.g. diphtheria/tetanus/pertussis, diphtheria/tetanus, inactivated poliomyelitis vaccine should not be given before 6 weeks of age, Japanese encephalitis not before 6 months and yellow fever not before 9 months of age. Because it may be difficult to reduce children's exposure to environmental dangers, it is particularly important to ensure that their routine vaccinations are fully up to date. A child who travels abroad before completing the full schedule of routine vaccines is at risk from vaccine-preventable diseases.

Adolescents and young adults

Adolescents and young adults make up the largest group of travellers and the group most likely to acquire sexually transmitted diseases or other travel-related infections. They are particularly at risk when travelling on a limited budget and using accommodation of poor standard (e.g. when backpacking), as well as from a lifestyle that may include risky sexual behaviour and other risks taken under the influence of alcohol or drugs. Because risk reduction through behaviour modification may not be reliable, this age group should be strongly encouraged to accept all appropriate vaccines before travel and to adhere to other precautions for avoiding infectious diseases.

Frequent travellers

Individuals who travel widely, usually by air, often become lax about taking precautions regarding their health. Having travelled numerous times without major health upsets, they may neglect to check that they are up to date with vaccination. Such travellers pose a special problem for health advisers who should, nonetheless, encourage compliance.

Pregnancy

Pregnancy should not deter a woman from receiving vaccines that are safe and will protect both her health and that of her unborn child. However, care must be taken to avoid the inappropriate administration of certain vaccines that could harm the unborn baby. Killed or inactivated vaccines, toxoids and polysaccharides can generally be given during pregnancy, as can oral polio vaccine. Live vaccines are generally contraindicated because of largely theoretical risks to the baby. Measles, mumps, rubella, BCG, varicella and yellow fever vaccines should therefore be avoided in pregnancy. The risks and benefits should nevertheless be examined in

Table 6.2 **Vaccination in pregnancy**

Vaccine	Use in pregnancy	Comments
BCG ^a	No	
Cholera	Yes, administer oral inactivated vaccine if indicated	
Hepatitis A	Yes, administer if indicated	Safety not determined
Hepatitis B	Yes, administer if indicated	
Influenza	Yes, administer if indicated	In some circumstances – consult a physician
Japanese encephalitis	No for live vaccine	Safety not determined
Measles ^a	No	
Meningococcal disease	Yes, administer if indicated	
Mumps ^a	No	
Poliomyelitis OPV ^a	Yes, administer if indicated	
IPV	Yes, administer if indicated	Normally avoided
Rubella ^a	No	
Tetanus/diphtheria	Yes, administer if indicated	
Rabies	Yes, administer if indicated	
Typhoid Ty21a ^a	Safety not determined	
Varicella ^a	No	
Yellow fever ^a	Yes, administer if indicated	Avoid unless at high risk

^a Live vaccine.

each individual case. Vaccination against yellow fever may be considered after the sixth month of pregnancy when the risk from exposure is deemed greater than the risk to the fetus (see Table 6.2). However, pregnant women should be advised not to travel to areas where there is a risk of exposure to yellow fever. For more detailed information, see the specific vaccine position papers at:

http://www.who.int/immunization/documents/positionpapers_intro/en/index.html

Elderly travellers

Vaccination of healthy elderly travellers does not differ in principle from vaccination of younger adults. However, special considerations arise if the elderly traveller has not been fully immunized in the past and/or has existing medical problems.

Many elderly people may have never been vaccinated with the vaccines used in routine childhood immunization programmes, or may have neglected to keep up the recommended schedule of booster doses. As a consequence, they may be susceptible to diseases such as diphtheria, tetanus and poliomyelitis as well as to other infections present at the travel destination.

Elderly travellers who have never been vaccinated should be offered a full primary course of vaccination against diphtheria, tetanus, poliomyelitis and hepatitis B. In addition, those who are not immune to hepatitis A should be vaccinated against this disease before travelling to a developing country.

Since the elderly are at risk for severe and complicated influenza, regular annual vaccination is recommended. For travellers from one hemisphere to the other, vaccine against the currently circulating strains of influenza is unlikely to be obtainable before arrival at the travel destination. Those arriving shortly before, or early during, the influenza season, and planning to stay for more than 2–3 weeks, should arrange vaccination as soon as possible after arrival. Pneumococcal vaccine may also be considered for elderly travellers in view of the risk of pneumococcal pneumonia following influenza infection.

Special considerations arise in the case of elderly travellers with pre-existing chronic health problems (see below).

Travellers with chronic medical problems

Travellers with chronic medical conditions involving impaired immunity, including cancer, diabetes mellitus, HIV infection and treatment with immunosuppressive drugs, may be at risk of severe complications following administration of vaccines that contain live organisms. Consequently, it may be advisable to avoid measles, oral polio, yellow fever, varicella and BCG vaccines for these travellers. For travel to a country where yellow fever vaccination is mandatory, a medical certificate will be required to obtain exemption.

Travellers with chronic cardiovascular and/or respiratory conditions or diabetes mellitus are at high risk for severe influenza and its complications. Regular annual vaccination against influenza is recommended. For travel from one hemisphere to the other shortly before, or early, during the influenza season, vaccination should be sought as soon as possible after arrival at the travel destination.

For those who lack a functional spleen, additional vaccines are advised: Hib, meningococcal vaccine (conjugate C or quadrivalent conjugate vaccine) and possibly pneumococcal vaccination should be considered, in addition to regular vaccination against influenza.

HIV-positive travellers

The likelihood of successful immunization is reduced in some HIV-infected children and adults. Asymptomatic HIV-infected children should be immunized according to standard schedules. With certain exceptions, symptomatic HIV-positive individuals should also be immunized as usual. Both measles and oral poliomyelitis vaccines may be given to persons with symptomatic HIV infection, but special attention should be paid to measles vaccination. Some vaccinations are contraindicated for this group:

- Measles vaccine has generally been recommended for individuals with moderate immunodeficiency if there is even a low risk of contracting wild measles from the community. A low level of risk is associated with use of measles vaccine in individuals who are HIV-infected and whose immune system is impaired. Where the risk of contracting wild measles infection is negligible, it may be preferable to avoid use of the vaccine.
- Yellow fever vaccine is not recommended for symptomatic HIV-positive adults and children. It is not certain whether yellow fever vaccine poses a risk for asymptomatic HIV-infected persons. Any adverse reactions to the vaccine occurring in HIV-positive individuals should be reported to WHO. In many industrialized countries, yellow fever vaccine is administered to people with symptomatic HIV infection or suffering from other immunodeficiency diseases, provided that their CD4 count is at least 200 cells/mm³ and if they plan to visit areas where epidemic or endemic yellow fever actually occurs.
- BCG vaccine should not be given to individuals infected with HIV, whether these individuals are symptomatic or not.

Adverse reactions and contraindications

Reactions to vaccines

While vaccines are generally both effective and safe, no vaccine is totally safe for all recipients. Vaccination may sometimes cause certain mild side-effects: local reaction, slight fever and other systemic symptoms may develop as part of the normal immune response. In addition, certain components of the vaccine (e.g. aluminium adjuvant, antibiotics or preservatives) occasionally cause reactions. A successful vaccine reduces these reactions to a minimum while inducing maximum immunity. Serious reactions are rare. Health workers who administer vaccines have an obligation to inform recipients of known adverse reactions and the likelihood of their occurrence.

A known contraindication should be clearly marked on a traveller's vaccination card, so that the vaccine may be avoided in future. In exceptional circumstances, the medical adviser may consider the risk of a particular disease to be greater than the theoretical risk of administering the vaccine and will advise vaccination.

Common mild vaccine reactions

Most vaccines produce some mild local and/or systemic reactions relatively frequently. These reactions generally occur within a day or two of immunization. However, the systemic symptoms that may arise with measles or MMR vaccine occur 5–12 days after vaccination. Fever and/or rash occur in 5–15% of measles/MMR vaccine recipients during this time, but only 3% are attributable to the vaccine; the rest may be classed as background events, i.e. normal events of childhood.

Uncommon, severe adverse reactions

Most of the rare vaccine reactions (detailed in Table 6.3) are self-limiting and do not lead to long-term problems. Anaphylaxis, for example, although potentially fatal, can be treated and has no long-term effects.

All serious reactions should be reported immediately to the relevant national health authority and marked on the vaccination card. In addition, the patient and relatives should be instructed to avoid the vaccination in the future.

Contraindications

Table 6.3 **Uncommon severe adverse reactions**

Vaccine	Possible adverse reaction	Expected rate ^a per million doses
BCG	Suppurative lymphadenitis	100–1 000 (mostly in immunodeficient individuals)
	BCG-osteitis	1–700 (rarely with current vaccines)
	Disseminated BCG infection	0.19–1.56
Cholera	NR ^b	—
DTP	Persistent crying	1 000–60 000
	Seizures	570
	Hypotonic–hypo-responsive episode	570
	Anaphylaxis	20

Vaccine	Possible adverse reaction	Expected rate ^a per million doses
<i>Haemophilus influenzae</i>	NR	—
Hepatitis A	NR	—
Hepatitis B ^c	Anaphylaxis	1–2
Influenza	Guillain–Barré syndrome	<1
Japanese encephalitis	Hypersensitivity	Rare 1 800–6 400
Measles	Febrile seizure	333
	Thrombocytopenic purpura	33–45
	Anaphylaxis	1–50
	Encephalitis	1 (unproven)
Meningococcal disease	Anaphylaxis	1
Mumps	Depends on strain – aseptic meningitis	0–500
Pneumococcal	Anaphylaxis	Very rare
Poliomyelitis (OPV)	Vaccine-associated paralytic poliomyelitis	1.4–3.4
Poliomyelitis (IPV)	NR	—
Rabies	Animal brain tissue only – neuroparalysis	17–44
	Cell-derived – allergic reactions	Rare
Rubella	Arthralgia/arthritis/arthropathy	None or very rare
Tetanus	Brachial neuritis	5–10
	Anaphylaxis	1–6
Tick-borne encephalitis	NR	—
Typhoid fever	Parenteral vaccine – various	Very rare
	Oral vaccine – NR	—
Yellow fever	Encephalitis (<6 months)	500–4 000
	Allergy/anaphylaxis	5–20
	Viscerotropic disease	0–04

^a Precise rate may vary with survey method.

^b NR = none reported.

^c Although there have been anecdotal reports of demyelinating disease following hepatitis B vaccine, there is no scientific evidence for a causal relationship.

The main contraindications to the administration of vaccines are summarized in Table 6.4.

Table 6.4 **Contraindications to vaccines**

Vaccine	Contraindications
All	An anaphylactic reaction ^a following a previous dose of a particular vaccine is a true contraindication to further immunization with the antigen concerned and a subsequent dose should not be given. Current serious illness
MMR, BCG, JE, varicella	Pregnancy Severe immunodeficiency
Yellow fever	Severe egg allergy Severe immunodeficiency (from medication, disease or symptomatic) Pregnancy HIV infection ^b
BCG	HIV infection
Influenza	Severe egg allergy
Pertussis-containing vaccines	Anaphylactic reaction to a previous dose Delay vaccination in case of evolving neurological disease (e.g. uncontrolled epilepsy or progressive encephalopathy).

^a Generalized urticaria, difficulty in breathing, swelling of the mouth and throat, hypotension or shock.

^b In many industrialized countries, yellow fever vaccine is administered to individuals with symptomatic HIV infection or who are suffering from other immunodeficiency diseases, provided that their CD4 count is at least 200 cells/mm³ and if they plan to visit areas where epidemic or endemic yellow fever actually occurs.

Further reading

Global Influenza Surveillance Network (FluNet): <http://www.who.int/GlobalAtlas/>

Information on safety of vaccines from the Global Advisory Committee on Vaccine Safety: http://www.who.int/vaccine_safety/en/

WHO information on vaccine preventable diseases: <http://www.who.int/immunization/en/>

WHO vaccine position papers: http://www.who.int/immunization/documents/positionpapers_intro/en/index.html

International certificate of vaccination

A revision of the International Health Regulations, referred to as IHR (2005), was unanimously adopted on 23 May 2005 by the World Health Assembly, and these Regulations entered into force in June 2007 (see Annex 2). As from 15 June 2007, the previous “International certificate of vaccination or revaccination against yellow fever” has been replaced by the “International certificate of vaccination or prophylaxis”, as follows:

International certificate of vaccination or prophylaxis

Model international certificate of vaccination or prophylaxis

This is to certify that [name], date of birth,
sex,
nationality, national identification document, if applicable
.....,
whose signature follows

has on the date indicated been vaccinated or received prophylaxis against [name of disease or condition] in accordance with the International Health Regulations.

Vaccine or prophylaxis	Date	Signature and professional status of supervising clinician	Manufacturer and batch no. of vaccine or prophylaxis	Certificate valid from until	Official stamp of administering centre
1.					
2.					

This certificate is valid only if the vaccine or prophylaxis used has been approved by the World Health Organization.¹

This certificate must be signed in the hand of the clinician, who shall be a medical practitioner or other authorized health worker, supervising the administration of the vaccine or prophylaxis. The certificate must also bear the official stamp of the administering centre; however, this shall not be an accepted substitute for the signature.

Any amendment of this certificate, or erasure, or failure to complete any part of it, may render it invalid.

The validity of this certificate shall extend until the date indicated for the particular vaccination or prophylaxis. The certificate shall be fully completed in English or in French. The certificate may also be completed in another language on the same document, in addition to either English or French.

¹ See http://www.who.int/immunization_standards/vaccine_quality/pq_suppliers/en/index.html WHO Technical Report Series, No. 872, 1998, Annex 1 (www.who.int/biologicals).
Note: since this list was issued, the following changes have taken place: Evans Medical is now Novartis Vaccines; Connaught Laboratories and Pasteur Merieux are now sanofi pasteur; Robert Koch Institute has ceased production.