

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 travellers will also be less likely to contaminate other travellers or the 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 rarely 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 (Chapter 3) should be followed carefully, regardless of any vaccines or other medication that have been administered. 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.

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 individual vaccines sections, as well as in WHO's vaccine position papers (www.who.int/immunization/documents/positionpapers/en/index.html). Summary tables for routine vaccinations can be found at www.who.int/immunization/policy/immunization_tables/en/index.html.

Recommendations on time intervals for administration of vaccines requiring more than one dose are provided; some slight variation can be made to accommodate

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 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.

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. Combination 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.

¹ IPV = inactivated poliomyelitis vaccine; Hib = *Haemophilus influenzae* type b [vaccine]; HepB = hepatitis B [vaccine].

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 (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 and Medina annually (Hajj) or at any time (Umrah).

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 before application for an entry visa for visitors arriving from countries reporting poliomyelitis cases). Updates are available on 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 www.who.int/ith/en/.

Vaccines for routine use

Recommendations on vaccines for routine use are provided by WHO in regularly updated position papers (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 these 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 www.who.int/vaccine_safety/en/.

WHO summary tables for recommendations for routine vaccinations can be found at www.who.int/immunization/policy/immunization_tables/en/index.html

DIPHTHERIA/TETANUS/PERTUSSIS

DIPHTHERIA

Cause	The bacterium <i>Corynebacterium diphtheriae</i> .
Transmission	Transmission of bacteria typically residing in the upper respiratory tract 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 another important source of infection
Nature of the disease	The infection commonly affects the throat and may lead to obstruction of the airways and death. There is toxin-induced damage to organs such as the heart. Nasal diphtheria may be mild, and chronic carriage of the organism frequently occurs; asymptomatic infections are common.
Geographical distribution	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

Cause	The bacterium <i>Clostridium tetani</i> .
Transmission	Tetanus is acquired through environmental exposure to the spores of <i>Clostridium tetani</i> , which are present in soil worldwide.
Nature of the disease	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.
Geographical distribution	Dirty wounds can become infected with the spores of <i>Clostridium tetani</i> 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	<p>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 <i>Haemophilus influenzae</i> 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.</p> <p>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.</p> <p>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.</p>

PERTUSSIS

Cause	The bacterium <i>Bordetella pertussis</i> .
Transmission	Pertussis (whooping cough) is a highly contagious acute bacterial disease involving the respiratory tract and caused by <i>Bordetella pertussis</i> . It is transmitted by direct contact with airborne discharges from the respiratory mucous membranes of infected persons.

Nature of the disease	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 apnoea. 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.
Geographical distribution	WHO estimated 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. Usually, aP or dTaP vaccines are used for vaccination of older children and adults.

HAEMOPHILUS INFLUENZAE TYPE B

Cause	<i>Haemophilus influenzae</i> type b (Hib).
Transmission	Respiratory droplets
Nature of the disease	<i>Haemophilus influenzae</i> type b 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.
Geographical distribution	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 5 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 one or more other vaccines, such as DTP, hepatitis B vaccine or IPV, 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.
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HEPATITIS B

Cause	Hepatitis B virus (HBV), belonging to the Hepadnaviridae family.
Transmission	Infection is transmitted from person to person by contact with infected body fluids. Sexual contact is an important mode of transmission, but infection is also transmitted by transfusion of contaminated blood or blood products, or by use of contaminated needles or syringes for injections. There is also a potential risk of transmission through other skin-penetrating procedures, including acupuncture, piercing and tattooing. Perinatal transmission may occur from mother to baby. There is no insect vector or animal reservoir.
Nature of the disease	Many HBV infections are asymptomatic or cause mild symptoms, which are often unrecognized in adults. When clinical hepatitis results from infection, it has a gradual onset, with anorexia, abdominal discomfort, nausea, vomiting, arthralgia and rash, followed by the development of jaundice in some cases. In adults, about 1% of cases are fatal. Chronic HBV infection persists in a proportion of adults, some of whom later develop cirrhosis and/or liver cancer.
Geographical distribution	Worldwide, but with differing levels of endemicity. In north America, Australia, northern and western Europe and New Zealand, prevalence of chronic HBV infection is relatively low (less than 2% of the general population is HBsAg-positive) (Map).
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 exposure to needles (e.g. acupuncture, piercing, tattooing or injecting drug use) that have not been appropriately sterilized. In addition, transmission from HBV-positive to HBV-susceptible individuals may occur through direct contact between open skin lesions following a penetrating bite or scratch.
Precautions	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. Also see precautions under "HIV/AIDS and other sexually transmitted diseases", Chapter 5.
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 provides 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 administration schedule for 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. The following very rapid administration schedule has also been proposed: 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 of day 0, 1 month and 2 months, with an additional dose at 12 months, and a very rapid schedule of 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

Cause	Human papillomavirus (HPV), belonging to the Papillomaviridae family.
Transmission	Genital HPV infections are transmitted primarily by sexual contact, predominantly but not exclusively through penetrative intercourse. HPVs are highly transmissible, and most sexually active men and women will acquire an HPV infection at some time in their lives.
Nature of the disease	Whereas most HPV infections are transient and benign, persistent genital infection with certain viral genotypes can lead to the development of anogenital precancers and cancers. Diseases caused by HPVs include cancers of the cervix, vagina, vulva, penis and anus; a subset of head and neck cancers; anogenital warts; and recurrent respiratory papillomatosis.
Geographical distribution	Human papillomavirus (HPV) is a family of viruses that are very common all over the world. In 2005, there were about 500 000 cases of cervical cancer worldwide and 260 000 related deaths. Cervical cancer incidence rates vary from 1 to 50 per 100 000 females; rates are highest in Latin America and the Caribbean, sub-Saharan Africa, Melanesia, and south-central and South-East Asia.
Risk for travellers	Transmission of HPV occurs most commonly through sexual activity; see precautions under “HIV/AIDS and other sexually transmitted diseases” (Chapter 5).
Vaccines	Since 2006, two HPV vaccines have been licensed; one vaccine targeting four HPV genotypes and the other two. 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

AVIAN INFLUENZA

See Chapter 5.

SEASONAL INFLUENZA

Cause	<p>Influenza viruses belonging to the family Orthomyxoviridae.</p> <p>The influenza viruses are classified into types A, B and C on the basis of their core proteins. Only types A and B cause human disease of any concern. The subtypes of influenza A viruses are determined by envelope glycoproteins possessing either haemagglutinin (HA) or neuraminidase (NA) activity. High mutation rates and frequent genetic reassortments of these viruses contribute to great variability of the HA and NA antigens. All of the currently identified 16 HA and 9 NA subtypes of influenza A viruses are maintained in wild, aquatic bird populations. Humans are generally infected by viruses of the subtypes H1, H2 or H3, and N1 or N2. Minor point mutations causing small changes ("antigenic drift") occur relatively often. Antigenic drift enables the virus to evade immune recognition, resulting in repeated influenza outbreaks during interpandemic years. Major changes in the HA antigen ("antigenic shift") are caused by reassortment of genetic material from different A subtypes. Antigenic shifts resulting in new pandemic strains are rare events, occurring through reassortment between animal and human subtypes, for example in co-infected pigs. Type B virus does not exhibit antigenic shifts and is not divided into subtypes.</p>
Transmission	<p>Respiratory transmission occurs mainly by droplets disseminated by unprotected coughs and sneezes. Short-distance airborne transmission of influenza viruses may occur, particularly in crowded enclosed spaces. Hand contamination and direct inoculation of virus is another possible source of transmission.</p>
Nature of the disease	<p>An acute respiratory infection of varying severity, ranging from asymptomatic infection to fatal disease. Typical influenza symptoms include fever with abrupt onset, chills, sore throat, non-productive cough and, often accompanied by headache, coryza, myalgia and prostration. Complications of influenza viral infection include: primary influenza viral pneumonitis, bacterial pneumonia, otitis media and exacerbation of underlying chronic conditions. Illness tends to be most severe in the elderly, in infants and young children, and in immunocompromised hosts. Death resulting from seasonal influenza occurs mainly in the elderly and in individuals with pre-existing chronic diseases.</p>

Geographical distribution	Influenza occurs all over the world, with an annual global attack rate estimated at 5–10% in adults and 20–30% in children. In temperate regions, influenza is a seasonal disease occurring typically in winter months: it affects the northern hemisphere from November to April and the southern hemisphere from April to September. In tropical areas there is no clear seasonal pattern, and influenza circulation is year around typically with several peaks during rainy seasons
Risk for travellers	Travellers, like local residents, are at risk in any country during the influenza season. In addition, groups of travellers that include persons from areas affected by seasonal influenza (e.g. cruise ships) may experience out-of-season outbreaks. Travellers visiting countries in the opposite hemisphere during the influenza season are at special risk, particular if they do not have some degree of immunity through recent infection or regular vaccination. The elderly, people with pre-existing chronic diseases and young children are most susceptible to complications.
Precautions	Whenever possible, avoid crowded enclosed spaces and close contact with people suffering from acute respiratory infections. Frequent hand-washing especially after direct contact with ill persons or their environment may reduce the risk of acquiring illness. Ill persons should be encouraged to practise cough etiquette (maintain distance, cover coughs and sneezes with disposable tissues or clothing, wash hands).
Vaccine	<p>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.</p> <p>Travellers with conditions that place them at high risk for complications of influenza should be vaccinated every year. In years in which the northern and southern hemisphere influenza vaccine strains differ, 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.</p> <p>Trivalent inactivated influenza vaccines are injected into the deltoid muscle (vaccinees aged >1 year) or the anterolateral aspect of the thigh (vaccinees</p>

aged 6–12 months). These vaccines should not be given to children under the age of 6 months; those aged 6–36 months should receive half the adult dose. Previously unvaccinated children aged under 9 years should receive 2 injections, administered at least 1 month apart. A single dose of the vaccine is appropriate for schoolchildren 9 years and over and healthy adults. 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.

INFLUENZA A (H1N1)

Cause	Influenza A(H1N1) virus is a new reassortment that has never before circulated among humans. This virus is not related to previous or current human seasonal influenza viruses.
Transmission	It is transmitted as easily as the normal seasonal influenza by infected droplets expelled by coughing or sneezing which can be inhaled or can contaminate hands or surfaces. To prevent spread of the infection, people who are ill should cover their mouth and nose when coughing or sneezing, stay home when they are unwell, clean their hands regularly, and keep away from healthy people as much as possible. There are no known instances of people being infected by exposure to pigs or other animals.
Nature of the disease	Similar to seasonal influenza with some key differences in the risk groups and complications. The majority of people who contract the virus experience mild disease and recover without antiviral treatment or medical care. Among the more serious cases, more than half of hospitalized people had underlying health conditions or weak immune systems as for seasonal flu but acute respiratory distress syndrome has also been seen in people with no known risk factors. Travellers should be aware of sign of severity and seek care quickly.
Geographical distribution	Worldwide.
Risk for travellers	Risk of acquiring influenza A (H1N1) now exists worldwide, especially in areas of overcrowding.
Precautions	See seasonal influenza
Vaccine	Regulatory authorities have licensed pandemic H1N1 vaccines in many countries.

MEASLES

Cause	Measles virus of the genus <i>Morbillivirus</i> of the family Paramyxoviridae.
Transmission	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.
Nature of the disease	Measles is a highly contagious infection; before vaccines became available, this disease affected most people by the time of adolescence. Common complications include middle-ear infection and pneumonia. High-risk

	groups for measles complications include infants and individuals suffering from chronic diseases and impaired immunity, or from severe malnutrition (including vitamin A deficiency).
Geographical distribution	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. In 2007, worldwide measles vaccination coverage had reached 82%, and between 2000 and 2007 the estimated annual number of deaths from measles dropped from 750 000 to 197 000.
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	<p>A number of live, attenuated measles vaccines are currently available, either as monovalent vaccine or as measles-containing vaccine combinations with one or more of rubella (R), mumps (M) and varicella vaccines. programmes. The measles/mumps/rubella triple (MMR) or measles/rubella (MR) vaccine is given in many countries instead of monovalent measles vaccine. The measles vaccines that are now internationally available are safe and effective and may be used interchangeably in immunization. Every child should receive two doses of measles vaccine. In industrialized countries, the first 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. Although generally administered at school entry (age 4–6 years), the second dose may be given as early as 1 month following the first dose, depending on the local programmatic and epidemiological situation.</p> <p>Special attention must be paid to all children and adolescent/young adult travellers who have not received two doses of measles vaccine. 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 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.</p> <p>A meta-analysis showed no increased risk of serious adverse events among HIV-positive children compared with uninfected children, although the antibody response may be lower. 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. Where the risk of contracting measles infection is negligible, physicians who are able to monitor CD4 counts may prefer to delay the use of measles vaccine until CD4 counts are above 200.</p>

MUMPS

Cause	Mumps virus belongs to the genus <i>Rubulavirus</i> of the family Paramyxoviridae.
Transmission	Humans are the only known natural host for mumps virus, which is spread via direct contact or by airborne droplets from the upper respiratory tract of infected individuals.
Nature of the disease	Mumps (parotitis epidemica) is a viral infection of humans, primarily affecting the salivary glands. Although it is mostly a mild childhood disease, with peak incidence occurring among those aged 5–9 years, the mumps virus may also affect adults, among whom complications such as meningitis and orchitis are relatively more common. Encephalitis and permanent neurological sequelae are rare complications.
Geographical distribution	Worldwide. 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. 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 1 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.

PNEUMOCOCCAL DISEASE

Cause	The bacterium <i>Streptococcus pneumoniae</i> .
Transmission	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.
Nature of the disease	Pneumonia with empyema and/or bacteraemia, febrile bacteraemia and meningitis are the commonest manifestations of invasive pneumococcal infection. Pneumococci are a frequent cause of non-bacteraemic pneumonia. In developing countries, non-bacteraemic pneumonia causes the majority of pneumococcal deaths in children. Middle-ear infections, sinusitis and bronchitis are non-invasive and less severe manifestations of pneumococcal infection but are considerably more common. Several chronic conditions predispose to serious pneumococcal disease. Increasing pneumococcal resistance to antibiotics underlines the importance of vaccination.

Geographical distribution	<p>Infection with pneumococcus is a major cause of morbidity and mortality worldwide. In 2005, WHO estimated that 1.6 million deaths were caused by this agent annually; this estimate includes the deaths of 0.7–1 million children aged under 5 years. Most of these deaths occur in poor countries, and children aged under 2 years are disproportionately represented among these deaths. In Europe and the United States, <i>S. pneumoniae</i> is the most common cause of community-acquired bacterial pneumonia in adults. In these regions, the annual incidence of invasive pneumococcal disease ranges from 10 to 100 cases per 100 000 population.</p>
Risk for travellers	<p>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 complications 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.</p>
Vaccine	<p>A conjugate vaccine containing seven serotypes of the pneumococcus is now available and is also safe and immunogenic 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. The primary series of PCV-7 consists of 3 intramuscular doses administered to infants at intervals of at least 4 weeks, starting at the age of 6 weeks or later. Some industrialized countries have adopted a schedule based on delivering 2 doses during infancy (for example, at 2 months and 4 months) and a third dose at 12–13 months. When the vaccine is initially introduced into childhood immunization programmes, a single catch-up dose of PCV-7 may be given to previously unvaccinated children aged 12–24 months and to children aged 2–5 years considered to be at high risk. This vaccine is licensed for children up to 5 years of age only.</p> <p>The 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. This vaccine is widely licensed for use in adults and children aged over 2 years who have certain underlying medical conditions. In some countries, such as the United States, routine vaccination is recommended for everyone aged over 65 years. 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. For primary immunization, PPV23 is administered as a single intramuscular dose (preferably in the deltoid muscle) or as a subcutaneous dose.</p>

POLIOMYELITIS

Cause	Poliovirus types 1, 2 and 3 (three closely related enteroviruses).
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Transmission	The virus is spread predominantly by the faecal–oral route, although rare outbreaks caused by contaminated food or water have occurred.
Nature of the disease	Poliomyelitis is a disease of the central nervous system. 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.
Geographical distribution	Significant progress has been made towards global eradication of poliomyelitis. There are now (2009) only four countries where indigenous wild poliovirus transmission has never been interrupted: Afghanistan, India, Nigeria and Pakistan (Map). Wild poliovirus importations from the four “endemic” countries into previously polio-free countries continue to occur, with some resulting in new outbreaks. As at mid-2009, imported wild poliovirus was circulating in 21 previously polio-free countries: Angola, Benin, Burkina Faso, Cameroon, Central African Republic, Chad, Cote d’Ivoire, Democratic Republic of the Congo, Ethiopia, Ghana, Guinea, Kenya, Liberia, Mali, Nepal, Niger, Sierra Leone, Somalia, Sudan, Togo and Uganda. Until wild poliovirus transmission has been stopped globally, all polio-free countries and areas remain at risk of importation and of renewed outbreaks.
Risk for travellers	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. 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. All travellers to and from polio-infected areas should be up to date with polio vaccination according to national immunization policy and 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 www.polioeradication.org/casecount.asp .
Vaccine	There are two types of vaccine: inactivated polio vaccine (IPV), which is given by injection, and oral polio vaccine (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 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, it has only limited effects in reducing

intestinal excretion of poliovirus. Following the first dose of polio vaccine given shortly after birth, usually between 1–2 months of age, 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. Whether OPV or IPV is recommended in these circumstances depends 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 live 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 1–12 months before 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

Cause	Rotaviruses, which belong to the family Reoviridae.
Transmission	Transmission is primarily by the faecal–oral route, directly from person to person or indirectly via contaminated fomites. A respiratory mode of transmission has also been proposed.
Nature of the 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 replicates in the enterocytes of the small intestine, causing extensive damage to the microvilli that results in malabsorption and loss of fluids and electrolytes.
Geographical distribution	Rotaviruses are found worldwide. They are the leading cause of severe, dehydrating diarrhoea in children under 5 years globally, with outpatients visits estimated at more than 25 million and hospitalizations attributable to rotavirus infections at more than 2 million each year. Fatal outcomes,

	estimated in 2004 to be 527 000 (475 000–580 000) annually, occur predominantly in low-income countries. In temperate climates, the incidence of rotavirus gastroenteritis typically peaks during the winter season, whereas in tropical settings rotavirus occurs year round. Reinfection of older children and adults is common, although the infection is usually sub-clinical.
Risk for travellers	The potential risk for adult travellers is extremely limited since most individuals will have good immunity through repeated exposures early in life. Children under the age of 5 years are at risk.
Vaccin	Two live, attenuated, oral rotavirus vaccines are internationally licensed and routine childhood vaccination has been initiated in a number of countries. The clinical efficacy of the rotavirus vaccines has been demonstrated in most parts of the world. WHO recommends the inclusion of rotavirus vaccination in all national immunization programmes, particularly in regions of high disease endemicity. The first dose of either RotaTeq™ or Rotarix™ should be administered at 6–15 weeks of age. The interval between 2 doses should be at least 4 weeks. The Rotarix™ vaccine is administered orally in a 2-dose schedule while RotaTeq™, is administered orally in a 3-dose schedule. All doses should be administered before the age of 32 weeks. Vaccination is not currently recommended for travellers or older children outside the routine childhood immunization schedule.

RUBELLA

Cause	The rubella virus, a togavirus of the genus <i>Rubivirus</i> .
Transmission	Rubella virus is transmitted by the respiratory route and the virus replicates in the nasopharyngeal mucosa and local lymph nodes. Humans are the only known host.
Nature of the disease	Acquired rubella is characterized by a transient, erythematous rash, conjunctivitis, coryza, postauricular and suboccipital lymphadenopathy, low fever and nausea. Arthralgia and arthritis rarely occur in children, but may affect up to 70% of adults, particularly women. Haemorrhagic manifestations, Guillain-Barré syndrome and encephalitis are rarely reported. Serological studies have shown that 20–50% of all rubella infections are subclinical. Congenital rubella infection and congenital rubella syndrome (CRS) are caused by infection in early pregnancy. From just before conception and during the first 8–10 weeks of gestation, rubella infection may result in multiple fetal defects in up to 90% of cases, and often causes miscarriage or stillbirth. 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.
Geographical distribution	Worldwide.
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 proved safe and efficacious, achieving 95–100% protection, possibly lifelong, after just one dose. Following well-designed and well-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 and other combinations. Rubella vaccination of pregnant women should be avoided, and pregnancy should be avoided within 1 month of receiving the vaccine.

TUBERCULOSIS (TB)

Cause	<i>Mycobacterium tuberculosis</i> , the tubercle bacillus.
Transmission	Infection is usually by direct airborne transmission from person to person.
Nature of the disease	<p>Exposure to <i>M. tuberculosis</i> may lead to infection, but most infections do not lead to disease. The risk of developing disease following infection is generally 5–10% during the lifetime but may be increased by various factors, notably immunosuppression (e.g. advanced HIV infection).</p> <p>Multidrug resistance refers to strains of <i>M. tuberculosis</i> that are resistant to at least isoniazid and rifampicin (MDR-TB). The resistant strains do not differ from other strains in infectiousness, likelihood of causing disease, or general clinical effects; however, if they do cause disease, treatment is more difficult and the risk of death will be higher. Extensively drug-resistant TB (XDR-TB) is TB that is resistant to at least isoniazid and rifampin, to any fluoroquinolone and to at least one of the injectable second-line anti-TB drugs capreomycin, kanamycin and amikacin.</p>
Geographical distribution	Worldwide. The risk of infection differs between countries, as shown on the map of estimated incidence.
Risk for travellers	Most travellers are at low risk for TB. The risk for long-term (>3 months) travellers 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.
Precautions	Travellers should avoid close contact with known TB patients. For travellers from low-incidence countries who may be exposed to infection in relatively high-incidence countries (e.g. health professionals, humanitarian relief workers, missionaries), a baseline tuberculin skin test is advisable for comparison with retesting after return. If the skin reaction to tuberculin suggests recent infection, the traveller should receive, or be referred for, treatment for latent infection. Patients under treatment for TB should not travel until the treating physician has documented, by laboratory examination of sputum, that the patient is not infectious and therefore of no risk to others. The importance of completing the prescribed course of treatment should be stressed.

Vaccine	<p>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.</p> <p>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.</p> <p>Many industrialized countries with a low incidence of TB have ceased giving BCG routinely to neonates.</p> <p>Booster doses of BCG are not recommended by WHO.</p>
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VARICELLA

Cause	Varicella zoster virus (VZV).
Transmission	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.
Nature of the disease	Varicella (chickenpox) is an acute, highly contagious disease. 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. 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, 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.
Geographical distribution	Worldwide.
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 to 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

Cause	<i>Vibrio cholerae</i> bacteria, serogroups O1 and O139.
Transmission	Infection occurs through ingestion of food or water contaminated directly or indirectly by faeces or vomitus of infected persons. Cholera affects only humans; there is no insect vector or animal reservoir host.
Nature of the disease	An acute enteric disease varying in severity. Most infections are asymptomatic (i.e. do not cause any illness). In mild cases, acute watery diarrhoea occurs without other symptoms. In severe cases, there is sudden onset of profuse watery diarrhoea with nausea and vomiting and rapid development of dehydration. In severe untreated cases, death may occur within a few hours due to dehydration leading to circulatory collapse.
Geographical distribution	Cholera occurs mainly in poor countries with inadequate sanitation and lack of clean drinking-water and in war-torn countries where the infrastructure may have broken down. Many developing countries are affected, particularly those in Africa and Asia, and to a lesser extent, those in central and South America (Map).
Risk for travellers	The risk for most travellers is very low, even in countries where cholera epidemics occur, provided that simple precautions are taken to avoid potentially contaminated food and water. Humanitarian relief workers in disaster areas and refugee camps are at risk.
Precautions	Cholera vaccination is not required as a condition of entry to any country. As for other diarrhoeal diseases, all precautions should be taken to avoid consumption of potentially contaminated food, drinks and drinking-water. Oral rehydration salts (ORS) should be carried to combat dehydration in case of severe diarrhoea (Chapter 3).
Vaccine	A vaccine consisting of killed whole-cell <i>V. cholerae</i> O1 in combination with a recombinant B-subunit of cholera toxin (WC/rBS) has been marketed

since the early 1990s. This vaccine is well tolerated and confers high-level (85–90%) protection for 6 months after the second immunization in all vaccinated subjects aged more than 2 years. The level of protection is still about 50% 3 years after immunization in those who were aged over 5 years at the time of vaccination. The vaccine also induces cross-protection against enterotoxigenic *Escherichia coli* (ETEC). Basic immunization of adults and children aged more than 6 years consists of 2 oral doses taken 7–14 days apart. Three doses are recommended for children aged 2–5 years. Intake of food or drinks should be avoided 1 hour before and after vaccination. If the second dose is delayed for more than 6 weeks, basic vaccination should be restarted. Protection against ETEC may be expected about 1 week following basic immunization. Booster doses are recommended after 2 years for adults and children aged more than 6 years, and every 6 months for children aged 2–5 years. This vaccine is not licensed for children aged under 2 years.

Type of vaccine:	Killed oral whole cell B-sub unit
Number of doses:	Two, at least 1 week apart (ideally 10–14 days apart)
Contraindications:	Hypersensitivity to previous dose
Adverse reactions:	Mild gastrointestinal disturbances reported
Before departure:	2 weeks
Consider for:	Travellers at high risk (e.g. emergency or relief workers)
Special precautions:	None

HEPATITIS A

Cause	Hepatitis A virus (HAV), a member of the picornavirus family.
Transmission	The virus is acquired directly from infected persons by the faecal–oral route or by close contact, or by consumption of contaminated food or drinking-water. There is no insect vector or animal reservoir (although some non-human primates are sometimes infected).
Nature of the disease	An acute viral hepatitis with abrupt onset of fever, malaise, nausea and abdominal discomfort, followed by the development of jaundice a few days later. Infection in very young children is usually mild or asymptomatic; older children are at risk of symptomatic disease. The disease is more severe in adults, with illness lasting several weeks and recovery taking several months; case-fatality is greater than 2% for those over 40 years of age and 4% for those over 60.
Geographical distribution	Worldwide but most common where sanitary conditions are poor and the safety of drinking-water is not well controlled (Map).
Risk for travellers	Non-immune travellers to developing countries are at significant risk of infection. The risk is particularly high for travellers exposed to poor conditions of hygiene, sanitation and drinking-water control.

Precautions	Travellers who are non-immune to hepatitis A (i.e. have never had the disease and have not been vaccinated) should take particular care to avoid potentially contaminated food and water.
Vaccine	<p>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.</p> <p>Current hepatitis A vaccines, all of which are 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.</p> <p>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.</p> <p>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.</p> <p>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.</p>

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

Cause	Japanese encephalitis virus – a flavivirus.
Transmission	The virus is transmitted by various mosquitoes of the genus <i>Culex</i> . It infects pigs and various wild birds, which represent the natural reservoir, as well as humans. Mosquitoes become infective after feeding on viraemic pigs or birds.
Nature of the disease	Most infections in humans are asymptomatic. In symptomatic cases, severity varies; mild infections are characterized by febrile headache or aseptic meningitis or encephalitis. Severe cases have a rapid onset and progression with headache, high fever and meningeal signs. Permanent neurological sequelae are common among survivors. Approximately 25% of severe clinical cases have a fatal outcome.
Geographical distribution	Japanese encephalitis (JE) is the leading cause of viral encephalitis in Asia and occurs in almost all Asian countries (Map). Largely as a result of immunization, its incidence has been declining in Japan and the Korean peninsula and in some regions of China, but the disease is increasingly reported from 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 particular in tropical climate zones. 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.
Risk for travellers	The risk for Japanese encephalitis for most travellers to Asia is very low but varies according to season, destination, duration of travel and activities. The risk is higher in long-term travellers and expatriates. 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. Whereas Japanese encephalitis in endemic countries is primarily a disease of children, it can occur among travellers of any age. Prevention is by avoidance of mosquito bites (Chapter 3) and by vaccination.
Vaccine	<p>Until recently, the inactivated mouse-brain-derived (IMB) vaccine against Japanese encephalitis was the most widely available commercially, but most manufacturers have ceased production. A cell-culture-derived live attenuated SA 14-14-2 vaccine is widely used in China and in an increasing number of countries within the region. The product is not licensed or marketed outside the endemic countries.</p> <p>A new Vero cell-derived inactivated JE vaccine was approved in 2009 in North America, Australia and various European countries. The vaccine is inactivated, alum-adsorbed, and based on the attenuated SA 14-14-2 attenuated JE viral strain. For primary immunization the manufacturer recommends intramuscular administration of two 0.5-ml doses 4 weeks apart. The durability of protective immunity and the need for and timing of a booster dose are still under investigation. This vaccine has been given concomitantly with hepatitis A vaccine without significant interference on</p>

the immune response or adverse events. Data on concomitant administration with other vaccines frequently used in travellers are currently unavailable. The vaccine is licensed for use in persons 17 years of age and older in the United States, and 18 years and above in other countries. Post-marketing safety studies are under way.

The Vero cell JE vaccine (VJE) by BIKEN was licensed by the Japanese authorities in February 2009. VJE uses the same strain of JE virus (Beijing-1) as the mouse-brain-derived vaccine. Four clinical trials evaluating the safety and immunogenicity of VJE have been completed. Seroconversion rates exceeded 95%. This vaccine is currently not available outside Japan.

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 JE
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) up to the age 10–15 years 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

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.

Type of vaccine:	Inactivated, alum-adsorbed, Vero cell-derived SA14-14-2 vaccine
Schedule:	2 intramuscular doses 4 weeks apart
Booster:	Need for and timing of booster doses have not yet been established
Contraindications:	History of hypersensitivity to any component of the vaccine
Adverse reactions:	Occasional mild local or systemic reactions
Special precautions:	Safety and effectiveness have not been established in pregnant women, nursing mothers, or in children and adolescents (younger than 17 years of age).
Before departure:	Immunization series should be completed at least 1 week before potential exposure to JEV.

MENINGOCOCCAL DISEASE

Cause	The bacterium <i>Neisseria meningitidis</i> . Most cases of meningococcal disease are caused by serogroups A, B and C; less commonly, infection is caused by serogroups Y (emerging in the United States) and W-135 (particularly in Saudi Arabia and west Africa)
Transmission	Transmission occurs by direct person-to-person contact and through respiratory droplets from the nose and pharynx of infected persons, patients or asymptomatic carriers. Humans are the only reservoir.
Nature of the disease	Most infections do not cause clinical disease. Many infected people become asymptomatic carriers of the bacteria and serve as a reservoir and source of infection for others. In general, susceptibility to meningococcal disease decreases with age, although there is a small increase in risk in adolescents and young adults. Meningococcal meningitis has a sudden onset of intense headache, fever, nausea, vomiting, photophobia and stiff neck, plus various neurological signs. The disease is fatal in 5–10% of cases even with prompt antimicrobial treatment in good health care facilities; among individuals who survive, up to 20% have permanent neurological sequelae. Meningococcal septicaemia, in which there is rapid dissemination of bacteria in the bloodstream, is a less common form of meningococcal disease, characterized by circulatory collapse, haemorrhagic skin rash and high fatality rate.
Geographical distribution	Sporadic cases are found worldwide. In temperate zones, most cases occur in the winter months. Localized outbreaks occur in enclosed crowded spaces (e.g. dormitories, military barracks). In sub-Saharan Africa, in a zone stretching across the continent from Senegal to Ethiopia (the African “meningitis belt”), large outbreaks and epidemics take place during the dry season (November–June). Recent reports of endemic occurrence of group Y meningococcal disease in the United States, and outbreaks caused by serogroup

	<p>W-135 strains in Saudi Arabia and sub-Saharan Africa, particularly Burkina Faso, suggest that these serogroups may be gaining in importance.</p>
Risk for travellers	<p>Generally low. 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.</p> <p>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.</p> <p>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.</p>
Precautions	<p>Avoid overcrowding in confined spaces. Following close contact with a person suffering from meningococcal disease, medical advice should be sought regarding chemoprophylaxis.</p>
Vaccine	<p><i>Polysaccharide vaccines</i></p> <p>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.</p> <p>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.</p> <p>A protective antibody response occurs within 10 days of vaccination. In schoolchildren 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.</p> <p>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.</p> <p>These vaccines do not provide any protection against group B meningococci, which are the leading cause of endemic meningococcal disease in some countries.</p> <p><i>Conjugate vaccines</i></p> <p>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.</p>

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

Cause	The rabies virus, a rhabdovirus of the genus <i>Lyssavirus</i> .
Transmission	Rabies is a zoonotic disease affecting a wide range of domestic and wild mammals, including bats. Infection of humans usually occurs through the bite of an infected animal as the virus is present in the saliva. Any other contact with a rabies-susceptible species such as a penetrating scratch with bleeding and licking of broken skin and mucosa in an area where rabies is present should be treated with caution. In developing countries, transmission is usually through dog bites. Person-to-person transmission other than via organ transplant has not been laboratory-confirmed.

Nature of the disease	An acute viral encephalomyelitis, which is almost invariably fatal. The initial signs include a sense of apprehension, headache, fever, malaise and sensory changes around the site of the animal bite. Excitability, hallucinations and aerophobia are common, followed in some cases by fear of water (hydrophobia) due to spasms of the swallowing muscles, progressing to delirium, convulsions and death a few days after onset. A less common form, paralytic rabies, is characterized by loss of sensation, weakness, pain and paralysis.
Geographical distribution	Rabies is present in mammals in many countries worldwide (Map). Most of the estimated 55 000 human rabies deaths per year occur in Africa and Asia alone and follow a dog bite. More information is available at www.who.int/rabies/rabnet/en .
Risk for travellers	<p>The risk to travellers in areas endemic for rabies (Map, or www.who.int/rabies/rabnet) is proportional to the probability of 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).</p> <p>Travellers should avoid contact with free-roaming animals, especially dogs and cats, and with wild, free-ranging 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.</p> <p>The map 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 and the availability of reliable laboratory-based surveillance data in these reservoir species. 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:</p> <p><i>Category 1:</i> no risk.</p> <p><i>Category 2:</i> 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.</p> <p><i>Category 3:</i> 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.</p>

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 through playing with animals, particularly with dogs and cats; they may receive more severe bites and are less likely 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 with 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 h, 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. 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.

^a For information on which vaccines are recommended for intradermal use, see: www.who.int/rabies/human/postexp/en/index.html.

^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.

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.

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

^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.

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 immune-globulin and vaccine immediately. 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
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^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. 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 (HRIG) or equine rabies immunoglobulin (ERIG) or F(ab')₂ products for category III exposure as well as in some category II exposures (see table, above). 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 initiation of the primary series of post-exposure prophylaxis (with cell-culture or embryonated egg rabies vaccine).

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 active 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.

3. Active immunization

Cell-culture or embryonated egg rabies vaccines should always be used for post-exposure prophylaxis. They 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.

- *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 purified chick embryo vaccine (Rabipur™).

For more details on intradermal regimens, see www.who.int/rabies/PEProphylaxisguideline.pdf

TICK-BORNE ENCEPHALITIS

Cause	The tick-borne encephalitis (TBE) virus is a flavivirus. Three subtypes of the causative agent are known: the European subtype, the Far Eastern subtype (spring-summer encephalitis) and the Siberian subtype. Other closely related viruses cause similar diseases.
Transmission	Infection is transmitted by the bite of infected ticks or by ingestion of unpasteurized milk. There is no direct person-to-person transmission. Some related viruses, also tick-borne, infect animals such as birds, deer (louping-ill), rodents and sheep.
Nature of the disease	Infection may induce an influenza-like illness, with a second phase of fever occurring in 10% of cases. Encephalitis develops during the second phase and may result in paralysis, permanent sequelae or death. Severity of illness increases with age. The Far Eastern subtype causes more severe symptoms and sequelae than the European subtype.
Geographical distribution	The European subtype is present in large parts of central and eastern Europe, particularly Austria, southern Germany and northern Switzerland, the Baltic states (Estonia, Latvia, Lithuania), the Czech Republic, Hungary and Poland; the Far Eastern subtype is found from north-eastern Europe to China and Japan, and the Siberian subtype from northern Europe to Siberia. The disease is seasonal; most cases occur during April to November. The risk is highest in forested areas up to an altitude of about 1400 m.
Risk for travellers	In endemic areas during the summer months, travellers are at risk when hiking or camping in rural or forested areas.
Precautions	Avoid bites by ticks by wearing long trousers and closed footwear when hiking or camping in endemic areas. If a bite occurs, the tick should be removed as soon as possible.
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. 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 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

Cause	<i>Salmonella typhi</i> , the typhoid bacillus, which infects only humans. Paratyphoid and enteric fevers are caused by other species of <i>Salmonella</i> , which infect domestic animals as well as humans.
Transmission	Infection is transmitted by consumption of contaminated food or water. Occasionally direct faecal–oral transmission may occur. Shellfish taken from sewage-polluted areas areas an important source of infection. Infection occurs through eating raw fruit and vegetables fertilized by night soil, and contaminated milk and milk products. Flies may transfer infection to foods, resulting in contamination that may be sufficient to cause human infection. Pollution of water sources may produce epidemics of typhoid fever, when large numbers of people use the same source of drinking-water.
Nature of the disease	A systemic disease of varying severity. Severe cases are characterized by gradual onset of fever, headache, malaise, anorexia and insomnia. Constipation is more common than diarrhoea in adults and older children. Without

	<p>treatment, the disease progresses with sustained fever, bradycardia, hepatosplenomegaly, abdominal symptoms and, in some cases, pneumonia. In white-skinned patients, pink spots (papules), which fade on pressure, appear on the skin of the trunk in up to 50% of cases. In the third week, untreated cases may develop additional gastrointestinal and other complications, which may prove fatal. Around 2–5% of those who contract typhoid fever become chronic carriers, as bacteria persist in the biliary tract after symptoms have resolved.</p>
Geographical distribution	Worldwide. The disease occurs most commonly in association with poor standards of hygiene in food preparation and handling and where sanitary disposal of sewage is lacking.
Risk for travellers	Generally low risk for travellers, except in parts of northern and western Africa, in southern Asia, in parts of Indonesia and in Peru. Elsewhere, travellers are usually at risk only when exposed to low standards of hygiene with respect to food handling, control of drinking-water quality, and sewage disposal. Even vaccinated individuals should take care to avoid consumption of potentially contaminated food and water as the vaccine does not confer 100% protection.
Precautions	<p>Observe all precautions against exposure to foodborne and waterborne infections (Chapter 3).</p> <ul style="list-style-type: none"> • Vaccine Oral Ty21a. This live, attenuated mutant strain of <i>Salmonella typhi</i> 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) contains 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. <p>Both vaccines are safe and effective.</p> <p>A combined typhoid/hepatitis A vaccine is also available in some countries.</p> <p>Precautions and contraindications</p> <p>Proguanil, mefloquine and antibiotics should be stopped from 3 days before until 3 days after giving Ty21a.</p> <p>No serious adverse effects have been reported following administration of Ty 21a or Vi CPS.</p> <p>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.</p>

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 insert ^a
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 Ty21a

^a The duration of protection following Ty21a immunization is not well defined and may vary with vaccine dose and possibly with subsequent exposures to *Salmonella typhi* (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 7 years (Canada) or 5 years (USA) for all, regardless of typhoid fever endemicity in the country of residence.

YELLOW FEVER

Cause	The yellow fever virus, an arbovirus of the Flavivirus genus.
Transmission	Yellow fever in urban and some rural areas is transmitted by the bite of infective <i>Aedes aegypti</i> mosquitoes and by other mosquitoes in the forests of Africa and South America. The mosquitoes bite during daylight hours. Yellow fever virus infects humans and monkeys. In jungle and forest areas, monkeys are the main reservoir of infection, with transmission from monkey to monkey carried out by mosquitoes. The infective mosquitoes may bite humans who enter the forest area, usually causing sporadic cases or small outbreaks. In urban areas, monkeys are not usually involved and infection is transmitted among humans by mosquitoes. Introduction of infection into densely populated urban areas can lead to large epidemics of yellow fever. In Africa, an intermediate pattern of transmission is common in humid savannah regions. Mosquitoes infect both monkeys and humans, causing localized outbreaks.
Nature of the disease	Although most infections are asymptomatic and not detected, some lead to an acute illness characterized by two phases. Initially, there is fever, muscular pain, headache, chills, anorexia, nausea and/or vomiting, often with bradycardia. About 15% of patients progress to a second phase after a few days, with resurgence of fever, development of jaundice, abdominal

	pain, vomiting and haemorrhagic manifestations; half of these patients die 10–14 days after the onset of illness.
Geographical distribution	Areas where yellow fever virus is present far exceed those officially reported. Some countries may have no reported cases simply because of a high level of vaccine coverage against yellow fever in the population or because of poor surveillance. The yellow fever virus is endemic in some tropical areas of Africa and central and South America (Map). Transmission can occur at altitudes up to 2300 m in the Americas and possibly higher in Africa.
Risk for travellers	Travellers are at risk in all areas where yellow fever is considered endemic (Country list and Annex 1). The risk is greatest for visitors who enter forest and jungle areas.
Precautions	Avoid mosquito bites during the day and evening (Chapter 3).
Vaccine	<p>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.</p> <p>With the few exceptions mentioned above, vaccination is recommended for all travellers to countries or areas where there is a risk of yellow fever transmission (Country list and Annex 1). The risk to unvaccinated individuals who visit countries where there may be yellow fever transmission is often greater than the risk of a vaccine-related adverse event. 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. While yellow fever vaccination should be encouraged as a key prevention strategy, it is important to screen travel itineraries, particularly of older travellers, and carefully evaluate the potential risk of systemic illness after yellow fever vaccination.</p> <p>Yellow fever vaccination is mandatory for visitors in selected countries (Country list).</p> <p>Precautions and contraindications</p> <p>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 (Chapter 9). 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.</p> <p>There have been recent reports of a small number of serious adverse events (including deaths) 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</p>

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 also be related to other population differences (e.g. previous vaccination or exposure to wild yellow fever virus). This risk appears to be limited to the first immunization. Potential risk factors are a history of thymus disease (e.g. thymoma) and age over 60. Adverse events 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 USA and Europe ranges between 0.19 and 0.8 per 100 000 doses.

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

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

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 (including airport transit) from countries 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.

Travellers 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 (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 from 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 *Neisseria 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 poliomyelitis 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 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 (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: www.who.int/immunization/documents/positionpapers_intro/en/index.html

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.

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 poliomyelitis, 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 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

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

Table 6.3 **Uncommon severe adverse reactions**

Vaccine	Possible adverse reaction	Expected rate ^a per million doses
BCG	Suppurative lymphadenitis	100–1000 (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	1000–60 000
	Seizures	570
	Hypotonic–hyporesponsive episode	570
	Anaphylaxis	20
<i>Haemophilus influenzae</i>	NR	—
Hepatitis A	NR	—
Hepatitis B ^c	Anaphylaxis	1–2
Influenza	Guillain–Barré syndrome	<1
Japanese encephalitis		Rare
	Hypersensitivity	1800–6400
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/arthrits/arthropathy	None or very rare
Tetanus	Brachial neuritis	5–10
	Anaphylaxis	1–6

Vaccine	Possible adverse reaction	Expected rate ^a per million doses
Tick-borne encephalitis	NR	—
Typhoid fever	Parenteral vaccine – various Oral vaccine – NR	Very rare —
Yellow fever	Encephalitis (<6 months) Allergy/anaphylaxis Viscerotropic disease	500–4000 5–20 0–4

^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.

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): www.who.int/GlobalAtlas/

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

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

WHO vaccine position papers: 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 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.