CHAPTER 6

Vaccine-preventable diseases and vaccines

6.1 General considerations

Vaccination is the administration of agent-specific, but relatively harmless, antigenic components that in vaccinated individuals can induce protective immunity against the corresponding infectious agent. In practice, the terms "vaccination" and "immunization" are often used interchangeably.

6.1.1 Disease prevention

Vaccination is a highly effective method of preventing certain infectious diseases. 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 infectious diseases that may be encountered abroad. However, satisfactory vaccines have not yet been developed against several of the most life-threatening infections, including tuberculosis, malaria and HIV/AIDS.

6.1.2 Vaccination and other precautions

Despite their success in preventing disease, vaccines rarely protect 100% of the recipients. The traveller should not assume that there is no risk of contracting the disease(s) against which he/she has been vaccinated. For example, immunization is not a substitute for avoiding potentially contaminated food and water. Therefore, all additional precautions against infection should be carefully considered (Chapter 3).

6.1.3 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. There is no single vaccination schedule that fits all travellers. Each schedule must be individualized according to the traveller's previous immunizations, countries to be visited, type and duration of travel, and the amount of time available before departure.

A medical consultation before departure is a good opportunity for the health care provider to review the immunization status of travellers and to offer missing routine vaccinations in addition to vaccines needed for the actual travel.

Following vaccination, the immune response of the vaccinated individual varies with the type of vaccine, the number of doses required, and whether the individual has been vaccinated previously 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, even when departure is imminent, there is still time to provide both advice and possibly some immunizations.

6.1.4 Vaccine schedules and administration

The vaccines that may be recommended or considered for travellers are summarized in Table 6.1. Further information on the schedules for administration of these vaccines can be found in the individual vaccine sections as well as in the corresponding WHO position papers (http://www.who.int/immunization/documents/positionpapers/en/index.html) Summary tables for routine vaccinations can be found at http://www.who.int/immunization/policy/immunization_tables/en/index.html.

The individual vaccine sections and the WHO position papers also provide information on the recommended dose intervals in multi-dose schedules, although here some adjustments can be made to accommodate the needs of travellers who may not be able to complete the schedule exactly as prescribed. In general, it is acceptable to lengthen the intervals between doses, and repeating previous vaccine doses is unnecessary unless this is explicitly stated in the package insert. On the other hand, significant shortening of the intervals is not recommended.

Table 6.1 **Vaccines for travellers**

Category	Vaccine
1. Routine vaccination	Diphtheria, tetanus, and pertussis Hepatitis B (Hep B) *Haemophilus influenzae* type b Human papillomavirus[a] Influenza[b] Measles, mumps, and rubella Pneumococcal Polio Rotavirus[a] Tuberculosis (BCG)[c] Varicella[a]
2. Selective vaccines for travellers to risk areas[d]	Cholera Hepatitis A[e] Japanese encephalitis[e] Meningococcal[e] Rabies Tick-borne encephalitis[e] Typhoid fever Yellow fever[e]
3. Required vaccination	Yellow fever (see Country list) Meningococcal (against serogroups A, C, Y, and W135) and polio (required by Saudi Arabia for pilgrims; updates are available on http://www.who.int/wer)

[a]So far, introduced into the routine immunization programme of a limited number of countries.
[b]Routine vaccination for certain age groups and for individuals potentially exposed to certain risk factors.
[c]No longer routine in most industrialized countries.
[d]For diseases in this category a summary of vaccine recommendations and other precautions is provided.
[e]These vaccines are also included in the routine immunization programme in several high-risk countries .

6.1.5 Safe injections

The administration of vaccines requires the same high standard of injection safety as any other injection. A sterile needle and syringe should be used for each injection and both 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 (*WHO best practices for injections and related procedures toolkit*. Geneva, World Health Organization, 2010; WHO/EHT/10.02).

6.1.6 Vaccine combinations and vaccines co-administration

Inactivated vaccines do not generally interfere immunologically with other inactivated or live vaccines. However, simultaneous administration requires a different anatomical injection site for each vaccine.

Most live vaccines can be given simultaneously provided that they are administered at different anatomical sites. However, if injectable live-virus vaccines are not administered on the same day, their injections should be separated by an interval of at least 4 weeks. Live oral polio vaccine (OPV) and the live oral Ty21a typhoid vaccine can be administered simultaneously with, or at any interval before or after, injectable live vaccines. Somewhat lower seroconversion rates for mumps, rubella and yellow fever (but not for measles) have been reported in subjects injected simultaneously with yellow fever vaccine and measles/mumps/rubella (MMR) vaccine compared with subjects receiving these vaccines 30 days apart.

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 of children, the combined diphtheria/tetanus/pertussis (DTP) and MMR vaccines are in widespread use. Other examples of combination vaccines are hepatitis A+B and hepatitis A+typhoid, IPV+DTP, IPV+DTP+Hib, MMR+varicella (MMRV), IPV+DTP+HepB+Hib.[1] A new combination vaccine based on *Haemophilus influenzae* type b and *Neisseria meningitidis* C vaccines (Hib/MenC) is now also available in Europe. 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. In general, licensed combination vaccines are just as safe and effective as the individual single-disease vaccines. However, comparing the adverse events following MMR and MMRV combinations, the first vaccine dose of MMRV is associated with a slightly elevated risk of post-vaccination febrile seizure.

6.1.7 Choice of vaccines for travel

Vaccines for travellers include: (1) basic vaccines used in most national routine programmes, particularly but not exclusively in children; (2) vaccines that are recommended before travel to particular countries or areas; (3) vaccines required by the International Health Regulations.

Several of the vaccines that are routinely administered in childhood require one or several booster doses to maintain an effective level of immunity. Adults often neglect the need for booster vaccinations, particularly if the risk of infection is low. Some adults,

[1] IPV = inactivated polio vaccine; Hib = Haemophilus influenza type b [vaccine]; HepB = hepatitis B [vaccine].

particularly elderly people, may never have been vaccinated at all. It is important to realize that diseases such as diphtheria and polio, which have been eliminated in most industrialized countries, may be present in countries frequently 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. Inhabitants of endemic areas who are travelling to non-endemic locations should be adequately vaccinated to prevent introduction/reintroduction of diseases such as polio, yellow fever, measles and rubella.

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.

Nowadays, only yellow fever vaccination is, in certain situations, required by the International Health Regulations. 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. In some non-endemic countries, yellow fever vaccination is a prerequisite for entry for those who have recently passed through yellow fever-endemic areas.

Vaccination against meningococcal disease (quadrivalent vaccine) is required by Saudi Arabia for pilgrims visiting Mecca and Medina for the Hajj or Umrah as well as for seasonal workers.

Some polio-free countries (see Country list) may also require travellers resident in countries or areas reporting wild polio viruses (updates available at http://www.polioeradication.org/Dataandmonitoring/Poliothisweek.aspx to be immunized against polio in order to obtain an entry visa, e.g. Brunei Darussalam, India, and Saudi Arabia (Chapter 9). Travellers should be provided with a written record of all vaccines administered (patient-retained record), preferably using the international vaccination certificate (which is required in the case of yellow fever vaccination). The certificate can be ordered from WHO at http://www.who.int/ith/en/.

6.2 Vaccines for routine and selective use

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

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. Travellers should ensure that all routine vaccinations are up to date. Information on the safety of routine vaccines can be found at http://www.who.int/vaccine_safety/en/.

Tables summarizing WHO recommendations for routine vaccinations can be found at http://www.who.int/immunization/policy/immunization_tables/en/index.html.

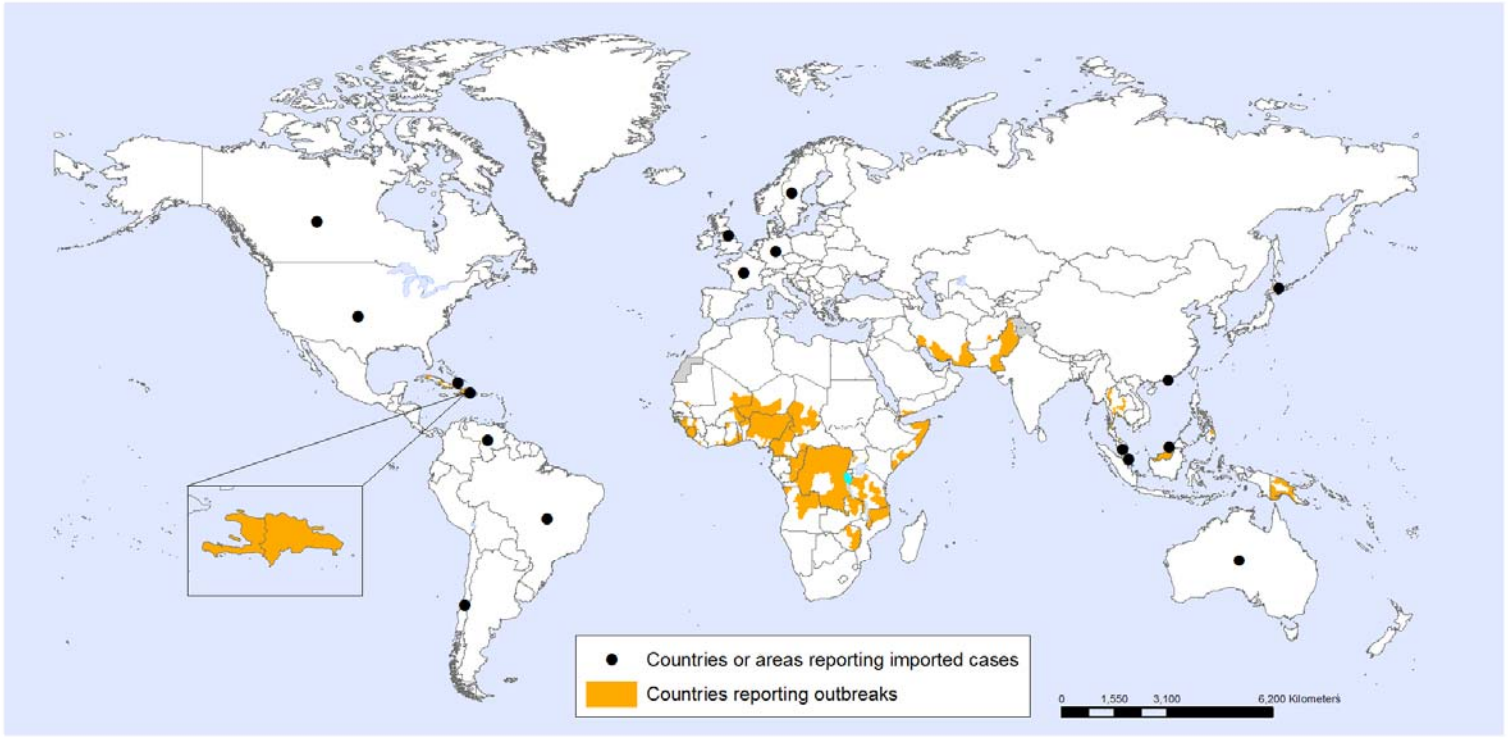
CHOLERA	
Cause	*Vibrio cholerae* bacteria of serogroups O1 and O139.
Transmission	Infection occurs through ingestion of food or water contaminated directly or indirectly by faeces or vomitus of infected individuals. Cholera affects only humans; there is no insect vector or animal reservoir host.
Nature 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 low-income countries that lack adequate sanitation and clean drinking-water and in war-torn areas where the infrastructure may have broken down. Many developing countries are affected, particularly in Africa and Asia and, to a lesser extent, in central and South America (see 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. However, humanitarian relief workers in disaster areas and refugee camps may be at risk.
General precautions	As for other diarrhoeal diseases, the consumption of potentially contaminated food, drinks and water should be avoided. Oral rehydration salts (ORS) should be carried to combat dehydration and electrolyte depletion in case of severe diarrhoea (Chapter 3). Cholera vaccination is not required as a condition of entry to any country.
Vaccine	A vaccine consisting of killed whole-cell *V. cholerae* O1 in combination with a recombinant B-subunit of cholera toxin (WC/rBS) has been marketed since the early 1990s. This killed vaccine is well tolerated and confers high-level (85–90%) protection for 6 months after the second immunization in all vaccinees aged more than 2 years. Three years after immunization the level of protection is still about 50% in vaccinees who were 5 years or older at the time of vaccination. Primary immunization consists of two oral doses 7–14 days apart for adults and children aged 6 years and over. For children aged 2–5 years, three doses are recommended. Intake of food and drinks should be avoided for 1 hour before and after vaccination. If the second dose is delayed for more than 6 weeks, vaccination should be restarted. Following primary immunization, protection against cholera

may be expected after about 1 week. Booster doses are recommended after 2 years for adults and children aged 6 years or more, and every 6 months for children aged 2–5 years. The vaccine is not licensed for children under 2 years of age.

In studies of travellers to countries or areas reporting cholera outbreaks, WC/rBS was found also to induce approximately 50% short-term protection against diarrhoea caused by enterotoxigenic *Escherichia coli* (ETEC).Two closely related bivalent oral cholera vaccines are available in India and Viet Nam. These killed whole-cell vaccines are based on *V. cholerae* serogroups O1 and O139 and do not contain the toxin B-subunit. They are reported to be safe and efficacious, providing 66–67% protection for at least 2 years against clinically significant cholera in countries or areas reporting outbreaks.

Type of vaccine:	a) Killed oral O1 with whole-cell with B-subunit b) Killed oral O1 and O139
Number of doses:	a) Two doses (minimum 1 week and maximum 6 weeks apart). Three doses for children aged 2–5 years (minimum 1 week and maximum 6 weeks apart) b) Two doses 14 days apart for individuals aged ≥2 year. One booster dose is recommended after 2 years
Contraindications:	Hypersensitivity to previous dose
Adverse reactions:	Mild gastrointestinal disturbances
Before departure:	2 weeks
Consider for:	Travellers at high risk (e.g. emergency/ relief workers)
Special precautions:	None

Cholera, areas reporting outbreaks, 2011–2012



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Data Source: World Health Organization
Map Production: Public Health Information and Geographic Information Systems (GIS)
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DIPHTHERIA/TETANUS/PERTUSSIS

DIPHTHERIA

Cause	Toxigenic *Corynebacterium diphtheriae (C. diphtheria)* and occasionally, toxigenic *Corynebacterium ulcerans (C. ulcerans).*
Transmission	*C. diphtheriae* typically resides in the upper respiratory tract and is transmitted from person to person through droplets and close physical contact. Transmission is facilitated by crowding and poor socioeconomic conditions. A cutaneous form of diphtheria caused by *C. ulcerans* is common in tropical countries. This bacterium is easily transmitted by close contact. Chronic carriage of *C. diphtheria* and *C. ulcerans* occurs frequently.
Nature of the disease	Diphtheria is caused by a potent bacterial toxin that can produce obstructive pseudo-membranes in the upper respiratory tract (croup) or damage to the myocardium and other tissues. Although asymptomatic or mild infections are most common, untreated diphtheria may be severe and sometimes fatal. *C. ulcerans* can cause respiratory or cutaneous diphtheria in non-immunized individuals and cutaneous, mostly non-toxic lesions even in fully vaccinated individuals.
Geographical distribution	Diphtheria is found worldwide, although it is not common in industrialized countries because of long-standing routine use of diphtheria/tetanus/pertussis (DTP) vaccine. Large epidemics occurred in several east European countries in the 1990s.
Risk for travellers	Non-immunized or incompletely immunized travellers have occasionally contracted diphtheria when visiting endemic areas. The disease occurs more frequently in parts of the world where DTP coverage is low.
Vaccine	All travellers should be vaccinated according to national recommendations. Vaccination against diphtheria is usually given as triple vaccine – DTP or DTaP (diphtheria/tetanus/acellular pertussis). After the initial course of three such doses, additional doses may be given as DT to children <7 years of age; individuals ≥7 years of age should receive a vaccine with reduced diphtheria content (dT). 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, adultboosters that contain TdaP are being introduced. Those who have received the primary series plus two booster doses, the last of which given in early adulthood, are unlikely to require further doses. Since the same schedule is now recommended for tetanus toxoid (see below) diphtheria toxoid and tetanus toxoid should normally be given together (as dT combination for individuals aged 7 years and over).

TETANUS

Cause	The bacterium *Clostridium tetani (C. tetani)*
Transmission	Tetanus is acquired through exposure to the spores of *C. tetani* which are present in soil worldwide. The disease is not communicable.
Nature of the disease	The disease is caused by the action of a potent bacterial neurotoxin released from wounds contaminated by *C. tetani*. Clinical symptoms are muscle spasms, initially of the muscles of mastication causing trismus or "lockjaw". Trismus can be followed by sustained spasm of the back muscles (opisthotonus) and by spasms of other muscles. Generalized tetanic seizures will ultimately lead to death unless intense supportive treatment is rapidly initiated.
Geographical distribution	Wounds can become infected with the spores of *C. tetani* anywhere in the world.
Risk for travellers	Every traveller should be fully vaccinated against tetanus. Almost any form of injury, from a simple laceration to a motor-vehicle accident, can expose the individual to the spores.
Vaccine	Tetanus vaccine is available as monovalent tetanus toxoid (TT), in bivalent combination with diphtheria toxoid (DT) or low-dose diphtheria toxoid (Td), or as trivalent vaccine that also includes whole-cell (wP) or acellular (aP) pertussis vaccine. In some countries, combination vaccines with hepatitis B, *Haemophilus influenzae* type b and/or IPV exist. Vaccines containing DT are used for children under 7 years of age and Td-containing vaccines for those aged 7 years and over. Vaccine combinations containing diphtheria toxoid (D or d) and tetanus toxoid, rather than tetanus toxoid alone, should be used when immunization against tetanus is indicated. A childhood immunization schedule of five doses is recommended. The primary series of three 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. Those who have received the primary series plus two booster doses, the last of which given in early adulthood, are unlikely to require further doses. 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 the primary series, or of subsequent booster injections, was given less than 5 years ago for dirty wounds or less than 10 years ago for clean wounds.

PERTUSSIS

Cause	The bacterium *Bordetella pertussis (B. pertussis*).
Transmission	*B. pertussis* is transmitted mainly by airborne droplets from the respiratory mucous membranes of infected individuals.
Nature of the disease	Pertussis (whooping cough) is a highly contagious acute bacterial disease involving the respiratory tract. Typical manifestations include several weeks of cough that gradually develops into severe coughing fits, ending in a characteristic "whoop", often with cyanosis and vomiting. In young infants, the cough may be absent and the disease may manifest with spells of apnoea. Although pertussis can occur at any age, most serious cases and fatalities are observed in early infancy. Major complications include pneumonia, encephalitis and malnutrition (due to repeated vomiting).
Geographical distribution	WHO estimated that about 16 million cases of pertussis occurred worldwide in 2008, 95% of which were in developing countries, and that some 195 000 patients died from this disease.
Risk for travellers	Unprotected young infants are at highest risk of severe pertussis, but older children, adolescents and adults may also contract the disease (often in mild and atypical form) if they are not fully immunized. Exposure to pertussis is more frequent in developing countries. All infants, including those who are HIV-positive, should be immunized against pertussis.
Vaccine	All travellers should be up to date with vaccination according to national recommendations. Both whole-cell (wP) and acellular (aP) pertussis vaccines provide excellent protection and are safe apart from minor adverse events. Both wP and aP are usually administered in combination with diphtheria and tetanus toxoids (DTwP or DTaP). WHO recommends a three-dose primary series, with the first dose administered at age 6 weeks; subsequent doses should be given 4–8 weeks apart, at age 10–14 weeks and 14–18 weeks. The last dose of the recommended primary series should be completed by the age of 6 months. Protection declines with time and probably lasts only a few years. A booster dose should be administered 1–6 years after the primary series, preferably during the second year of life. Some countries now offer an adolescent/adult booster, in particular to health care workers and young parents. Previously unvaccinated adolescents/adults should receive three doses of wP or aP vaccine with an interval of 2 months between the first and second, and 6–12 months between the second and third doses.

HAEMOPHILUS INFLUENZAE TYPE B

Cause	The bacterium *Haemophilus influenzae* type b (Hib).
Transmission	Respiratory droplets.
Nature of the disease	*Haemophilus influenzae* type b is a common cause of pneumonia and meningitis and of a number of other serious and potentially life-threatening conditions, including epiglottitis, osteomyelitis, septic arthritis and septicaemia. Rarely occurring in infants under 3 months of age or children 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.
Geographical distribution	It is estimated that each year Hib causes 7–8 million cases of pneumonia and hundreds of thousands of deaths, mainly in developing countries. The disease has practically disappeared in countries where routine Hib 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	WHO recommends the inclusion of conjugate Hib vaccines in all infant immunization programmes using any of the following schedules: three primary doses without a booster (3p+0); two primary doses plus a booster (2p+1); and three primary doses with a booster (3p+1). The age at first dose and the number of primary doses should be set after consideration of the local epidemiology, vaccine presentation (Hib conjugate monovalent vaccine or Hib conjugate vaccine in combination with other antigens) and how this fits into the overall routine immunization schedule.

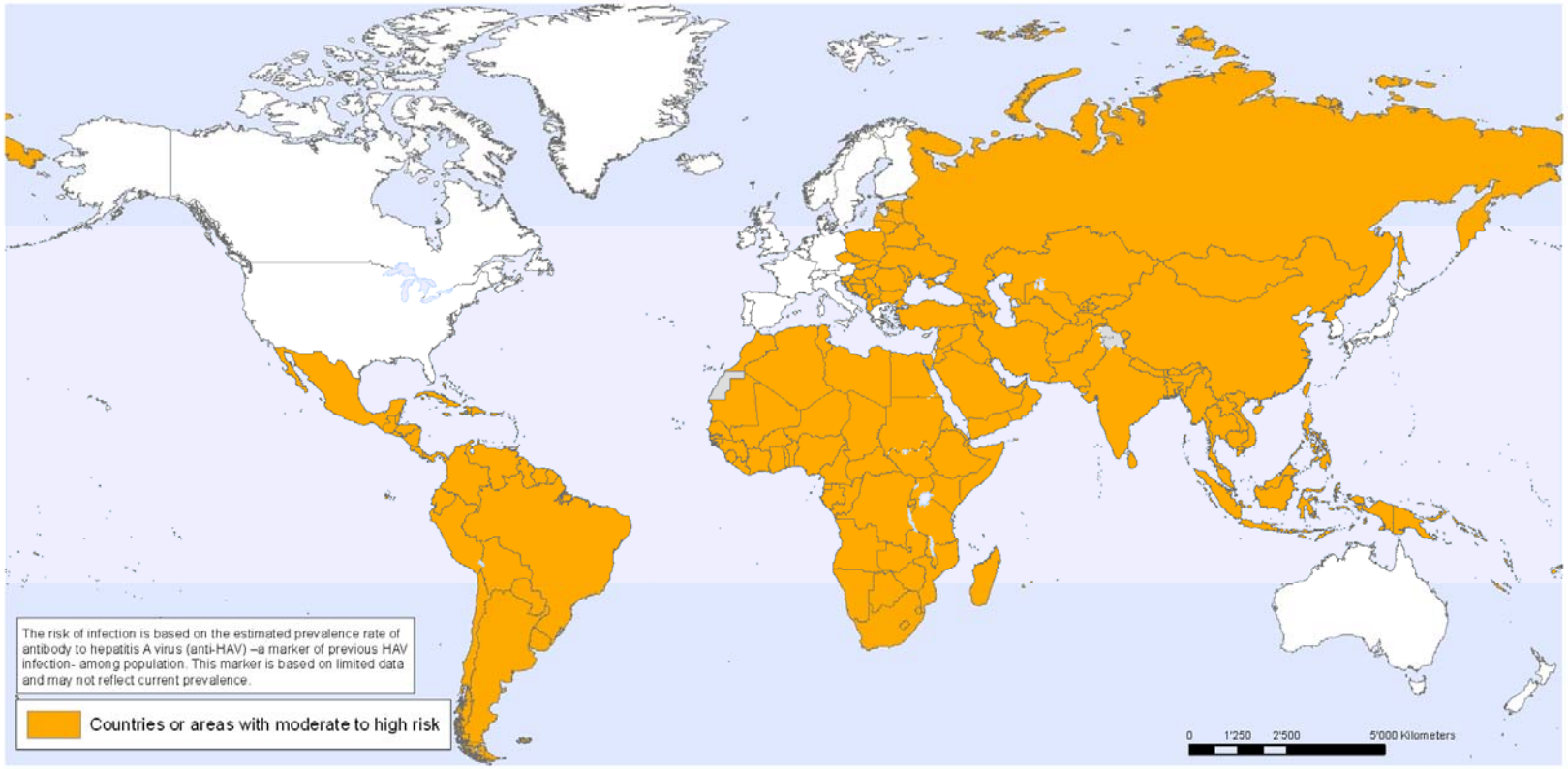
HEPATITIS A

Cause	Hepatitis A virus (HAV), a member of the *Picornaviridae* family.
Transmission	The virus is acquired through close contact with infected individuals or through faecally contaminated food or drinking-water. There is no insect vector or animal reservoir.
Nature of the disease	Acute viral hepatitis is characterized by abrupt onset of fever, malaise, nausea and abdominal discomfort, followed by jaundice a few days later. In very young children infection is usually mild or asymptomatic whereas in older children symptomatic disease is common. The disease is often more severe in adults and full recovery may take several months. Case-fatality is greater than 2% for those over 40 years of age and about 4% for those aged 60 years or more.
Geographical distribution	Worldwide, but most common in areas where sanitary conditions are poor (see map).
Risk for travelers	Non-immune travellers to developing countries are at significant risk of infection, particularly in settings with poor food and drinking-water control and poor sanitation.

	People born and raised in developing countries, and those born before 1945 in industrialized countries, have usually been HAV-infected in childhood and are likely to be immune.
Precautions	Avoid or boil potentially contaminated food and water. Short-term protection through injection of human immune globulin is gradually being replaced worldwide by hepatitis A vaccination.
Vaccine	Two types of HAV vaccines are currently available internationally: 1) Formaldehyde-inactivated vaccines: Inactivated HAV vaccines are used in most countries. Monovalent inactivated HAV vaccines are available in paediatric dose (0.5 ml) for children aged 1 year to 15 years, and in adult dose (1 ml). 2) Live attenuated vaccines (based on H2 or LA-1 HAV strains): These vaccines are manufactured and used mainly in China and sporadically in the private sector in India. 1. Inactivated hepatitis A vaccines are safe and highly effective. Traditionally, a two-dose schedule is recommended, particularly in travellers at substantial risk of contracting hepatitis A and in immunocompromised individuals. However, in healthy individuals, comparable effectiveness has been achieved with a single dose. Results from mathematical models indicate that, after completion of the primary two-dose series, anti-HAV antibodies may persist for 25 years or more. Serological testing to assess antibody levels after vaccination is not indicated. A combination hepatitis A/typhoid (ViCPS) vaccine, administered as a single dose, confers high levels of protection against both these waterborne diseases. A combination vaccine that provides protection against both hepatitis A and hepatitis B should be considered for travellers who may be exposed to both organisms (see under Hepatitis B vaccines). 2. The Chinese live attenuated hepatitis A vaccines have been shown to be safe and highly protective (95%) against clinical infection for at least 3 years.

Type of vaccine:	Inactivated or live, both given i.m.
Number of doses:	Inactivated vaccine: two; live vaccine: one
Schedule:	Inactivated vaccine: two doses, the second dose normally 6 months after the first. If needed, this interval may be extended to 18–36 months). In healthy individuals, a single dose seems to be similarly efficacious. Live vaccine: one dose Minimum age for HAV vaccination is 1 year
Boosters:	May not be necessary
Contraindications:	Hypersensitivity to previous dose
Adverse reactions:	Inactivated vaccine: mild local reaction of short duration, mild systemic reaction Live vaccine: few reported
Before departure:	Inactivated and live vaccines: protection is achieved 2–4 weeks after first dose. 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.
Recommended for:	Hepatitis A vaccination should be considered for individuals aged ≥1 year who are travelling to countries or areas with moderate to high risk of infection. Those at high risk of acquiring severe disease, such as immunosuppressed patients and patients with chronic liver disease, should be strongly encouraged to be vaccinated regardless of where they travel.
Special precautions:	None

Hepatitis A, countries or areas at risk



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Data Source: World Health Organization.
Jacobsen KH, Wiersma ST. Hepatitis A virus seroprevalence by age and world region, 1990 and 2005. Vaccine 2010 Sep;28(41):6653-7
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

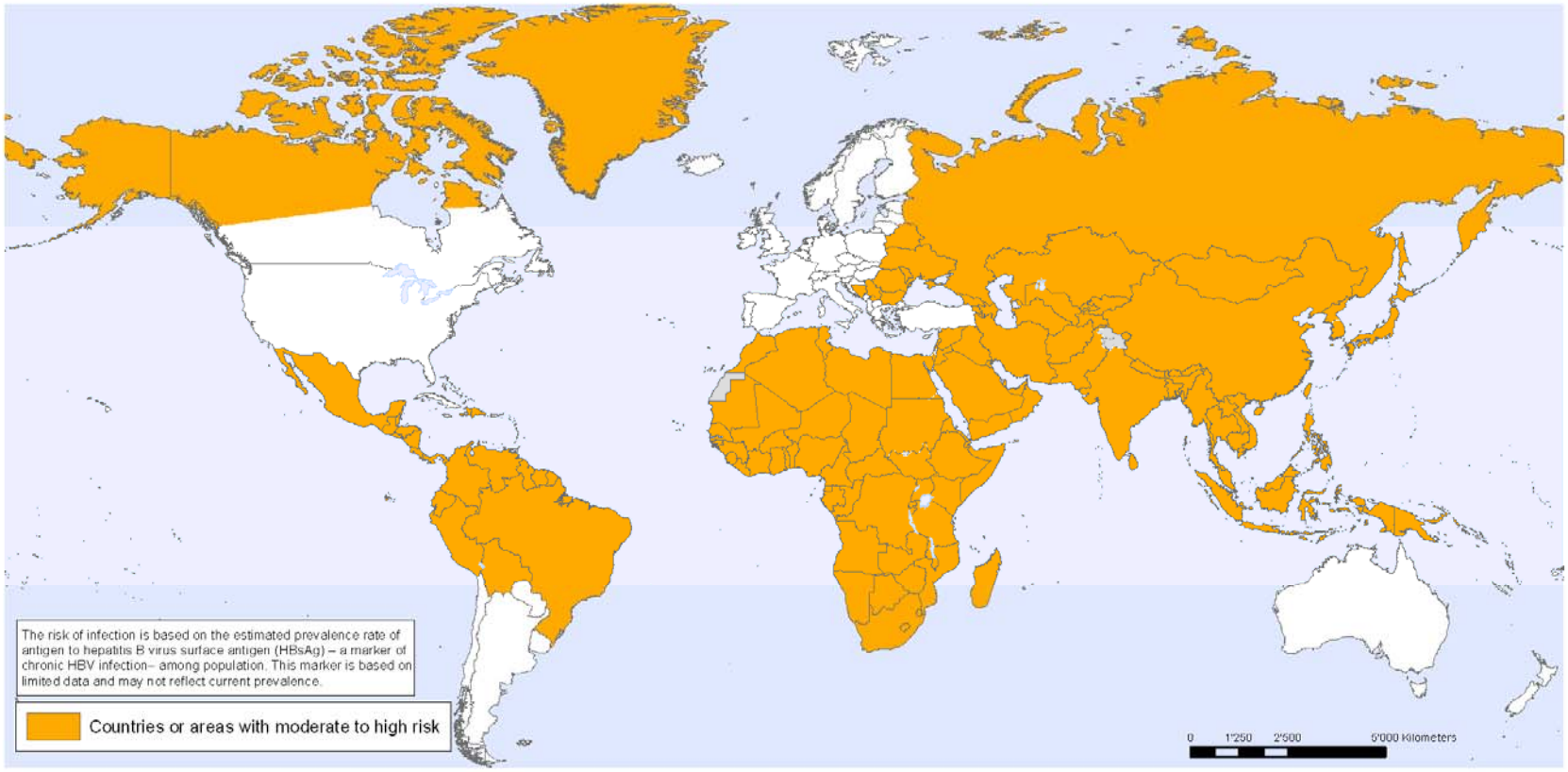
World Health Organization

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 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	Most acute HBV infections are asymptomatic or cause mild symptoms, which are often unrecognized. Symptomatic acute disease occurs in about 1% of perinatally infected individuals, in 10% of children infected between 1 and 5 years of age, and in about 30% of individuals infected after the age of 5 years. Clinical acute hepatitis B 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 develops in <5% of HBV-infected adults but more often in young children and in the majority of those infected perinatally. In some cases of chronic HBV infection, cirrhosis and/or liver cancer develop later.
Geographical distribution	The endemicity of HBV in a population is described by the prevalence of HBsAg, an HBV-specific component found in the blood (and other body fluids) in both acute and chronic stages of the infection. HBV is found worldwide, but with differing levels of endemicity. The majority of the world's population live in countries where the prevalence of HBsAg in the general population is high (≥8%) or intermediate (2–7%). In certain areas of North America, northern and western Europe, the southern cone of South America, Australia and New Zealand, prevalence of chronic HBV infection is relatively low (<2%) (see map).
Risk for travellers	The risk depends on (1) the prevalence of HBV infection in the country or area of destination, (2) the extent of direct contact with blood or body fluids or of sexual contact with potentially infected individuals, and (3) the duration and type of travel. Principal risky activities include unprotected sexual intercourse with an infected person; health-care interventions (medical, dental, laboratory or other) that entail direct exposure to human blood or body fluids; receipt of a transfusion of blood that has not been tested for HBV; 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.
General precautions	See under "HIV/AIDS and other sexually transmitted infections", Chapter 5.

Vaccine	Hepatitis B vaccine is produced by recombinant DNA technology, most commonly in yeast. The complete vaccination series consists of three doses of vaccine; the first two doses are usually given 1 month apart, with the third dose 1–12 months later. The WHO-recommended schedule for hepatitis B immunization of children consists of a dose within 24 hours of birth followed by a second and third dose of hepatitis B-containing vaccines at intervals of at least 4 weeks. A complete series of immunization provides protection for at least 25 years and, according to current scientific evidence, probably for life. Boosters are not recommended for routine immunization programmes. 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. A combination vaccine that provides protection against both hepatitis A and hepatitis B should be considered for travellers who may be 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.
Recommended for	Hepatitis B vaccine should be considered for all non-immune individuals travelling to countries or areas with moderate to high risk of infection. It can be administered to infants from birth.

Hepatitis B, countries or areas at risk



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Data Source: World Health Organization/CDC
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

World Health Organization

HEPATITIS E

Cause	Hepatitis E virus, which has not yet been definitively classified (formerly classified as a member of the Caliciviridae).
Transmission	Hepatitis E is usually a waterborne disease acquired from contaminated drinking-water. Direct faecal–oral transmission from person to person is also possible. There is no insect vector. Various domestic animals, including pigs, may be reservoirs of hepatitis E.
Nature of the disease	The clinical features and course of the disease are generally similar to those of hepatitis A. As with hepatitis A, there is no chronic phase. Young adults are most commonly affected. In pregnant women, there is an important difference between hepatitis E and hepatitis A: during the third trimester of pregnancy, hepatitis E takes a much more severe form, with a case–fatality rate reaching 20% or higher.
Geographical distribution	Worldwide. Most cases, both sporadic and epidemic, occur in countries with poor standards of hygiene and sanitation.
Risk for travellers	Travellers to developing countries may be at risk when exposed to poor conditions of sanitation and drinking-water control.
Precautions	Travellers should follow the general conditions for avoiding potentially contaminated food and drinking-water (Chapter 3).
Vaccine	An Hepatitis E vaccine has been recently commercially developed and licensed in China. The vaccine contains a recombinant viral capsid protein. The available data for this vaccine relate to pre-exposure protection after administration of three doses over a 6-month period, and to a limited extent following that of the first two doses. The vaccine appears to be effective for at least 2 years; future follow-up studies should provide data on whether the vaccine provides longer-term protection. Limited data on safety during pregnancy are available .

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. HPV is 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 HPV 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	HPV is very common all over the world. In 2005, there were an estimated 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 infections", Chapter 5.
Vaccines	Since 2006, two HPV vaccines have been licensed; one vaccine targets four and the other two HPV genotypes. Both vaccines are designed to protect against about 70% of cervical cancer cases worldwide (the tetravalent vaccine also protects against genital warts). Both vaccines are intended to be administered to females before the onset of sexual activity – that is, before first exposure to HPV infection. Most countries that have licensed these vaccines, recommend their use in girls aged 10–14 years. In some countries the tetravalent vaccine is offered to girls as young as 9 years. WHO recommends that routine HPV vaccination be included in national immunization programmes, provided that: prevention of cervical cancer or other HPV-related diseases, or both, constitutes a public health priority; vaccine introduction is programmatically feasible; sustainable financing can be secured; and the cost–effectiveness of vaccination strategies in the country or region is considered. The primary target populations are girls within the age range 9–10 to 13 years. The complete series of quadrivalent vaccine is administered at day 0; 2 months; and 6 months. The bivalent vaccine is administered at day 0; 1 month; and 6 months. Repeating previous doses is not necessary if the three-dose programme has been interrupted. Booster doses are currently not recommended.

INFLUENZA

For zoonotic influenza, see Chapter 5.

SEASONAL INFLUENZA

Cause	Influenza viruses belonging to the family *Orthomyxoviridae*. The influenza viruses are classified into types A, B and C on the basis of their nucleoproteins. 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. The majority of the currently identified 17 HA and 10 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. In 2009, global outbreaks caused by the A(H1N1) strain attained pandemic proportions, gradually evolving into a seasonal epidemiological pattern in 2010.
Transmission	Respiratory transmission occurs mainly by droplets disseminated by unprotected coughs and sneezes. Airborne transmission of influenza viruses occurs particularly in crowded spaces. Hand contamination followed by direct mucosal inoculation of virus is another possible source of transmission.
Nature of the disease	Influenza is 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 and non-productive cough, often accompanied by headache, coryza, myalgia and prostration. Complications of influenza include primary viral pneumonitis, bacterial pneumonia, otitis media and exacerbation of underlying chronic conditions. Illness tends to be most severe in elderly people, in infants and young children, and in immunocompromised individuals. Death resulting from seasonal influenza occurs mainly in elderly people and in individuals with pre-existing chronic diseases.
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-round, typically with several peaks during rainy seasons.
Risk for travellers	Travellers, like local residents, are at risk during the influenza season. In addition, groups of travellers (e.g. on cruise ships) that include individuals from areas affected by seasonal influenza may experience out-of-season outbreaks. Travellers visiting countries in the opposite hemisphere during the influenza season are at special risk, particularly if they do not have some degree of immunity through recent infection or regular vaccinations.
Precautions against influenza	During influenza outbreaks, crowded enclosed spaces and close contact with people suffering from acute respiratory infections should be avoided if possible. 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 maintain distance, cover coughs and sneezes with disposable tissues or clothing, and to wash hands. In some situations, physicians may recommend antiviral prophylaxis or early treatment using neuraminidase inhibitors, particularly for individuals at special risk.
Vaccine	Both trivalent (or quadrivalent) inactivated and live attenuated influenza vaccines are available. There are three types inactivated vaccines : whole-virus vaccines, split-virus vaccines, and subunit

vaccines. In most countries, whole-virus vaccines have been replaced by less reactogenic split virus and subunit vaccines. Inactivated vaccines are the only influenza vaccines licensed for vaccination of children <2 years of age, for persons aged ≥50 years, and for pregnant women. Healthy non-pregnant individuals aged 2–49 years may receive live attenuated influenza vaccines. There are inactivated influenza vaccines licensed for ages 6 months and higher, although specific age groups vary by product. Inactivated influenza vaccine may be used to prevent influenza among individuals aged ≥ 6 months, including healthy persons and those with high risk medical conditions.

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. Therefore, the composition of influenza vaccines is reviewed annually, separately for the two hemispheres. During years when the composition of the seasonal influenza vaccines differs antigenically between the northern and southern hemispheres, vaccines designed for one hemisphere may offer only partial protection against the prevailing strains of the other.

Available seasonal influenza vaccines do not protect against so-called avian influenza.

Travellers with conditions that place them at high risk for complications of influenza should be vaccinated every year. In years when the vaccine strains differ between the northern and southern hemispheres, high-risk individuals travelling from one hemisphere to the other shortly before or during the other hemisphere's influenza season should obtain the vaccination recommended for the opposite hemisphere two weeks before travel. Where this is not possible, the traveller should arrange vaccination as soon as possible after arriving at the travel destination.

Inactivated influenza vaccines are injected into the deltoid muscle (vaccinees aged >1 year) or the anterolateral aspect of the thigh (vaccinees 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 less than 9 years should receive two injections, administered at least 1 month apart. A single dose of the vaccine is appropriate for schoolchildren aged 9 years and over and for healthy adults. Mild local reactions such as pain or swelling at the injection site are common; systemic reactions such as fever are less common.

Contraindications and precautions

Vaccination is contraindicated in case of severe egg allergy, including anaphylactic reaction.

JAPANESE ENCEPHALITIS

Cause	Japanese encephalitis virus belonging to the mostly vector-borne Flaviviridae family.
Transmission	Pigs and various wild birds represent the natural reservoir of this virus, which is transmitted to new animal hosts and occasionally humans by mosquitoes of the genus *Culex*.
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 followed by an uneventful recovery; 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 virus is the leading cause of viral encephalitis in Asia and occurs in almost all Asian countries (see map). Transmission occurs principally in rural agricultural locations where flooding irrigation is practised – some of which may be near or within urban centres. Transmission is related mainly to the rainy season in south-east Asia but may take place all year round, particularly 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. Largely as a result of immunization, the incidence of Japanese encephalitis has been declining in Japan and the Republic of Korea, in some regions of China, and more recently in Nepal, Sri Lanka, Thailand and Viet Nam. However, transmission of the virus remains unaffected by immunization, and non-immunized individuals remain at risk. The disease is also reported from Bangladesh, parts of India and Pakistan, and from Cambodia, the Lao People's Democratic Republic, the Philippines and other countries in the region (see map).
Risk for travellers	The risk of Japanese encephalitis is very low for most travellers to Asia, particularly for short-term visitors to urban areas. However, the risk varies according to season, destination, duration of travel and activities. Vaccination is recommended for travellers with extensive outdoor exposure (camping, hiking, working, etc.) during the transmission season, particularly in endemic countries or areas where flooding irrigation is practised. In areas at risk, Japanese encephalitis is primarily a disease of children, but it can occur in travellers of any age. Prevention is by avoidance of mosquito bites (Chapter 3) and by vaccination.
Vaccine	The inactivated mouse brain-derived (IMB) vaccine is now commonly replaced by cell culture-based vaccines. A live attenuated vaccine based on the SA 14-14-2 strain of the JE virus is widely used in China and in an increasing number of countries within the Asian region, including India, the Republic of Korea, Sri Lanka, and Thailand. A Vero cell-derived, inactivated and alum-adjuvanted JE vaccine based on the SA 14-14-2 strain was approved in 2009 in North

America, Australia and various European countries. The primary two doses are administered 4 weeks apart. A booster dose is recommended 1–2 years after the primary immunization. This vaccine has been given concomitantly with hepatitis A vaccine without significant interference with the safety and immunogenicity of either vaccine. Data on concomitant administration with other vaccines frequently used in travellers are currently unavailable. The vaccine is licensed for use in individuals 17 years of age and older in the United States, and 18 years and above in other countries. Paediatric and post-marketing safety studies are under way.

Another Vero cell-derived inactivated JE vaccine was licensed by the Japanese authorities in February 2009 and a similar Japanese vaccine was licensed in 2011. These two vaccines use the same strain of JE virus (Beijing-1) as the mouse-brain-derived vaccine. Clinical trials have shown that the vaccines are safe and immunogenic, with seroconversion rates exceeding 95%.

In addition, a new live attenuated, JE–yellow fever chimeric vaccine has recently been licensed in Australia and Thailand. A single dose of this chimeric JE vaccine was found to be safe, highly immunogenic and capable of inducing long-lasting immunity in both preclinical and clinical trials.

Type of vaccine and schedules:	1) Live attenuated vaccine (SA 14-14-2 strain). In China, the first dose is given subcutaneously at age 8 months, followed by a booster dose at 2 years of age. In some areas, an additional booster is offered at 6–7 years of age. However, protection for several years may be achieved with a single dose of this vaccine, and in many countries one dose without subsequent boosters is recommended. 2) Inactivated, Vero cell-derived, alum-adjuvanted vaccine (SA 14- 14-2 strain). Primary immunization consists of two intramuscular doses, 4 weeks apart. A booster is recommended after 1 year. 3) Inactivated Vero cell-derived vaccines (Beijing-1 strain). Primary immunization consists of three doses at days 0, 7 and 28, or two doses given preferably 4 weeks apart (0.25 ml for children <3 years, 0.5 ml for all other ages). One booster is recommended 12–14 months after completion of the primary immunization and thereafter every 3 years. 4) Live chimeric vaccine (with yellow fever 17D as backbone). A single dose is recommended; the need for and timing of a possible booster dose have not yet been determined
Adverse reactions:	Occasional mild local or systemic reactions
Contraindications and precautions	A hypersensitivity reaction to a previous dose is a contraindication. In principle, the live attenuated vaccine should be avoided in pregnancy unless there is a high risk of exposure to the infection. Rare, but serious, neurological adverse events attributed to IMB vaccine have been reported, but no causal relationship has been confirmed. As occasional allergic reactions to components of the vaccine may occur up to 2 weeks after administration, it is advisable to ensure that the complete course of vaccination is administered well in advance of departure.

Japanese encephalitis, countries or areas at risk*

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization/CDC
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

World Health Organization

MEASLES	
Cause	Measles virus, genus *Morbillivirus* and family Paramyxoviridae.
Transmission	Transmission, which is primarily by airborne 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 had affected most people by the time of adolescence. Epidemics may still occur every 2 or 3 years in areas where there is low vaccination coverage. In countries where measles has been largely eliminated, cases imported from other countries remain an important continuing source of infection. In 2009, worldwide measles vaccination coverage had reached 82%, and between 2000 and 2008 the estimated annual number of deaths from measles dropped from 733 000 to 164 000. The classical signs and symptoms of measles include fevers, cough, nasal congestion, and rashes. Common complications include bacterial middle-ear infection and pneumonia. In addition to infants, high-risk groups for measles complications include individuals suffering from chronic diseases and impaired immunity or from severe malnutrition (including vitamin A deficiency).
Geographical distribution	Before vaccines became available, measles outbreaks occurred all over the world. Since the introduction of large-scale measles immunization, indigenous transmission has virtually stopped in the Americas and in many industrialized countries worldwide.
Risk for travellers	Measles is still common in many countries and travel in densely populated areas may favour transmission. Travellers who are not fully immunized against measles are at risk. Special attention must be paid to all children and adolescent/young adult travellers who have not received two doses of measles vaccine.
Vaccine	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. The measles/mumps/rubella (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 programmes. Every child should receive two doses of measles vaccine. The second dose may be given as early as 1 month following the first, depending on the local programmatic and epidemiological situation. For infants travelling to countries experiencing extensive measles transmission, a dose of vaccine may be given as early as 6 months of age. However, children who receive the first dose between 6 and 8 months of age should subsequently receive the two conventional doses according to the national schedule. Older children or adults who did not receive the two lifetime doses should consider measles vaccination before travel. Given the severe course of measles in patients with advanced HIV infection, measles vaccination should be routinely administered to

potentially susceptible, asymptomatic HIV-positive children and adults. Measles vaccination may be considered even in individuals with symptomatic HIV infection, provided that they are not severely immunosuppressed. Where the risk of contracting measles infection is negligible, physicians who are able to monitor CD4 counts in HIV patients receiving antiretroviral treatment may prefer to delay the use of measles vaccine until CD4 counts are above 200. Following measles vaccination, no increased risk of serious adverse events has been demonstrated in HIV-positive compared with HIV-negative children, although lower antibody levels may be found in the former group.

MENINGOCOCCAL DISEASE

Cause	*Neisseria meningitides* bacteria, in most cases serogroups A, B and C, less commonly Y and X. Serogroup W-135 is of increasing concern.
Transmission	Transmission occurs by direct person-to-person contact and through respiratory droplets from patients or asymptomatic meningococcal carriers. Humans are the only reservoir.
Nature of the disease	As a rule, endemic disease occurs primarily in children and adolescents, with highest attack rates in infants aged 3–12 months; in meningococcal epidemics, rates may rise also in older children 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 the "meningitis belt" of sub-Saharan Africa, a zone stretching across the continent from Senegal to Ethiopia, large outbreaks and epidemics take place during the dry season (November to June). Recent reports of group Y meningococcal disease in the United States, and outbreaks caused by serogroup W-135 strains in Saudi Arabia and sub-Saharan Africa, particularly Burkina Faso, Chad and Niger, and serogroup X in Burkina Faso and Niger, suggest that these serogroups may be gaining in importance.
Risk for travellers	The risk of meningococcal disease in travellers is generally low. Those travelling to industrialized countries may be exposed to sporadic cases, mostly of A, B or C. Outbreaks of meningococcal C disease occur in schools, colleges, military barracks and other places where large numbers of adolescents and young adults congregate.

	Travellers to the sub-Saharan meningitis belt may be exposed to outbreaks, most commonly of serogroup A and serogroup W135 disease, with comparatively very high incidence rates during the dry season. Long-term travellers living in close contact with the indigenous population may be at greater risk of infection. Pilgrims visiting Mecca for the Hajj or Umrah are at particular risk.
General precautions	Avoid overcrowding in confined spaces. Following close contact with an individual suffering from meningococcal disease, medical advice should be sought regarding possible chemoprophylaxis and vaccination.
Vaccines	*Polysaccharide vaccines* Internationally marketed meningococcal polysaccharide vaccines are bivalent (A and C), trivalent (A, C and W-135) or tetravalent (A, C, Y and W-135). The vaccines are purified, heat-stable, lyophilized capsular polysaccharides from meningococci of the respective serogroups. Following one dose, both group A and group C vaccines have documented short-term efficacy levels of 85–100% in older children and adults. However, group C vaccines do not prevent disease in children under 2 years of age, and the efficacy of group A vaccine in children under 1 year of age is unclear. Group Y and W-135 polysaccharides have been shown to be immunogenic only in children over 2 years of age. A protective antibody response occurs within 10 days of vaccination. In schoolchildren and adults, one dose of these polysaccharide vaccines appears to provide protection for at least 3 years, but in children under 4 years of age the levels of specific antibodies decline rapidly after 2–3 years. **Adverse events and precautions – polysaccharide vaccine** The internationally available polysaccharide vaccines are safe, and significant systemic reactions are very rare. The most common adverse reactions are erythema and slight pain at the site of injection for 1–2 days. Fever exceeding 38.5 ºC occurs in up to 2% of vaccinees. No significant change in safety or reactogenicity has been observed when the group-specific monovalent vaccines are combined into bivalent or tetravalent meningococcal vaccines. Special precautions: Children under 2 years of age are not protected by the vaccine *Conjugate meningococcal vaccines* Conjugation of the bacterial polysaccharide to a protein carrier induces a T-cell-dependent immune response characterizedby increased immunogenicity among infants, prolonged duration of protection, and reduced nasopharyngeal carriage of meningococci. Conjugate meningococcal vaccines are available as monovalent serogroup A and serogroup C vaccines; bivalent serogroups A, C vaccine; and tetravalent serogroups A, C, Y, W-135 vaccine. These vaccines are highly immunogenic (>90%), although protective antibody titres are not long-lasting in young children. Cross-

protection between different meningococcal serogroups does not occur.

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.

A combination vaccine based on *Haemophilus influenzae* type b and *Neisseria meningitidis* serogroup C vaccines (HibMecC) is also marketed.

In 2010, a conjugated serogroup A meningococcal vaccine designed particularly for use in the African meningitis belt received regulatory approval in India and in a few African countries. This vaccine, which is licensed for single-dose immunization of individuals 1–29 years of age, has proved to be safe and highly immunogenic.

Three tetravalent conjugate vaccines against serogroups A, C, Y and W-135 meningococci are now licensed internationally. They differ in the conjugate carrier protein (CRM 197, tetanus toxoid, and diphtheria toxoid), but all are administered intramuscularly and show similar immunogenicity. In Canada and the United States, these vaccines are licensed for single-dose immunization of individuals 2–55 years of age. In addition, two of these vaccines offer a two-dose schedule for children aged 9–23 months.

In 2012, a conjugate tetravalent vaccine that can be administered as a single dose from the age of 1 year was licensed in Europe.

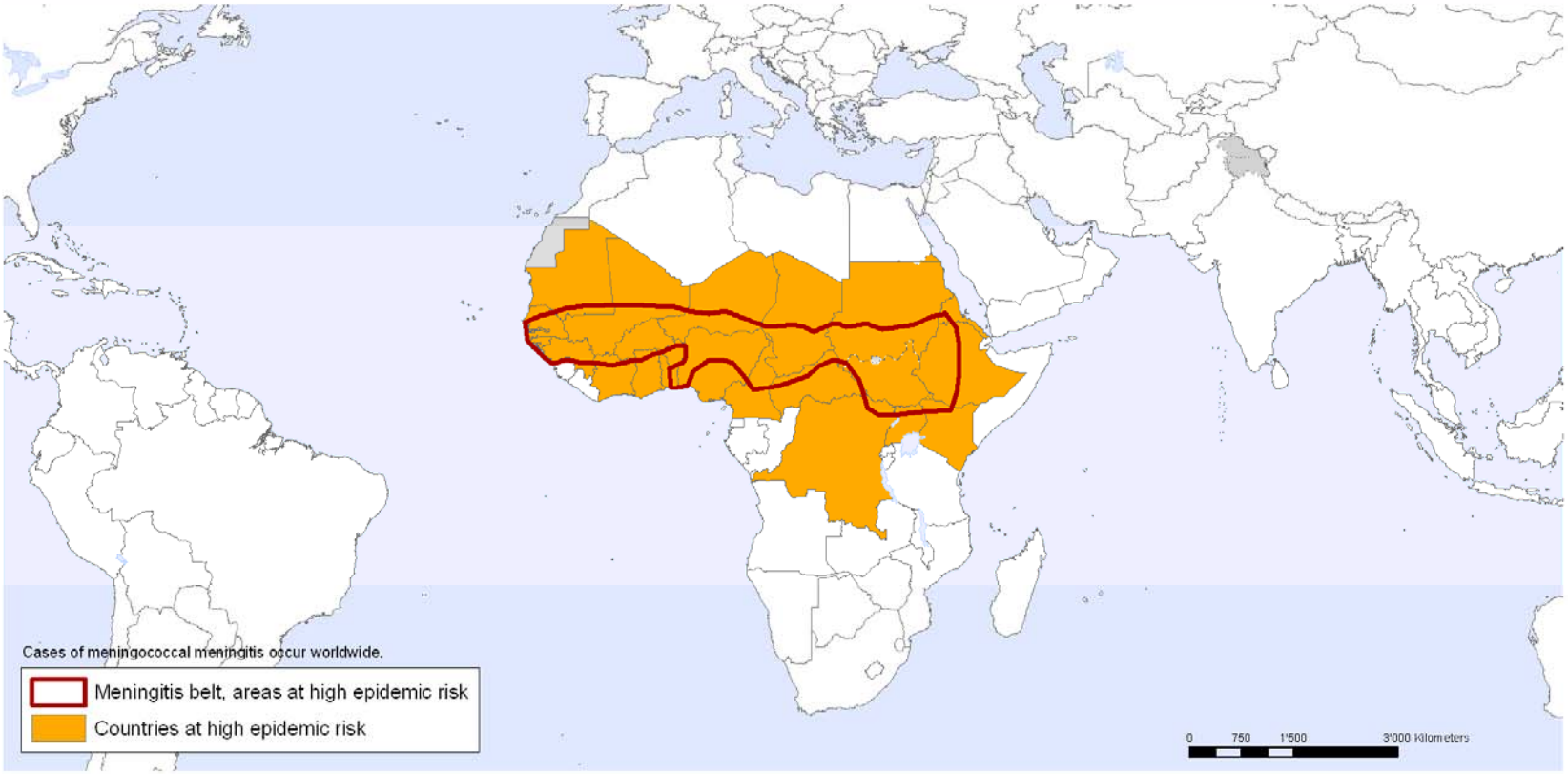
Adverse events and precautions – conjugated vaccines

All meningococcal conjugate vaccines have an excellent safety record. None has been associated with any serious adverse effects during clinical trials or in post-marketing surveillance. Redness, swelling and pain at the site of injection may occur, however. Such reactions usually start within the first day after immunization and last 1–3 days. Less commonly, children may develop a fever or be irritable for a short period.

Travellers should be aware that protection induced by meningococcal vaccines is strictly serotype-specific and that tetravalent vaccine offers the widest range of protection. However, tetravalent meningococcal vaccines do not protect against meningococci of serogroups B and X which are common causes of meningococcal disease in some countries.

Required vaccinations: Saudi Arabia demands proof of recent meningococcal vaccination (tetravalent vaccine) as a visa requirement for pilgrims and guest workers. See 6.4 “Required vaccinations”.

Meningococcal meningitis, countries or areas at high risk, 2011



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MUMPS	
Cause	Mumps virus, genus *Rubulavirus*, 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, in whom complications such as meningitis and orchitis are relatively more common. Encephalitis and permanent neurological sequelae are rare complications.
Geographical distribution	Except in countries with high coverage of mumps-containing vaccines, the annual mumps incidence in most parts of the world is in the range 100–1000 per 100 000 population, with epidemic peaks every 2–5 years.
Risk for travellers	Travellers who are not fully immunized against mumps are at risk.
Vaccine	The mumps vaccine is usually given in combination with measles and rubella vaccine (MMR). The attenuated strains of mumps virus that are currently used for the production of live mumps vaccines are all considered to be safe and efficacious. 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. A single dose of mumps vaccine, either as single antigen or in combination, has a protective efficacy of 90–96%.The second dose provides protection to most individuals who did not respond to the first and should be given after a minimum interval of 1 month. In some countries the second dose is given at the age of 4–6 years.

PNEUMOCOCCAL DISEASE	
Cause	Many serotypes of the bacterium *Streptococcus pneumoniae*.
Transmission	Infection is acquired mainly through pneumococci contained in respiratory droplets. There are many healthy, asymptomatic carriers of the bacteria but 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	Pneumococcal infection 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 included the deaths of

	0.7–1 million children aged under 5 years. Most of these deaths occurred in poor countries and included a disproportionate number of children under the age of 2 years. In Europe and the USA, *S. pneumoniae* 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.
Risk for travellers	While travel itself does not normally increase the risk of acquiring pneumococcal disease, access to optimal health care may be limited during travel, increasing the risk of a poor outcome should disease occur. Thus, before travel to countries with limited medical resources is undertaken, vaccination against invasive pneumococcal disease is advisable for children <2 years of age and for children and adults considered to be at particular risk of serious disease. Conditions predisposing to complications of pneumococcal infections include sickle-cell disease and other haemoglobinopathies, chronic renal failure, chronic liver disease, immunosuppression after organ transplantation, 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.
Vaccines	*Conjugate vaccines* Conjugate vaccines that contain 10 (PCV-10), or 13 (PCV-13) pneumococcal serotypes are currently available. A pneumococcal conjugate vaccine containing 7 serotypes (PCV-7) is gradually being removed from the market. **Indication and administration** Although the exact labelling details may differ by country, both PCV10 and PCV13 are licensed for immunization of infants and children from 6 weeks to 5 years of age against invasive disease, pneumonia and acute otitis media caused by the respective vaccine serotypes of *S. pneumoniae*. In addition, PCV13 is licensed for the prevention of pneumococcal disease in adults >50 years of age. For PCV administration to infants, WHO recommends three primary doses (given at 6, 10 and 14 weeks or 2, 4 and 6 months) or two primary doses plus a booster (given between the age of 9 and 15 months). The favourable safety and reactogenicity profiles of pneumococcal conjugate vaccines are well established, and compatibility with major childhood vaccines has been demonstrated. *Polysaccharide vaccine* The 23-valent polysaccharide vaccine (PPV23) represents pneumococcal serotypes that are responsible for 85–90% of invasive pneumococcal infections in USA and some other industrialized countries. The vaccine is efficacious against invasive pneumococcal disease and pneumonia in healthy young adults but shows limited efficacy in this regard in other age groups. PPV23 is licensed only for individuals aged >2 years. The vaccine is commonly recommended for children and adults who have certain underlying medical conditions predisposing for pneumococcal infection, although its efficacy in several of these conditions is not well documented. In

some countries, such as USA, routine vaccination is recommended for everyone over 65 years of age.

For primary immunization, PPV23 is administered as a single intramuscular dose (preferably in the deltoid muscle) or as a subcutaneous dose. The optimal timing, frequency and clinical effectiveness of additional doses of PPV23 are poorly defined, and national recommendations regarding revaccination vary. However, on the basis of data on the duration of vaccine-induced protection, WHO suggests one single revaccination >5 years after a first vaccination. In resource-limited settings where there are many competing health priorities, evidence does not support routine immunization of elderly people and high-risk populations with PPV23. Local adverse reactions may be more frequent in recipients of a second dose of PPV23 but are generally self-limiting and not severe.

POLIOMYELITIS (POLIO)

Cause	Poliovirus types 1, 2 and 3 (three closely related enteroviruses).
Transmission	Polio viruses are spread predominantly by the faecal–oral route. In settings with high standards of hygiene, the oral–oral route of transmission may also be common.
Nature of the disease	Poliomyelitis, also known as polio or infantile paralysis, is a disease of the central nervous system. Following primary asymptomatic infection of the alimentary tract, fewer than 1% develop paralytic disease. In developing countries, 65–75% of cases occur in children under 3 years of age and 95% in children under 5 years of age. The resulting paralysis is permanent, although some recovery of function is possible. There is no cure.
Geographical distribution	Significant progress has been made towards global eradication of polio. As of March 2014, wild poliovirus remains endemic in three countries – Afghanistan, Nigeria and Pakistan. . In 2013, outbreaks following importation of wild poliovirus from endemic countries occurred in the Horn of Africa (Somalia, Ethiopia, Kenya), Syria and Cameroun. Evidence of wild poliovirus transmission was also documented in Israel Polio cases due to circulating vaccine-derived poliovirus (cVDPV) were reported in 2013 from Nigeria, Niger, Chad, Cameroun, Pakistan, Afghanistan, Somalia and Yemen.
Risk for travellers	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 countries and areas infected by wild or circulating vaccine-derived poliovirus should be adequately vaccinated. Updates on countries which are considered to be polio infected currently can be found at www.polioeradication.org/casecount.asp.
Vaccines	Both orally administered, live attenuated polio vaccines (OPV) and inactivated polio vaccines (IPV) for intramuscular (or subcutaneous) injection are widely used internationally. OPV has been the vaccine of choice for controlling poliomyelitis in many countries, and for the

global polio eradication initiative, because of the ease of oral administration, its superiority in conferring intestinal immunity in immunologically naive individuals, and its low cost. The only very rare adverse event associated with OPV use is vaccine-associated paralytic poliomyelitis (VAPP), which may occur in vaccine recipients or their contacts. The overall risk of VAPP is estimated at 1 case per 2.4 million doses administered. Outbreaks of polio due to circulating vaccine-derived polioviruses continue to be detected occasionally, mainly in areas of low immunization coverage . As long as transmission of wild poliovirus has not been interrupted globally, WHO recommends that OPV should remain the vaccine of choice for routine infant immunization in most countries. However, WHO also recommends that all countries currently using only OPV add at least 1 dose of IPV to the schedule. In polio-endemic countries and in countries at high risk for importation and subsequent spread, WHO also recommends an OPV dose at birth (also called 'zero dose'), followed by the primary series of 3 OPV doses and at least 1 IPV dose.

The primary series consisting of 3 OPV doses plus 1 IPV dose can be initiated from the age of 6 weeks with a minimum interval of 4 weeks between the OPV doses. If only 1 dose of IPV is used in the schedule, it should be given from 14 weeks of age (when maternal antibodies have diminished and immunogenicity is significantly higher) and can be co-administered with an OPV dose. Countries may have alternative schedules based on local epidemiology, including the documented risk of VAPP prior to 4 months of age.

Routine vaccination with IPV alone should be used only in countries with high immunization coverage (> 90%) and at low risk of wild poliovirus importation and spread. A primary series of three IPV doses should be administered, beginning at 2 months of age. If the primary series begins earlier (e.g. with a 6-, 10- and 14-week schedule), a booster dose should be administered after an interval of at least 6 months (four- dose IPV schedule). Some such countries may use a sequential schedule of IPV followed by OPV.

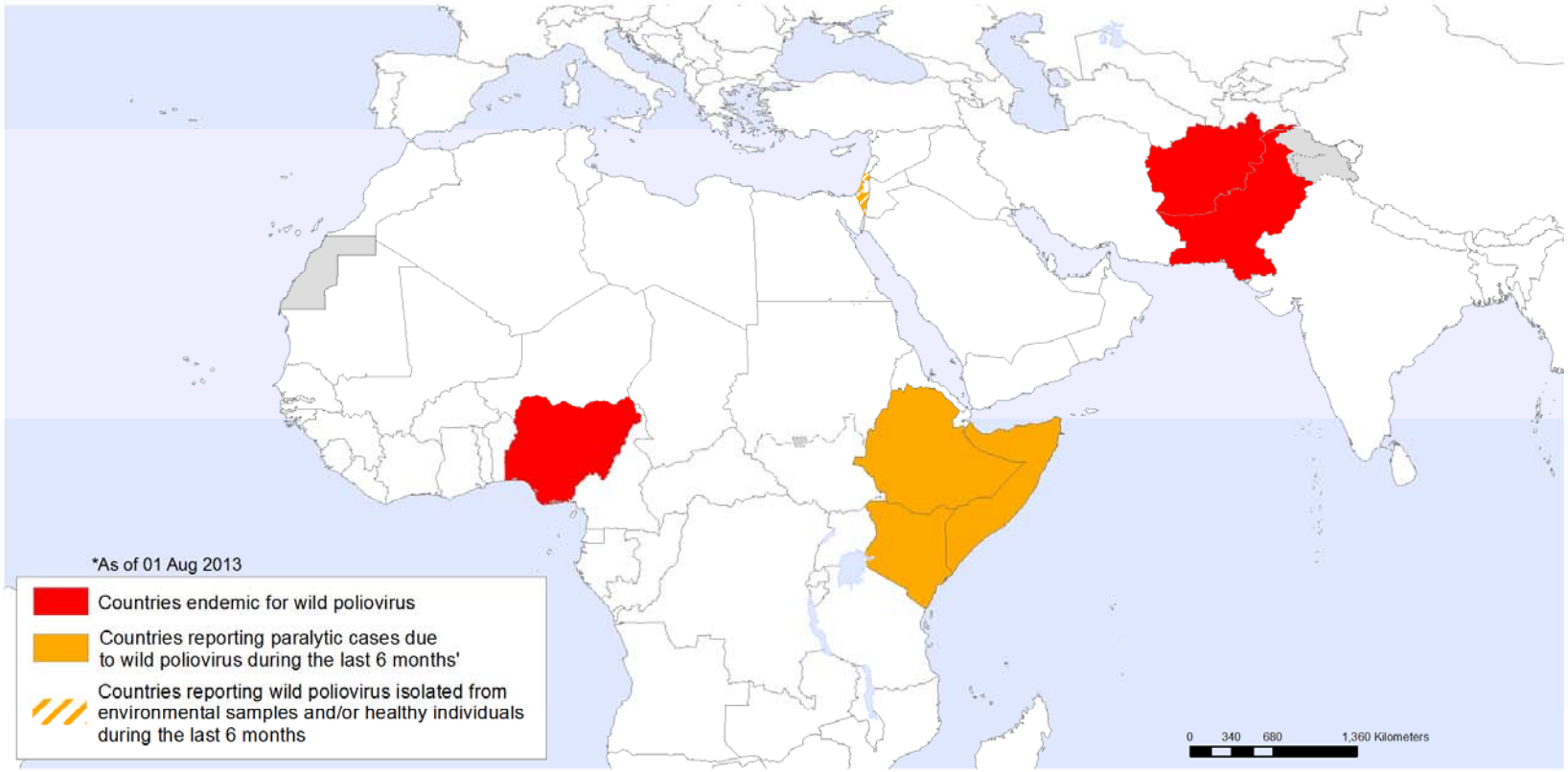
Before travelling to areas with active poliovirus transmission, travellers from polio-free countries should ensure that they have completed the age-appropriate polio vaccine series, according to their respective national immunization schedule. Adult travellers to polio-infected areas who have previously received three or more doses of OPV or IPV should also be given another one-time booster dose of polio vaccine. Travellers to polio-infected areas who have not received any polio vaccine previously should complete a primary schedule of polio vaccination before departure.

Before travelling abroad, persons of all ages residing in polio-infected countries (i.e. those with active transmission of a wild or vaccine-derived poliovirus) and long term visitors to such countries (i.e. persons who spend more than 4 weeks in the country), should have completed a full course of vaccination against polio in compliance with the national schedule. Travellers from infected areas should receive an additional dose of OPV or IPV within 4 weeks to 12 months of travel, in order to boost intestinal mucosal immunity and reduce the risk of poliovirus shedding, which could lead to re-

introduction of poliovirus into a polio-free area. For persons who previously received only IPV, OPV should be the choice for the booster dose, if available and feasible. In case of unavoidable last – minute travel, travellers should still receive one dose of OPV or IPV prior to departure, if they have not received documented dose of polio vaccine within the previous 12 months. Some polio-free countries may require such travellers from polio-infected countries to provide documentation of recent vaccination against polio in order to obtain an entry visa, or they may require that travellers receive an additional dose of polio vaccine on arrival, or both.

All travellers are advised to carry their written vaccination record (patient-retained record) in the event that evidence of polio vaccination is requested for entry into countries being visited. Preferably travellers would use the IHR 2005 International Certificate of Vaccination or Prophylaxis. The certificate is available from the WHO web site at http://www.who.int/ihr/IVC200_06_26.pdf.

Polio infected countries for which WHO recommends Polio immunization or boosting to travellers*



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Data Source: World Health Organization
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

World Health Organization

RABIES

Cause	Lyssavirus of the family Rhabdoviridae.
Transmission	Rabies is a zoonotic disease affecting a wide range of domestic and wild mammals, including bats. The virus is present primarily in the saliva, and infection of humans usually occurs through the bite of an infected animal, usually a dog, which may not show signs of rabies. Transmission may occasionally occur also through other contact with a rabid animal, for example following a penetrating scratch with bleeding, or through licking of broken skin and mucosa. Laboratory-confirmed person-to-person transmission other than via organ transplant has not been reported.
Nature of the disease	Rabies is 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 abnormal fear of drafts of air (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 paralysis and loss of sensation, weakness and pain.
Geographical distribution	Rabies is present in mammals in most parts of the world (see map). Most of the estimated 55 000 human rabies deaths per year occur in Africa and Asia. More information on rabies is available at http://www.who.int/rabies/rabnet/en.
Risk for travellers	The risk to travellers in areas where rabies occurs (see map, or http://www.who.int/rabies/rabnet/en) is proportional to the probability of contact with potentially rabid mammals. In most developing countries, the estimated ratio of dogs, both owned and ownerless, to humans is 1:10 and an average 100 suspected rabid dog bites per 100 000 inhabitants are reported annually. As rabies is a lethal disease, medical advice should be sought immediately at a competent medical centre – ideally, the rabies treatment centre of a major city hospital. First-aid measures should also be started immediately (see "Post-exposure prophylaxis", below). Travellers should avoid contact with free-roaming animals, especially dogs and cats, and with wild, free-ranging or captive animals. For travellers who participate in caving or spelunking, casual exposure to cave air is not a concern, but cavers should be warned not to handle bats. In most countries of the world, suspect contact with bats should be followed by post-exposure prophylaxis. The map shows the WHO categories of risk, from no-risk (rabies-free) countries or areas to countries or areas of low, medium and high risk (dog rabies). Categorization is based primarily on the animal host species in which the rabies virus is maintained, e.g. bats and/or other wildlife and/or dogs, and on the availability of reliable laboratory-based surveillance data from 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 (see below), pre-exposure

immunization against rabies is recommended for travellers with certain characteristics:

Category 1: no risk.

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

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

Category 4: high risk.
In these countries, travellers spending a lot of time in rural areas and involved in activities such as running, bicycling, camping or hiking should receive pre-exposure prophylaxis. Prophylaxis 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 the development of clinical rabies 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. 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 countries or areas at risk. 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 countries or areas at risk, where they provide an easy target for rabid animals. Pre-exposure vaccination is also recommended for individuals travelling to isolated areas or to areas where immediate access to appropriate medical care is limited or to countries where modern rabies vaccines are in short supply and locally available rabies vaccines might be unsafe and/or ineffective.

Pre-exposure rabies vaccination consists of three full intramuscular (i.m.) doses of cell-culture- or embryonated-egg-based 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 1 year 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 (i.d.) 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. 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.

Periodic booster injections are 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, individuals 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 patients who have previously received a complete vaccination series.

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 intramuscular or 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 or 0.5 ml/dose depending on the vaccine) or i.d. (0.1 ml/inoculation site)[a]
Boosters:	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 country or area at risk, especially if the area to be visited is far from major urban centres and appropriate care, including the availability of post-exposure rabies prophylaxis, cannot be 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, individuals 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.

Post-exposure prophylaxis

In countries or areas at risk of rabies, 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 of 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

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

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

[d]Post-exposure prophylaxis should be considered for individuals who have been in close contact with bats, particularly following bites or scratches or exposure to mucous membranes.

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 should be used for category III exposures as well as for some category II exposures (see table above). Passive immunization should be administered just before or shortly after 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 correct dose of rabies immunoglobulin is too small to infiltrate all wounds, as might be true of a severely bitten individual, it can be diluted in physiological buffered saline to ensure greater wound coverage.

3. Active immunization

Cell-culture- or embryonated-egg-based rabies vaccines should always be used for post-exposure prophylaxis. They can be administered either i.m. or i.d.

Intramuscular regimens: Both a five-dose and a four-dose i.m. regimen are recommended for post-exposure vaccination; the five-dose regimen is the more commonly used:

- The five-dose regimen is administered on days 0, 3, 7, 14 and 28 into the deltoid muscle.
- The four-dose regimen is administered as two doses on day 0 (one dose in the right and one in the left arm (deltoid muscles), and then one dose on each of days 7 and 21 into the deltoid muscle.

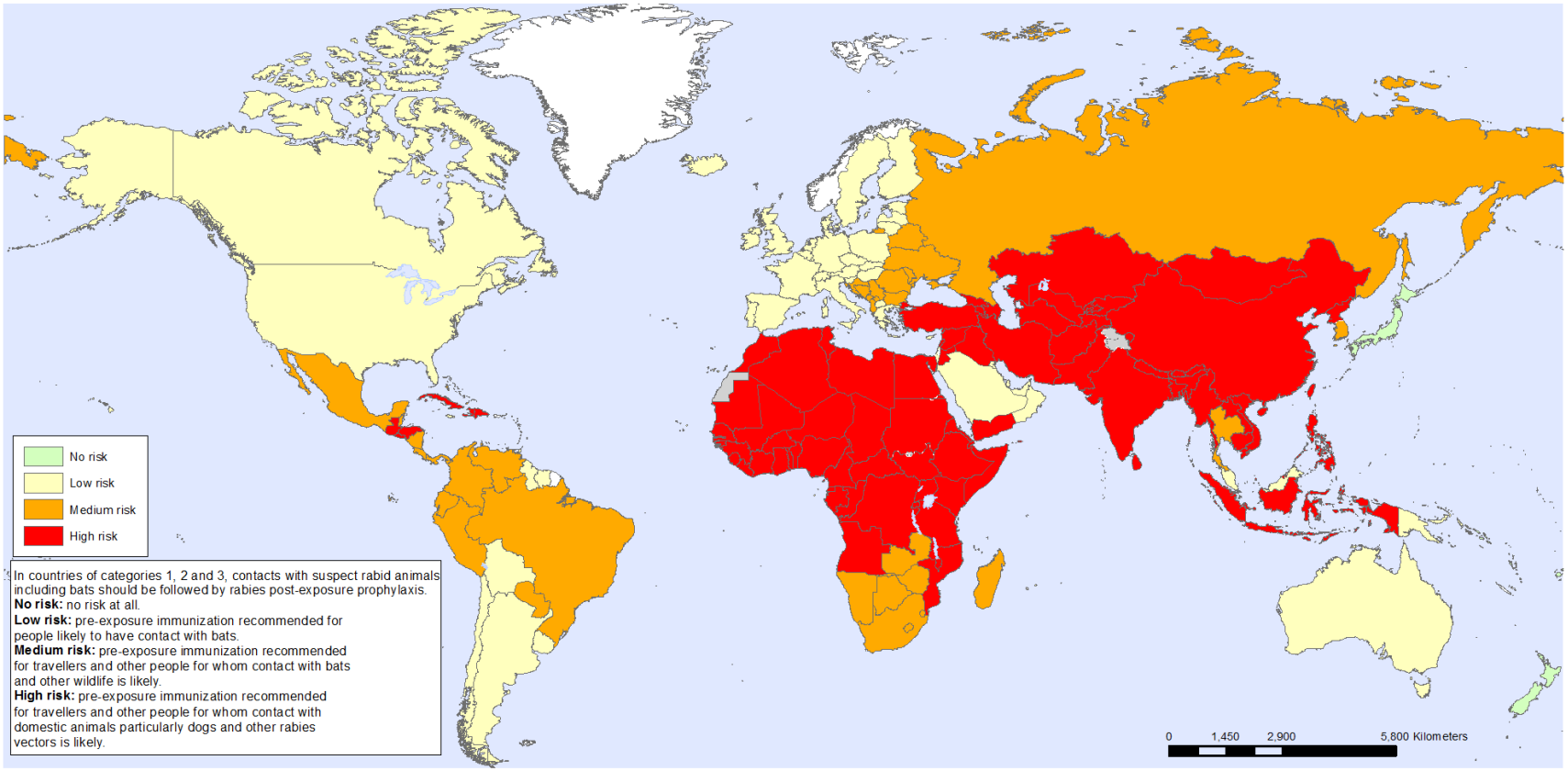
An alternative post-exposure regimen for healthy, fully immuno-competent exposed people who receive wound care plus high-quality rabies immunoglobulin plus WHO-prequalified rabies vaccines consists of four doses administered i.m. on days 0, 3, 7 and 14.

Intradermal regimens: Intradermal administration of cell-culture- and embryonated-egg-based rabies vaccines has been successfully used in many developing countries that cannot afford the five- or four-dose i.m. schedules.

- The two-site i.d. method: one i.d. injection at two sites on days 0, 3, 7 and 28.

The volume per intradermal injection should be 0.1 ml with both purified Vero cell rabies vaccine, and purified chick embryo rabies vaccine.

Rabies, countries or areas at risk



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Data Source: WHO Control of Neglected Tropical Diseases (NTD)
Map Production: Health Statistics and Information Systems (HSI)
World Health Organization

World Health Organization

ROTAVIRUS	
Cause	Viruses belonging 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 requiring rehydration therapy can occur, especially in very young infants. The virus replicates in the enterocytes of the small intestine, causing extensive damage to the microvilli and resulting 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: outpatient visits are estimated at more than 25 million and hospitalizations attributable to rotavirus infections at more than 2 million each year. WHO estimates that in 2008 453 000 (420 000 – 494 000) child deaths occurred due to rotavirus gastroenteritis worldwide. Fatal outcomes occur predominantly in low-income countries. In temperate climates, the incidence of rotavirus gastroenteritis typically peaks during the winter season, whereas in tropical settings this type of gastroenteritis occurs year round. Reinfection of older children and adults is common, although reinfections are usually sub-clinical.
Risk for travellers	The risk for adult travellers is negligible since most individuals will have good immunity through repeated exposures early in life. Children under the age of 5 years are at risk.
Vaccines	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 countries at high risk of severe disease and fatal outcomes. Rotarix vaccine should be administered orally in a two-dose schedule at the time of the first and second doses of DTP and with an interval of 4 weeks between the doses. RotaTeq requires an oral three-dose schedule administered with DTP1, DTP2, and DTP3 and with an interval of 4–10 weeks between doses. WHO recommends that the first dose of rotavirus vaccine be administered as soon as possible after 6 weeks of age, along with diphtheria–tetanus–pertussis (DTP) vaccination. Because most severe cases of rotavirus gastroenteritis occur earlier in life, vaccination of children older than 24 months is not encouraged.
Vaccine safety	Post-marketing surveillance of both currently available rotavirus vaccines has detected a small increased risk of intussusception (about 1–2/100 000 infants vaccinated) in some settings shortly after administration of the first dose. This risk is 5–10 times lower than

	that observed with the previously licensed vaccine, and the benefits of rotavirus vaccination against severe diarrhoea and death from rotavirus infection far exceed the risk of intussusception.

RUBELLA

Cause	Rubella virus, a togavirus of the genus *Rubivirus*.
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 reported rarely. 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 the 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 China and Japan. Rubella vaccine is commercially available in a monovalent form, in a bivalent combination with measles vaccine, as the trivalent measles/mumps/rubella (MMR) vaccine and in a few countries, also in a tetrarivalent measles/mumps/rubella/varicella (MMRV) combination. Rubella-containing vaccines are usually administrated at 12–15 months of age but may be offered to children as young as 9 months. In principle, rubella vaccination of pregnant women should be avoided, and pregnancy should be avoided within 1 month of receiving the vaccine due to the theoretical, but never demonstrated, risk of vaccine-induced CRS.

TICK-BORNE ENCEPHALITIS

Cause	Tick-borne encephalitis virus (TBEV) of the family Flaviviridae. Three subtypes of the causative agent are known: the European (Western), the Far Eastern (spring-and-summer encephalitis) and the Siberian.
Transmission	TBEV is transmitted by the bite of infected ticks (which often remain firmly attached to the skin for days) or occasionally by ingestion of unpasteurized milk. There is no direct person-to-person transmission.
Nature of the disease	Infection may induce an influenza-like illness followed, in about 30% of cases, by high fever and signs of central nervous involvement. Encephalitis developing during this second phase may result in paralysis, permanent sequelae or death. Severity of illness increases with age of the patient.
Geographical distribution	Tick-borne encephalitis (TBE) tends to occur focally even within endemic areas. Currently, the highest incidences of clinical cases are being reported from foci in the Baltic States, the Russian Federation and Slovenia. High incidencesare also reported from foci in the North-Western Federal Area of the Russian Federation. Other countries that have reported cases within their territories, or that are considered to be at risk because of focally high prevalence of the virus in ticks, include Albania, Austria, Belarus, Bosnia, Bulgaria, China, Croatia, Denmark, Finland, Germany, Greece, Hungary, Italy, Mongolia, Norway, Poland, the Republic of Korea, Romania, Serbia, Slovakia, Slovenia, Sweden, Switzerland, Turkey and Ukraine.
Risk for travellers	Travellers to endemic areas may be at risk during April to November. The risk is highest when hiking or camping in forested areas up to an altitude of about 1500 m.
Precautions	Prevent blood-feeding ticks from becoming attached to the skin by wearing appropriate clothing, including long trousers and closed footwear, when hiking or camping in countries or areas at risk. The whole body should be inspected daily and attached ticks removed as soon as possible. The consumption of unpasteurized dairy products should also be avoided in those areas.
Vaccine	The vaccine should be offered only to at-risk travellers. *Western European vaccines:* In western Europe, two vaccines are available in both adult and paediatric formulations. Although these vaccines are based on the European subtype, immunity is induced against all subtypes of the TBE virus. The vaccines contain a suspension of purified TBEV grown on chick embryo cells and are inactivated with formaldehyde. Both TBE vaccines provide safe and reliable protection. Little information is available on the duration of protection following completion of the primary three-dose immunization. Outside countries or areas at risk, TBE vaccines may not be licensed and will have to be obtained by special request. *Russian vaccines:*

The two inactivated TBE vaccines manufactured in the Russian Federation are based on the Far Eastern subtype of the virus and propagated in primary chicken embryo cells. These vaccines are considered efficacious for individuals aged ≥3 years although supporting data are more limited for the Russian products.

Adverse reactions

With the western European vaccines, adverse events are commonly reported, including transient redness and pain at the site of injection in ≤45% of cases and fever ≥38 °C in ≤5–6%. However, none of these events is life-threatening or serious.

Both the Russian vaccines have been reported to be moderately reactogenic but without inducing severe adverse reactions. (However, some lots of the Russian vaccine Encevir were recently withdrawn because of frequent high fever and allergic reactions, particularly in children; this vaccine is currently not recommended for individuals 3–17 years of age.)

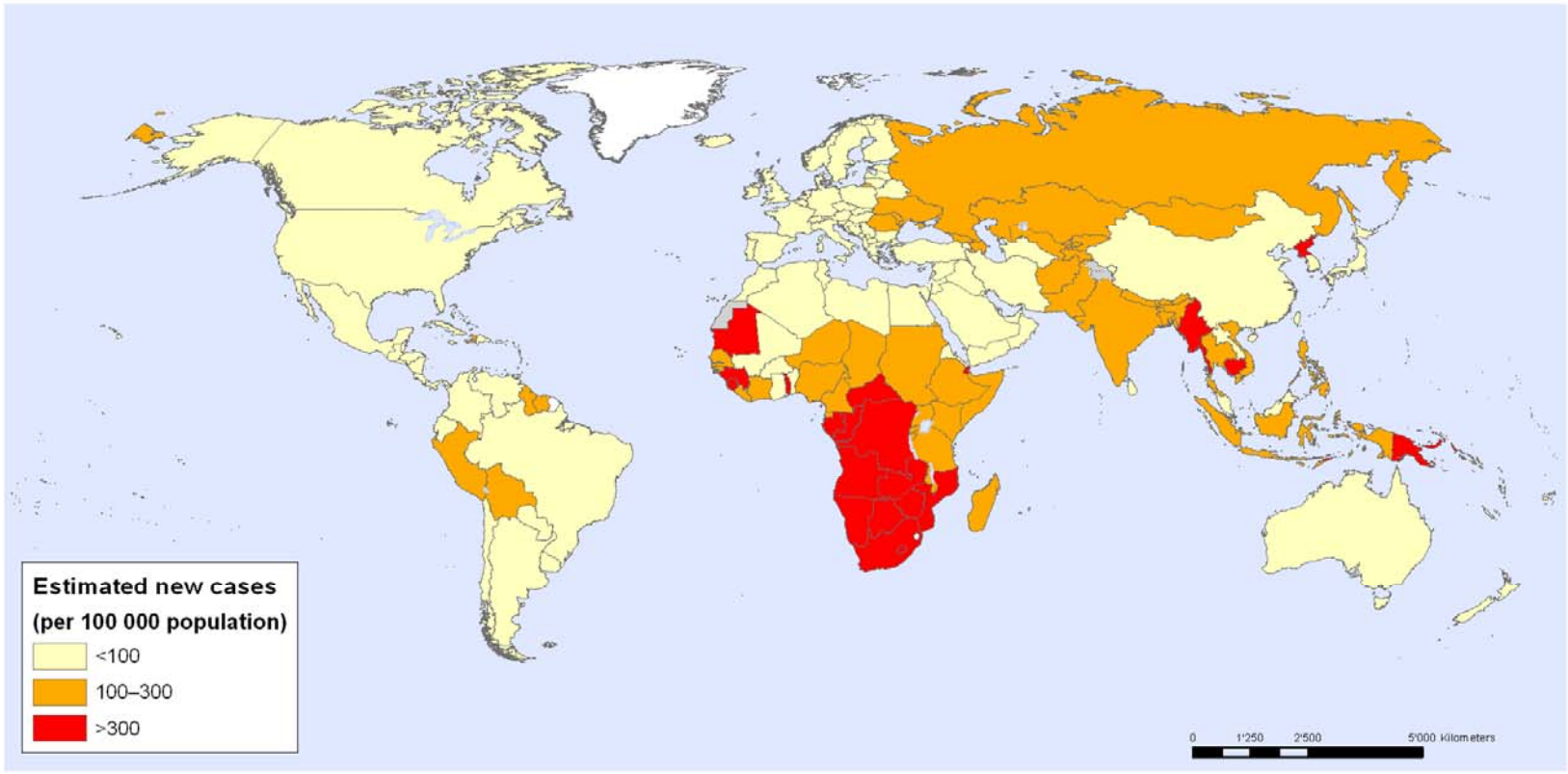
Type of vaccine:	Killed
Number of doses:	*Western European vaccines*: primary series, three i.m. doses, administered at intervals of 4–12 weeks between the first and second, and 9–12 months between the second and third doses. *Russian vaccines*: primary series, three doses administered at intervals of 1–7 months between the first and second, and 12 months between the second and third doses.
Boosters:	*Western European vaccines*: In healthy individuals aged <50 years booster doses are conventionally offered at intervals of 3–5 years if the risk continues, although in some endemic areas (Switzerland) intervals of ≤10 years are now used. In individuals aged 50 years and above, booster intervals of 3–5 years are recommended until more definitive information becomes available. Accelerated schedules for travellers: depending on the choice of TBE vaccine, the manufacturer recommends either a rapid schedule based on immunization on day 0, day 14 and month 5–7, or an accelerated schedule based on immunization on day 0, day 7 and day 21. *Russian vaccines:* Booster doses are recommended every 3 years for those at continued risk of exposure.
Contraindications:	Hypersensitivity to any vaccine component; adverse reaction to previous dose
Before departure:	Second dose 2 weeks before departure
Recommended for:	High-risk individuals only
Special precautions:	Prevent blood-feeding ticks from becoming attached to the skin through use of appropriate clothing; remove ticks as soon as possible

TUBERCULOSIS (TB)

Cause	The tubercle bacillus *Mycobacterium tuberculosis*.
Transmission	In most cases, infection is transmitted by inhalation of *M. tuberculosis*-containing microscopic droplets originating from cases of active pulmonary tuberculosis
Nature of the disease	Exposure to *M. tuberculosis* 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). Multidrug resistant tuberculosis (MDR-TB) refers to strains of *M. tuberculosis* that are resistant to at least isoniazid and rifampicin. The resistant strains do not differ from other strains in infectiousness, likelihood of causing disease, or general clinical effects; if they do cause disease, however, 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.
Geographical distribution	Worldwide. The risk of infection differs between countries, as shown on the map of estimated tuberculosis 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. Individuals 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 they are not infectious and are therefore of no risk to others. The importance of completing the prescribed course of treatment should be stressed.

Vaccine	All versions of the BCG vaccine are based on live, attenuated mycobacterial strains descended from the original, attenuated bacillus Calmette–Guérin. The vaccine is administered intradermally and can be given simultaneously with other childhood vaccines. BCG vaccine is contraindicated for individuals with severely impaired immunity and individuals with HIV infection. BCG vaccine is of very limited use for travellers. In the first year of life it provides good protection against severe forms of TB (miliary TB and meningitis). In countries with high TB prevalence, infants are generally immunized with a single dose of BCG as soon after birth as possible. Children who are known to be HIV-infected, even if asymptomatic, should not be immunized with BCG vaccine. Other protective benefits of the vaccine are uncertain. One dose of BCG should be considered for unvaccinated infants travelling from an area of low incidence to one of high incidence. Many industrialized countries with a low incidence of TB have ceased giving BCG routinely to neonates. Booster doses of BCG are not recommended by WHO

Tuberculosis, estimated new cases, 2010



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Data Source: World Health Organization
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

World Health Organization

TYPHOID FEVER

Cause	The typhoid bacillus *Salmonella typhi*, which infects humans only. Paratyphoid and enteric fevers are caused by other species of *Salmonella*, which infect domestic animals as well as humans.
Transmission	The typhoid bacillus is transmitted by consumption of contaminated food or water. Occasionally, direct faecal–oral transmission may occur. Shellfish taken from sewage-polluted areas are an important source of infection; transmission also occurs through eating raw fruit and vegetables fertilized by human excreta and through ingestion of contaminated milk and milk products. Flies may cause human infection through transfer of the infectious agents to foods. 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	Typhoid fever is 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 treatment, some patients develop sustained fever, bradycardia, hepatosplenomegaly, abdominal symptoms and, occasionally, pneumonia. In white-skinned patients, pink spots, which fade on pressure, appear on the skin of the trunk in up to 20% of cases. In the third week, untreated cases may develop gastrointestinal and cerebral complications, which may prove fatal in up to 10–20% of cases. The highest case–fatality rates are reported in children <4 years of age. Around 2–5% of those who contract typhoid fever become chronic carriers, as bacteria persist in the biliary tract after symptoms have resolved.
Geographical distribution	There is a higher risk of typhoid fever in countries or areas with low standards of hygiene and water supply facilities.
Risk for travellers	The risk for travellers is generally low, 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. Even vaccinated travellers should take care to avoid consumption of potentially contaminated food and water as the vaccine does not confer 100% protection.
General precautions	For general precautions against exposure to foodborne and waterborne infections, see Chapter 3.
Vaccine	Currently, two typhoid vaccines of demonstrated safety and efficacy are available on the international market: 1) The oral vaccine based on the live, attenuated mutant strain *of S. typhi* Ty21a (Ty21a vaccine), is supplied in enteric coated capsules. In Australia and Europe, three tablets are given on days 1, 3, and 5; this series is repeated every year for individuals travelling from non-endemic to endemic countries, and every 3 years for individuals living in countries or areas at risk. In North America, four 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 risk in the country or area of residence.

	The duration of protection following Ty21a immunization is not well defined and may vary with vaccine dose and possibly with subsequent exposures to *S. typhi* (natural booster). 2) The injectable Vi capsular polysaccharide vaccine (ViCPS vaccine) is given intramuscularly in a single dose. Protection is induced about 7 days after the injection. In countries or areas at risk, the protective efficacy 1.5 years after vaccination is about 72%; after 3 years it is about 50%. The vaccine is licensed for individuals aged >2 years. To maintain protection, revaccination is recommended every 3 years. A combined typhoid/hepatitis A vaccine is also available in some countries. **Contraindications and precautions** Both typhoid vaccines are safe and there are no contraindications to their use other than previous severe hypersensitivity reactions to vaccine components. Proguanil, mefloquine and antibiotics should be stopped from 3 days before until 3 days after the administration of Ty21a. These vaccines are not recommended for use in infant immunization programmes due to insufficient information on their efficacy in children under 2 years of age.
Recommended for:	Typhoid fever vaccination may be offered to those travelling to destinations where the risk of typhoid fever is high, especially individuals staying in endemic areas for >1 month and/or in locations where antibiotic-resistant strains of *S. typhi* are prevalent.

VARICELLA

Cause	The varicella zoster virus (VZV), a herpesvirus belonging to the sub-family of Alphaherpesviridae.
Transmission	Transmission is via droplets, aerosol or direct contact, or indirectly by touching freshly soiled contaminated items. Patients are usually contagious from a few days before onset of the rash until the rash has crusted over.
Nature of the disease	Varicella 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 individuals. 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 individuals and elderly people.
Geographical distribution	Worldwide.

Risk for travellers	Most adult travellers from temperate climates are immune to varicella as a result of natural childhood disease or vaccination, whereas non-vaccinated young individuals from areas of low varicella endemicity may be at risk of infection when travelling to countries of high endemicity. Immunocompromised individuals are at particular risk of severe disease.
Vaccine	Various formulations of the live attenuated vaccine, based on the so-called Oka strain of VZV, are in use, both as single antigen and in combination (MMRV). From both a logistic and an epidemiological point of view, the optimal age for varicella vaccination is 12–24 months. In some countries, one dose of the vaccine is considered sufficient, regardless of age. In the United States, two 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.

YELLOW FEVER

Cause	Yellow fever virus (YFV), an arbovirus of the Flavivirus genus.
Transmission	Yellow fever occurs in urban and rural areas of Africa and central South America. In jungle and forest areas, monkeys are the main reservoir of infection, which is spread by mosquitoes from monkey to monkey and, occasionally, to humans. In urban settings mosquitoes transmit the virus from human to human, and 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 where mosquitoes infect both monkeys and humans, causing localized outbreaks.
Nature of the disease	Although most infections are asymptomatic, 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; up to half of these patients die 10–14 days after the onset of illness.
Geographical distribution	In tropical areas of Africa and Central and South America (see maps) YFV transmission can occur at altitudes up to 2300 metres (in Africa, possibly higher). Countries or areas where the YFV 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, or because of poor surveillance. A revision of the risk classification of countries and areas recommended for yellow fever vaccination is reflected in this year's edition of *International travel and health* (Country list and Annex 1).
Risk for travellers	Apart from areas of high yellow fever endemicity, YFV transmission may take place also in areas of low endemicity if the traveller's

	itinerary implies heavy exposure to mosquitoes, for example during prolonged travel in rural areas.
General precautions	Avoid mosquito bites; the highest risk for YFV transmission is during the day and early evening (Chapter 3).
Vaccine	The 17D vaccine, which is based on a live, attenuated viral strain, is the only commercially available yellow fever vaccine. It is given as a single subcutaneous (or intramuscular) injection. Yellow fever vaccine is highly effective (approaching 100%). All individuals aged 9 months or older and living in countries or areas at risk should receive yellow fever vaccine.

Precautions and contraindications

With the exception of very rare cases of vaccine-associated neurotropic and viscerotropic disease (see below), the 17D vaccine is generally considered to be safe. Contraindications include severe hypersensitivity to egg antigens and severe immunodeficiency. Conditions and treatments considered to be severely immuno-compromising include: primary immunodeficiencies, thymus disorder, symptomatic HIV infection or CD4 T-cell values <200 per mm^3, malignant neoplasm treated with chemotherapy, recent haematopoietic stem cell transplantation, drugs with known immunosuppressive or immunomodulatory properties (e.g. high-dose systemic corticosteroids, alkylating drugs, antimetabolites, TNF-α inhibitors, IL-1 blocking agent, or other monoclonal antibodies targeting immune cells), and current or recent radiation therapies targeting immune cells.

Noting that yellow fever vaccine is a live vaccine, a risk–benefit assessment should be undertaken for all pregnant and lactating women. In areas where YF is endemic, or during outbreaks, the benefits of YF vaccination are likely to far outweigh the risk of potential transmission of vaccine virus to the fetus or infant. Pregnant women and nursing mothers should be counselled on the potential benefits and risks of vaccination so that they may make an informed decision about vaccination. Lactating women should be advised that the benefits of breastfeeding far outweigh alternatives. Vaccination is recommended, if indicated, for pregnant or breastfeeding women travelling to endemic areas when such travel cannot be avoided or postponed.

The YF vaccine is contraindicated in infants under 6 months of age and is not recommended for those aged 6–8 months, except during epidemics when the risk of YFV transmission may be very high.

Viscerotropic disease: Vaccine-associated viscerotropic disease is a recently described adverse event that on very rare occasions has occurred after the first immunization with the yellow fever 17D vaccine. Onset is within 10 days of vaccination and the pathological process is characterized by severe multi-organ failure and an overall case–fatality rate in excess of 60%. Known risk factors include a history of thymus disease (e.g. thymoma or thymectomy) and age ≥60 years. In the USA the risk of contracting viscerotropic disease after YF vaccination for persons over 70 years of age is estimated to be 2.4 cases/100 000 vaccine doses.

Neurotropic disease: Increased incidence of vaccine-associated neurotropic disease (e.g. meningoencephalitis, acute disseminated encephalomyelitis and Guillain–Barré syndrome) has been reported in infants under 6 months of age and in vaccine recipients aged 60 years and older. The reported rate of vaccine-associated neurotropic disease in travellers from the United States and Europe ranges between 0.13 and 0.8 per 100 000 doses.

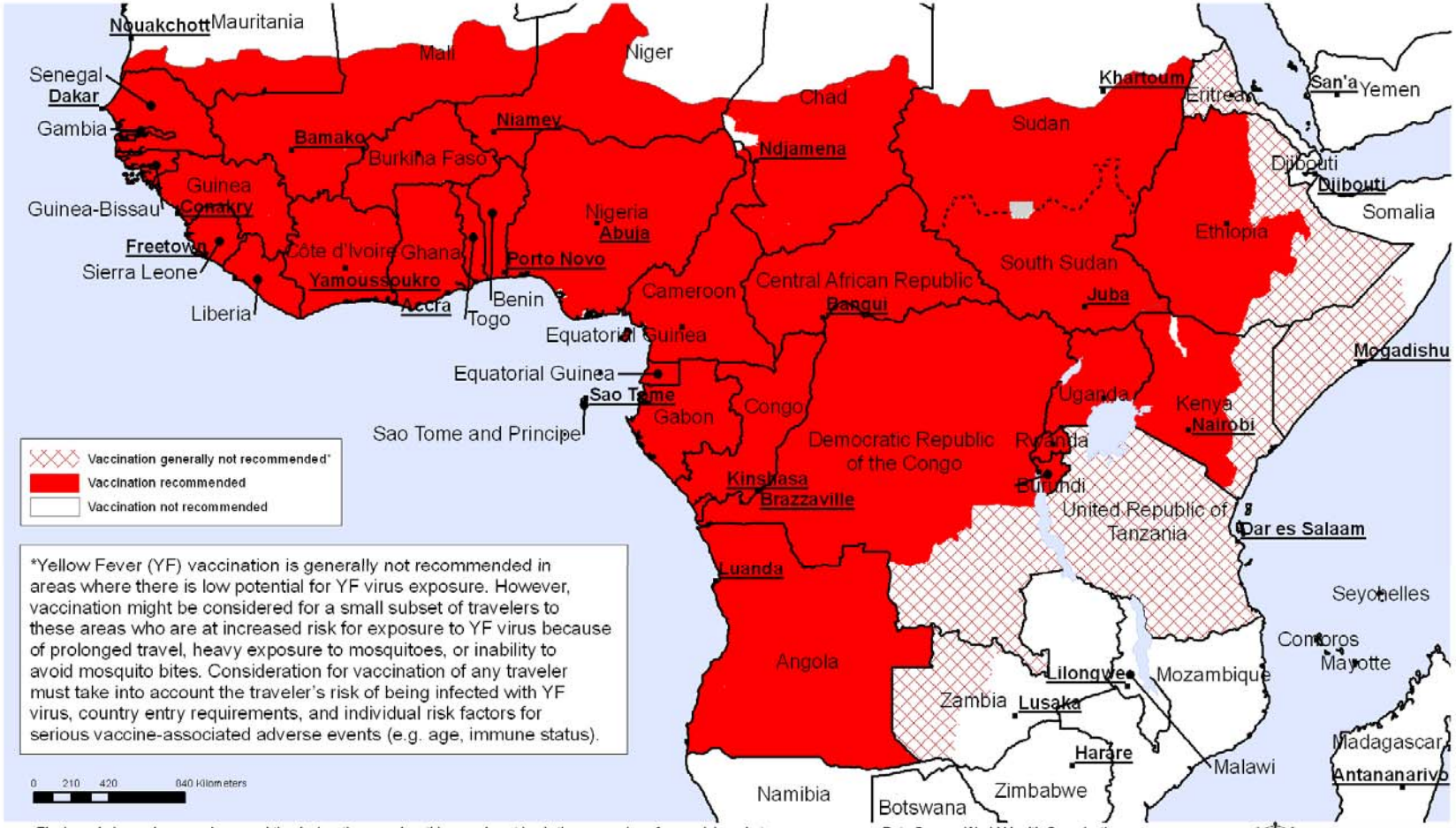
Yellow fever vaccination is required for travellers to certain countries and is recommended for all travellers to countries or areas with risk of yellow fever transmission (see Country list and Annex 1).

While yellow fever vaccination should be encouraged as a key prevention strategy, it is important to screen travel itineraries and carefully evaluate the potential risk of systemic illness after yellow fever vaccination. 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. Although vaccination is generally not recommended for travellers going to areas where the risk of exposure is low, any risk (e.g. as a result of prolonged travel or heavy exposure to mosquito bites) should be weighed against individual risk factors for vaccine-associated adverse events (e.g. altered immune status).

Type of vaccine:	Live, attenuated
Number of doses:	One dose of 0.5 ml
Boosters:	A single dose of YF vaccine is sufficient to confer sustained lifelong protective immunity against YF disease; a booster dose is not necessary for protection but may still be required by some countries. Adjustments of the provisions for the duration of validity of certificates under the IHR are ongoing.
Contraindications:	Infants aged less than 6 months; history of severe allergy to egg or to any of the vaccine components, or hypersensitivity to a previous dose of the vaccine; thymoma or history of thymectomy, immunodeficiency from medication, disease or symptomatic HIV infection
Adverse reactions:	Rarely, neurological (encephalitis) or multi-organ failure resembling wild-type yellow fever.
Before departure:	International certificate of vaccination becomes valid 10 days after vaccination.
Recommended for:	All travellers to countries and areas with risk of yellow fever transmission and when required by countries.
Special precautions:	Not recommended for infants aged 6–8 months, except during epidemics when the risk of YF virus transmission may be very high. The risks and benefits of vaccination in this age group should be carefully considered before vaccination. The vaccine should be avoided during pregnancy or breastfeeding. However, pregnant or nursing women may be vaccinated during epidemics or if travel to a country or area at risk of transmission is unavoidable.

For the international certificate of vaccination, see below under "Required vaccinations".

Yellow Fever Vaccination Recommendations in Africa, 2011



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Data Source: World Health Organization
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

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Yellow Fever Vaccination Recomendations in the Americas, 2013

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Data Sources: World Health Organization
Yellow Fever Working Group

World Health Organization

6.3 Required vaccinations

6.3.1 Yellow fever

Vaccination against yellow fever is required to prevent the importation of yellow fever virus into countries where the disease does not occur but where the mosquito vector and non-human primate hosts are present. In those settings, vaccination is an entry requirement for all travellers arriving (including airport transit)[1] from countries where there is a risk of yellow fever transmission.

If yellow fever vaccination is contraindicated for medical reasons, a letter of medical exemption is necessary.

The international certificate of vaccination for yellow fever vaccine becomes valid 10 days after primary vaccination. Although a booster dose after 10 years is not necessary for protection, it may still be required by some countries. Adjustments of the provisions for the duration of validity of certificates under the International Health Regulations are ongoing.

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.

Explanatory notes on the international certificate of vaccination are included at the end of this chapter. A revision of the International Health Regulations was adopted on 23 May 2005 by the World Health Assembly, and these Regulations entered into force in June 2007 (see Annex 2). As from June 2007, the previous "International certificate of vaccination or revaccination against yellow fever" has been replaced by the "International certificate of vaccination or prophylaxis". It should be noted that the main difference between this and the previous certificate is the requirement to specify in the space provided that yellow fever is the disease for which the certificate is issued.

6.3.2 Meningococcal disease

Vaccination against meningococcal disease is required by Saudi Arabia for pilgrims visiting Mecca for the Hajj (annual pilgrimage) or for the Umrah. The same requirements apply to guest workers.

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.[2]

6.3.3 Polio

Some polio-free countries may require travellers from countries or areas reporting polio viruses (see http://www.polioeradication.org/Dataandmonitoring/Poliothisweek.aspx) 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.

[1] A few hours transit spent in an air-conditioned international airport in an endemic area should not be considered a realistic risk of contracting yellow fever and hence should not be seen as an indication for yellow fever vaccination or restrict entry of non-vaccinated individuals into non-endemic countries.

[2] Most recently: Weekly Epidemiological Record. 2012; 87(30):277–80.

6.4 Special groups

6.4.1 Infants and young children

Because not all vaccines can be administered to the very young, it is especially important to ensure protection of those age groups against health hazards such as foodborne illnesses and mosquito bites by means other than vaccination.

Some vaccines can be administered at birth (BCG, oral polio vaccine, hepatitis B). Others, e.g. diphtheria/tetanus/pertussis, cannot be given before a certain age; Japanese encephalitis cannot be given before 6 months and yellow fever not before 9 months. 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.

6.4.2 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), or when their lifestyle includes 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.

6.4.3 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 adequately vaccinated. Such travellers pose a special problem for health advisers who should, nonetheless, encourage compliance.

6.4.4 Pregnant women

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 such as influenza vaccine, toxoids, polysaccharides and conjugated vaccines can generally be given during pregnancy. Except for oral poliovaccine, live vaccines are generally contraindicated because of largely theoretical risks to the baby; measles, mumps, rubella, 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 in early pregnancy depending upon the risk (see Table 6.2). For more detailed information, see the specific vaccine position papers at: http://www.who.int/immunization/documents/positionpapers_intro/en/

6.4.5 Elderly travellers

In general, vaccination of healthy elderly travellers does not differ 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 polio as well as to other infections present at the travel destination.

Table 6.2 **Vaccination in pregnancy**

Vaccine	Use in pregnancy	Comments
BCG[a]	No	
Cholera	Yes, administer oral inactivated vaccine if indicated	
Hepatitis A (inactivated)		Yes, administer if indicated
Hepatitis A (live vaccine)	No	
Hepatitis B	Yes, administer if indicated	
Influenza	Yes, administer if indicated	Use inactivated vaccine
Japanese encephalitis	No for live vaccine	Safety not determined
Measles[a]	No	
Meningococcal disease	Yes, administer if indicated	
Mumps[a]	No	
Polio:		
OPV[a]	Yes, administer if indicated	
IPV	Yes, administer if indicated	
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 who have never been vaccinated should be offered a full primary course of vaccination against diphtheria, tetanus, polio 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 elderly people are at risk for severe and complicated influenza, regular annual vaccination should be considered. Unless the seasonal influenza vaccines are identical in the two hemispheres, elderly travellers from one hemisphere to the other shortly before, or during, the influenza season may arrange to receive the appropriate influenza vaccine before leaving home or shortly after arrival at the destination. Pneumococcal polysaccharide vaccine has not been demonstrated to prevent non-bacteraemic pneumonia among elderly and other individuals at the highest risk of influenza-related morbidity and mortality.

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

6.4.6 Travellers with chronic medical problems

Travellers with chronic medical conditions associated with 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 for these travellers to avoid measles, oral polio, yellow fever, varicella and BCG vaccines. For travel to a country where yellow fever vaccination is required, a letter of medical exemption should be issued.

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. Unless the seasonal influenza vaccines are identical in the two hemispheres, high-risk travellers from one hemisphere to the other shortly before, or during, the influenza season may arrange to receive the appropriate influenza vaccine before leaving home or shortly after arrival at the destination.

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

6.4.7 HIV-positive travellers

See Chapter 9.

6.5 Adverse reactions and contraindications (see Tables 6.3 and 6.4)

6.5.1 Reactions to vaccines

While vaccines are generally both effective and safe, no vaccine is totally safe for all recipients. Vaccination may sometimes cause 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.

6.5.2 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. The systemic symptoms (mainly fever and/or rash) that are reported in 5–15% of measles/MMR vaccine recipients 5–12 days after vaccination are commonly attributable to background events, i.e. normal events of childhood.

6.5.3 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 vaccine in the future.

6.5.4 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
Haemophilus influenzae	NR	—
Hepatitis A	NR	—
Hepatitis B[c]	Anaphylaxis	1–2
Influenza	Guillain–Barré syndrome	<1
Japanese encephalitis	Neurological event (mouse-brain only)	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 disease	Anaphylaxis	Very rare
Polio (OPV)	Vaccine-associated paralytic	1.4–3.4 polio
Polio (IPV)	NR	—
Rabies	Animal brain tissue only – neuroparalysis	17–44
	Cell-derived – allergic reactions	Rare
Rubella	Arthralgia/arthritis/arthropathy transient	In non-immune adult women: arthralgias: 25%, arthritis: 12%
Tetanus	Brachial neuritis	5–10
	Anaphylaxis	1–6
Tick-borne encephalitis	NR	(data on western vaccines only)
Typhoid fever	Parenteral vaccine – various	Very rare
	Oral vaccine – NR	—
Yellow fever	Encephalitis (<6 months)	500–4000
	Allergy/anaphylaxis	5–20
	Viscerotropic disease	0–24

[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 (no absolute contraindication; depends on the risk of exposure) Severe immunodeficiency
Yellow fever	Severe egg allergy Severe immunodeficiency (from medication or disease, or symptomatic) Pregnancy HIV infection[b]
BCG	HIV infection
Influenza	Severe egg allergy

[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 who have symptomatic HIV infection or who are suffering from other immunodeficiency diseases, provided that their CD4 count is at least 200 cells/mm^3 and if they plan to visit countries or areas at risk.

Further reading

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

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

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

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

International certificate of vaccination

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

International certificate of vaccination or prophylaxis

Model international certificate of vaccination or prophylaxis

This is to certify that [name].....

date of birth ..... sex .....

nationality.....

national identification document, if applicable .....

whose signature follows .....

has on the date indicated been vaccinated or received prophylaxis against [name of disease or condition].....

in accordance with the International Health Regulations.

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

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

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

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

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

[1] See http://www.who.int/immunization_standards/vaccine_quality/pq_suppliers/en/index.html, WHO Technical Report Series, No. 872, 1998, Annex 1 (http://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.