Travel Medicine

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Before travelling to other countries, thorough travel advice should be provided. Not only information about diseases of specific countries but also general advice for travelling should be given on this consultation.

The following topics should be included in the travel advice consultation:

- Vaccinations (general and country specific)
- Country-specific diseases
- Malaria prophylaxis
- Mosquito prophylaxis (wearing bright long-sleeved clothes, avoiding perfume, staying in air-conditioned rooms, using a mosquito net, using insect repellents, staying inside at dawn and dusk)
- Food consumption and drinking overseas (no consumption of ice cubes, uncooked meals, salads and food, which is exposed to flies, limited alcohol consumption)
- UV protection (using sun cream, avoiding sun exposure between 11.00 and 15.00 o'clock, remaining in shaded areas, wearing a hat and covering skin)
- Fitness assessment for travelling, flying and diving
- Challenges of different climates and their effects on the personal health (dehydration, hyperthermia)
- Medications
- Thrombosis counselling
- Counselling on symptoms on return, which require review (fever, skin changes, abnormal bleeding, lymphadenopathy, diarrhoea)
- Sexual transmitted diseases
- Contraception
- Rabies

The following items should be asked to enable to give the appropriate advice:

- Risk assessment of the travel in a particular country (transport, area of stay/ rural or resort, reason for travelling, appropriate conduct overseas, pre-existing diseases and medications)
- Vaccination status
- Accomodation and stopovers
- Duration of the stay

The vast majority of up-to-date travel information and information about tropical disease are available on WHO (World Health Organization) or CDC (Centres for Disease Control and Prevention) websites. Information on these websites are frequently updated. Before giving appropriate advice based on these online resources, it should be checked, which medications are available in the particular countries. Hence, recommendations need to be adjusted individually. Usually, a medication record is required at the customs. However, it might be sufficient, if the original medication box has the patients and prescribing doctors details (Table 32.1).

32.1 Malaria

Malaria is a tropical disease transmitted by the female *Anopheles* mosquito. The distribution of malaria is primarily in the tropics and subtropics of Africa, Central and South America, Asia, Papua New Guinea and the Western Pacific Islands. As popular diving spots are located in these areas, malaria prophylaxis and advice should be given. The WHO (World Health Organization) estimates the worldwide number of people affected by malaria with about 198 million and 1,200,000 deaths (2013). The *Plasmodium* parasites need temperatures above 20 °C in order to complete the entire growth cycle. Therefore, malaria occurs in some places only seasonal. Additionally, there are differences in *Anopheles* species regarding the affinity to the host and their local distribution. Some genetic factors are protected against malaria. For example, sickle cell anaemia gives a certain protection against *P. falciparum* and Duffy negative blood group against *P. vivax*. It appears that after recurrent malaria infections, the body adapts to the disease. This means that an infection is possible, but the symptoms of malaria seem to be reduced. Children and pregnant women have an increased risk of being affected by malaria. Additionally, children have a high mortality rate. During pregnancy the resistance against malaria is reduced.

Table 32.1 DVT prophylaxis

Risk	Risk factors	Prophylaxis
Minimal risk	Age < 40, no health issues	[a]
Low risk	Age > 40, obesity, acute inflammation, minor surgery <3 days	[a]Compression stockings
Medium risk	Varicose veins, poorly controlled heart failure, acute myocardial infarction <6 days, oestrogen therapy and OCD, polycythemia, pregnancy and postpartum, injury or paralysis of the lower limbs <6 weeks	[a]Aspirin (if there are no contra-indications; not in pregnancy; effectiveness not proven), compression stockings
High risk	Previous DVT or pulmonary embolism, thrombocytophilia (AT III, protein C and protein S deficiency, APC resistence, factor II-dimorphism, dysfibrinogenemia, hyperhomocysteinemia, factor V-Leiden, etc.), major surgery <6 weeks, previous stroke, neoplasia, family history of DVT and pulmonary embolism	[a, b]Anticoagulation with low molecular weight heparin (e.g. dalteparin 5000 IE, enoxaparin 40 mg) or an off label use of a single dose of rivaroxaban (Xarelto®) 10 mg before and 3 days after the flight

[a]Extension of legs and ankles, no luggage under seat in front of the passenger, frequent walking, avoiding sleeping crippled over, high fluid intake, avoiding alcohol, coffee or tea
[b]Approval of anticoagulants for VTE prophylaxis depends on national regulations; contraindications prior administration need to be excluded

It also poses an increased risk for the unborn child (low birth weight). *Anopheles* is active especially at sunrise and sunset. Different kinds of mosquitoes are rather active during the day and can transmit other diseases such as dengue. Especially *P. falciparum* and *P. vivax* have resistances against antimalaria drugs. There are different *Plasmodium* pathogens:

- *P. falciparum*: Worldwide tropical and subtropical distribution, mainly in Africa; pathogen of severe malaria causes 1 million deaths per year; rapid growth in the blood with haemolysis and emboli due to cyto-adherence of affected erythrocytes; 7–30 days of incubation, irregular fever spikes.
- *P. vivax*: mainly in Asia, Latin America and some countries in Africa; the disease can be activated after months or years. Incubation period of 12–18 days; fever spikes every 2 days.
- *P. ovale*: mainly West Africa and the Western Pacific Islands. Similar to the *P. vivax*, it can also infect people with Duffy-negative blood group; incubation period of 12–18 days; fever spikes every 2 days.
- *P. malariae*: worldwide distribution; typical 3-day cycle, untreated can lead to lifelong chronic malaria; incubation period 16–50 days; fever spikes every 3 days.
- *P. knowlesi*: Southeast Asia, mainly infected animals.

32.1.1 Aetiology and Pathogenesis

After the *Anopheles* mosquito aspirates with gametocytes infected blood, the gametocytes develop to gamete in the mosquito's intestines. In the blood of the mosquito, the microgametes (male) penetrate the macrogametes (female), forming zygotes. Then cells are changed to an elongated, motile ookinete. This evolves into an oocyst. After the oocyst bursts, sporozoites are released and get in the saliva of the mosquito. The entire cycle inside the mosquito takes 8–16 days. If sporozoites enter the human bloodstream through the saliva of the

mosquito, liver cells via the bloodstream get infected. They penetrate liver cells and turn into schizonts (exo-erythrocytes cycle). With the exception of *P. oval*, merozoites are released in the bloodstream after the liver cycle (exo-erythrocytic cycle). *P. vivax* and *P. ovale* produce hypnozoites, which can stay dormant in liver cells. Merozoites enter red blood cells and multiply there asexually. By rupturing erythrocytes, merozoites are released, which some of them are infecting other erythrocytes. The cycle repeats every 2 or 3 days. The blood stage parasites are responsible of the typical malaria symptoms. Some merozoites differentiate into gametocytes, after being aspirated by the mosquitoes. Again, in a mosquito infected with the pathogen, transfer of the parasite to someone else is possible (■ Table 32.2, ■ Fig. 32.1).

32.1.2 Symptoms

Symptoms of malaria appear after the incubation period. The incubation period varies depending on the pathogen. It can be between a few weeks and also takes up to several months or even a year (*P. vivax* or occasionally *P. ovale*). Malaria can be divided in three different forms:

- *Malaria tertiana*: Pathogen: *P. vivax* and *P. ovale*; fever every second day with one day without fever, spontaneous remission after max. 5 years
- *Malaria quartana*: Pathogen: *P. malaria*; fever every third day with 2 days without fever, no spontaneous remission
- *Malaria tropica*: Pathogen: *P. falciparum*, irregular fevers due to the lack of synchronisation of the parasite reproduction, severe form of malaria (Malaria maligna) with high fatality, recurrence up to 2 years

The fever has a specific pattern. In the first hour, strong rigors and increasing fever typically develop. The fever can reach 40 °C and more for duration of about 4 h. It is often associated with flushing, vomiting and nausea. The fever stage is followed by an approximately 3-h stage of severe sweating with decreasing fever.

■ **Table 32.2** Comparison of mild and severe malaria symptoms

Mild symptoms	Severe symptoms
Fever, rigors	Altered level of consciousness, confusion, coma,
Cough	GCS < 11 (adults), Blantyre coma scale <3 (children)
Malaise	Shock
Diaphoresis	Icterus (bilirubin >3 mg/dL or 50 µmol/L)
Myalgia, arthralgia	Acute renal failure (creatine >265 µmol/L, urea >20 mmol/L); oliguria (<400 mL/24 h)
Abdominal pain	Seizures >2/d
Headache	Hyperparasitaemia >2%
Vomiting, nausea	Extreme weakness (requires assistance for sitting up)
Diarrhoea	Shortness of breath (pulmonary oedema, shock)
Anorexia	SaO_2 < 92%, respiratory rate > 30/min
Hepatosplenomegaly	Acidosis (pH < 7,25, plasma bicarbonate <15 mmol/L)
Mild anaemia	Hypoglycaemia (<40 mg/dL), haematocrit >15% (children) and >20% (adults)
Mild thrombocytopenia (important parameter for the staging of severity)	Severe Anaemia (Hb < 5 g/dL)
	Severe thrombocytopenia with spontaneous bleeding

Severe forms of malaria can be fatal in within few days. Causes of death are cerebral malaria, respiratory failure with ADRS and kidney failure. The main reason of these complications is the cyto-adherence ("bonding") of the erythrocytes. It results in a failure of the microcirculation followed by ischaemia of vital organs.

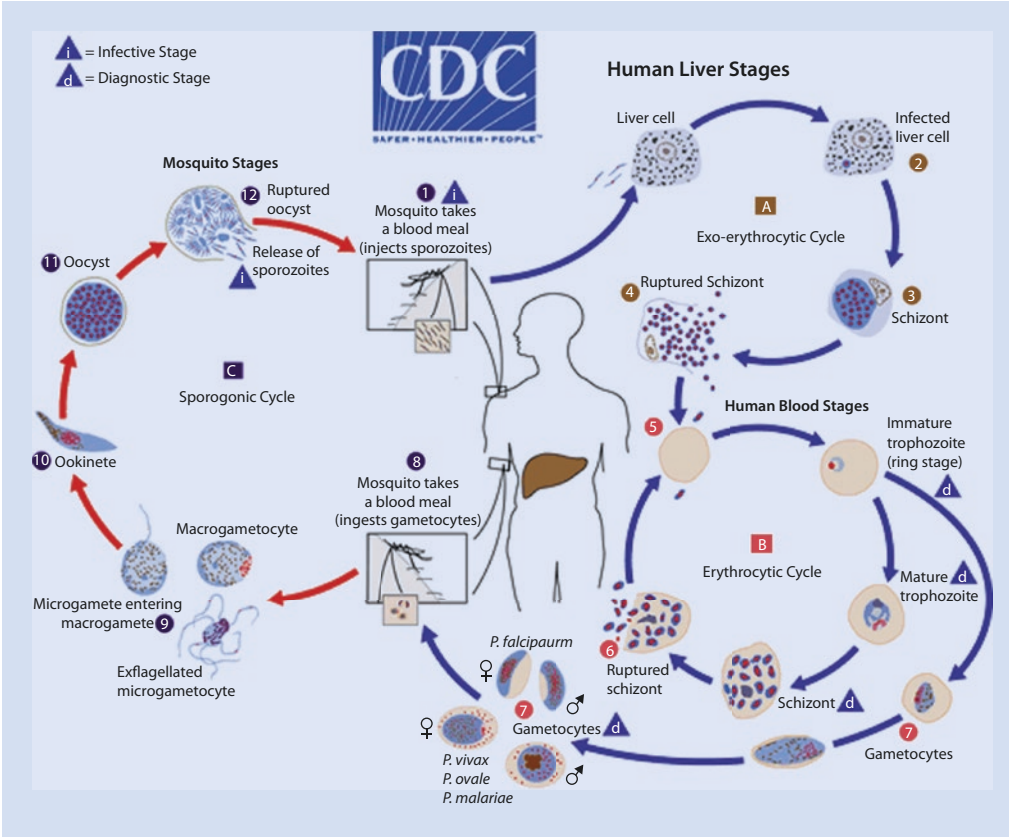

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Fig. 32.1 Plasmodium life cycle. (CDC)

32.1.3 Diagnosis

In case of pyrexia of unknown origin, the patient always should be asked about previous stays overseas. Additionally to the symptoms, a blood test is the most important diagnostic tool. The parasite can be demonstrated using a blood smear and thick drop. A single negative smear does not exclude malaria. A negative smear should be repeated three times within 12–24 h. In the thick drop, existing parasites with a low count can be accumulated and detected. After a positive test, the number of parasites in the erythrocytes should be calculated. A parasite count >2% might be an indication for complicated malaria. A PCR-test for *Plasmodium* DNA is a good diagnostic tool and commonly used. It is slightly more sensitive than the blood smear. It also allows a discrimination of the malaria species. Another test is the antigen detection. These immunologic tests often use a dipstick or cassette format and provide results within 2–15 min. Hence, they are referred as "Rapid Diagnostic Tests" (RDTs). RDTs should be followed up by microscopy. RDTs and smear microscopy currently provide the best results in testing for malaria. The *Plasmodium* antibody test is not suitable in the initial phase, as antibodies only can be detected after 6–10 days. It is only to retrospectively confirm a previous infection. Regular monitoring of the blood count and renal function and a careful fluid balance is necessary during the treatment of malaria. A CXR may be necessary, if respiratory symptoms are present.

32.1.4 Treatment

The treatment depends on the severity and the pathogen. In *complicated malaria*, admission to the intensive care should be considered, if more than one of the following criteria exists:

- Inability of the oral intake of medication
- Parasite load of erythrocytes >2%
- Severe symptoms of malaria (see table above)

The treatment options of complicated malaria are:

- *Artesunate* (allowed only in some countries): 2.4 mg/kg/bw iv; first dose on admission, repeated after 12 and 24 h, minimum duration of therapy 24 h and then once a day, till oral therapy is tolerated.
  or
- Combination of quinine + doxycycline or clindamycin.
  - *Quinine:*
    - First dose: 20 mg/kg/bw iv over 4 h or 7 mg/kg/bw iv over 30 min with subsequent administration of 10 mg/kg/bw iv over 4 h.
    - Maintenance therapy: 10 mg/kg/bw iv over 4 h three times a day, beginning 4 h after the completion of the first dose.
    - Exemption: if the patient received three or more doses of quinine in the last 48 h or had an Mefloquine prophylaxis in the last 24 h or received a Mefloquine treatment in the last 3 days.
      +
  - *Doxycycline*: 100 mg iv twice daily for 7 days (iv or oral)
    or
  - *Clindamycin*:
    - Initial dose: 10 mg/kg/bw
    - Maintenance dose: 5 mg/bw every 8 h for 7 days (iv or oral)
- After clinical improvement medication can be changed to a complete cycle of the oral therapy of an uncomplicated malaria (Riamet® or quinine with doxycycline or clindamycin).

Uncomplicated malaria can be handled on the normal ward. Outpatient therapy with close supervision can be considered under the following conditions:

- Parasite load of erythrocytes <1%.
- Age > 12 months.
- No co-morbidity.
- Pregnancy is excluded.
- Ability of oral medication intake.
- *P. falciparum* is excluded.
- Clinically stable under medical therapy for the last 24 h.

A daily blood smear is necessary during treatment to follow the process of the disease. The patient can be discharged from the hospital and continue treatment at home; if oral therapy is tolerated, a clinical improvement is achieved and the parasite count decreases. A week and a month after discharge, blood smears should be repeated. Primaquine as eradication therapy is approved in some countries. It is the only drug that can be used to eliminate hypnozoites, which are the dormant forms of the malaria parasites that occur with *P. ovale* and *P. vivax*. Because primaquine causes haemolysis in G-6-PD deficiency, G-6-PD status prior therapy needs to be established. If an eradication with primaquine is required in patients with G-6-PD deficiency, a dose up to 45 mg weekly for 8 weeks, with monitoring for haemolysis, could be considered. In children methaemoglobinaemia can be provoked by giving primaquine. A single dose of primaquine 45 mg for *P. falciparum*, *P malaria* and *P. knowlesi* can be given to sterilise the gametocytes. If malaria caused by *P. vivax* or *P. ovale* or co-infection with these parasites is suspected, a 14-day treatment with 15 mg of primaquine twice a day is recommended.

Treatment of uncomplicated malaria:

- Artemether 20 *mg* + *Lumefantrine 120 mg (Riamet®)*: four tablets (appropriate dose for children, 5–14 kg; one tablet; 15–24 kg, two tablets; 25–34 kg, three tablets) in following time interval: 0, 8, 24, 36, 48 and 60 h; for *P. falciparum*, site of action: inhibits nucleic acid and protein synthesis

or

- *Atovaquone 250 mg* + Proguanil 100 *mg (Malarone®):* four tablets (appropriate dose for children: 11–20 kg, one tablet; 21–30 kg, two tablets; 31–40 kg, three tablets) with a high-fat meal or milk daily for 3 days; for *P. vivax* (Papua New Guinea and Indonesia) and *P. falciparum*; site of action: inhibits metabolic enzymes and thus the growth of parasite

or

- *Mefloquine (Lariam®):* first dose 750 mg, second dose 500 mg (6–8 h after the first dose), third dose 250 mg (only at bw > 60 kg, 6–8 h after the second dose); for *P. falciparum* and *P. vivax*; site of action: schizoid

or

- *Chloroquine*: Dose first day 10 mg/kg/bw, second day 10 mg/kg/bw, third day 5 mg/kg/bw; for *P. malariae*, *P. knowlesi* and *P. falciparum* (if there is no chloroquine resistance); site of action: erythrocytic, unknown mechanism

or

- *Chloroquine* + *primaquine* (with normal G-6-PD)
  - Chloroquine: Dose first day 10 mg/kg/bw, second day 10 mg/kg/bw, third day 5 mg/kg/bw; site of action: erythrocytes
  - Primaquine: 15 mg twice a day for 14 days (adults), 0.25–0.5 mg/kg/bw daily for 14 days (children); *P. Ovale* and *P. vivax* (all countries except Papua New Guinea or Indonesia and no chloroquine resistance); site of action: extra-erythrocytic inhibits plasmodium mitochondria

  or

- *Combination therapy* (except for patients, who had Malarone® as prophylaxis); for *P. Falciparum* and *P. vivax* (Papua New Guinea and Indonesia)
  - *Quininsulfat*: 600 mg (children 10 mg/kg/bw) three times a day for 7 days; site of action: unknown, probably inhibits the *Plasmodium* DNA transcription/replication

  +
  - *Doxycycline*: 100 mg twice a day *or* clindamycin 300 mg (children 5 mg/kg/bw) three times a day for 7 days; site of action: probably inhibits the dissociation of peptidyl t-RNA at the ribosome, inhibits protein synthesis by binding onto the 50 s ribosome subunit

  or
  - *Clindamycin* 20 mg/kg/bw three times daily for 7 days; site of action: inhibits protein synthesis by binding onto the 30 s and 50 s ribosome subunit

32.1.5 Prophylaxis

Exposure Prophylaxis

Before commencing holidays overseas, medical advice should be given in order to assess the malaria risk of the particular country. In nearly all tropical areas, there is a risk of getting infected with malaria. In some tourist areas, this risk might be small, but infection is still possible. In particular day trips to more remote areas pose a risk. Some areas have malaria outbreaks and therefore should be avoided. In general, mosquito bites should be avoided to minimise the risk of any mosquito-borne infections. Mosquitoes transmitting malaria are mainly active at night, sunrise and sunset. However, mosquito bites are also possible throughout the day. Long-sleeved shirts, long pants and closed shoes cover the skin and provide protection against insect bites. Insect repellent for the skin and clothes offer additional protection. Higher concentrations offer better and longer protection. The protection period of a normal insect repellent lasts usually only 1–2 h. Slow release products can prolong the effect. Mosquitoes avoid air-conditioned rooms. So staying in air conditioned rooms itself provides certain protection. Spraying insecticides in rooms and surroundings can be helpful to repel and minimise the quantities of mosquitoes. The bed should be covered with a mosquito net (Fig. 32.2).

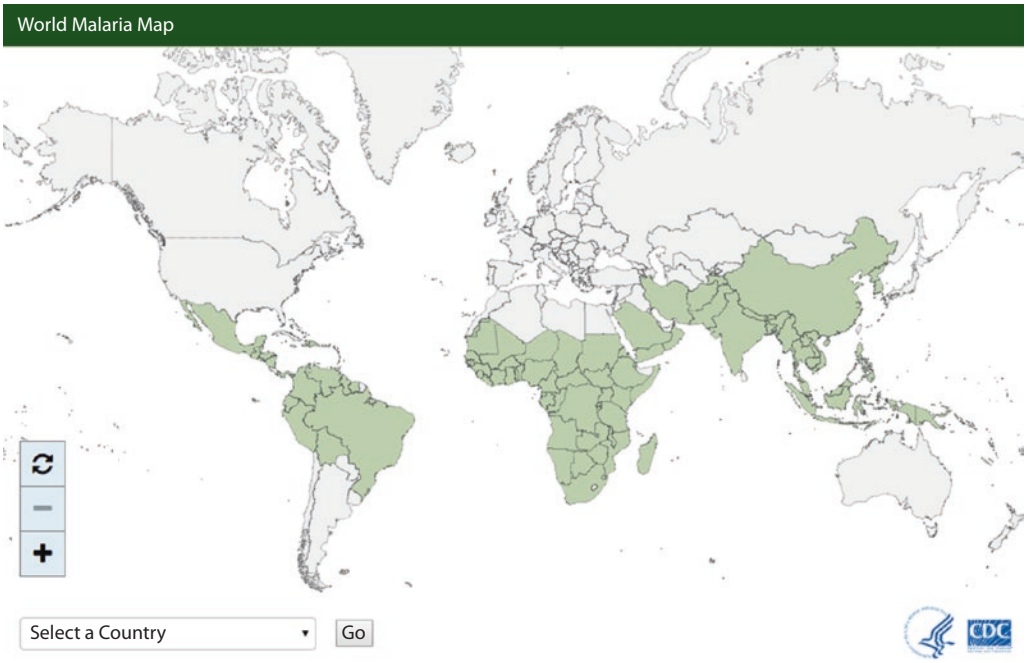


Fig. 32.2 Malaria map. (CDC)

Chemoprophylaxis

Chemoprophylaxis is important, because the main cause of malaria deaths is still inadequate chemoprophylaxis. There are different drugs for chemoprophylaxis available. They are subject to the travel location and the parasite's resistances to certain drugs. In addition, they differ in side effects, dosage and cost. Except Malarone®, all other drugs for the chemoprophylaxis against malaria have to be taken 4 weeks after leaving the country as they aren't sufficiently effective against the primary liver stages of malaria. Mefloquine (Lariam®) is the only malaria prophylaxis without absolute contraindication in pregnancy.

- *Chloroquine*: schizontocidal; 300 mg (<75 kgbw), 450 mg (>80kgbw)/week; begin 1 week before entering the malaria-endemic country and 4 weeks after return. Adverse reactions: gastrointestinal, photosensitivity, haemolysis (with G-6-PD deficiency), neuropathy (with long-term treatment), cardiomyopathy, eye damage (deposit in the cornea and irreversible retinopathy), narrow therapeutical window
- *Doxycycline*: chemoprophylaxis for *P. falciparum* with Mefloquine resistance, 100 mg/d. Begin 1–2 days before entering the malaria-endemic country and 4 weeks after return. Adverse reactions: gastrointestinal, photosensitivity contraindication, lactation and children <8 years of age
- *Atovaquone* + *Proguanil* (*Malarone®*): 250/100 mg/d for adults, the dose for children is weight dependent; Begin 1–2 days for entering the malaria-endemic country till 7 days after return; Adverse reactions: gastrointestinal, headaches and vivid dreams
- *Mefloquine* (*Lariam®*): 250 mg/week; long half-life (21 days). Adverse reactions: gastrointestinal, elevation of transaminases, psychiatric (anxiety, agitation, depression, vivid dreams, hallucinations, seizures, suicidal ideations), AV-block, bradycardia, leuco- and thrombocytopenia, rash, alopecia, extrasystoly; contraindication for

diving (decrease in vigilance); 2–3 weeks (at least 1 week) before entering the malaria-endemic country and 4 weeks after return; Lariam® is a category B medication and is the only medication against malaria without absolute contraindication in pregnancy. The use in the first trimester should only be considered, if the expected benefits justify the potential risk to the foetus. However, recent studies suggest that even in the first trimester this medication is safe to take.

32.2 Other Mosquito-Borne Diseases

32.2.1 Dengue

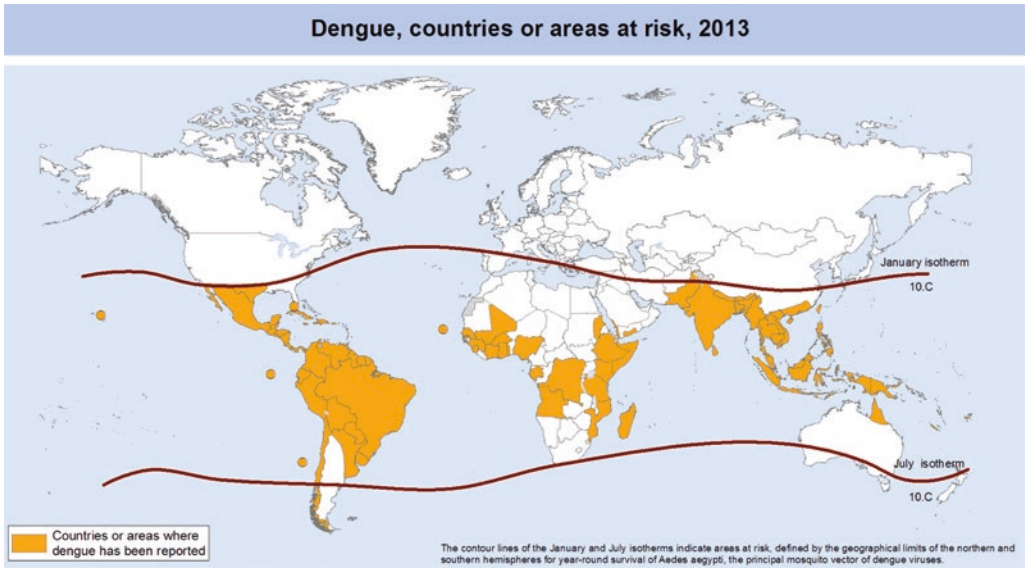
Introduction

The dengue virus is an arbovirus. It has four different serotypes (DENV 1–4). Dengue has a worldwide distribution in the tropics and subtropics, especially in Asia and South America. Approximately 50–100 million cases and about 100,000 with serious complications per year occur. There is a 10% mortality, which can be reduced to 1% with timely diagnosis and appropriate treatment. It has an increased risk for children under 15 years and persons with previous dengue infections. The dengue virus is transmitted by the Aedes aegypti mosquitoes. These mosquitoes mainly bite at day and in twilight (◘ Fig. 32.3).

Symptoms

The incubation period is 2–10 days. There is a wide range in severity of dengue symptoms. The majority of infections cause minor symptoms. But dengue infections can be also quite severe (◘ Table 32.3). In particular recurrent infections with dengue are associated with complications and severity of the disease. It is important for the treating doctor to remember that after the initial fever, the critical phase follows. Therefore, the patient must be monitored closely during this time. The disease goes through three stages:

- Fever phase (day 1–3): sudden high fever 40 °C occasional associated with bradycardia; myalgia mainly in the spine, arms and legs ("breakbone fever"), headache; retrobulbar pain; rigors; metallic/bitter taste; vomiting; and dehydration.



◘ **Fig. 32.3** Dengue distribution; 2013 (WHO)

Table 32.3 Dengue classification

Grade 1	Grade 2	Grade 3	Grade 4
Fever Positive blood pressure cuff test High permeability of the blood vessels Hepatomegaly Thrombocytopenia	Plasma leakage Spontaneous bleeding (skin, epistaxis)	Early shock Disseminated intravascular coagulation (DIC)	Shock Severe bleeding

- Critical phase (day 4–5): normal temperature with possible mild fever later on, leucopenia, exanthema, petechiae and lymphadenopathy. Severe dengue: abdominal pain, spontaneous bleeding, volume shift in to the peritoneal space ("plasma leak"), pleural effusion, hepatomegaly (≥2 cm), rapid increase in haematocrit and decreasing thrombocytes, shock (dengue haemorrhagic shock = DHS or dengue shock syndrome = DSS), increased bleeding (dengue haemorrhagic fever = DHF) and organ failure (particularly liver).
- Remission (after 6 days lasting sometimes for weeks): risk of hyperhydration is given when extravascular fluid is reabsorbed without reducing the intravenous fluid administration. In particular in long remissions, fatigue and depression may be present. Normally there are no long-term damages after a dengue infection, and the vascular changes recover completely.

Treatment

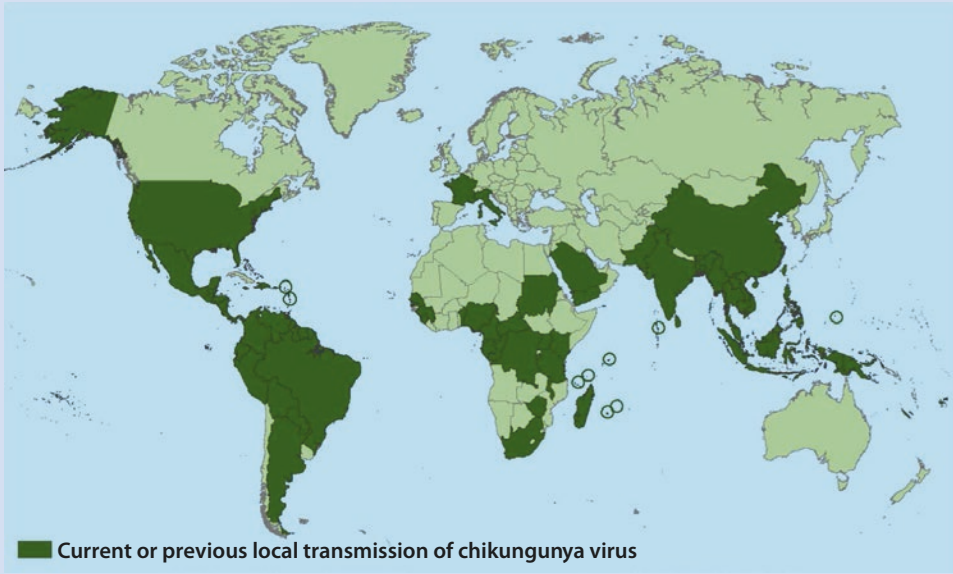
There is no medication available to treat dengue directly. The diagnosis of dengue can be demonstrated by PCR in the initial phase and using IgM and IgG a few days later. Due to severe complications, the haematocrit, coagulation parameters, leukocytes and platelets have to be tested daily. Thrombocytes <100,000 cells/mm^3 can rise the suspicion of DHF. If pleural effusion is suspected, a CXR should be obtained. By tightening a blood pressure cuff petechiae can be provoked (medium pressure of the systolic and diastolic pressure for 5 min). This can be used as a diagnostic tool. An increase of the haematocrit of >20%, pleural effusion, ascites or hypoproteinaemia could be a sign for extravascular fluid loss. The extravascular fluid loss is typically found in the initial phase. Hence, fluid replacement therapy is crucial in this phase. As the extravascular fluid loss can come to an end quite quickly, a complication of the fluid replacement therapy is hyperhydration. Decrease of haematocrit of >20% after fluid administration can represent a fluid excess and hyperhydration. Hence, careful monitoring of the fluid balance and weight are necessary. The therapy is adjusted according to its severity. If necessary, DIC, blood loss or shock require specific treatment.

32.2.2 Chikungunya

Like dengue, Chikungunya is a mosquito-borne disease. The species transmitting the Chikungunya virus (CHIKV) are *Aedes aegypti* in the tropics and subtropics and *Aedes albopictus* in colder regions (Fig. 32.4).

These mosquitoes bite day and night, but mainly in the early morning hours and late afternoon. The incubation period is between 2 and 12 days. The symptoms are similar to that of dengue. Patients suffer from sudden fever with headache, skin rash, fatigue, strong limbs and muscle pain. Affected joints often are swollen. The symptoms generally last for few days but can persist for weeks and years. The disease has no long-term effects. For diagnosis RT-PCR and virological methods can be used in the initial phase. Later, it can be diagnosed by IgM and IgG. IgM peaks after 3–5 weeks and can be detected up to 2 months. The treatment requires analgesia only.

Countries and territories where chikungunya cases have been reported*
(*as of April 22, 2016*)



*Does not include countries or territories where only imported cases have been documented. This map is updated weekly if there are new countries or territories that report local chikungunya virus transmission.

Data table: Countries and territories where chikungunya cases have been reported

AFRICA
Benin
Burundi
Cameroon
Central African Republic
Comoros
Dem. Republic of the Congo
Equatorial Guinea
Gabon
Guinea
Kenya
Madagascar
Malawi
Mauritius
Mayotte
Nigeria
Republic of Congo
Reunion
Senegal
Seychelles
Sierra Leone
South Africa
Sudan
Tanzania
Uganda
Zimbabwe

ASIA
Bangladesh
Bhutan
Cambodia
China
India
Indonesia
Laos
Malaysia
Maldives
Myanmar (Burma)
Pakistan
Philippines
Saudi Arabia
Singapore
Sri Lanka
Taiwan
Thailand
Timor
Vietnam
Yemen

EUROPE
France
Italy

AMERICAS
Anguilla
Antigua and Barbuda
Argentina
Aruba
Bahamas
Barbados
Belize
Bolivia
Brazil
British Virgin Islands
Cayman Islands
Colombia
Costa Rica
Curacao
Dominica
Dominican Republic
Ecuador
El Salvador
French Guiana
Grenada
Guadeloupe
Guatemala
Guyana
Haiti
Honduras
Jamaica
Martinique
Mexico
Montserrat
Nicaragua
Panama
Paraguay
Peru
Puerto Rico
Saint Barthelemy
Saint Kitts and Nevis
Saint Lucia
Saint Martin
Saint Vincent & the Grenadines
Sint Maarten
Suriname
Trinidad and Tobago
Turks and Caicos Islands
United States
US Virgin Islands
Venezuela

OCEANIA/PACIFIC ISLANDS
American Samoa
Cook Islands
Federal States of Micronesia
French Polynesia
Kiribati
New Caledonia
Papua New Guinea
Samoa
Tokelau
Tonga

Fig. 32.4 Distribution of Chikungunya 2015. (CDC)

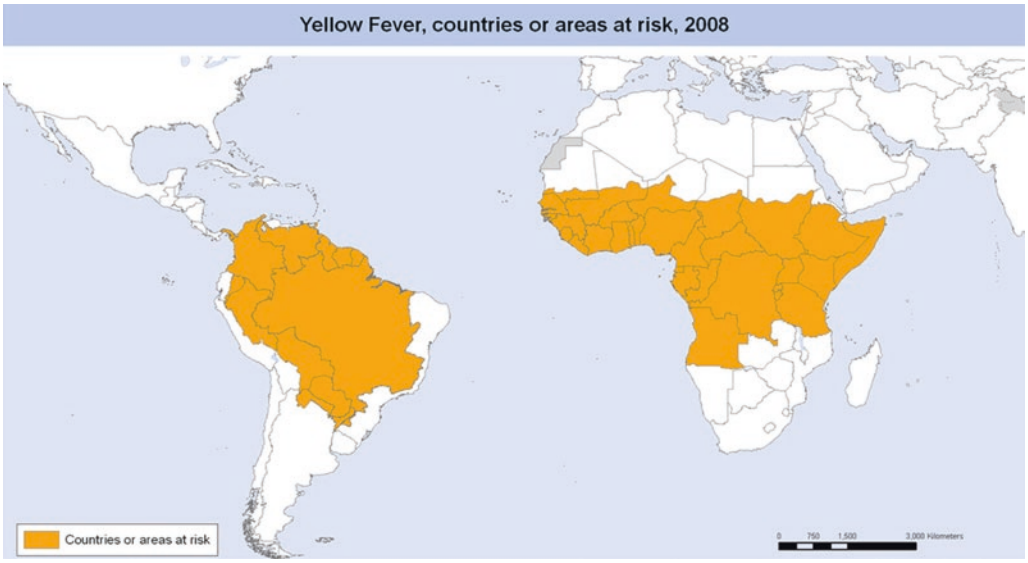


Fig. 32.5 Yellow fever 2008 (WHO)

32.2.3 Yellow Fever

Yellow fever is a disease transmitted mainly by the *Aedes aegypti* mosquito but also by other mosquitoes or ticks. The pathogen is a RNA-containing Flavivirus. It has approximately 200,000 infections with approximately 30,000 deaths annually. 90% of cases occur in Africa and the remaining 10% in South America. The risk of getting infected with yellow fever is with 1:200–2000 in Africa and higher than 1:20000 in South America (Fig. 32.5).

The transmission occurs in rainforest areas (jungle or sylvatic cycle), where mosquitoes transfer the virus from monkeys to humans, in endemic areas of the savannah (savannah or intermediate cycle) either transferred from monkeys or human to humans via mosquitoes or in urban areas from human to human via mosquitoes.

The incubation period is 3–6 days. The disease has two phases. The acute phase comes with fever, headache, myalgia, head- and backache, loss of appetite, nausea, vomiting and diarrhoea. The second phase occurs only in approx. 15% of infected humans within the next 24 h. Jaundice, abdominal pain and vomiting are rapidly developing, followed by diffuse bleeding (epistaxis and GI bleeding) and multi-organ failure (mainly kidneys). If symptoms of the more severe second phase develop, 50% of the patients die within the next 10–15 days. Patients who survive usually recover without significant organ damage.

The diagnosis can be made via a blood or tissue biopsy of the liver. There is no cure for yellow fever and only supportive measures can be taken. However, a very effective life-vaccination (Stamaril®) is available. Only authorised doctors are authorised to prescribe and give the vaccine. Severe side effects of these vaccinations are severe allergic reaction (1:55000), vaccine-associated neurotropic disease/post-vaccinal encephalopathy (1:125000) and vaccine-associated viscerotropic disease/multi-organ failure (1:400000). For travelling into countries where yellow fever is endemic, vaccination is mandatory. The side effects seem to be age-related and occur increasingly with progressive age or in young children. The vaccination is contraindicated in children

below 9 month and during pregnancy. Analysis of yellow fever vaccines adverse events demonstrated an increased frequency of serious adverse events in persons age 60 years and older. The risk of viscerotropic side effects in <65 years is 1:400000, in a population of 65–75 years of age 1:40000 and in >75 years of age 1:4000. A failure to be vaccinated or being documented can lead to a refusal of entry into other countries or to a certain time in quarantine when leaving the area where yellow fever occurs. If there is a clinical indication against receiving yellow fever vaccine (e.g. children <9 month or poor immune status), a written medical exemption can be granted, to enable to travel to these countries without vaccination.

Absolute contraindications for a yellow fever vaccination are:

- Allergy against the vaccine or egg protein
- Age < 6 months
- Immunodeficiency
- Neoplasia
- Transplantations
- Immunosuppressive therapies

Relative contraindications for a yellow fever vaccination are:

- Age 6–9 months
- Age > 60
- Asymptomatic HIV infections and CD4+ T lymphocytes 200–499/mm^3 (15–24% of the total in children <6 years of age)
- Pregnancy
- Lactation

32.2.4 Others

Aedes aegypti spreads also the *Zika virus*. However, it is also sexually, intrauterine and perinatal transmitted. Currently the main distribution is countries in South and North America as well as the Caribbean Islands, Singapore and some countries in South Pacific Islands. Symptoms of Zika infection may be fever, rash, arthralgia, myalgia, headache and conjunctivitis. But in most cases, an infection is asymptomatic (~80%). These symptoms are lasting for several days to a week. The incubation period is 3–14 days but is likely to be a few days to a week. The diagnosis can be made via PCR or serology. Blood PCR can be detected only in the first week of the disease. Urine PCR can detect the virus up to 2 weeks. There is no specific treatment available. Deaths are unlikely. There is a potential risk during pregnancy, as microcephaly or other birth defects (~20%) may develop. The Zina virus cane be also transferred via semen and can affect unborn life.

Ross River virus (RRV) is transmitted by the bites of Culex annulirostris, Aedes vigilax, Aedes normanensis and Aedes notoscriptus in Australia, Papua New Guinea, parts of Indonesia and the Western Pacific Islands. The main transmission time is in the humid summer month from December till March. The main symptoms are fever, rash, headache, myalgia, arthralgia and fatigue. The initial symptoms with fever last usually for 1–2 weeks. Myalgia and arthralgia usually last longer. Symptoms of fatigue and depression can be late complications. The incubation time is between 3 days and 3 weeks. The diagnosis is made with IgM. There is only symptomatic treatment available.

Barmah Forest virus (BFV) is transmitted by the same species as the RRV. It mainly can be found in Australia. Many people don't develop any symptoms. The incubation time is 3–11 days. If symptoms appear, they are similar to the one of RRV. The initial symptoms last for 1–2 weeks, and the arthralgia and myalgia may last for 6 months. The diagnosis is made with IgM. There is only symptomatic treatment available.

Sindbis virus (SINV) is related to the Chikungunya virus. It is mainly transmitted via the Culex and Culiseta mosquitoes. It can be found in Europe, Africa, Asia and Oceania. The symptoms and the duration of the symptoms are quite similar to RRV and BFV. The diagnosis is made with IgM. There is only symptomatic treatment available.

The *o'nyong-nyong virus (ONNV)* is related to the Chikungunya virus but is restricted

to Africa. It has similar symptoms as the Chikungunya virus but has additionally mainly cervical lymphadenopathy, and the affected joins rarely show signs of an effusion.

32.3 Gastrointestinal Infections

Most of the gastrointestinal tract infections are caused by poor hygienic conditions of the travel destination. Occasionally ingested seawater can cause intestinal infections too. The main transmission routes are either food-borne or by contact. However, the most common cause for gastrointestinal infections is eating contaminated food. Old, warmed up food, salads, unpeeled fruits, poorly cooked food, contaminated water (ice and already opened bottles with refilled water) and ice cream often have substantial quantities of pathogens and pose a risk. Hence, the best protection against GI infections is avoiding contaminated food or drinks. Usually gastrointestinal infections last for a few days and are self-limiting. If diarrhoea contains blood or mucus in combination of high fever for more than 2 days, more thorough assessment is required. Blood and mucus without fever are most likely related to a parasitic disease. If fever is present, it's most likely a bacterial or viral disease. But also climate change by itself or dehydration may be caused by autonomic dysregulation gastrointestinal symptoms such as nausea, weakness, vomiting and diarrhoea.

With dehydration the DCI risk increases. Rehydration and supply of certain electrolytes such as sodium, chloride and potassium are the most important treatments for gastroenteritis. Fatigue is a common associated symptom. Tannins of black tea boiled for more than 10 min might be beneficial for diarrhoea. The consumption of bananas is recommended because of the high content of potassium. But the best options are rehydration preparations in form of drinks, powders or icy poles. Loperamide may slow down the peristaltic and give some relief from diarrhoea. Probiotics may support recovery. A low fibre diet is recommended in the active phase of diarrhoea. Administration of antibiotics is rarely necessary and indicated. It only is used for serious illnesses or symptoms.

32.3.1 Salmonellosis (Salmonella Typhimurium + Enteritidis)

- Reservoir: poultry or meals prepared with egg
- Incubation: 8–48 h
- Symptoms: fever, vomiting nausea, diarrhoea, occasionally blood and mucous in the stool
- Duration: 4–7 days
- Treatment: symptomatic; azithromycin 1 g OD for 5 days or ciprofloxacin 500 mg BD for 7 days or ceftriaxone 2 g OD

32.3.2 Typhus (Salmonella Typhi + Paratyphi)

- Reservoir: water and food
- Incubation: 1–2 weeks
- Symptoms: headache, myalgia, bradycardia, roseola in the abdominal area, continuous fever 39–40 °C, porridge – like diarrhoea, intestinal bleeding and decrease of the fever after 4 weeks
- Treatment: symptomatic; azithromycin 1 g OD for 5 days or ciprofloxacin 500 mg BD for 7 days or ceftriaxone 2 g OD; vaccination available

32.3.3 Shigellosis

- Reservoir: human, flies, food and faeces
- Incubation: 2–5 days
- Symptoms: fever, diarrhoea, sometimes with blood and mucus in the stool and severe abdominal pain
- Treatment: symptomatic; ciprofloxacin 500 BD for 5 days, norfloxacin 400 mg BD for 5 days or bactrim 160/800 mg BD for 5 days

32.3.4 ETEC (Enterotoxic *E. Coli*)

- Reservoir: food and water
- Incubation: 0–2 days
- Symptoms: mild to severe diarrhoea with fever and blood and mucous in the stool, most common cause for diarrhoea overseas
- Treatment: symptomatic; norfloxacin 400 mg OD and ciprofloxacin 500 mg OD

32.3.5 Amoebiasis (*Entamoeba histolytica*)

- Reservoir: food (particular strawberries) and water
- Incubation: 1–4 weeks
- Symptoms: diarrhoea like raspberry jelly, no fever! Blood and mucous in the stool, risk for developing a liver abscess
- Treatment: symptomatic, asymptomatic carrier, paromomycin 500 mg TDS for 7 days; invasive, tinidazole 2 g OD for 3 days or metronidazole 400 mg TDS for 7 to 10 days

32.3.6 Cholera (*Vibrio cholerae*)

- Reservoir: contaminated food and water
- Incubation: 0–5 days
- Symptoms: often mild GI symptoms, 5–10% develop severe symptom with nausea vomiting, rice water-like diarrhoea and severe dehydration, mortality risk of 25–50%
- Treatment: rehydration, electrolyte substitution; vaccination available; azithromycin 1 g single dose, ciprofloxacin 1 g single dose

32.3.7 Hepatitis A

- Reservoir: food (in particular sea food) and water
- Incubation: 15–50 days
- Symptoms: initial phase (2–7 days) – flulike symptoms, gastrointestinal, hepatomegaly; hepatic manifestation (4–8 weeks), no jaundice (approx. 70%), jaundice (30%) with dark urine, jaundice, pruritus; hepatitis A has no chronic form, rarely fatal (fatality is age dependent)
- Treatment: symptomatic, bed rest, avoidance of liver toxic substances (alcohol, medication); vaccination available

32.4 Japanese Encephalitis

Japanese encephalitis is caused by a *Flavivirus*, which is transmitted by mosquitoes (*Culex particularly C. tritaeniorhynchus*). The hosts are usually pigs and water birds. In humans there are usually not sufficiently high concentrations of virus to serve as a host. The distribution is the Asia, especially in rural areas. Epidemics occur every 2–15 years (◘ Fig. 32.6).

The transmission can occur throughout the year but frequently peaks in the rainy season. There are about 68,000 cases per year. Only about 1% of the patients are symptomatic. However, if symptoms develop, the mortality rate is 20–30%. Approx. 30–50% of patients who survive have long-term neurological or psychiatric complications. Mild courses of Japanese encephalitis may be accompanied by mild fever and headache. Severe cases show high fever, neck stiffness, photophobia, headache, disorientation, coma, convulsions, spastic paralysis or death. Consequential damages may be behavioural disorders, convulsions, paralysis and speech disorders. The diagnosis can be established with blood tests and lumbar puncture. There is currently no treatment option. The vaccination is usually well tolerated and available for prophylaxis.

32.5 Other Tropical Diseases

There are various tropical diseases, which are present in poorer countries causing more or less severe symptoms. These diseases are termed "neglected tropical diseases" (NTD). The more common NTDs are summarised in this chapter.

Geographic Distribution of Japanese Encephalitis Virus

Data Table: Countries in which Japanese encephalitis virus has been identified			
Australia	India	Pakistan	Sri Lanka
Bangladesh	Indonesia	Papua New Guinea	Taiwan
Brunei*	Japan	Philippines	Thailand
Burma	Laos	Russia	Timor-Leste
Cambodia	Malaysia	Saipan	Vietnam
China	Nepal	Singapore	
Guam	North Korea	South Korea	

*No data but presumed to be endemic.

Fig. 32.6 Japanese encephalitis 2007. (CDC)

32.5.1 Trypanosomiasis

There are three main conditions caused by these pathogens.

The *African trypanosomiasis (sleeping sickness)* is transmitted by the tsetse fly. The distribution is only in some countries of the sub-Saharan Africa. Seventy percent occur in the Democratic Republic of Congo.

Tsetse flies are mainly found in rural areas. There are two forms causing sleeping sickness, *T. brucei rhodesiense* and *T. brucei gambiense*. *T. brucei gambiense* has an incubation period of months to years and *T. brucei rhodesiense* weeks to months. The initial phase is the haemolytic-lymphatic phase, in which pathogens replicate in tissues, blood and lymphatic tissues. Symptoms are intermittent fever, headache, myalgia and pruritus. Additionally, a painless, indurated chancre on the skin 5–15 days after the bite and lymphadenopathy (axillary and inguinal) can be associated. In the second phase, the CNS affected causes continuous headache, behavioural disorders (mood swings and depression), delirium, sensitivity disorders, coordination problems and disruptions of the sleeping cycle (daytime somnolence). The diagnosis is mainly made clinically. Only for the T. b. rhodesiense, a blood test (centrifuged or wet preparation) to

Table 32.4 Treatment of sleeping sickness

Species	Drug of choice	Adult dosage
T. brucei rhodesiense, haemolymphatic stage	Suramin	1 gm IV on days 1, 3, 5, 14 and 21
T. brucei rhodesiense, CNS involvement	Melarsoprol	2–3.6 mg/kg/day IV × 3 days. After 7 days, 3.6 mg/kg/day × 3 days. Give a third series of 3.6 mg/kg/d after 7 days.
T. brucei gambiense, haemolymphatic stage	Pentamidine	4 mg/kg/day IM or IV × 7–10 days
T. brucei gambiense, CNS involvement	Eflornithine	400 mg/kg/day in 4 doses × 14 days

detect the parasite is available. Examination of buffy coat increases sensitivity. A biopsy of the lymph node to detect the pathogens can be diagnostic for *T. brunei gambiense* or be used for a culture and PCR. The card agglutination test for trypanosomiasis (CATT) is a field test suitable for mass population screening in endemic areas for T. b. gambienses but has a low specificity and is hence only used for identifying suspected cases. All diagnosed patients need to have their cerebrospinal fluid examined for staging, which influences treatment options (Table 32.4). The treatment is dependent on the pathogen and the staging. If untreated, infections of both forms lead to coma and death.

Leishmaniasis has three forms: visceral, cutaneous and mucosal (Kala-Azar). There are about 30 different pathogens, from which approx. 20 are held responsible for these diseases. The disease is transmitted by mosquitoes or sandflies (*Phlebotomus* and *Lutzomyia*). The cutaneous form is the most common one, which causes skin ulcerations. Typically this form appears weeks to months after the initial mosquito bite. Initially papules are formed, which later ulcerate. They can be painful or painless. The visceral form affects organs, especially the liver, spleen and bone marrow. Therefore, this form can be quite dangerous. The changes occur within months and years. Hepatosplenomegaly and pancytopenia develop. The mucus form is rare. Ulcerative changes of the mucous membranes (e.g. nose, mouth and throat) are typical for this. Endemic areas for leishmaniasis are East Africa, some Arabic countries, India, Bangladesh, Brazil and some other South American countries. Historically, the diagnosis was made by taking a biopsy (skin, bone marrow or other tissues) for culture. Now PCR or serological testing with high sensitivity replaced biopsies for making diagnosis. As the visceral disease is fatal without treatment, it needs to be treated in any case. All other forms require normally no treatment. Following medication is available:

- Pentavalent antimonial (Sb^V) compounds (20 mg per day IV or IM for 28 days)
- Liposomal amphotericin B (3 mg OD IV on day 1–5, 14 and 21)
- Miltefosine (in adults > 45 kg 50 mg 3 times daily for 28 days)
- Azoles (fluconazole 200 mg OD for 6 weeks, itraconazole 200 mg BD for 28 days, ketoconazole 600 mg OD for at least 28 days)
- Paromomycin (uncommonly used)
- Pentamidine isethionate (uncommonly used)

The *Chagas' disease* is transmitted via an insect bite ("kissing bug") or by contaminated food. It occurs in Central and South America. It has

Table 32.5 Treatment of Chagas' disease

Drug	Age group	Dosage and duration
Benznidazole	<12 years	5–7.5 mg/kg per day orally in two divided doses for 60 days
	12 years or older	5–7 mg/kg per day orally in two divided doses (max 300 mg/d) for 60 days
Nifurtimox	≤10 years	15–20 mg/kg per day orally in three or four divided doses for 90 days
	11–16 years	12.5–15 mg/kg per day orally in three or four divided doses for 90 days
	17 years or older	8–10 mg/kg per day orally in three or four divided doses for 90 days

an acute and chronic phase. In the acute phase within 1–2 weeks after the infection, localised swelling of the area of the insect bite (skin or mucous membranes), lymphadenopathy, bilateral orbital oedema, meningoencephalitis and myocarditis can occur. 20–30% of all infections become chronic, causing arrhythmias with risk of "sudden death", cardiomyopathy and enlargement of the oesophagus (megaoesophagus) or of the colon (megacolon) even after years or decades. The cardiomyopathy consists of fibrosing myocarditis, causing arrhythmia (RBBB, left anterior fascicular block, ST changes, premature ventricular beats and bradycardia) and ventricular failure. The diagnosis in the acute phase is made by a blood smear (thick and thin) to visualise the parasite. A serological test is also available.

Treatment is recommended in the acute phase and in patient up to the age of 50 and no advanced cardiomyopathy with chronic Chagas' disease (Table 32.5). In age groups above 50, benefits and risk need to be outweighed.

32.5.2 Helmetides

Worm infections are a major problem in underdeveloped countries. They occur mainly in rural areas. These conditions may cause insignificant symptoms but also lead to serious consequences or even cause death. Because some dive sites are located far away from tourist centres, these infections should be discussed before travelling.

Ascariasis (Roundworm)

This kind of roundworm is found in the tropical and subtropical regions of Africa and Southeast Asia. The transfer follows on oral intake of eggs by contaminated food. The larvae are entering the bloodstream after hatching in the intestine. They reach the lungs via the blood and penetrate the lung tissue, and the larvae can be coughed up. If the sputum is swallowed again, the larvae reach the intestine, mature there within the next 2–3 months and lay eggs, which are then excreted via the faeces. The adult worms live about 1–2 years. Infection is usually asymptomatic. However, abdominal pain, flulike symptoms, allergic skin manifestations, malnutrition, productive cough and a stridor can occur. The diagnosis can be made by examining the faeces (eggs, worms) or sputum (larvae).

Ancylostomiasis (Hookworm)

Hookworms are found in tropical and subtropical regions of Africa and Latin America. The transmission is percutaneously or orally by ingestion of contaminated soil. In contaminated soil the larva is able to survive for about 3–4 weeks. Larvae can penetrate the skin and enter the blood and reach the alveoli in the

lungs. From there they ascend in the airways, are swallowed again and finally get into the intestines. There larvae mature to adult worms. The worms attach themselves to the wall of the intestine and feed on blood. The eggs are excreted in the faeces and reach again the soil. The eggs can survive up to 2 years. Common symptoms are pruritus and rash at the entry site, abdominal pain, diarrhoea, weight loss, anaemia and extreme fatigue. The diagnosis can be made of the faeces.

Filariasis

Filariasis has a worldwide distribution in tropical and subtropical regions. It is caused by *Wuchereria bancrofti* and *Brugia malayi*. It is transmitted by mosquitoes. The infective filariform grow inside mosquitoes and enter via its saliva during the bite. They migrate to the lymphatic vessels and lymph nodes where they develop into adults. They can live there for about 6 years. The female worms produce microfila, which are circulating in the blood. Absorbed by mosquitoes they develop within 1–2 weeks to the infective filariform. Initially there are no symptoms. Later lymph oedema in extremities or genitals is a common symptom. In men hydrocele can develop. The skin typically swells and hardens ("elephantiasis"). The diagnosis is made via the blood. Detection in the blood smear has to be performed at night, as larvae only circulate in the blood at night. There is also a serological detection of anti-filaria IgG4 available for diagnosis. The treatment with DEC is the drug of choice. Concurrent disease of Loa Loa or onchocerciasis is a contraindication for DEC, because of the serious side effects (encephalopathy and deaths). Ivermectin is used as a prophylaxis, but not as a therapy.

Schistosomiasis (Bilharziose)

Schistosomiasis can be found in tropical and subtropical regions worldwide. In addition to malaria, it is the most common parasitic disease. The parasite schistosoma is housed in freshwater snails. By being exposed to freshwater in these regions, infections can occur. The eggs are excreted in urine or faeces of the host. They hatch under optimal conditions and release miracidia. These miracidia infect freshwater snails and develop into sporocysts. These develop into cercariae and get released into the water, where they can penetrate the skin of the host. There, they shed their tail and become schistosomulae and migrate to the liver. In the liver they mature into adults. The paired adult worms migrate to the bowel and bladder, where they lay the eggs. A rash ("swimmers itch") may develop at the entry site on the skin. Suprapubic pain and haematuria, abdominal pain, myalgia, fever, swelling of the lymph nodes, liver and spleen enlargement and eosinophilia can be additional symptoms. The risk of bladder cancer is increased with schistosomiasis. The diagnosis can be made in the stool and urine. The maximum excretion of eggs in the urine is between 12 and 3 pm.

Trichuriasis (Whipworm)

Whipworms have a worldwide distribution in the humid tropics. The eggs are orally absorbed via soil or unwashed vegetables or fruits. The whipworm grows in the large intestine. The eggs are excreted via the faeces. In the soil the eggs pass through various stages before getting absorbed again. The symptoms are abdominal pain, chronic diarrhoea, nausea, vomiting, inflammation of the intestine, anaemia and eosinophilia. The diagnosis is made with a stool sample. The treatment on the infection is dependent on the parasite (Table 32.6).

32.5.3 Leptospirosis

Leptospirae are long, motile spirochetes. They have a worldwide distribution, but infections occur more commonly in tropical and subtropical regions. They spread through infected urine, which enters water or soil. Leptospires can survive for several weeks and

Table 32.6 Overview over the common tropical worm infestations

Drugs	Ascariasis	Ancylostomiasis	Filariasis	Schistosomiasis	Trichuriasis
Albendazole single dose 400 mg	x	x			x
Mebendazole 100 mg/d for 3 days or single dose 500 mg	x	x			x
Ivermectin single dose 200 µg/kg/bw	x				x
Diethylcarbamazine (DEC) 6 mg/kg/bw/d for 1–12 days			x		
Pyrantel 11 mg/kg/bw For 3 days (max. 1 g)		x			
Praziquantel twice daily for one days 4 h apart, 40[a] or 60[b] mg/kg/bw				x	

[a]For S. Mansoni, S. Haematobium, S. Intercalatum; [b]for S. Japonicum, S. mekongi

months. Infections can be caused by contact with either direct contact with the urine or other body fluids except saliva as well as with contaminated soil and water. The bacteria enter the body through the skin or mucous membranes. A broken skin increases the risk of infection. Increased risk is after heavy rainfall or flooding. The incubation period is usually 5–14 days, but can range from 2–30 days. Symptoms vary greatly. Usually sudden onset of headaches, fever, chills, myalgia, nausea and vomiting, diarrhoea, rash and jaundice are common signs of the first phase for 3–8 days. If the patient doesn't recover the second phase (Weil's disease) develops, with renal failure, ARDS, hepatomegaly, jaundice, haemorrhage and meningitis. This has a fatality rate of 1–5%. Untreated symptoms can persist for several months. Treatment is either doxycyclin 100 mg BD or benzylpenicillin 1.2 g QID or ceftriaxone 1 g OD for 7 days.

32.5.4 Rickettsial (Spotted and Typhus Fever) and Related Infections (Anaplasmosis and Ehrlichiosis)

Infections caused by *Rickettsia*, *Orienta*, *Ehrlichia*, *Neorickettsia*, *Neoehrlichia* and anaplasma are summarised as Rickettsial infections. Rickettsias are divided into the typhus group and the spotted fever group. Orienta make up the typhus group. The reservoir is found in mainly animals, like rodents, but some species are found in fish. The vector is commonly ticks. In scrub typhus the vectors are larval mites. Others have fleas and lice as a vector. Infection occurs either by bites of the vectors or by direct contact, inoculation or inhalation of contaminated fluids or faeces. The clinical presentation varies. Mild symptoms are headache, myalgia, abdominal pain, cough and rash. Some rickettsial infections,

like Rocky Mountains and Brazilian spotted fevers, Mediterranean spotted fever, scrub typhus and endemic typhus, have a fatality rate up to 20–60%. Diagnosis is made clinical and by serology. The treatment should be started early by suspicion as serology reports can take quite some time and a delay in treatment may be fatal. Doxycyclin 100 mg BD for 7 days or azithromycin 500 mg OD at the first day 250 mg OD for further 4 days are the antibiotics of choice.

32.5.5 Q-Fever

Q-fever is a zoonosis caused by the protozoa *Coxiella burnetii*. The bacterium is quite resilient due to its sporelike life cycle and remains virulent for months even up to more than a year. The primary reservoir is cattle, goats, sheep and other wildlife like kangaroos, rats and cats. Rarely is it transmitted by tick bites or by ingestion of unpasteurised milk or dairy products. The incubation time is usually 2–3 weeks but can range from 2 days to 6 weeks. The initial acute Q-fever comes with sudden onset of high fever up to 40 °C, headache (retrobulbar), myalgia, chills, non-productive cough and sweats. The symptoms settle within 5–14 days. 50% of all infections are however asymptomatic. Often thrombocytopenia and abnormal LFTs are found. Complications are ARDS, endocarditis and meningoencephalitis. The diagnosis is based on detecting phase II and phase I antibodies (IgG) 4 weeks apart. The initial test (phase II) should be taken at the end of the first week of illness. IgM and IgG rise almost at the same time. A fourfold rise is diagnostic. An initial negative titre doesn't rule out Q-fever. Seroconversion occurs usually between days 7 and 15 but is almost always present by 21 days. PCR testing can be used in the first 2 weeks but before antibiotic administration. However, a negative PCR result doesn't rule out Q-fever. Chronic Q-fever develops in 0.2–4%. It can result in endocarditis, aneurysms, osteomyelitis, hepatitis, neurogic (mononeuritis, optic neuritis), pulmonary (interstitial fibrosis, pseudotumor) and renal (glomerulonephritis) disease. Chronic Q-fever usually develops shortly after the infection. However, chronic endocarditis may not come apparent until 2–4 years or even longer. Chronic fatigue syndrome is described in approx. 10%. Typically in chronic Q-fever, the initial IgG titre is increasing (>1:800). The treatment for acute Q-fever is doxycyclin 100 mg BD for 14 days or for at least 3 days after fever subsides and until clinical improvement. As serological confirmation takes time, treatment should not be delayed. Early treatment is effective at preventing severe complications. For chronic Q-fever, 18 months of doxycyclin 100 mg BD and hydroxychloroquine 200 mg TDS is recommended as standard treatment.

32.6 Rabies

Rabies has an almost worldwide distribution. More than 95% of deaths occur in Africa and Asia. About 40% are children under 15 years of age. Dogs are the main vectors. In Asia, there is also a risk of transmission through monkeys. In addition to other diseases, like the Lyssavirus, bats or flying foxes can transfer rabies. It is transmitted by bites or scratch wounds but also by inoculation of saliva onto mucous membranes or eye of an infected animal. Thorough cleaning of the wound and vaccination within hours can prevent the disease.

The incubation period is usually 1–3 months but can be less than 1 week and more than a year. Initial symptoms include paraesthesia in the wound area. The disease can pass in two forms. The *hyperactive* form (70%) shows up with hyperactivity, manic behaviour, paranoia, hallucinations, delirium, hydrophobicity and occasionally aerophobia (triggered by the extremely painful spasms in the larynx area). The *paralytic form* (30%) is characterised by a slow but steady increasing paralysis. The paralysis begins in the area of the infection. The diagnostics can be established on the animal that has inflicted the wound. The tissue samples of the animal are taken from the brain (brainstem and cerebel-

lum). The diagnosis in humans is difficult and unreliable. Investigation of blood (antibodies), saliva (PCR), spinal fluid (antibodies) and skin biopsies (rabies Antigen) are available. The vaccine and the immune globulin can be given during pregnancy. Typical side effects of the vaccine are headache, myalgia, malaise, fatigue and nausea.

Treatment after potential infection (post-exposure prophylaxis PEP) includes:

- Irrigation of the wound for a minimum of 15 min and washing of the wound with water, soap, iodine or other disinfecting substances
- Rabies vaccine
- Rabies immunoglobulin into the wound area within 7 days after the first vaccination

Following data should be recorded when a rabies vaccine is given overseas:

- Address, email and telephone of the practice or hospital
- Date of vaccinations
- Batch number, name of the vaccine and manufacturer
- How many vaccinations are given
- Application: subcutaneous or intramuscular injection

WHO recommends the following approach with potential rabies after animal contact:

- *Category 1*: Feeding of animals, touching animals or being licked at the intact skin; no PEP
- *Category 2*: Nibble of unprotected skin, minor scratches without bleeding; immediate PEP and rabies vaccination
- *Category 3*: Single or multiple bites (transdermal), scratches, licking of open wounds, mucous membrane contact with saliva, contact with bats or fruit bats; instant PEP, rabies vaccination and rabies immunoglobulin

Vaccination against rabies is recommended for:

- Travellers, who for more than 1 month in areas, in which rabies is present
- Professions that deal with bats or fruit bats
- Professions, in which might get with rabies in contact (e.g., veterinary surgeon or nurse)
- Laboratory workers who handle objects with rabies or Lyssavirus
- After animal contact category 2 + 3

Pre-exposure prophylaxis (PreP) includes three vaccinations on day 0, 7 and 21–28. The dose is 0.1 ml intramuscularly or subcutaneously. The vaccination lasts for 10 years. Follow-up vaccinations (post-exposure prophylaxis = PEP) include four vaccinations on day 0, 3, 7 and 14. The dose is 1.0 ml intramuscularly. Immunocompromised patients should receive five vaccinations with an additional vaccination on the 28th day. With previous vaccinations, two vaccinations are recommended on day 0 and 3 after exposure. It is not recommended to change the brand or the manufacturer during the course of vaccinations. However, it is possible, if that particular vaccine is not available. Immunoglobulin should be administered with the first vaccination. The dose is 20 IU/kgbw. The immunoglobulin preferably should be given in proximity of the wound. The immunoglobulin can be diluted, if the wounds is large, to enable to cover the entire wound area. The immunoglobulin is not recommended, if the first vaccination was given more than 7 days ago, if PreP or PEP was completed or if an adequate serologic detection of VNAb titres (≥0.5 IU/ml) is present.

To avoid infection, no animals should be fed. Bringing your own food or carrying items like handbags, water bottles, etc. should be avoided, if you stay in the range of monkeys. Distance should be maintained to stray cats and dogs.

32.7 MERS

The Middle East respiratory syndrome (MERS) is caused by a corona virus. Corona viruses can cause mild flulike symptoms but also severe symptoms like the severe acute respiratory syndrome (SARS). The MERS-CoV occurs

mainly on the Arabian Peninsula (Iran, Jordan, Kuwait, Lebanon, Oman, Qatar, Saudi Arabia, United Arab Emirates and Yemen). But through international travel, it can spread worldwide. Recently it resulted in some cases in Korea. MERS has 37% mortality. The disease is transmitted through droplets or direct contact. The MERS-CoV also has a wide range of symptoms, from mild common cold symptoms and infections of the upper respiratory tract to a rapidly progressive pneumonitis, respiratory failure, septic shock and multi-organ failure. It seems the MERS-CoV has a low virulence, since the transmission occurs usually only through close contact by human to human, such as the care of a person suffering from MERS. Camels seem to be the original reservoir. Mild forms with fever and mild respiratory symptoms, MERS should be considered, if close contact with infected people existed prior to these symptoms.

MERS can be asymptomatic but also lead to respiratory failure and death. Typical symptoms include fever, cough and shortness of breath. Pneumonia or pneumonitis is often associated with MERS. Sometimes gastrointestinal symptoms such as diarrhoea and vomiting can occur. It has a high mortality of 36%. The treatment depends on the severity of the disease. Caution in contact with camels in affected countries should be taken. Eating insufficient heated camel meat and milk should be avoided.

A suspicion of MERS should be considered in individuals with the following risk profile:

- Fever and pneumonia/pneumonitis and stay in endemic areas or contact with a symptomatic person from an endemic area within 14 days before onset of symptoms
- Fever and pneumonia/pneumonitis and hospitalisation in endemic areas or contact with camels and camel products in an endemic area within 14 days before onset of symptoms
- Fever and pneumonia/pneumonitis and contact with a MERS diseased person within 14 days before onset of symptoms
- Cluster of patient (especially medical personnel) with severe respiratory symptoms with unclear aetiology

32.8 Tuberculosis (TB)

Tuberculosis is caused by an acid-resistant *Mycobacterium*. *M. tuberculosis* is responsible for tuberculosis in more than 95%. It has global distribution but occurs more frequently in countries with low hygienic standards. Tuberculosis spreads around the globe through international travel and immigration. It also shows a rising rate of resistances to conventional therapies. The time between the initial infection and tuberculin conversion takes approx. 8 weeks. The transmission is caused by droplets. Initial infections can be asymptomatic or cause unspecific symptoms such as cough, night sweats, loss of appetite, fatigue or erythema nodosum. People with normal immunity develop symptoms of tuberculosis only to 10%. The initial infection usually turns into latent tuberculosis. Tuberculosis can affect other organs to approximately 20%. The latent tuberculosis can be reactivated at a later stage when the immune system is weakened. The tuberculosis has three stages:

- *Exudative stage:* Caseation with cavern formation or caseous pneumonia
- *Productive stage:* Tubercle formation
- *Secondary changes:* Scarring and calcification

Complications of primary infection are hilum lymph node tuberculosis, pleurisy, miliary tuberculosis, caseous pneumonia and Landouzy sepsis (usually only people with immunodeficiency).

The diagnosis can be made with the tuberculin skin test (TST/Mendel Mantoux). 3 days after the strictly intradermal injection of the substance, the induration at the injection site is measured. An induration of >5 mm may be suggestive of tuberculosis. It is considered a positive test if either the patient has a radiological proof, had close contact with someone with tuberculosis, and has symptoms of tuberculosis, is HIV positive or suffers from immunodeficiency. An induration >10 mm is considered as positive, when the patient who travelled to a country with high TB prevalence

is an iv. drug user, homeless and a resident of nursing home or prison and has diabetes mellitus, silicosis, M. Hodgkin's or end-stage renal failure. An induration >15 mm is considered as evidence of tuberculosis without any risk factors or symptoms. The TST can be negative in the first 8 weeks after an infection as well as in patients suffering from miliary tuberculosis, M. Hodgkin, sarcoidosis, viral infections, and lowered immunity, receiving an immunosuppressive therapy or at high age. A false-positive test can occur after multiple TSTs, after vaccination against tuberculosis and infection of other mycobacteria. The interferon-γ test (QuantiFERON® TB gold) offers an alternative testing method. This test has the same sensitivity as the TST but a higher specificity. Moreover, this test is a confirmation test and isn't affected by previous BCG-immunisations. It consists of three parts, the control (to determine the baseline-interferon-γ), mitogen control (determining the ability of an immune response) and antigen detection (detection of prior infections). A CXR may demonstrate caverns or hilar lymph nodes, but is not a diagnostic tool to exclude tuberculosis.

The treatment duration of uncomplicated tuberculosis is 6 months, of complicated tuberculosis 9–12 months (◘ Table 32.7). It's a combination treatment of different drugs.

Medications for the tuberculosis treatment are:

- *Isoniazid*: 5 mg/kgbw, max. 300 mg /d; side effects: elevated serum transaminases, polyneuropathy, prophylaxis to avoid side effects of pyridoxine 40–80 mg/d
- *Rifampicin*: 50 mg/kgbw, max. 600 mg/d; side effects: elevated serum transaminases, cholestasis, anaphylaxis, thrombocytopenia and flu syndrome
- *Pyrazinamide*: 25 mg/kgbw max. 1500–2500 mg/ d; side effects: elevated serum transaminases, hepatitis, nausea, flush, myopathy, arthralgia and hyperurikaemia
- *Ethambutol*: initial 25 mg/kgbw, max. 2500 mg/d; side effects: retrobulbar neuritis

◘ **Table 32.7** Treatment of uncomplicated and complicated tuberculosis

2 Month	4 Month
Isoniazid	Isoniazid
Rifampicin	Rifampicin
Pyrazinamide	
Ethambutol	

A vaccination BCG vaccine is not recommended due to its side effects and the lack of efficacy.

32.9 Travel Vaccination

All vaccinations should be given 28 days before travelling. Minimum time for a sufficient protection is 2 weeks (◘ Table 32.8).

32.10 Diving Organisations

32.10.1 Description

DAN

Divers Alert Network (DAN) is a non-profit organisation for divers. They provide medical information and articles, diving insurance, life insurance and travel insurance. They also offer courses, support and research. DAN has an international hotline for support and coordination of diving accidents but also for general medical advice overseas.

EUBS

European Underwater and Baromedical Society (EUBS) is a European organisation for diving and hyperbaric medicine. They provide guidelines for hyperbaric treatment and training of medical professionals for the hyperbaric medicine.

GETÜM

The German organisation for diving and hyperbaric medicine is the "Gesellschaft für Tauch- und Überdruckmedizin" (GETÜM).

Table 32.8 Travel vaccinations

Vaccine	Combinations	Vaccination schema	Comments
Hepatitis A (e.g. Havrix®)	(Twinrix: Hepatitis A + B, Vivaxim: Hepatitis A + Typhus)	Two vaccinations (0 and 6 month)	
Hepatitis B (e.g. Engerix®)	(Twinrix – hepatitis A + B)	Three vaccinations (0, 2 and 6 month)	
Influenza (e.g. Vaxigrip®)		Annual	Updated influenza A + B
Measles (e.g. MMR-Priorix®)	Measles + mumps + rubella	Two vaccinations (0 and 6 months) no further vaccinations necessary	
Polio (Ipol®)	Boostrix: diphtheria + tetanus + pertussis + polio Infarix: diphtheria + tetanus + pertussis + polio + hepatitis B + *Haemophilus influenzae* Type b	After three vaccination (0, 2 and 6 months) vaccinations every 10 years (only for polio or Boostrix)	
Japanese encephalitis (e.g. Jespect® or Imojev®)		Jespect: two vaccinations 28 days apart, further vaccinations within the two years (between first and second year).	Imojev: Only single dose required (only available in Australia)
Meningococcus (quadrivalent meningococcal conjugate vaccines, e.g. Menveo®, Nimenrix®)		Every 3 or 5 years	Menveo or Nimenrix preferred for protection overseas, Menveo: Meningococcal group A, C, W_{135} and Y conjugate vaccine; Nimenrix Meningococcal group A, C, W_{135} and Y tetanus toxoid conjugate vaccine
Rabies (e.g. Rabipur®)		Three vaccinations (day 0, 7 and 21 or 28) further vaccination with antibody-titre ≥0,5 IE/ml	Post-exposure treatment after vaccination recommended with WHO category II and III; also with I, if it can't be clearly defined: two doses at day 0 and 3
Tuberculosis			Generally not recommended as risk outweighs benefits
Typhus (e.g. Typhim® or Vivaxim®)	Vivaxim: hepatitis A + typhus	Every 3 years	

(continued)

Table 32.8 (continued)

Vaccine	Combinations	Vaccination schema	Comments
Cholera (e.g. Dukoral®)		Two doses at least 1 week apart	Commonly not required, protection for approx. 2 years (adults); protection against *Vibrio cholerae* and ETEC
Varicella		2 vaccinations	
Yellow fever (e.g. Stamaril®)		Single dose	Certificate is valid for 10 years, a new vaccination may be required after 10 years to renew the certificate

They provide guidelines for hyperbaric treatment and training of medical professionals for the hyperbaric medicine.

SPUMS

The South Pacific Underwater Medicine Society (SPUMS) is the organisation for diving and hyperbaric medicine in Australia. They provide guidelines for hyperbaric treatment and training of medical professionals for the hyperbaric medicine.

UHMS

The Undersea and Hyperbaric Medical Society (UHMS) is the organisation for diving and hyperbaric medicine in the United States. They provide guidelines for hyperbaric treatment and training of medical professionals for the hyperbaric medicine.

VDST

The organisation for German recreational divers "Verband Deutscher Sporttaucher" (VDST) provides diving curses, information about environmental issues, research, sportive diving activities and an emergency hotline.

32.10.2 Contact Details

- DAN Europe: C/da Padune, 11 – 64026 Roseto – Italy, Tel: +39-085-893-0333, Fax: +39-085-893-0050; Emergency contact: +39-06-4211-8685
- *DAN International*

  America: 6 West Colony Place, Durham, NC 27705 USA, Tel: +1-919-684-2948 or +1-800-446-2671, Fax: +1-919-490-6630, or +1-919-493-3040 (medical); Emergency-Hotline: +1-919-684-9111.

  Brazil: 150 – Térreo- Edif. Galleria Plaza, Campinas – SP, CEP: 13091–611, Brazil; Office: Tel: +1-919-684-2948, Emergency-Hotline: +1-919-684-9111.

  Japan: Japan Marine Recreation Association, Kowa-Ota-Machi Bldg, 2F, 47 Ota-Machi 4 Chrome Nakaku, Yokohama City, Kagawa 231–0011,Japan; Office: Tel: +81-45-228-3066, F ax: +81-45-228-3063; Emergency-Hotline: +81–3–3812-4999;

  Asia-Pacific:PO Box 384, Ashburton, VIC3147, Australia;Office: Tel: +61-3-9886-9166, Fax: +61-3-9886-9155, Emergency-Hotline: 1800-088-200 (inside Australia), +61-8-8212-9242 (outside of Australia).

  Southern Africa: Private Bag X197, Halfway House, Midrand 1685, South Africa; Tel: 0860–242-242 (Sharecall in South Africa), +27-11-266-4900 (Int.), Fax: +27-11-312-0054 (Int.); Emergency-Hotline: 0800–020-111 (inside Southern Africa), +27-828-10-60-10 (outside Southern Africa),

- *EUBS*: webmaster@eubs.org
- *GTUEM*: c/o BG-Unfallklinik, Professor-Kuentscher-Str. 8, D-82418 Murnau, Tel: +49-8841-48-2167, Fax +49-8841-48-2166
- *SPUMS*: 630 St Kilda Road, Melbourne, Vic, 3004
- *UHMS*: 631 US Highway 1, Suite 307, North Palm Beach, FL 33408, Tel.: +1-919-490-5140, Fax: +1-919-490-5149
- *VDST*: Berliner Str. 312, 63067 Offenbach, Tel.: +49-699819025, Fax: +496998190298

32.11 Web Links

- *CDC*: ▶ www.cdc.gov
- *DAN*: ▶ www.diversalertnetwork.org
- *DAN Europe*: ▶ www.daneurope.org
- *Emedicine*: ▶ http://emedicine.medscape.com
- *EUBS*: ▶ www.eubs.org
- *GTUEM*: ▶ www.gtuem.org
- *The Rubicon Research Repository*: ▶ http://archive.rubicon-foundation.org
- *SPUMS*: ▶ www.spums.org.au
- *UHMS*: ▶ www.uhms.org
- *VDST*: ▶ www.vdst.de
- *WHO*: ▶ www.who.int.

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