17. Traveling with HIV

Thomas Weitzel

HIV patients are fond of traveling. In 1995, an American study revealed that 20% of HIV patients had traveled in the previous two years, with 60% of those having visited developing countries (Kemper 1995). In a 1996 study from the Netherlands, 20% of the HIV patients reported traveling abroad within the past year (Simons 1999). Ever since, increasing expectancy and quality of life have caused a further rise in the travel activities of HIV patients.

Travel preparations

Depending on their immune status, HIV patients bear an increased risk of travel-associated complications. In particular, if CD4+ T-cell counts are below 200/µl, there is a substantial threat of severe gastrointestinal and other opportunistic infections, which can be acquired while traveling. Furthermore, the effectiveness of vaccinations in this group of patients is reduced.

Therefore, HIV-infected individuals should carefully plan their travel. According to the destination and style of travel, the latest travel advice should be observed. A general overview of travel recommendations can be accessed through different Internet sites (Frädrich 2000). Especially before traveling to tropical or subtropical countries, it is recommended to obtain additional information from travel medicine specialists. Long-term travelers should, in advance, clarify the treatment possibilities of HIV-related problems at their destination.

A first-aid kit for HIV-infected travelers should contain, besides the usual drugs (local antihistaminics, disinfectants, sun protection, analgesics, antipyretics, antiemetics, and antidiarrheals), an antibiotic for the empirical treatment of acute diarrhea (see below).

Antiretroviral therapy (ART)

A newly started antiretroviral regimen should be proven to be effective and well tolerated for at least three months before long-term traveling takes place. Depending on the destination and the activities planned, interruption of therapy can be considered. If ART is being continued during traveling, the following aspects should be considered:

- A sufficient amount of antiretroviral drugs should be packed, preferably in the hand luggage (suitcases can get lost…).
- The availability of the ART at destination should be checked beforehand. When necessary, prescriptions and a medical letter in English should be taken along.
- For some countries it may be useful to pack antiretroviral drugs in neutral packages because of entry regulations (see below).
Storage requirements for the drugs (refrigeration, etc.) must be checked in advance – especially when traveling over long distances.

Steps to cope with an unplanned therapy interruption during travel should be discussed with the patient in advance.

**General precautions**

The higher risk of gastrointestinal infections for HIV patients demands the adherence to the principles of food and water hygiene (see links below). The following food and drink are to be avoided:

- Raw fruit or vegetables that are not peeled
- Raw or undercooked meat or fish dishes
- Tap water
- Ice cubes made from tap water
- Unpasteurized milk or milk products
- Food prepared or distributed under insecure hygienic circumstances (e.g. street vendors)

Even brushing teeth or swimming carries the risk of swallowing small amounts of potentially contaminated water. In the lack of hygienic beverages, tap water should be boiled. In areas up to 2,000 meters above sea level, a boiling time of one minute kills all potential pathogens; at higher altitudes, the boiling time should be prolonged to three minutes. Chemical or filtration methods of water treatment are less reliable.

Certain vector-transmitted infections, e.g. leishmaniasis, pose a special risk to HIV-infected patients (see below). Repellents are helpful in avoiding those threats. Products containing at least 24 % DEET are internationally recommended. Sun protection has to be applied before repellent. Sleeping areas should be mosquito safe (a mosquito net is the best repellent!). Impregnation of clothes and mosquito nets with permethrine offers additional safety. Outdoors, long and bright clothes should be worn and outdoor stays during dawn or night ought to be avoided (see links).

Since condoms and lubricants abroad are not always of reliable quality, a sufficient amount of these products should be brought, to guarantee safe sex during the holiday.

Because of possible *Strongyloides stercoralis* infection (see below), direct skin contact to fecally contaminated soil should be avoided. It is wise to wear closed shoes and place a towel underneath when lying on the ground.

Precautions against zoonotic infections such as salmonellosis or cryptosporidiosis include proper hand washing following animal contact.

**Vaccinations**

A travel medicine consultation is an opportunity to check and complete routinely recommended immunizations such as tetanus/diphtheria, pneumococcal, influenza, and hepatitis B vaccinations. It has to be kept in mind that the southern hemisphere influenza season is from April to September, while in the tropics influenza can oc-
cur all year long. Additional immunizations have to be considered according to travel style, duration, and destination. Open immunization questions usually require the consultation of a specialized institution (see links). Further details on this issue can be seen in the chapter on vaccinations in this book.

**Malaria prophylaxis**

The interactions between antiretroviral drugs and drugs available for malaria prophylaxis, such as chloroquine, mefloquine, doxycycline, and Malarone™ (atovaquone/proguanil), are inadequately evaluated.

In healthy volunteers taking mefloquine (Lariam™) together with ritonavir, a 30% reduction of the steady-state plasma level of ritonavir was reported; however, mefloquine did not change the ritonavir level after a single dose of ritonavir (Khaliq 2001). The explanation is probably a reduced bile production caused by mefloquine. No relevant interactions seem to occur if mefloquine is coadministered with nelfinavir or indinavir (Schippers 2000).

Chloroquine is metabolized by CYP2D6, but is also significantly excreted by the kidneys; explicit data on interactions of chloroquine with HIV drugs are lacking. In vitro, chloroquine inhibits HIV replication and shows synergistic effects together with protease inhibitors (Savarino 2001 and 2004). On the other hand, PIs display an inhibitory effect on plasmodia (Parikh 2005). Whether these observations could have an impact on the clinical management of HIV infection or malaria is still uncertain.

Clinical data on the interactions of atovaquone and proguanil with HIV drugs are missing. In vitro data indicate that ritonavir causes a reduced level of atovaquone and an increased level of proguanil. Atovaquone decreases the indinavir level by 20% and increases the acyclovir level by 30%.

Doxycycline is not metabolized by the cytochrome p450 system. Thus, relevant interactions with HIV drugs are not anticipated.

Available data and clinical experience indicate that mefloquine as well as doxycycline and chloroquine can be safely and effectively used in patients taking antiretroviral therapy. Although clinical studies are lacking, the same applies for Malarone™. Thus, recommendations for malaria prophylaxis are not limited by concomitant HIV medication.

Common drugs for malaria stand-by treatment are chloroquine, mefloquine, Malarone™, and Riamet™ (artemether/lumefantrine). Both components of Riamet™ are substrates of CPY3A4; due to incalculable increases in drug exposure, Riamet™ is contraindicated with protease inhibitors (see Riamet™ product information). With this exception, HIV patients should follow the same recommendations as healthy travelers. However, mefloquine is often unfavorable because of frequent neurological comorbidity in HIV patients.

**Entry regulations and travel insurance**

Although contentious as a measure of health policy and not recommended by the WHO, more than 150 countries, including the USA, refuse entry to HIV infected individuals. This particularly affects long-term stays in connection with work or
Traveling with HIV

To avoid problems, information on entry regulations should be obtained beforehand. Peter Wiessner and Karl Lemmen’s brochure “Schnellfinder” provides an excellent and comprehensive overview on entry policies. In cooperation with David Haerry of the Swiss Aids Info Docu, a regularly updated version of this databank is available online (see links).

The American foreign ministry also publishes a list of countries with HIV-specific entry restrictions (see links). Under certain circumstances, e.g. visits to conferences, family members, or business travel, journeys to the USA are possible for HIV patients if they apply for a “visa waiver”. However, the procedure is time consuming and the passport endorsement can complicate further travel to the USA or other countries.

Travel insurances usually exclude existing illnesses and often refuse HIV patients explicitly. For that reason, special HIV travel insurances have been made available in the UK and USA (see links).

Special risks

Enteric infections

Reduced immunological defense and diminished gastric acid production increase the risk for gastrointestinal infections in HIV patients. Furthermore, bacterial enteric infections such as salmonellosis, shigellosis, and Campylobacter infections bear a high risk of bacteremia and relapse. Infections caused by Cryptosporidium sp., Isospora belli and microsporidia are dangerous due to chronicity. Therefore, HIV-infected patients must strictly observe proper water and food hygiene (Hayes 2003).

Prophylactic use of antibiotics, although reducing the prevalence of travel-associated diarrhea, is not generally recommended in HIV patients. In individual situations, e.g. HIV patients with advanced immunodeficiency traveling under poor hygienic conditions, prophylaxis with ciprofloxacin (500 mg per day) could be considered. In Southeast Asia, an increasing rate of quinolone resistance makes azithromycin a useful alternative. Because of widespread bacterial resistance, cotrimoxazole and doxycycline are not sufficient.

Travel-associated diarrheal diseases should be empirically self-treated for five to seven days with ciprofloxacin (500 mg per day) or alternatively azithromycin (400 mg per day). In afebrile episodes of non-bloody diarrhea, short-term use of loperamide is justified. Adequate oral rehydration has to be maintained.

Malaria

Malaria does not behave like an opportunistic infection. However, the details on the interaction between HIV and malaria are widely unknown. Malaria seems to increase HIV replication through proinflammatory cytokines. HIV-infected women appear to have a higher malaria risk. Malaria-HIV co-infection in pregnancy is associated with increased parasitemia and a higher incidence of prematurity as well as low birth weight (Ayisi 2003, ter Kuile 2004). Until recently, the clinical influence of HIV infection on malaria was considered to be small except for the above mentioned problems in pregnancy. However, new data on HIV-infected ma-
Malaria patients demonstrated a negative influence of the HIV infection on the clinical course of malaria (Grimwade 2004), a higher risk for severe malaria in patients with low CD4+ T-cell counts, and a high frequency of atypical malaria manifestation, e.g. respiratory or intestinal symptoms (Cohen 2005).

The efficacy of antimalarial prophylaxis and therapy is not influenced by HIV. Accordingly, recommendations for malaria therapy are generally applicable to HIV patients. As described above, drug interactions of antimalarial and HIV drugs are insufficiently established. The treatment of complicated malaria is especially problematic since the indicated drugs, quinine, quinidine, or artemisinin derivatives, are all metabolized by CYP3A4. The coadministration of these drugs with CYP3A4 inhibitors, especially protease inhibitors, efavirenz, and delavirdine, requires intensive care monitoring and, when possible, drug level monitoring.

**Measles**

Measles, considered on a global level, is a common infection. In 2002, more than 200 million measles cases with about 600,000 deaths were reported worldwide (WHO, 2004). In HIV-infected patients, measles often runs a severe course. American studies showed a mortality rate of 40%, mostly due to giant-cell pneumonitis (Kaplan, 1996). Non-immune HIV patients should therefore consider active or passive immunization before traveling to areas with a high prevalence of measles.

**Leishmaniasis**

Visceral leishmaniasis (kala azar), caused by parasites of the *Leishmania donovani* complex, is a life-threatening opportunistic infection with limited therapeutic options. An analysis of imported cases in Germany showed that most cases of visceral leishmaniasis were acquired in European Mediterranean countries, long-term travelers were affected in particular, and HIV patients had a higher infection risk than healthy travelers (Weitzel 2005). Most frequently, HIV patients with CD4+ T-cell counts below 200/µl are affected (Kaplan 1996). Due to the infection’s potentially extended latency period, symptoms can occur long after exposure in endemic areas. Diagnosis is challenging, mostly requiring cooperation with a specialized center. Cutaneous leishmaniasis does not seem to occur more frequently in HIV patients. Severely immunocompromised HIV patients must be informed of the risk of leishmaniasis even when traveling to Mediterranean countries. Preventive measures against mosquito bites should be followed in order to avoid leishmanial infections (see above); because of the vector’s small size, the use of an impregnated mosquito net of small mesh size is advisable.

**Tuberculosis**

Globally, tuberculosis is the most prevalent HIV-associated opportunistic infection. Before and after long-term travel to countries of high tuberculosis endemicity, a tuberculin skin test should be performed. Patients with a positive tuberculin skin reaction or with a known high risk exposure should receive a course of treatment for latent tuberculosis (see chapter “Tuberculosis”). HIV-infected individuals should avoid risk areas such as hospitals, prisons or homeless-shelters or wear adequate facemasks.
**Endemic mycoses**

Endemic mycoses are rare infections. Nevertheless, they are able to cause life-threatening opportunistic infections in HIV patients even years after stays in endemic areas. Most agents of endemic mycoses are thought to enter the pulmonary tract after inhalation of infective spores. In areas endemic for *Penicillium marneffei* (South East Asia, Southern China) and *Coccidioides immitis* (south-west parts of the USA, parts of Central and South America), increased exposure to dust or soil should be avoided (e.g. construction sites, agriculture, garden work, excavations, storms). *Histoplasma capsulatum* is prevalent worldwide in soil contaminated with bird and bat droppings. Exposure might happen during eco or adventure tourism and should be avoided by HIV-infected persons. In individual cases, e.g. severely immunocompromised HIV patients with a foreseeable contact to agents of endemic mycoses, primary prophylaxis can be considered. Depending on the expected pathogen, either fluconazole or itraconazole should be prescribed.

Another fungus causing severe infections in HIV patients is *Sporothrix schenckii*. This pathogen, which occurs worldwide, enters the body through cutaneous lesions.

**Sexually transmitted diseases**

A recent study reported the high sexual activity and frequency of risk behavior (unprotected sex) in young British tourists (Bellis 2004). In Germany, an estimated 5 to 10 % of HIV infections are acquired during holidays. HIV-positive travelers should be aware of the special risks that sexually transmitted diseases and HIV reinfection present to them.

**Other parasites**

Due to hygienic and climatic circumstances, the following parasitic pathogens are more frequently found in developing countries and carry the risk of severe infection in HIV patients:

- *Strongyloides stercoralis* is prevalent in most tropical and subtropical areas. The parasite is transmitted by cutaneous larval invasion after skin contact with contaminated soil. In HIV patients, there is the risk of a “hyperinfection syndrome” with a high fatality rate (Gompels 1991). Besides HIV infection, corticosteroid use seems to be an additional risk factor, as these drugs seem able to increase larval maturation triggering a cycle of massive autoinfection.

- *Trypanosoma cruzi* is endemic in large parts of Latin America. This protozoan causes Chagas disease and is transmitted by triatomine bugs. Chagas disease, which often persists asymptomatically for many years, can reactivate in severely immunocompromised HIV patients. In these cases, lesions radiologically resembling cerebral toxoplasmosis are often found in the central nervous system (Rocha 1994).

- *Babesia sp.*, prevalent worldwide, are able to cause infections in a broad spectrum of vertebrates and are transmitted by ticks. Severe infections, clinically mimicking malaria or manifesting as fever of unknown origin, mainly occur in
patients after splenectomy, but have also been reported in severely immuno-compromised HIV patients (Falagas et Klempner 1996).

- Free-living ameba (Acanthamoeba sp. and Balamuthia mandrillaris) are ubiquitous, living in soil and water. In HIV-infected and other immunocompromised patients, these organisms are capable of causing severe infections of the central nervous system (granulomatous encephalitis), as well as local infections of the skin and cornea (Sison 1995).

Medical problems after traveling

The threat presented by the diseases discussed in this chapter makes it imperative that any symptom occurring after travel be checked. Because most tropical diseases are quite rare in temperate countries, diagnosis is often delayed. An analysis of imported visceral leishmaniasis revealed a median time span of 85 days until the diagnosis was established (Weitzel 2005). Furthermore, tropical diseases often manifest atypically in HIV patients (Karp et Neva 1999). In any event, differential diagnosis of febrile syndromes in HIV-infected individuals is very broad; after traveling abroad the clinical situation can become even more complex needing close cooperation of HIV and Tropical Medicine specialists.

References


Links
- Travel Medicine
  http://www.cdc.gov/travel/
  http://www.who.int/ith/
  http://www.crm.de/
- Tropical Medicine institutions in Germany
  http://dtg.org/98.html
- German recommendations for malaria prophylaxis and therapy
  http://dtg.org/malaria.html
- Entry regulations and HIV-associated restrictions
  http://www.aidsnet.ch/linkto/immigration/
  http://travel.state.gov/travel/HIVtestingreqs.html
- Travel insurance and HIV infection
  http://www.nat.org.uk/
- Drinking water & mosquito protection