Respiratory infections and other diseases of close personal contact

Author: Dr Mike Townend, MB, ChB (Hons), Diploma in Travel Mdicine, Fellow of the Faculty of Travel Medicine of the Royal College of Physicians and Surgeons, Glasgow. Executive Committee member of the British Travel Health Association and member of the International Society of Travel medicine and the International Society for Mountain Medicine.

Viral respiratory tract infections

Viral respiratory tract infections are among the commonest illnesses in the general population but there is little published evidence about their incidence in travellers. It is reasonable to suppose that they occur as frequently in travellers but their symptoms are familiar, and travellers might not, therefore, report them as travel-related illness. If travellers are confined in close contact for prolonged periods, for example during air travel, they may transmit viral infections by means of respiratory droplets. Such spread is likely to occur only to adjacent passengers as re-circulated air passes through HEPA (High Efficiency Particulate Arresting) filters[1] that prevent re-circulation of infection.

Influenza vaccination prior to travel should be considered for all the groups of patients for whom it would be advised in standard UK practice. The epidemiology of influenza[2] is such that the influenza season at the traveller's destination may differ from that of the UK. The World Health Organisation tracks the progress of the influenza virus and consulting its website – www.who.int - may be useful in updating information about the influenza situation in other countries.

Other respiratory tract infections

Lower respiratory tract infections with organisms such as *Streptococcus pneumoniae, Chlamydia, Mycoplasma* and *Haemophilus influenzae* may occur in travellers.

If they occur in the returning traveller it is important to realise that their patterns of antibiotic resistance may be different from those of strains normally encountered in the UK. This is due to differences in the use of antibiotics in other countries. *Strep. pneumoniae*, for example, is more likely to be penicillin resistant[3] when penicillins are freely available without prescription or are over-prescribed by physicians.

Legionella

What is it?

Infection by *Legionella pneumophila* has been recognised as a potential hazard for travellers since the late 1970s[4]. *Legionella* grows in water at a temperature of 25-42^{o}C and is transmitted to humans by inhalation of a water aerosol, often from shower heads, taps or air conditioning systems, but possibly from other sources such as cooling towers or whirlpool baths.

Who gets it?

Those most at risk of developing the infection are:

- The elderly
- Travellers with reduced immune function for whatever reason. This includes patients who are taking, or who have recently taken, any immunosuppressive drugs such as corticosteroids, cancer chemotherapy, disease-modifying drugs for rheumatoid arthritis and immunosuppressive drugs following an organ transplant.

How do they present?
Infection with *Legionella* produces a pneumonia, usually of lobar distribution, with fever and often with myalgia. Cerebral and gastrointestinal symptoms including confusion, hallucinations and diarrhoea may also be present.

These symptoms may not appear until the traveller has returned home, as the incubation period may be up to 10 days.

Diagnosis
The diagnosis may be suspected from the severity of symptoms, and the presence of symptoms or signs in systems other than just the respiratory tract. Chest X ray is likely to show the presence of pneumonia, and a serological test will help to confirm the diagnosis.

Management and prognosis
In severe cases death may occur, but otherwise the infection will usually respond to the administration of erythromycin or rifampicin. It is resistant to penicillins such as ampicillin.

Tuberculosis

In recent years there has been a worldwide resurgence in tuberculosis, much of it in association with HIV infection[5] and in multi-drug resistant infections.

What is it?
Tuberculosis is a chronic granulomatous infection caused by *Mycobacterium tuberculosis*. Although it is capable of producing pathological changes in any bodily system it is most often acquired and most often seen as a pulmonary infection.

Who gets it?
For most travellers the risk of infection is not great, though there has been some concern about the spread of infection to other passengers when a passenger on an aircraft has open tuberculous infection[6]. As was previously stated in connection with viral infections, the cabin air filtration system is effective in removing bacteria from re-circulated air, but there have been reports of cases caused by direct droplet spread to adjacent passengers.

Patients at principal risk of acquiring tuberculous infection are those travelling to developing countries or other countries with a high prevalence of tuberculosis and/or HIV infection, who intend to live or work in close contact with the local population for prolonged periods. Such travellers include:

- Aid workers

- Healthcare workers
- Teachers

HIV positive travellers are also at particular risk.

How do they present?
In the presence of immunosuppression the infection may present in a variety of ways. In pulmonary infection:

- Cough for more than three weeks
- Sputum production
- Loss of weight

In extrapulmonary disease:
- Wasting and weight loss
- Pyrexia
- Cervical lymphadenopathy

Headache and a deteriorating level of consciousness may indicate tuberculous meningitis.

Diagnosis
If sputum is being produced it should be examined for the presence of acid-fast bacilli. Other investigations would depend on the suspected site of infection and may include chest X ray, aspiration of lymph nodes or lumbar puncture.

Examination
Heaf testing and BCG vaccination is widespread in the UK though not universal. Travellers in high risk categories should be checked for the presence of a BCG scar. If there is no scar a BCG vaccination should be offered, though there is no evidence to support its use in patients over the age of 40 years[7]. It must also not be given to HIV positive travellers. Returning travellers who have been at high risk of infection should be screened for the disease on their return.

Diphtheria is causedby *Corynebacterium diphteriae* and is passed from person to person by droplet transmission.

Who gets it?
Following the demise of the Soviet Union, diphtheria has re-emerged in many former USSR countries[8] as a result of a breakdown in public health infrastructures. It is also present in many developing countries with ineffective or non-existent vaccination programmes. As with tuberculosis, the risk of infection is not great for most travellers, but there are particular groups who are at higher risk. Again, they include:
- Aid workers
- Healthcare workers
- Teachers

Those groups are at risk from droplet infection by being in close contact with the local population for prolonged periods.

How do they present?
Diphtheria presents as a membranous pharyngotonsillitis which may lead to respiratory obstruction. *C. diphteriae* also produces a toxin which may cause myocarditis or polyneuritis. It may also present with skin ulceration.

Treatment
C. diphteriae can be treated with penicillins. Antitoxin should also be administered at the first sign of toxaemia.

Prevention
Diphtheria is a routine part of the UK immunisation schedule and most travellers are likely to have received the vaccine in childhood.

- Travellers in one of the high risk categories already outlined should have their immunisation record investigated
- If they have received a primary course and have not been given a booster dose in the last 10 years they should be given a booster dose of the adult vaccine.
- Children of expatriate families should also be given the adult vaccine if they are over the age of 10 years
- Adults and children over the age of 10 years who have not been given a primary course should start on a primary course using the adult vaccine.

Meningococcal infection

What is it?
Neisseria meningitidis, the causative organism of meningococcal infection, is commonly found in the nasopharynx of healthy individuals, from which it is transmitted by droplet infection.

Who gets it?
Because of its mode of transmission the risk of infection is not great for most travellers, but is, again, highest for groups such as aid workers, healthcare workers and teachers. Those groups are at risk from droplet infection by being in close contact with the local population for prolonged periods.

The areas of greatest risk for these travellers are the “meningitis belt” across Sub-Saharan Africa

The peak periods for transmission are in the hot dry season when droplets travel more easily. Pilgrims on the Hajj pilgrimage to Mecca are also at increased risk and vaccination is now mandatory for the pilgrimage.

How do they present?
When *Neisseria meningitidis* becomes invasive it produces a rapid onset of septicaemia and meningitis, leading to death or disability if not rapidly treated.

Management and prognosis

- Meningococcal vaccination is now included in the UK immunisation schedule for children
- The vaccine gives protection against the C serotype but is ineffective against other serotypes including the B serotype, which also causes many cases in the UK and for which no vaccine is yet available in this country
- It is also ineffective against the A serotype which is often found in other countries
- It is also ineffective against other serotypes of the organism including W-135 which has been found in Europe associated with pilgrims returning from the Hajj pilgrimage
- Adults travelling to endemic areas, and who fall into one of the high risk groups already outlined, have usually been given the A + C vaccine. But in view of the rising incidence of other strains such as Y and W-135 it would now be wise to use the quadrivalent A/C/W/Y vaccine
- Children travelling with them should receive similar protection even if they have previously been given the routine C vaccine
- A gap of one month after C vaccination is recommended before giving A + C or A/C/W/Y vaccines[9]
- The quadrivalent should always be used for at-risk travellers to areas where the Y and W-135 serotypes are prevalent. This includes Hajj pilgrims, who should be given the A/C/Y/W-135 vaccine
- Meningococcal vaccination is not required by the majority of package tourists to endemic areas as their contacts with local people are likely to be neither close nor prolonged
- It is also doubtful whether, for example, all trekkers travelling to Nepal, who are often given meningococcal vaccine as routine, are at particular risk of infection. Many of them will mix mainly with their fellow-travellers
- Those sharing accommodation with local people in homes and lodges may be at greater risk, though there are no reports of recent cases of meningococcal infection in trekkers[10]

Hepatitis B & C

What is hepatitis B?

Hepatitis B[11] is a viral infection transmitted via contact with blood and other body fluids.

Who gets it?

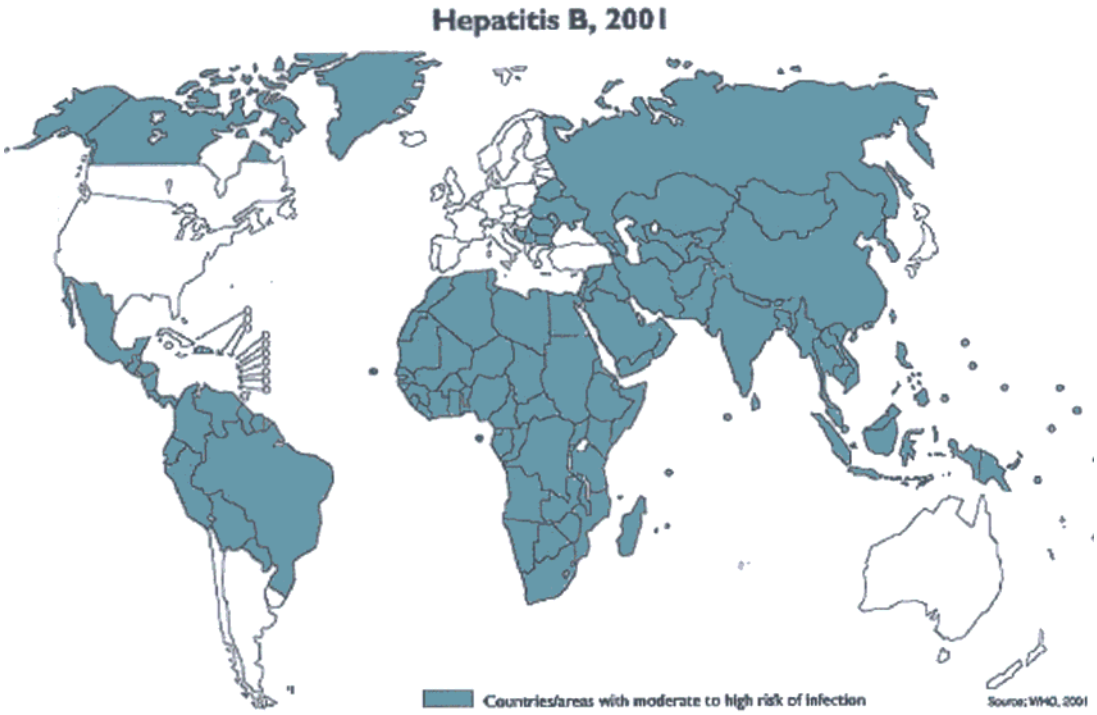
It is present throughout the world but the highest risk areas are shown in Figure 1. Modes of transmission include:

- Use of unscreened blood transfusions or blood products
- Contact with blood as a result of:
    - Trauma
    - Re-use of needles and other medical equipment
    - Sexual contact
    - Sharing of needles by intravenous drug users
    - Tattooing and body piercing

Vertical transmission from mother to baby occurs, and infants born to carrier mothers have a 90% chance of developing chronic liver disease and liver cancer.

Travellers most at risk of hepatitis B infection are long-term travellers and expatriates in countries with a high prevalence of the disease. The length of their stay means that they run a greater risk of exposure to infection as a result of trauma, medical treatment or unwise sexual liaisons.

Figure 1
(World Health Organisation)



How do they present?
Hepatitis B may be subclinical. Otherwise it may present with:

- Headache
- Malaise and fever
- Nausea and vomiting
- Abdominal pain

These symptoms are followed by:

- Jaundice
- Pale stools
- Dark urine

More rarely there may be a fulminating course with rapid progression to severe illness or death. In those not succumbing to the acute stage, outcomes range from recovery and immunity, to the chronic carrier state, hepatic cirrhosis and hepatocellular carcinoma.

Diagnosis

The presence of hepatitis B surface antigen (HBsAg) in the blood indicates acute infection and distinguishes the illness from other types of hepatitis. But it is also present in the chronic carrier state.

The presence of hepatitis B e-antigen (HBeAg) indicates the presence of active viral replication and therefore high infectivity when found in the acute stage or the chronic carrier.

The presence of anti-HBsAg antibody indicates immunity due to previous infection or vaccination.

The presence of anti-HBeAg antibody is present in either the recovery stage from active infection or chronic carrier stages of relatively low infectivity.

Immunity due to vaccination may be distinguished from that due to previous infection by the presence of hepatitis B core antigen in the blood of those who have had the infection. It is absent from those who have been vaccinated.

Management and prognosis

- Hepatitis B vaccination is a wise precaution for all high-risk travellers
- Screening for hepatitis B may be advisable for long-term expatriates on their return
- Incubation period varies from 6 weeks to 6 months and this should be borne in mind when screening returned travellers
- Holidaymakers and other short-stay travellers are less likely to develop hepatitis B, but should be advised about the risks from the activities outlined above and vaccinated if this seems appropriate

Around 10% of adults with clinical disease develop chronic hepatitis, and hepatitis B is a major cause world-wide of cirrhosis and liver cancer.

What is hepatitis C?
Hepatitis C[11] is also a viral infection. The incubation period is 6 to 8 weeks.

Who gets it?
The modes of transmission and clinical features are similar to those of hepatitis B, from which it can be distinguished by serological testing.

Management and prognosis

- There is no vaccine available at present
- Those who have been given hepatitis B vaccination should be counselled that they are still at risk of hepatitis C
- Safe sex and the use of condoms should be advised if sexual activity is likely
- Questionable medical facilities, needle sharing, tattooing and body piercing should be avoided

The incidence of chronic liver disease and liver cancer is higher than that occurring in hepatitis B, with 20 to 30% of those affected developing chronic liver disease.

Other sexually transmitted infections

HIV/AIDS

The human immunodeficiency virus (HIV) is a retrovirus that is transmitted by:

- Exchange of body fluids during heterosexual or homosexual activity (vaginal, oral or anal)
- Invasive medical procedures such as unscreened blood transfusion, use of other unscreened blood products or inadequate sterilisation of instruments
- Sharps injuries in health care staff
- Sharing of needles by intravenous drug users and possibly by other activities such as tattooing and body piercing with inadequate sterilisation of equipment

Who gets it?

- In 2001 5 million people became infected with HIV world-wide
- 0.8 million of them were children[12]
- No part of the world has been spared in the global pandemic
- In sub-Saharan Africa, the area with the highest prevalence, there are 28.5 million living with HIV
- The incidence is rising in Asia, where around 1% of the population of India and Thailand and up to 50% or more of intravenous drug users (IVDUs) are infected
- Prevalence is also rising in Eastern Europe, again with a high prevalence in IVDUs
- Sexual activity is responsible for about 75% of all infections world-wide[13], although transmission also occurs by means of infected blood, blood products and other invasive procedures
- It has been estimated that the risk of female to male infection per single sexual contact in Thailand is 0.031 compared with a risk of 0.001 in the North America[13]
- The risk is greater for anal than for vaginal intercourse
- In North America, Western Europe and Australasia transmission of infection occurs mainly among homosexual and bisexual men, though heterosexual transmission is increasing
- In sub-Saharan Africa heterosexual transmission is the most important route, with transmission by blood transfusion and other medical procedures playing a smaller part
- In Asia, North Africa and Eastern Europe transmission is largely among sex workers, their clients and families, and IVDUs, though homosexual transmission also occurs, as does “imported” infection from individuals from other infected areas and from unscreened blood products from other countries
- The presence of ulcerative genital infections such as herpes and chancroid predisposes to invasion by the HIV virus
- Vertical transmission from mother to baby via the placenta, during vaginal delivery and by breastfeeding occurs when the mother is infected

How do they present?

Infection may be symptomless, though there may sometimes be a seroconversion illness with fever and rash up to three months after the initial exposure.

After this three month period anti-HIV antibodies can be found in the blood. There may follow a latent period of up to ten years or more. As the CD4 lymphocyte count begins to fall below 400 x 10^9L a variety of non-specific symptoms such as tiredness, headaches, fever, myalgia and weight loss may occur, together with lymphadenopathy, rashes, oral or vaginal thrush, herpes zoster, diarrhoea and a variety of other infections.

Clinical acquired immune deficiency syndrome (AIDS) is characterised by the presence of opportunistic infections such as:

- Systemic candidiasis
- *Pneumocystis carinii* pneumonia
- Cryptococcal meningitis
- Toxoplasmosis

and neoplasms such as Kaposi's sarcoma.

Wasting and mental deterioration leading to dementia in some cases also occur. The use of retroviral drugs has greatly prolonged the interval between the onset of clinical AIDS and death, but the treatment of HIV/AIDS is beyond the scope of this course.

Diagnosis

The diagnosis of HIV infection is usually confirmed by testing for the presence of anti-HIV antibodies, either by an ELISA (Enzyme-Linked Immunosorbent Assay) test or by the Western Blot method. A period of up to three months following exposure to infection is required for the test to become positive.

There are other more sophisticated tests, some of which are very expensive, but it is now possible to test less expensively for the presence of viral DNA in white blood cells.

The CD4 lymphocyte count is an important measure of the degree of immune suppression present. CD4 counts of less than 400 x 10^9L indicate that HIV infection has begun to affect the individual's immune function and counts of less than 200 x 10^9L show a very significant degree of immune suppression.

Other sexually transmitted infections (STIs)

The publicity given to HIV infection has tended to drive out of the public mind the existence of other STIs.

- ***Chlamydia*** is the most widespread bacterial STI in the developed world and is likely to become common in developing countries
- ***Genital herpes, trichomonas*** and ***human papilloma*** virus are also widespread in the developed world. While their prevalence is not clear in developing countries, they are also likely to be commonly found here

- ***Syphilis*** is still prevalent in developing countries, with 5 to 20% of women attending antenatal clinics being seropositive[13] (up to 70% in the case of sex workers)
- ***Gonorrhoea*** is also widespread
- ***Chancroid*** is an ulcerating genital infection not commonly found in the UK but it is much more frequently encountered in South East Asia, and Africa
- ***Donovanosis*** is also an ulcerating genital infection, sometimes with skin lesions at other sites. It is found in India and Papua New Guinea and in some other parts of Asia, Africa and South America
- ***Lymphogranuloma venereum*** produces enlargement of inguinal and femoral lymph nodes. It is uncommon in the UK but is found in Africa, South-East Asia and South America including the Caribbean

HIV and other STIs can be avoided only if patients abstain from sexual contact during travel with anyone other than their usual sexual partners. This is probably a counsel of perfection, and travellers need to be advised about safe sexual practices, including the use of condoms, preferably purchased prior to travel and carrying a recognised quality mark.

Returning travellers who have had sexual contact during travel should be screened for HIV infection and other STIs even if they have attempted to practise safe sex.

Sexual behaviour of travellers
A study of German travellers[14], defined as "sex tourists" those who travel from an industrialised country to a third world country, staying for a limited period and paying for sex with local women, though the wider definition of the term would also include those seeking sex with men.

The characteristics of sex tourists in this study were:

- Age range 19 to 74 years, with an increased representation of 20 to 40 year olds in the heterosexual travellers and of 40 to 50 year olds in the homosexual travellers
- More single men and men separated from their wives
- More sexually active on holiday than they were at home
- Less reliable in the use of condoms: 45% used condoms regularly and 30% did not use them at all, whereas 90% of clients of sex workers in their home country reported condom use
- More than 50% of the men stayed for several days with the same sex worker and all were older than their selected sexual partners
- 50% to 78% had travelled to other sex tourism locations in the previous five years
- Those who had planned their trips specifically for sexual activity were less likely to have used condoms, and married men were also less likely to use them
- The more frequent the sexual activity the less likely was the use of condoms, but condom use was more likely if they were supplied by the sex worker

This study gives a good insight into the risk-taking behaviour of those who plan to travel in search of sex and those who have frequent sexual contact during their

travelling. To what extent they would be likely to change this risk-taking behaviour as a result of medical advice prior to travel is difficult to predict, but it is none the less important that tactful enquiries should be made of single male travellers about the nature of their intended activities while abroad and advice given about condom use. A more profitable approach may be to educate and empower women in developing countries to make them less economically reliant on sex for their income and to educate those who remain in such employment about condom use.

There are travellers, both male and female, who do not necessarily travel for the express purpose of seeking sex but who nevertheless become involved in sexual activity while abroad. As this activity is completely unpredictable there is an argument for including advice or leaflets about safe sex in the advice given to all who travel unaccompanied by a regular sexual partner.

Haemorrhagic fevers

What are they?

Viral haemorrhagic fevers (VHFs) have a high profile in the media but are rare in practice in travellers[15]. The types of viruses, the associated diseases and the modes of transmission are summarised in Figure 2.

Class of virus	Disease	Source	Person to person spread
Arenavirus	Argentine haemorrhagic fever (Junin)	Rodent	Occasional
	Bolivian haemorrhagic fever (Machupo)	Rodent	Occasional
	Brazilian haemorrhagic fever (Sabia)	Rodent	Occasional
	Lassa fever	Rodent	Yes
	Venezuelan haemorrhagic fever (Guanarito)	Rodent	Occasional
Bunyavirus	Crimean/Congo haemorrhagic fever	Tick	Yes
	Haemorrhagic fever/renal syndrome (Hantaan)	? Animals	Occasional
	Rift Valley Fever	Mosquito	Not reported
Filovirus	Ebola	N/K	Yes
	Marburg	N/K	Yes
Flavivirus	Dengue	Mosquito	Not reported
	Kyasanur Forest disease	Tick	Not reported
	Omsk haemorrhagic fever	Tick	Not reported
	Yellow fever	Mosquito	Not reported
Togavirus	Chikungunya	Mosquito	Not reported

Figure 2 The types of viruses, the associated diseases and the modes of transmission. The names in brackets are alternative names sometimes used both colloquially and in medical literature

Who gets them?
Not only are VHFs rare in travellers, they are also, contrary to popular belief, difficult to acquire[15]. Bites from mosquitoes or contact with urine or faeces of rodents such as rats are the main methods of transmission. Person to person transmission is much less likely and requires contact with blood or other body fluids via mucous membranes or broken skin, though inhalation of respiratory droplets may also result in infection. Health care workers looking after patients with a VHF may become infected but few such cases have been reported. Person to person transmission, without such a high level of contact, is unlikely.

How do they present?
Some cases may be mild or even subclinical, but established cases have a high mortality rate. Early symptoms include sore throat and fever, making early diagnosis difficult, before progressing to severe illness with haemorrhagic manifestations. If a careful travel history is taken it should be possible to identify travellers who have: visited an area where VHFs occur - in circumstances which have put them at risk – and whose symptoms are of a severity that arouses suspicion.

- Some VHFs are specific to a country and have not been reported elsewhere, e.g. Argentine and Bolivian VHFs
- Some are specific to a region e.g. Ebola in sub-Saharan Africa
- Some are found in several continents such as Crimean/Congo HF

Eastern Europe, Central Asia, India, China, Australia and South-East Asia have all had VHFs reported, either specific to them or members of a more widespread group of viruses[*].

In order not to overlook a possible diagnosis of a VHF the clinician must be aware that such infections are possible in travellers to sub-Saharan Africa (especially West Africa) in particular, but may occasionally be seen in travellers to South America, Australia and parts of Asia.

Diagnosis

Initial diagnosis of a VHF is not easy, as symptoms may be relatively mild and non-specific such as fever, headache and myalgia, often with a sore throat. It is therefore important to consider such a diagnosis at an early stage if no other cause for fever is discovered in a returned traveller.

A careful travel history must be obtained, with a history of the degree to which the traveller may have been exposed to animals, especially rodents, and to mosquito or tick bites. Examination should include looking for evidence of mosquito and tick bites. Deterioration in the patient's general condition and the appearance of haemorrhagic manifestations may be rapid, and as VHFs may be transmitted from person to person it is important to arrange the admission to hospital and isolation of suspected cases as soon as possible.

Learning points

- Respiratory tract infections are common in travellers

- Diseases such as diphtheria, tuberculosis and meningococcal infection are a high risk for travellers likely to be in close and prolonged personal contact with the indigenous population
- Legionella infection is most likely to occur in the elderly and in those with reduced immune function
- Hepatitis B is widespread and is a potential risk for long term travellers or expatriates and for travellers likely to suffer trauma or indulge in I/V drug use or unprotected sex
- HIV infection is widespread and in many countries is transmitted chiefly by heterosexual contact, commercial sex and needle sharing.

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Useful websites

Travax - www.travax.scot.nhs.uk
Fit for Travel - www.fitfortravel.scot.nhs.uk
World Health Organisation – **www.who.int**
Centers for Disease Control and Prevention – www.cdc.gov
Health Protection Agency – www.hpa.org.uk