The HIV infected traveller (Adapted from HIV Manual www.hivmanual.hk)

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CME / CNE / PEM point accreditation *(please refer to the attached test paper for the number of credit points awarded)*

Introduction

As a result of the improved quality of life and survival benefits brought forth by the use of effective antiretroviral therapy, people living with HIV/AIDS (PLWHA) are leading relatively normal life. Travel is now more common for PLWHA, especially from developed countries to tropical and subtropical areas of the world.[1] This trend has created unique health concerns because of the defective immune response arising from low CD4 count and an increased risk of complications from exotic diseases acquired at their travel destinations.

Studies in North America have shown that only half of PLWHA consulted with a physician prior to travel.[2] While travel medicine and the concept of pre-travel health consultation are still at their developmental stage in Hong Kong, physicians should alert PLWHA of the importance of obtaining pre-travel advice, especially when planning for trips to developing countries where the infection risk is anticipated to be higher. Likewise, HIV physicians need to counsel their clients with regard to a wide variety of health issues not only limited to infectious diseases, but also non-infectious aspects of travelling including time-zone changes, temperature extremes, altitude medicine, diving medicine, environmental hazards and personal safety. Constant update on destination-specific diseases and environmental conditions, and basic knowledge across the health specialties is desirable in order to offer individualised risk assessment and to discuss the prevention strategies and management plan with PLWHA.

Basic principles of healthy travelling

Like any other travellers, an HIV traveller should plan ahead of his/her trip and seek not only general travel-related advice regarding infectious and non-infectious travel risks in their destination, but also specific advice in regards to one's current health status. Visits should be made at least 4-6 weeks in advance of departure to allow for the consideration of vaccination and modification of treatment regimen and observing potential side effects of prophylactic treatment should these be required. [Algorithm]

Apart from obtaining routine travel information as listed (Table 1), physicians should also provide specific information on one's health status, specifically the most recent CD4 count and its trend, the latest HIV viral load, the current highly active antiretroviral therapy (HAART) regimen and drug adherence. An integration of all information could be used to assess the degree of immunocompromise and physical fitness of an HIV traveller for the journey and to offer general and specific health advice.

In the past, a CD4 count <200/μL and a history of AIDS were used to define a compromised immune system. But since most PLWHA in care these days are already on HAART to achieve viral suppression, those who have no replicating virus are not thought to be immunocompromised (unless CD4 cell count is severely diminished) and should be approached like uninfected travellers. For those with CD4 count <200/μL who are not yet on treatment or with a detectable viral load, history of ADI, or those with clinical manifestations of symptomatic HIV, they are considered to have severe immunosuppression and should generally be advised to delay their travel whenever possible.[3] Such a delay is preferred when the individuals undergo immune reconstitution with the initiation of antiretroviral treatment, firstly because it is not uncommon for them to suffer from side effects of the treatment during the initial months; secondly, immunologic recovery will minimise the risk of acquiring new infections and potentially lead to a better response to vaccinations.

An HIV traveller on treatment should ensure an ample supply of antiretroviral medications to prepare for unanticipated delay during their trip. Special consideration has to be taken on dosing interval when travelling across time zones. Whenever possible, new medication change just prior to travel should be avoided. Medications are best kept in the original bottles in their carry-on luggage and not the check-in luggage. It is advisable to obtain a letter from the physician with a brief summary of the medical history and list of medications to expedite the customs process when crossing borders. Reliable medical institutions at the destination should be located before travelling so that prompt medical care can be sought if one becomes ill while travelling. Medical insurance coverage should be verified and evacuation insurance should be considered depending on the type of travel and itinerary.

As in the case of traveller's diarrhoea, HIV travellers should be reminded that all of the preventive strategies against specific conditions do not guarantee protection. They should be advised to seek expert medical assistance early in the case of any febrile illness during or after the trip.

Table 1. Basic and specific information to be obtained from an HIV traveller as pre-travel assessment

Basic Information	
Regarding the trip	Destinations, including countries and areas within countries and transit cities (e.g. rural vs. urban areas) Detailed itinerary (including types of accommodations and activities involved) Season of travel Duration (Dates of departure and return) Nature of travel (business, leisure, missionary, visiting friends and relatives [VFR], study or teaching etc.) Travel format (tour group, backpack, luxury travel etc.)
Regarding the traveller	Medical history Drug history (including both trade name and generic name and the exact dosage) Allergic history Immunisation history Reproductive status (women) Experience of travel
Specific Information	
Immune status	Recent CD4 count and its trend
Antiretroviral therapy and the chemoprophylaxis	Need of refrigeration Dosing interval Adherence

Food- and water-borne disease and traveller's diarrhoea

Immunocompromised HIV travellers are more prone to either chronic diarrhoea from parasitic enteric infections, e.g. *Cyclospora, Cryptosporidium and Cystoisospora*; or more severe diseases from associated bacteraemia with the bacterial pathogens, e.g. *Campylobacter* species, *Shigella* species, and *Salmonella* species. The same precautions against food and waterborne diseases for all travellers should be emphasised when counselling PLWHA. They should be advised to avoid any uncooked foods, raw fruits and vegetables, raw or undercooked seafood or meat, tap water, ice made from tap water, unpasteurised milk and dairy products, and food and beverages purchased from street vendors. Frequent hand washing and use of proper hand hygiene with water and soap or alcohol-based solutions should be reinforced and advised as the best prevention against enteric infections.

Water should be either boiled or bottled, and when these are not feasible, alternative methods including use of portable water filtration units together with chemical treatment with e.g. iodine, tetraglycine hydroperiodide tablets, and chlorine can be considered. However, travellers should be warned that all of these methods have caveats to their use, thus they should not be falsely reassured of their safety, and the basic precautions above should be vigilantly observed throughout the trip.

As some animals are known to be associated with infections e.g. *Salmonella, Campylobacter, Cryptosporidium, Brucella* etc., HIV travellers should be advised to wash their hands after handling pets, avoid contact with pet faeces, and refrain from contact with reptiles, birds, and young farm animals.

Traveller's diarrhoea can occur despite strict adherence to the precautions as mentioned. Routine antimicrobial prophylaxis for traveller's diarrhoea is not recommended for HIV travellers, due to concerns of adverse effects and the possibility of promoting drug resistance.[4] In the event of severe manifestations (severe diarrhoea, abdominal cramp and fever), treatment of traveller's diarrhoea using oral rehydration solutions in combination with antidiarrhoeal agents and presumptive antibiotic regimen with azithromycin (but not clarithromycin) or a fluoroquinolone such as ciprofloxacin and levofloxacin may be considered. These agents are safe, as they are not known to have significant interactions with HAART drugs. Fluoroquinolones, however, should be used with caution as resistant strains of campylobacter have been increasingly reported in Southeast Asia. Rifaximin is a non-absorbable antibiotic that has been shown to be active against several enteric pathogens. However, it is not readily available in Hong Kong and its use is limited by its cost and inconvenient thrice-daily dosing schedule.

Other waterborne infections (e.g. cryptosporidiosis, giardiasis, schistosomiasis or leptospirosis, *Acanthamoeba sp*) may also result from swallowing or even being exposed to some bodies of water during recreational activities. HIV travellers should be advised to limit their exposure to fresh water (including rivers and ponds) and be careful not to swallow water while swimming. They should wear shoes and protective clothing to limit their exposure to soil with possible faecal contamination. For those with unavoidable exposure to water potentially contaminated with leptospira, chemoprophylaxis with a weekly dose of doxycycline at 200mg is recommended.[5]

Vector-borne disease and malaria

General advice on preventing exposure

HIV travellers are more prone to severe sequelae of certain insect-borne illnesses, e.g. leishmaniasis and Chagas disease. They need to take personal protective measures to avoid bites from different insects, such as mosquitoes (vectors for malaria, dengue fever, Japanese encephalitis, yellow fever, West Nile virus, and other arboviral infections), sandflies (vectors for leishmaniasis and *Bartonella bacilliformis*), ticks/mites/lice/fleas (vectors for rickettsiosis). They should be advised to put on light-colored clothing that covers most of the body surface, to use repellent-impregnated mosquito nets and to avoid shrubby areas and other infested habitats. The most effective repellent against a wide range of arthropods is N, *N*-

diethyl-3-methylbenzamide (known as DEET). Insect repellents that contain DEET at concentrations up to 50% (range from 30-50%) are recommended for adults, and DEET up to 30% has been shown to be safe when applied to children older than 2 months according to the directions on the product labels. Repeated applications are necessary as DEET can be washed off with perspiration or rain. Permethrin can be used to spray clothes and bed nets, and permethrin-treated bed nets and clothing are also available as alternatives. Combined use of all of these measures can reduce insect bites substantially.

Malaria

Existing data on the relationship between HIV infection and incidence or severity of malaria are complex, and malaria has not been regarded as an HIV-related opportunistic infection. However, recent evidence has shown that HIV RNA plasma levels are increased during malaria infection, and CD4 counts are lowered in patients on HAART. In vitro studies also indicate that immune activation mediated by proinflammatory cytokines may contribute to HIV disease progression. HIV infection has been associated with recurrent malaria parasitaemia and reinfections, with increased clinical severity.[6] A thorough discussion of malaria prevention should be included in the pre-travel consultation with travellers visiting malaria endemic areas. Apart from personal protection measures against insect bites, an HIV traveller should be strongly urged to start chemoprophylaxis before the trip and be reminded of the importance of drug adherence. The regimen should be tailored according to the specific area of travel and the local resistance to antimalarial drugs. Special consideration, however, has to be taken for potential drug-drug interactions, e.g. between ritonavir (RTV) and atovaquone-proguanil, chloroquine, and mefloquine, between efavirenz (EFV) and atovaquone-proguanil and doxycycline, and between cobicistat (COBI)-boosted regimen with mefloquine, although no clinically relevant events have been reported and no dosage adjustments are recommended. Mefloquine carries the risk of additional neurological toxicity when used with EFV, and atovaquone-proguanil has been known to increase the level of zidovudine (ZDV), thus, close monitoring of haemoglobin level is warranted. The up-to-date regional prophylaxis recommendations from CDC can be found at https://www.cdc.gov/malaria/travelers/country_table/a.html. In general, doxycycline and atovaquone-proguanil are considered to be the drugs of choice for malaria prophylaxis among PLWHA receiving antiretroviral drug therapy in view of the safety profile, tolerability and lack of clinically significant drug interactions.[7]

In contrast, antimalarial treatment regimens, including artemisinin derivatives and quinine/quinidine, may have potential interactions with many non-nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), COBI-boosted regimen, and with the CCR5 receptor antagonist. Expert advice should be sought when treating patients for malaria who are also on HAART.[3,7]

Vaccine issues in HIV travellers

Travel-related vaccines can be categorised into 3 main groups: (a) routine vaccines; (b) recommended vaccines, depending on the destination and travel itinerary; and (c) required vaccines to acquire visa/entry permission for certain countries. Physicians should take the opportunity to update routine immunisation and to offer required and recommended destination-specific vaccinations for their HIV clients during the pre-travel consultation after careful evaluation of the risk of disease acquisition versus the safety and efficacy of respective vaccines.

As a general rule, killed or inactivated vaccines are safe for use in PLWHA. Live vaccines should be avoided, especially when the CD4 count is <200/μL (except for highly selected circumstances that measles or yellow fever vaccine may be considered when the risk of acquiring the infection outweighs the potential risk of the vaccination). Besides, the degree of immunocompetence also correlates with the degree of immunologic response to vaccinations. Studies have demonstrated a suboptimal antibody titre following vaccination at lower CD4 counts. Revaccination is recommended at least 3 months after immune reconstitution with antiretroviral therapy for any vaccines given while CD4 counts are <200/μL.[3] (Table 2) summarises the recommendations for specific vaccines relevant to adult HIV travellers.

Table 2. Immunisations for adult HIV-infected travellers

Vaccine type	Composition	CD4 >200/μL and asymptomatic infection	CD4 <200/μL	Remarks
Required in specific destination				
Yellow Fever vaccine	Live attenuated	*Consider if substantial high-risk exposure anticipated	No; provide exemption letter	Give at 10 days prior to travel; available only at sites designated by local health departments. [§] ↓ response reported in PLWHA. Booster every 10 years required for immunity
Meningococcal vaccine	Conjugated (inactivated)	√	√	Safe; ↓ response to serotype C reported in PLWHA; required/recommended when travelling to the 'meningitic belt' in sub-Saharan Africa or to attend the Hajj pilgrimage in Saudi Arabia
	Polysaccharide (inactivated)	√	√	
Recommended when travel to endemic areas				
Typhoid vaccine	Live attenuated Ty21a oral typhoid vaccine	No	No	
	Inactivated typhoid Vi capsular polysaccharide (intramuscular)	√	√	Safe; decreased response in those with CD4 <200 count /μL; Recommended for travel to rural areas of countries endemic of typhoid or in any area of an outbreak, usually in Latin America, Southeast Asia, the Indian subcontinent and Africa
Japanese Encephalitis vaccine	Inactivated (vero-cell vaccine, SA14-14-2 strain))	√, if substantial risk	if substantial risk	2-dose regimen, booster dose ≥1 year after primary series is needed. No data on immune response in HIV-infected persons
	Live attenuated (YF17D/SA14-14-2)	No	No	
Polio vaccine	Inactivated	√	√	Indicated when travelling to some areas of western Africa and the Indian subcontinent
	Live attenuated	No	No	
Rabies vaccine	Inactivated	√	√	Consider in travellers with occupational risk and those with extended travel to endemic areas; no data on immune response
Routine				
Influenza vaccine	Inactivated	√	√	
	Live attenuated	No	No	
Pneumococcal vaccine	Conjugated vaccine (PCV13)	√	√	For those who have not received PCV13 or 23vPPV: administer PCV13 followed by 23vPPV at least 8 weeks after PCV13; for those who have already received 23vPPV, PCV13 should be administered at least 1 year later; for those who have already received any PCV13, a single dose of 23vPPV should be administered at least 8 weeks later
	Polysaccharide vaccine (23vPPV)	√	√	
Tetanus, diphtheria, pertussis vaccine (Tdap/Td)	Toxoid/Inactivated	√	√	Safe; substitute 1-time dose of Tdap for Td booster, then boost with Td every 10 years; no data on immune response
Hepatitis A vaccine	Inactivated	√	√	Safe; 2-dose regimen; response improves after immune reconstitution with ART
Hepatitis B vaccine	Inactivated	√	√	Safe; 3-dose regimen; response improves after immune reconstitution with ART
Measles-mumps-Rubella vaccine	Live attenuated	√, for non-immune persons	No	May consider measles immunoglobulin for those with CD4 <200/μL travelling to measles endemic area
BCG	Live attenuated	No	No	

[§]Travel Health Service, Department of Health. http://www.travelhealth.gov.hk
ART, antiretroviral therapy

Sexual health and blood-borne viral risks

It has been shown that sexual activity increases during international travel, with only a limited number of travellers reporting consistent use of condoms. A study of the practices of HIV travellers revealed that over 20% reported having had casual sexual activity with new partners while travelling.[8] Physicians should take the opportunity during the pre-travel consultation to provide counselling on risks of exposure to other sexually transmitted infections (STI) as well as the risk of transmitting HIV and acquiring a new strain of HIV, and remind PLWHA on safer-sex preventive strategies.

Entry restriction

Border regulations relating to HIV status are a unique and important part to consider while planning for international travel. Most countries do not have entry restrictions to PLWHA for short-term stay, so holidaymakers do not usually have any problems. USA has lifted the ban in 2010. But there are still countries that impose restrictions on the entry of PLWHA and immigrants. In case of doubt, HIV travellers should be advised to check with the embassies or consulates of destination countries to get the most up-to-date information and policy about HIV test requirements and other possible health-related visa requirements, e.g. vaccination requirement and proof of immunity, TB test and chest x-ray, etc.

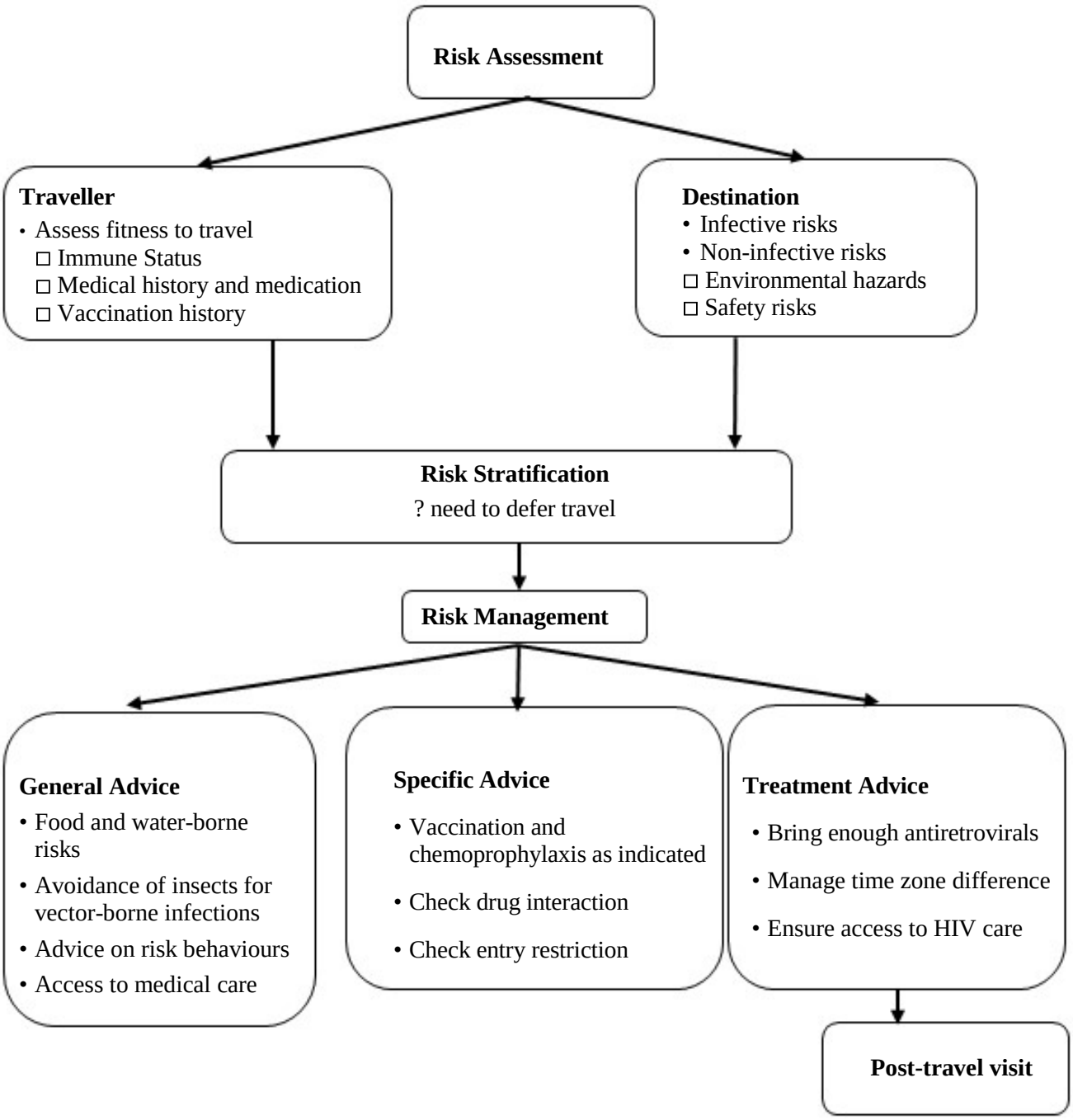
Approach to post-travel management of HIV travellers

When a returning HIV traveller presents with illness for post-travel assessment, a detailed history including the onset of symptoms in relation to the itinerary, the exact arrival and departure dates, specific risk behaviours (e.g. intake of 'high-risk' food/drinks, contact/bites by animals, fresh water exposures, insect bites, new sexual partners, hospitalisation in foreign countries etc.), history of any pre-travel vaccination and chemoprophylaxis and the adherence to such treatment during and after the trip should be obtained to determine the potential exposure to infectious agents and the likely incubation period.

Because of its complexity, any returning, febrile HIV traveller should be evaluated immediately, preferably by an infectious disease clinician or tropical medicine specialist. Physicians should be aware of the presence of HIV infection or AIDS, which can pose a diagnostic challenge as the natural history of infectious disease could be altered in different ways and that patients may present with atypical clinical manifestations. Apart from geographically focal infections for inclusion in the list of differential diagnoses, physicians should always consider commonly encountered infections.

For febrile travellers returning from a malaria-endemic area, irrespective of the history of chemoprophylactic treatment and its adherence, all should be managed as medical emergency with a working diagnosis of malaria until proven otherwise. If chemoprophylaxis has been given, the same medicine should not be used for treatment.

Algorithm. Pre-travel consultation



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Test paper - The HIV infected traveller (Adapted from HIV Manual www.hivmanual.hk)

Expiration Date: 28 April 2021

CME point / CNE point: 1 / PEM point: 0 (Midwifery related) #

- Please choose the best option.
- Answer these on the answer sheet and make submission by fax to Special Preventive Programme, Department of Health.

 # Please contact respective authorities directly for CME/CPD accreditation if it is not on listed below.

Accreditors	CME Point
Department of Health *(for practising doctors who are not taking CME programme for specialists)*	1
Anaesthesiologists	1
Community Medicine	1
Dental Surgeons	1
Emergency Medicine	1
Family Physicians	1
Obstetricians and Gynaecologists	1
Ophthalmologists	0.5
Orthopaedic Surgeons	0
Otorhinolaryngologists	pending
Paediatricians	1
Pathologists	1
Physicians	1
Psychiatrists	1
Radiologists	1
Surgeons	1

1. Which of the following is true of the HIV infected traveller after effective antiretroviral therapy became available?

   (a) Travelling has not become more common because of entry restrictions imposed by many countries
   (b) HIV ceases to be a factor in travel-related advice once it is verified that the HIV viral load has been suppressed
   (c) In Hong Kong, it is now routine practice that the HIV infected traveller receive advice by a travel medicine specialist before beginning his travel
   (d) The traveller should preferably visit a travel medicine specialist as close as possible to the onset of travel
   (e) None of the above

2. In assessing the risk of travel, which of the following information regarding the trip is NOT required?

   (a) All destinations and dates, including transit airports
   (b) The reason of travel (e.g. visiting friends, business meetings)
   (c) The travel format (e.g. tour group, solo, etc)
   (d) Types of accommodation arranged or to be arranged
   (e) All of the above information is required

3. In assessing the risk of travel, which of the following information regarding the HIV disease status is NOT required?

   (a) The most recent viral load
   (b) The current antiretroviral regimen
   (c) The nadir CD4 count
   (d) The current regimen of chemoprophylaxis
   (e) All of the above information is required

4. Which of the following circumstances related to an HIV infected traveller should prompt consideration to postpone the trip?

   (a) Recent viral rebound to 1000/ml after three years of viral load suppression; current CD4 count is 180/uL; the patient intends to go to Tibet for four weeks
   (b) An asymptomatic patient with a CD4 count of 450/uL and not on treatment who intends to holiday in Tokyo for 10 days
   (c) An asymptomatic patient newly started on antiretroviral treatment 3 months ago; his pre-treatment viral load was 150,000 copies/mL and CD4 count 500/uL; he intends to go to London for five days for a business meeting
   (d) A and B
   (e) A and C

5. Which of the following is NOT recommended measure against water-borne diseases and traveller's diarrhoea?

   (a) Limit sport activities in rivers and ponds
   (b) Avoid using ice made from tap water
   (c) Seek to chemically treat tap water before use. If not feasible, resort to boiled water
   (d) Frequent hand hygiene
   (e) Avoid contact with animals

6. After assessing the risk posed to the traveller, which of the following chemoprophylaxis may be indicated?

   (a) Weekly doxycycline against leptospirosis
   (b) Weekly ceftibuten against gonorrhoea
   (c) Malarone against malaria
   (d) A and C
   (e) B and C

7. Which of the following vaccinations is not considered in pre-travel consultation?

   (a) Inactivated Japanese encephalitis vaccine
   (b) Inactiviated polio vaccine
   (c) Yellow fever vaccine
   (d) Live MMR vaccine
   (e) BCG

8. It is important to avoid mosquito bites. Which of the following infections is not transmitted in this way??

   (a) West Nile virus
   (b) Japanese encephalitis
   (c) Zika virus
   (d) Leishmaniasis
   (e) Chikungunya

9. Which of the following organisms is associated with exposure to freshwater?
   (a) *Acanthamoeba sp*
   (b) *Babesia sp*
   (c) *Histoplasma capsulatum*
   (d) *Trypanosoma cruzi*
   (e) *Penicillium marneffei*

10. Which of the following is true regarding the risk of sexually transmitted diseases in travellers?

   (a) Unprotected sex with casual partners is more common with travelling
   (b) Genital infection with drug resistant *Chlamydia trachomatis* is likely with travel to Africa
   (c) Chemoprophylaxis with metronidazole and azithromycin is indicated if the traveller is unwilling or unable to use condom
   (d) Chemoprophylaxis with azithromycin against chancroid is indicated for travel to highly endemic countries even if condom will be used
   (e) All of the above