THE IMMUNE-COMPROMISED TRAVELLER

The immune-compromised traveller is clearly at higher risk from travel-related infections.

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Infectious diseases are a complex interplay between pathogen and host. Immune-compromised hosts are more susceptible to infection, including those from organisms that are not normally pathogenic. The infections they acquire are more severe as a result of more rapid progression and a higher rate of invasiveness. Immunisation, one of the key preventive components of travel medicine, is less effective. Furthermore, live vaccines can cause severe disease in the severely immune compromised.

There is a burgeoning population of individuals with acquired immune deficiency. The most obvious example of this phenomenon is the HIV pandemic in southern Africa. But there is also an increasing population of individuals treated with long-term corticosteroids and other immunosuppressant therapy. Congenital immune-deficiency syndromes are rare, but survival to adulthood is becoming increasingly common. However, in view of the rarity of the congenital syndromes and their diverse nature, this article will only cover the traveller with common acquired immune-deficiency states: HIV infection, immunosuppressant therapy and asplenia (usually after splenectomy). Specialist advice is recommended for other immune-deficiency states.

Many authorities recommend advising immune-suppressed patients not to travel. While this is sound conservative advice, it disempowers patients and is seldom necessary. Clearly it is imprudent to travel shortly after commencing either immune suppressants to prevent rejection of transplants or highly active antiretroviral therapy (HAART) in HIV infection. However, once patients are stabilised on therapy and prevention measures against opportunistic infections are being followed, safe travel is possible.

ASSESSING IMMUNE SUPPRESSION AND NON-TRAVEL-RELATED PREVENTION MEASURES

Establishing the level of immune suppression is a critical component of pre-travel assessment as this will determine the risk of infections as well as the immunisation strategy (see 'Immunisation' below). Prior to travel it is important to establish that routine prevention measures directed against opportunistic infections are correctly implemented in order to prevent the development of an opportunistic infection while travelling to destinations where health care facilities are limited.

Assessing the level of immune suppression is relatively straightforward in HIV infection — the CD4+ lymphocyte (T-helper cell) count is an accurate reflection of the level of immune suppression. Patients with a CD4+ lymphocyte count < 200 cells/µl are significantly immune suppressed. However, patients with significant HIV-related symptoms (Table I) are also significantly immune suppressed until they have been on effective HAART for 6 months or more. All patients with either low

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Table I. **HIV-related symptoms/diseases indicating significant immune suppression irrespective of CD4+ lymphocyte count**

Non-AIDS diagnoses
Oral thrush or hairy leukoplakia
Unexplained weight loss > 10% body weight
Pathogen-negative diarrhoea > 4 weeks

AIDS diagnoses
Pneumocystis pneumonia
Kaposi's sarcoma
Non-Hodgkin's lymphoma
Oesophageal thrush
Mucocutaneous herpes simplex ulcers > 4 weeks

*Conditions which are almost always associated with CD4+ lymphocyte counts < 200 cells/ml have been omitted.

CD4 counts or significant symptoms should receive prophylactic co-trimoxazole. This will afford only limited protection against travel-related infections, as resistance is common among enteric pathogens and *Plasmodium falciparum* malaria in most developing countries. Treatment of latent tuberculosis infection should probably only be commenced after travel, unless a long stay is anticipated. Annual influenza immunisations are recommended in HIV infection.

Patients on long-term corticosteroids are considered significantly immune suppressed if their daily dose is ≥ 20 mg of prednisone or equivalent. Patients on other immune-suppressant drugs will generally all be significantly immune suppressed. Immune-suppressant drugs result in impaired functioning of all arms of the immune response, but the predominant defect is usually impaired T-lymphocyte function. Many of the infections seen in these patients are similar to those seen in advanced HIV. In these patients prevention strategies are less clearly defined. Annual influenza immunisation is recommended. Prophylactic co-trimoxazole is generally only given in the year after transplant and seldom for other patients on immune-suppressant drugs. Treatment of latent tuberculosis infection is recommended in these patients, but is seldom given. As noted above, this should be commenced only after travel, unless a long stay is expected.

Asplenic patients are at risk of rapidly progressive infections caused by encapsulated bacteria (particularly pneumococci) and intracellular protozoan infections such as malaria. These infections are termed overwhelming post-splenectomy infections. This risk is highest in the first few years after splenectomy, but persists lifelong. All asplenic individuals should have pneumococcal vaccination every 5 years and have a Medic Alert bracelet/necklace. They should carry a course of antibiotics active against pneumococci (e.g. amoxicillin 500 mg 8-hourly) to take when they develop pyrexia. Prophylactic antibiotics with penicillin V 250 mg 12-hourly should be taken for the first 2 years (for adults) or 5 years (for children) after splenectomy. Some authorities recommend lifelong antibiotic prophylaxis. The reason for the splenectomy is an important factor in assessing the level of immune suppression — individuals with lymphoma who have undergone staging splenectomy are at higher risk of overwhelming post-splenectomy infection than those whose splenectomy followed trauma. Immune suppression in patients with lymphoma persists even when patients are in remission.

IMMUNISATION

There are three important facets to be considered before immunising the immune-compromised patient:

- assessing the level of immune suppression (see above)
- recognition of impaired immune responses to active immunisation

Table II. **Summary of immunisation guidelines for the immune-compromised traveller**

Immune suppression	Examples	Live vaccine	Killed/subunit vaccine
Severe	HIV CD4 < 200 OR significant symptoms Corticosteroid ≥ 20 mg prednisone Asplenia with lymphoma	Avoid	Safe but poor response
Mild/moderate	HIV CD4 > 200, no significant symptoms	Probably safe	Safe with fair response
	Corticosteroid < 20 mg prednisone	Probably safe	
	Asplenia without other condition	Safe	

- potential dangers of vaccination with live organisms.

Impaired immune responses

Immune responses to active immunisation are very poor in severely immune-suppressed patients. Passive immunisation (e.g. immune globulin for protection against hepatitis A) should be used whenever possible in this setting. HIV-infected patients who have had a good response to HAART still display poor responses to immunisation if their CD4+ lymphocyte count was < 200 cells/ml when they started HAART (i.e. the CD4 nadir rather than the CD4 count after HAART should be used to assess likely responses to immunisation). HIV-infected individuals experience a significant but transient rise in HIV RNA (the viral load) after active immunisation, but this is not thought to affect the course of their illness.

Potential dangers of vaccination

Patients who are not severely immune suppressed can probably be safely vaccinated with live organisms (Table II — summary of immunisation guidelines). In the context of travel health the live vaccine for which there is no substitute is yellow fever (live polio vaccines should be avoided and inactivated vaccine used instead). However, vaccination should clearly benefit the patient. If the risk of yellow fever is extremely low, but vaccination is required for travel to a certain area, then a waiver letter (see box below) should be considered for patients with mild to moderate immune suppression (asplenic patients without additional factors are not at risk from live vaccines).

Waiver letter for immunisation

A doctor's letter stating the contraindication to vaccination is acceptable to certain governments. Ideally, the letter should be written on letterhead stationery and bear the stamp used by health department and official vaccination centres to validate the International Certificate of Vaccination. When planning to use a waiver letter, the traveller should also obtain specific and authoritative advice from the embassy or consulate of the country or countries she/he plans to visit. Waivers of requirements obtained from embassies or consulates should be documented by appropriate letters and retained for presentation with the International Health Certificate.

SELECTED INFECTIONS

Malaria is more severe in HIV-infected individuals and probably also in patients on immunosuppressant therapy. Malaria is particularly severe in asplenic individuals. Therefore, in addition to anti-mosquito measures, effective chemoprophylaxis should be taken by immune-compromised travellers, even if they are travelling to low-risk areas or during low-risk seasons. Levels of atovaquone, which is used in a fixed-dose combination with proguanil (Malanil), are reduced by protease inhibitors, the significance of which is uncertain. However, it would be prudent to avoid Malanil use in HIV-infected patients on protease inhibitors. Treatment of malaria in patients on HAART is problematic because of significant drug interactions that affect quinine as well as artemether and lumefantrine (Coartem). This topic is outside the scope of this article; advice can be sought from infectious disease specialists or the Medicines Information Centre, tel (021) 406-6829.

Enteric infections are the commonest infections afflicting travellers. Enterotoxigenic *Escherichia coli* (ETEC) is the commonest cause of traveller's diarrhoea, but does not pose a special risk to immune-suppressed patients as it is not invasive. However, patients with severe immune suppression (advanced HIV, those on significant immunosuppressant therapy and asplenic patients with lymphoma) are at risk of life-threatening disease with invasive bacterial pathogens causing dysentery. The organism most associated with bacteraemia in these patients with severe immune suppression is non-typhoidal *Salmonella* species. Because of this risk, patients should be provided with a 3-day course of a fluoroquinolone (e.g. ciprofloxacin) for self-treatment. Prophylactic antibiotics (usually with a fluoroquinolone) for the

duration of stay should be considered for the most severely immune-suppressed travellers. Severe, chronic watery diarrhoea may occur after infection with one of the following protozoa: *Cyclospora cayetenensis, Cryptosporidium parvum, Isospora belli, Giardia lamblia* and microsporidiosis. The immune-suppressed traveller should therefore be very well educated about standard prevention measures to limit the risk of food and waterborne infections.

Meningococcal infections are likely to be fulminant in asplenic patients. Immunisation should therefore be offered to all such patients before travel.

DISCRIMINATION AGAINST THE HIV-INFECTED TRAVELLER

Many countries restrict or prevent entry to people who have HIV infection, despite the fact that the World Health Organization does not endorse this practice. This is particularly true of the prospective long-stay traveller seeking employment. Mandatory HIV testing is often demanded in this setting. Confidential enquiry before travel is essential. If HIV-infected individuals choose not to disclose their status, they run the risk of discovery and harassment if they carry antiretroviral therapy with them or if they carry waiver letters stating that live virus vaccines are contraindicated.

Further reading

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IN A NUTSHELL

The population of people living with acquired immune deficiency is burgeoning.

Immune compromised patients should be stable on therapy and receive routine prophylaxis against opportunistic infections before travel.

Assessment of the level of immune compromise is essential before immunisation.

Severely immune-suppressed patients must not be given live vaccines — an official waiver letter should be issued for countries requiring yellow fever vaccination.

Severely immune-suppressed patients respond poorly to active immunisation — where possible passive immunisation should be given.

Enteric pathogens that are invasive or associated with chronic diarrhoea can cause severe morbidity in immune-compromised patients.

Many countries discriminate against HIV-infected travellers.

SINGLE SUTURE

TAKE TIME OFF

Analysis of the Whitehall II study reports an association between what the authors describe as 'sickness presenteeism', i.e. not taking any time off, and serious coronary events. During the 3-year follow-up period of the study, 17% of unhealthy male British civil servants took no time off work. The incidence of non-fatal and fatal myocardial infarcts over 9 years was twice as high in this group as in unhealthy employees who had taken a moderate amount of time off work. Overworked doctors take note!

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