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Post-travel illness

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Abstract

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An estimated 50 million people travel from industrialised countries to less developed areas of the world annually. Between 20% and 70% of these travellers will experience ill-health whilst abroad. Although most of these ailments are minor, between 1% and 5% of travellers will seek medical advice either whilst abroad or on their return home. Additionally, one should consider groups such as refugees and asylum seekers who will present to doctors in industrialised nations with diseases endemic to their home countries. In travellers, the most common health problems are diarrhoea, respiratory infections and skin conditions, relatively minor complaints that can be easily managed at the primary care level. One to three per cent of post-travel patients will be febrile and, if they have travelled to an area endemic for malaria, should be investigated as a matter of urgency to exclude potentially life-threatening *P. falciparum* infection. The range of possible diagnoses in a post-travel patient is diverse and can be daunting. Taking a thorough travel and exposure history and considering incubation times can result in a more workable differential diagnosis.

Introduction

An estimated 50 million people travel from the industrialised world to the less developed world each year. Between 20% and 70% of these travellers will develop illness related to their travels.[1] Whilst most of these ailments are minor, 1–5% of travellers will seek medical advice for their travel-related illness either whilst abroad or on their return home.[2] Thus, it is to be expected that doctors in Australia and NZ will frequently be consulted by patients who have acquired illness whilst travelling.

Post-travel patients are diverse, with each group having unique potential exposures. Apart from the leisure traveller, one should consider special groups such as humanitarian workers, missionaries, religous pilgrims, the military, international students, business people, long-term expatriates and their families, adventure travellers, those travelling for sex and so on. It is not just travellers from the industrialised world to the less developed world who should be considered when looking at post-travel problems. One should also consider those moving in the opposite direction; refugees, immigrants, asylum seekers and migrant workers may all present with illness endemic to their home country.

As in all fields of medicine, a thorough history will provide the majority of the information required to produce a workable differential diagnosis. In the case of post-travel presentation this is arguably even more important than usual, as the range of possible illness is so broad and diverse.

The recent outbreak of SARS has highlighted the role that international travel can play in the spread of emerging diseases. The world's population is now incredibly mobile – at any time a patient may walk into our clinics or emergency rooms having departed from any point on the globe within the last 24 to 48 hours.

Epidemiology

Data are increasingly being collected to analyse the epidemiology of travellers' illness. One American study conducted in a travel medicine clinic analysed data collected from 780 individuals who had travelled to less developed countries for a period of less than three months. Of this cohort, 64% reported illness during their travels, the most common complaints being diarrhoea (46%), respiratory

FIGURE 1
ILLNESS IN A USA POST-TRAVEL CLINIC (ref 3)

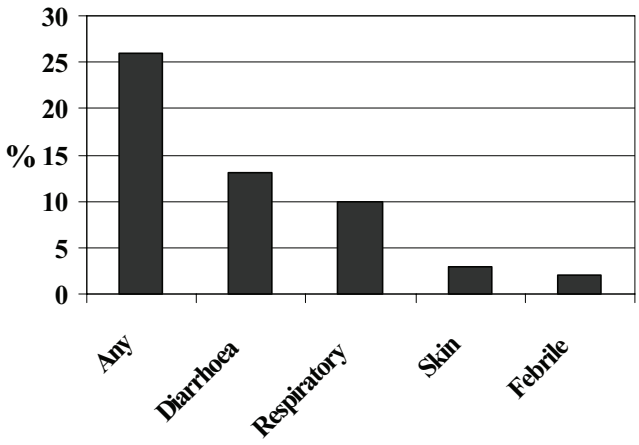

TABLE 1
10 MOST FREQUENT DIAGNOSES AT CIWEC TRAVEL MEDICINE CENTER, KATHMANDU, NEPAL

DIAGNOSIS	%
Acute bacterial diarrhoea	19
Acute respiratory infection	14
Skin condition (rash, infection, dermatitis)	5
Acute parasitic diarrhoea	5
Laceration, sprain, fracture	4
Healthy	3
Acute diarrhoea, unknown aetiology	2
Anxiety	2
Asthma	2
Animal bite/rabies post-exposure prophylaxis	2

TABLE 2
THE MINIMUM REQUIREMENTS FOR A POST-TRAVEL MEDICAL HISTORY

- Departure and return dates
- Countries and regions visited
- Illness whilst abroad
- Medications taken abroad
- Illness amongst fellow travellers
- Specific exposures: unsafe sex, swimming in fresh water or consumption of certain foodstuffs
- Pre-travel vaccinations: date(s) of administration
- Anti-malaria prophylaxis and compliance with prescribed regimen
- Detailed geographical history
- Activities undertaken
- Timescale of potential exposures

tract symptoms (26%) and skin problems (8%). Of the study group, 26% reported illness on their return home. Once again, the most common complaints were diarrhoea (13%), respiratory tract symptoms (10%) and skin problems (3%) (Figure 1).[3]

Similar figures are reported from the CIWEC Travel Medicine Center in Kathmandu, Nepal (P. Pandey, personal communication). This Western-run travellers' clinic sees approximately 6,000 patients annually and collects data on all patient visits. These unique data provide an excellent insight into the health problems of travellers whilst in a destination country. Of 8,900 travellers analysed, the most common complaints were acute bacterial diarrhoea (19%), acute respiratory infection (14%), skin conditions (5%), parasitic diarrhoea (5%), and injuries such as sprains, fractures and lacerations (4%), followed by a variety of other conditions (Table 1).

Thus, it is apparent that the majority of post-travel patients will present with relatively minor complaints that can be dealt with easily at the primary-care level. The febrile post-travel patient has more potential to be a medical emergency, but accounts for only 2–3% of ill travellers. Life-threatening conditions such as *Plasmodium falciparum* malaria must be excluded in these patients as a matter of urgency. An analysis of 232 febrile post-travel patients admitted to the Royal Melbourne Hospital showed malaria to be the most common diagnosis (27%), followed closely by respiratory tract infections (24%), then gastroenteritis (14%), dengue fever (8%), enteric fever (3%) and a variety of other conditions (Figure 2).[4]

FIGURE 2
FEBRILE POST-TRAVEL PATIENTS ADMITTED TO THE ROYAL MELBOURNE HOSPITAL (ref 4)

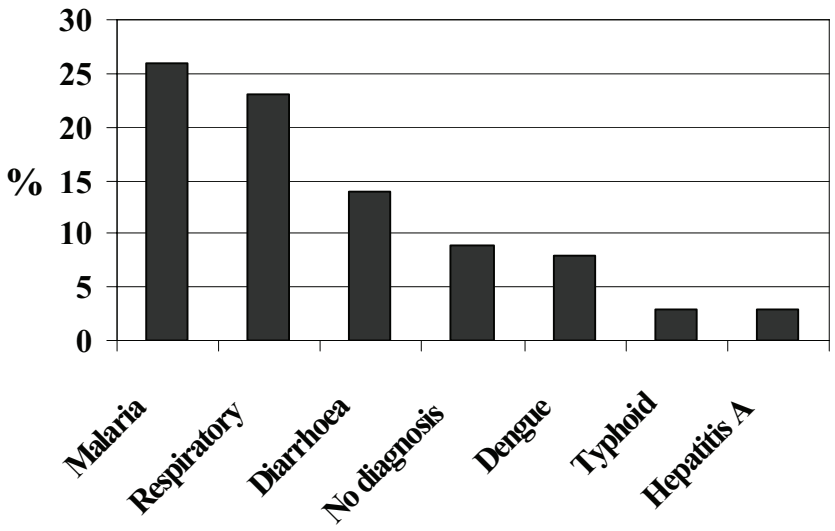

TABLE 3
TYPICAL INCUBATION TIMES FOR SELECTED TROPICAL DISEASES
(NB. This is not a comprehensive list)

SHORT (<10 days)
- Arboviral e.g., Japanese b encephalitis, dengue fever, yellow fever
- Bacterial diarrhoea
- Bacterial meningitis
- Haemorrhagic fevers e.g., Lassa, Marburg, Ebola
- Influenza
- Legionnaires' disease
- Leptospirosis
- Lyme disease
- Malaria
- Rabies
- SARS
- Streptococcal pharyngitis
- Typhoid and paratyphoid
- Typhus – African tick bite, flea-borne, scrub, Rocky Mountain spotted fever

MEDIUM (10–21 days)
- Amoebiasis
- Arboviral e.g., Murray Valley encephalitis, tick-borne encephalitis, Japanese b encephalitis
- Haemorrhagic fevers e.g., Congo-Crimean, Lassa, Marburg, Ebola
- Leptospirosis
- Lyme disease
- Malaria
- Measles
- Q fever
- Rabies
- Schistosomiasis (acute)
- Toxoplasmosis
- Trypanosomiasis
- Typhoid
- Typhus
- Hepatitis A (rarely)

LONG (>21 days)
- Amoebic liver abscess
- Brucellosis
- Filariasis
- Hepatitis, viral
- HIV
- Lyme disease
- Malaria
- Q fever
- Rabies
- Schistosomiasis (acute)
- Trypanosomiasis
- Tuberculosis
- Typhoid

Taking a post-travel history

Apart from the standard medical history, a travel history should be taken in as much detail as possible (Table 2). At a minimum this should include departure and return dates, all countries and regions visited, illnesses that occurred whilst abroad, medications taken abroad, illness amongst fellow travellers and specific exposures such as unsafe sex, swimming in fresh water or consumption of certain foodstuffs. Pre-travel vaccinations and their date of administration should be reviewed, as should the appropriateness of anti-malaria prophylaxis and patient compliance with the prescribed regimen.

A detailed geographical history will help exclude many potential pathogens and may also provide very specific clues. Activities undertaken can also offer specific clues. For instance, white-water rafting is associated with leptospirosis, walking safaris in southern Africa with African tick bite fever, and sexual contact with HIV. An accurate timescale of potential exposures and knowledge of incubation times are essential as these parameters may be used to exclude many aetiologies (Tables 3 and 4).

A thorough examination with a particular emphasis on temperature, lymphadenopathy, skin, chest, liver and spleen is imperative and may add further clues. Baseline investigations for a febrile patient should include: full blood count (FBC), three malaria smears, antigen testing, liver function tests, urea, electrolytes, blood culture, urinalysis, chest X-ray, stool and serum for relevant serology.

Fever in the post-travel patient

Febrile travellers must be assessed with urgency, in particular to exclude potentially life-threatening *P. falciparum* malaria. The 'big four' illnesses to exclude in the febrile traveller are malaria, dengue fever, enteric fever and hepatitis. The list of potential diagnoses is extensive and will not be covered in this review. A recent review article by Schwartz provides a timely methodological approach for the evaluation of fever in the returned traveller.[5]

MALARIA

Malaria has been covered in detail in a previous article in this series and will not be discussed again.[6] It is, however, important to emphasise that malaria remains the most frequently diagnosed disease in the febrile traveller and may be rapidly fatal.[4] The fever pattern in malaria is variable and may not be continuous, and the absence of fever at the time of evaluation should not exclude the possibility of malaria. At least three negative malaria smears read by a competent pathologist over a period of 48 hours are required to exclude the diagnosis. Most would agree that all patients with *P. falciparum* should be admitted to hospital for treatment as their clinical status may deteriorate rapidly.

DENGUE FEVER

Dengue fever is increasingly being recognised as a risk to travellers. Dengue viruses are the most common cause of arboviral disease in the world and are estimated to cause 50–100 million cases of dengue fever annually.[7]

The principal vector of dengue, *Aedes aegypti*, is found throughout the world between the latitudes of 35^{O} North and South. It is a highly efficient vector and over the past 60 years the incidence, distribution and clinical severity of dengue has increased dramatically.[7] An analysis of European travellers who had contracted dengue abroad showed that over 50% of cases were acquired in Asia. Thailand and India in particular are high-risk destinations.[8] Of patients admitted to the Royal Melbourne Hospital with dengue, 61% acquired their illness in Thailand.[4]

Dengue has a short incubation period of four to seven days and in the classical presentation common symptoms include the abrupt onset of high fever, severe headache, retro-orbital pain, myalgias, arthralgias and sometimes a maculopapular rash. Laboratory findings commonly associated with dengue include neutropenia, lymphocytosis, and thrombocytopenia.[7] Diagnosis is by virus isolation or positive serology. There is no specific treatment available for dengue. Patients should be watched for signs of dengue haemorrhagic fever (DHF), the more severe manifestation of the illness. DHF is primarily a disease of children under 15 in hyperendemic areas, characterised by haemorrhagic manifestations and a platelet count of less than 100,000.[7]

ENTERIC FEVER

Enteric fever is the clinical syndrome caused by *Salmonella typhi* (typhoid fever) or 'paratyphi' Salmonella species (paratyphoid fever). The dominant symptoms are sustained fever and headache. Patients have constipation, abdominal pain, and a dry cough. Leukopenia and thrombocytopenia may be present on FBC. The most common destination for acquiring the illness is the Indian subcontinent (India and Nepal), which now has increasing species of quinolone-resistant *Salmonella*. Eighty per cent of the cases of typhoid fever treated at the CIWEC Travel Medicine Center in Kathmandu, Nepal, this year have been resistant to ciprofloxacin (W. Cave, personal communication). Interestingly, older drugs such as co-trimoxazole are being found to treat the illness successfully. Diagnosis is made by culture. Blood culture is approximately 50% sensitive, whilst bone marrow is more reliable and offers approximately 90% sensitivity. Without treatment, the case fatality rate of enteric fever is 10%. This is reduced to less than 1% with appropriate antibiotic therapy.

HEPATITIS

Theoretically, hepatitis A should no longer be a cause of fever in travellers since the advent of a highly effective vaccine. It is therefore disturbing to see that hepatitis A still accounted for 3% of the patients in the Royal Melbourne Hospital series. This reflects a failure of travellers to seek appropriate advice pre-travel, or of healthcare providers to offer adequate pre-travel vaccination advice.

Hepatitis E is endemic in Nepal and there is currently no vaccine available. Like hepatitis A, it is food and water borne and presents clinically in a manner indistinguishable from hepatitis A. Hepatitis E is a particularly serious disease in pregnant women resulting in a 30% maternal and fetal mortality rate if contracted in the final trimester. A vaccine trial is currently underway in Kathmandu; unblinding of the results will occur in May of this year. Interestingly, this study has been conducted in members of the Royal Nepalese Army and has shown an incidence rate of 5% in the study population (R. Scott, personal communication). The diagnosis is made on serology and should be considered in all cases of hepatitis in travellers, particularly in those to the Indian subcontinent. Treatment is supportive.

TABLE 4
SPECIFIC EXPOSURES FOR SELECTED TRAVEL-RELATED DISEASES

Untreated water
Hepatitis A and E, bacterial diarrhoea, cholera
Unpasteurised dairy products
Brucellosis, Q fever
Undercooked meat
Cestodes, trichinosis, bacterial diarrhoea
Animal contact/bites
Rabies, Q fever, typhus, echinococcosis, leptospirosis
Mosquitoes
Malaria, dengue fever, yellow fever, arboviruses
Sand flies
Leishmaniasis
Tsetse flies
Trypanosomiasis
Ticks
Rickettsial disease
Fleas
Murine typhus, plague
Freshwater exposure
Schistosomiasis, leptospirosis
Barefoot exposure
Strongyloidiasis, cutaneous larva migrans
Sexual contact
HIV, other STDs
IV drug use/tattoos/transfusions
HIV, hepatitis B and C, malaria
Sick contacts
Meningitis, TB

Diarrhoea

Acute traveller's diarrhoea has previously been discussed in these review articles.[9] Chronic diarrhoea (diarrhoea of greater than two weeks' duration) is more likely to present to the doctor evaluating a post-travel patient. Chronic diarrhoea is more commonly parasitic than bacterial in origin, however a bacterial cause should always be excluded. In Kathmandu, *Campylobacter* is the second most commonly found pathogen in patients with diarrhoea lasting for two to four weeks (P. Pandey, personal communication). The most common parasitic causes of prolonged diarrhoea in travellers are *Giardia lamblia, Entamoeba histolytica*, *Cryptosporidium* and *Cyclospora*.[10]

GIARDIASIS

Giardia lamblia is the most common protozoan infection in returning travellers.[10] At the CIWEC clinic it accounts for 5% of cases of traveller's diarrhoea. *G. lamblia* tends to cause a prolonged, low-grade illness characterised by two to five loose bowel motions daily with accompanying nausea, mild fatigue and abdominal discomfort. 'Sulphurous burps' are often mentioned in travel books as being specific to *G. lamblia*, however analysis of data collected at CIWEC has shown that they are no more common in patients with *G. lamblia* than those with any other pathogen.

G. lamblia is diagnosed by stool examination, but may be difficult to find. Antigen testing can also be carried out and this gives a more reliable result. Empiric treatment for giardiasis is often suggested if a bacterial cause has been excluded in a patient with chronic diarrhoea post-travel. Tinidazole, 2 g daily for two days, is the standard protocol. In some areas of the world e.g., Kathmandu, tinidazole resistance is now developing. Treatment with quinacrine, 100 mg three times daily (TDS) for five days, is effective treatment in these refractory cases.

AMOEBIASIS

Entamoeba histolytica is an unusual cause of diarrhoea in travellers. The most important point to raise regarding *E. histolytica* is the identification of two distinct but morphologically identical strains of amoebae.[11] *E. histolytica* is a pathogen that can cause disease ranging from asymptomatic to liver abcess and fatal colitis. *E. dispar* is non-pathogenic. The two strains are indistinguishable under the microscope and can only be differentiated using *E. histolytica* antigen testing. *E. dispar* does not require treatment whereas *E. histolytica* should be treated with tinidazole 2 g daily for three days followed by diloxanide furoate 500 mg TDS for 10 days.

OTHER PARASITES

Cryptosporidiosis is also uncommon in travellers but should be considered in all cases of prolonged diarrhoea post-travel. The laboratory should be specifically requested to look for *Cryptosporidium*; at 4 microns (mm) diameter it is best diagnosed using an acid fast stain and fluorescent microscope. In immunocompromised individuals, *Cryptosporidium* can be a debilitating illness and there is currently no highly effective treatment.

Cyclospora accounts for 5% of the diarrhoea seen in Kathmandu, a city known to be highly endemic for the parasite. *Cyclospora* appears during the hot, rainy monsoon months in Nepal (June to October) and is characterised by the abrupt onset of watery diarrhoea accompanied by upper abdominal symptoms. Profound fatigue is commonly reported. The parasite is 8 mm in diameter and can be identified by the naked eye by an experienced microscopist, but is more easily identified with acid fast staining. Once again, the laboratory should be specifically asked to look for *Cyclospora*. Treatment is with trimethoprim-sulphamethoxazole double strength, twice daily for one week. Unfortunately there is no alternative treatment for those with sulphur allergy and without treatment the illness lasts on average six weeks.

If travellers have been on antibiotics, the diagnosis of *Clostridium difficile* should also be entertained and a request for *C. difficile* toxin made on stool examination.

TROPICAL SPRUE

Tropical sprue is a malabsorption syndrome acquired in the tropics and associated with weight loss, fatigue and decreased appetite. The cause of the disease remains unclear; however, it often occurs after an episode of acute bacterial diarrhoea when travelling. Diagnosis is made after empiric treatment for parasitic causes has failed, if the clinical criteria are fulfilled and the patient has an abnormal D-xylose test. Treatment is with 250–500 mg tetracycline four times daily for four to six weeks, and folate 5 mg daily. If there is no response after four weeks of treatment an alternative diagnosis should be considered and the patient should be referred to a gastroenterologist.[10]

Patients with chronic diarrhoea who do not respond to empiric treatment for bacteria and parasites, have a clear stool, no evidence of colitis, no weight loss and a normal D-xylose test are a problematic group. Dietary manipulation may be helpful, for instance avoidance of dairy products. It is important that they are reassured they do not have a hidden parasite and do not waste their time doctor shopping in order to find a solution. Post-infectious irritable bowel syndrome (IBS) is the most likely diagnosis and should be managed along standard lines for the treatment of IBS.

One should also be aware of the possibility of inflammatory bowel disease presenting for the first time post-travel. Thus, if there is weight loss, evidence of colitis or any concerning clinical features the patient should be referred to a gastroenterologist.

Skin conditions

CUTANEOUS LARVA MIGRANS

Cutaneous larva migrans is the most commonly reported skin condition in travellers returning from tropical countries.[12] It is caused by the larvae of animal hookworms *Ancylostoma braziliense* or *A. caninum*. Humans are infected as a result of skin contact with contaminated soil. Humans are only an incidental host, however, so whilst the larva burrows through intact skin it remains in the upper dermis.[13] Time from exposure to the onset of symptoms is one to six days and classically the lesion will start as an erythematous papule that then becomes serpiginous as the larva burrows along the upper dermis. It is usually intensely pruritic and it is this symptom that causes people to seek treatment. Complications such as impetigo and allergic reactions may occur. Whilst it is a self-limiting condition (spontaneous healing usually occurs within weeks or months), treatment with ivermectin or albendazole will usually result in rapid resolution of troublesome symptoms.[14]

LEISHMANIASIS

Leishmaniasis results from infection with one of the protozoan parasites of the *Leishmania* species. The organism is transmitted to humans by the bite of an infected sandfly and occurs in tropical and subtropical areas throughout the world except Australia. Worldwide, over two million cases occur each year and leishmaniasis is increasingly recognised as a risk to travellers.[15] The majority of cases in travellers are contracted in central and South America.[16] There are three quite distinct clinical syndromes – visceral leishmaniasis, cutaneous leishmaniasis and mucocutaneous leishmaniasis. The majority of cases in travellers are of cutaneous leishmaniasis. An ulcerous skin lesion develops at the site of the bite. These lesions are typically painless and slowly progressive and will heal spontaneously after between three and six months.[17] Diagnosis is made by biopsy and the patient should be referred to an infectious diseases specialist.

MYIASIS

Myiasis is caused by the invasion of skin by larval maggots of various *Diptera* fly species – most commonly the botfly in South America and the tumbu fly in Africa.[17] The botfly is the common name for *Dermatobia hominis*. The botfly lays its eggs on another insect, usually a mosquito, which then transfers the eggs onto human skin whilst feeding. These eggs penetrate the skin and then slowly develop into larvae, thus creating a subcutaneous nodule. At this stage, the larva remains in contact with the air and thus there is a punctum in the nodule through which the larva breathes.[18] Afflicted patients often feel a sensation of movement within the nodule as the larva grows. After about four to six weeks the larva matures and emerges from the lesion; however, most people seek medical attention before this occurs. Treatment consists of removal of the larva by occluding the punctum with vaseline or an occlusive dressing for 12 hours and then gentle removal. Antibiotics are not required unless there is evidence of secondary infection. Prevention is by use of insect repellent.

In Africa, the tumbu fly will present in a similar fashion. However, the eggs of the fly are usually laid on people's clothes as they are hung out to dry. When the infected clothes are worn the eggs hatch and penetrate the skin, and multiple lesions are the norm. Prevention is by ironing all clothes before wearing them.

Other common skin conditions include pyoderma, insect bite dermatitis, tungiasis and urticaria.

Schistosomiasis

Special mention should be made of schistosomiasis as it is common for travellers to present to their primary-care doctor requesting that they be checked for infection after travel to an endemic area. Schistosomiasis is caused by various species of blood flukes belonging to the genus *Schistosoma*.[19] The majority of infected travellers will be exposed to schistosomiasis in Africa, particularly by swimming in freshwater lakes such as Lake Malawi. There are four species of schistosomes that infect man but they all have the same lifecycle. Eggs are voided from humans in their stool and urine. On reaching fresh water, these eggs hatch and their larvae then infect specific species of aquatic snail (the intermediate host). After a period of time, the microscopic larvae are released into the water. Humans then become infected by exposure to the fresh water.

If patients are symptomatic, they will most commonly present with haematuria, dysuria or urinary frequency if infected with *S. haematobium*, or with abdominal pain, diarrhoea and rectal bleeding if infected with *S. mansoni*.[20] The majority of infected individuals are, however, asymptomatic and present for screening as they are aware that they may have been exposed. As infection can result in delayed serious complications, all travellers requesting investigation should undertake the following, ideally at least 12 weeks after their final exposure: FBC, schistosomiasis serology, one stool sample and urine dipstick. Eosinophilia is not a reliable finding. Serology is far more reliable with the ELISA test being >95% sensitive for *S. mansoni* and 90% sensitive for *S. haematobium*. Stool and urine microscopy provides additional support for a positive serological result. However, most travellers have a low parasite burden and hence rarely show eggs on microscopy. Positive serology requires treatment with praziquantel 20 mg per kg body weight.

Investigating the asymptomatic post-travel patient

Travellers will often present requesting a 'post-travel checkup'. A thorough history should be taken that looks

for particular exposure risks, especially sexually transmitted diseases and schistosomiasis. A thorough examination should also be performed. A basic work up would include a FBC, one stool sample for ova/cysts/parasites (O/C/P) and serology as relevant e.g., for schistosomiasis or an STD checkup. This is a good opportunity to offer any vaccine boosters that may be required, or to undertake a post-travel Mantoux test if required. One should also keep in mind psychological problems that may occur after travel. In particular, readjustment disorder (reverse culture shock) for long-term travellers and expatriates is a well-recognised phenomenon and may present with somatisation.

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