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Whilst the text is directed to health professionals possessing appropriate qualifications and skills in ascertaining and discharging their professional (including legal) duties, it is not to be regarded as clinical advice and, in particular, is no substitute for a full examination and consideration of medical history in reaching a diagnosis and treatment based on accepted clinical practices.

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Travel health

Unit 524 January–February 2016

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- Applied professional knowledge and skills
- Population health and the context of general practice
- Professional and ethical role
- Organisational and legal dimensions

RACGP
More Australians than ever before are now travelling to other countries, with rates increasing 2.5 times between 2000 and 2013 to more than 7.63 million visits. General practitioners (GPs) are best placed to provide expert advice to travellers on risks associated with specific destinations. In particular, travellers need to be aware of infectious diseases that may be acquired when visiting other countries; GPs can provide information about how to best avoid or minimise contact with sources of infection, as well as provide appropriate vaccinations.

Schistosomiasis is an infectious disease that affects an estimated 240 million people globally, with more than 700 million living in an endemic area. In a systematic review on the sexual behaviours associated with international travel, about 50% of travellers who engaged in new sexual relationships inconsistently used condoms. The review also found that the risk of developing a sexually transmissible infection while travelling increased threefold. Influenza causes an estimated 3500 deaths, 18,000 hospitalisations and more than 300,000 GP consultations each year in Australia. Japanese encephalitis is a mosquito-borne viral disease that is most prevalent in many parts of Asia and most cases in Australia are from returning travellers. In 2011–12, there were more than 350 notifications of overseas-acquired malaria in Australia, mainly from travellers returning from the Asia-Pacific region, Africa and the Middle East.

This edition of check considers the management and treatment of travel health that may present in general practice.

**LEARNING OUTCOMES**

At the end of this activity, participants will be able to:

- describe the assessment of a returned traveller presenting with fever
- discuss the diagnosis of schistosomiasis
- outline protective and preventive measures against Japanese encephalitis
- summarise the recommendations for investigating and treating influenza
- list current options for malaria chemoprophylaxis
- review the management of sexually transmissible infections in returned travellers.

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**REFERENCES**


**ACRONYMS**

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Description</th>
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<tbody>
<tr>
<td>ASPREN</td>
<td>Australian Sentinel Practices Research Network</td>
</tr>
<tr>
<td>BCG</td>
<td>Bacillus Calmette-Guérin</td>
</tr>
<tr>
<td>CDC</td>
<td>Centers for Disease Control and Prevention</td>
</tr>
<tr>
<td>CRP</td>
<td>C-reactive protein</td>
</tr>
<tr>
<td>dTPa</td>
<td>diphtheria, tetanus and pertussis</td>
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<tr>
<td>ELISA</td>
<td>enzyme-linked immunosorbent assay</td>
</tr>
<tr>
<td>FBE</td>
<td>full blood evaluation</td>
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<tr>
<td>GP</td>
<td>general practitioner</td>
</tr>
<tr>
<td>HBV</td>
<td>hepatitis B virus</td>
</tr>
<tr>
<td>HIV</td>
<td>human immunodeficiency virus</td>
</tr>
<tr>
<td>IAMAT</td>
<td>International Association for Medical Assistance to Travellers</td>
</tr>
<tr>
<td>ISTM</td>
<td>International Society for Travel Medicine</td>
</tr>
<tr>
<td>JE</td>
<td>Japanese encephalitis</td>
</tr>
<tr>
<td>LFT</td>
<td>liver function test</td>
</tr>
<tr>
<td>MDR</td>
<td>multidrug-resistant</td>
</tr>
<tr>
<td>MERS</td>
<td>Middle East respiratory syndrome</td>
</tr>
<tr>
<td>MMR</td>
<td>mumps, measles and rubella</td>
</tr>
<tr>
<td>NAAT</td>
<td>nucleic acid amplification test</td>
</tr>
<tr>
<td>NAI</td>
<td>neuraminidase inhibitor</td>
</tr>
<tr>
<td>NICE</td>
<td>National Institute for Health Care and Excellence</td>
</tr>
<tr>
<td>PHU</td>
<td>Public Health Units</td>
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<tr>
<td>RADT</td>
<td>rapid antigen detection test</td>
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<tr>
<td>RNA</td>
<td>ribonucleic acid</td>
</tr>
<tr>
<td>STI</td>
<td>sexually transmissible infection</td>
</tr>
<tr>
<td>TB</td>
<td>tuberculosis</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
</tbody>
</table>
CASE 1

JANE HAS A FEVER

Jane, 29 years of age, is a registered nurse who presents to you with a two-day history of fever, dry cough and abdominal pain. She has no significant past medical history and her only regular medication is the oral contraceptive pill. She has no known allergies.

QUESTION 1

What further information should you obtain from Jane? What physical examination would you perform?

FURTHER INFORMATION

Jane tells you that she returned to Australia three weeks ago after a four-week trip to Kenya, Uganda and Madagascar. She spent 10 days in Uganda, which included a trek in the Ruwenzori mountains, then three days relaxing on the coast of Kenya in Mombasa, before a two-week 'eco tourism' project in Madagascar. Jane travelled with four friends, one of whom developed a fever and itchy rash yesterday. Her friend’s general practitioner (GP) had suggested she was having an allergic reaction, perhaps to the doxycycline she was still taking for malaria prophylaxis.

Jane was vaccinated against yellow fever, hepatitis A and typhoid prior to her trip. She had previously completed hepatitis B vaccination, mumps, measles and rubella (MMR) and diphtheria, tetanus and pertussis (dTPa) vaccinations as part of her occupational requirement. She had discussed rabies vaccine with the clinic but decided against it, and had proven immunity to varicella. She had taken atovaquone/proguanil for malaria prophylaxis, as directed, and had experienced no side effects.

She recalled many insect bites, had one casual sexual encounter in Uganda with a British traveller (but had used a condom), experienced no animal bites, and drank no raw dairy products. About one week after arriving in Madagascar, she visited the Lily Waterfall and had a very quick swim, only for about five minutes.

On examination, Jane’s temperature is 38.5°C, heart rate is 92 beats per minute and blood pressure is 125/80 mmHg. She looks only mildly unwell. She has no rash or lymphadenopathy. Her chest examination reveals bilateral wheeze. Her abdomen is soft and she has some mild peri-umbilical tenderness.

QUESTION 2

What are your differential diagnoses? What tests would you order?

FURTHER INFORMATION

Jane’s malaria smears are negative, her blood tests are normal (apart from a very mild eosinophilia), urinalysis is normal and her chest X-ray is also reported as normal.

QUESTION 3

What is your working diagnosis?
QUESTION 4
What are the common signs and symptoms of acute schistosomiasis? How is it diagnosed?

QUESTION 5
How common is acute schistosomiasis? Where is it found and how is it treated?

QUESTION 6
What follow-up should Jane be advised to undertake?

QUESTION 7
Should Jane’s travelling companions be tested?

QUESTION 8
What advice should travellers who are going to schistosomiasis-endemic areas be given before travel?
CASE 1 ANSWERS

ANSWER 1
The usual history taking would apply as for any standard consultation. It would be easy to dismiss this presentation as just another respiratory tract infection. However, it is important to ask any febrile patient the simple question, “Have you travelled anywhere in the past 12 months?”.

A positive answer should prompt further enquiry into the exact itinerary, travel dates in each destination, date of return to Australia, specific exposures, pre-travel vaccinations and, if appropriate, whether antimalarial medication was prescribed and taken as directed. Specific exposure enquiries should include sexual contacts, the use of personal protective measures against insects, insect bites noted, exposure to fresh water, animal bites, contact with farm animals, and consumption of other potentially contaminated foods and fluids (eg raw foods). It can also be helpful to enquire if any of Jane’s fellow travellers had been sick either on the trip or after returning to Australia.1

Physical examination should ensure standard vital signs are recorded, followed by a particular focus on the chest, abdomen and skin.

ANSWER 2
It is important to consider all diseases that you would consider in a non-traveller. A proportion of febrile illness post-travel is caused by non-travel-related infections such as pneumonia or urinary tract infection. Given Jane’s sexual encounter and abdominal pain, pregnancy should be excluded, as should sexually transmissible infections (STIs).

Although Jane took her antimalarial medication as directed, it remains important to exclude malaria in any febrile traveller who has returned from a malaria endemic area within the previous 12 months—Plasmodium falciparum is the priority diagnosis.1 Note, the Northern Territory guidelines recommend testing travellers who have returned from endemic malaria regions in the past two years.2

The list of differential diagnoses is long; however, the initial focus should be on identifying any diseases that are rapidly progressive, treatable or transmissible including:3

- malaria
- typhoid
- leptospirosis
- acute human immunodeficiency virus (HIV)
- hepatitis E
- amoebic liver abscess
- East African trypanosomiasis
- acute schistosomiasis.

The incubation period of longer than three weeks makes dengue fever, chikungunya and rickettsial spotted fevers unlikely.3 Initial investigations should include:

- malaria smear and rapid test x 3 at 12- to 24-hour intervals
- full blood evaluation (FBE)
- blood cultures

ANSWER 3
The incubation period, clinical symptoms and signs, and mild eosinophilia, combined with Jane’s freshwater exposure at the Lily Waterfalls in Madagascar point to a diagnosis of acute schistosomiasis, also known as Katayama fever.4,5

ANSWER 4
The diagnosis of acute schistosomiasis remains a challenge.

The clinical stages of schistosomiasis reflect the life cycle of the parasite (Figure 1).6

Some individuals, 5–100% in various studies, develop a diffuse pruritic maculopapular rash within 24 hours of exposure to fresh water. This reflects a reaction to the transcutaneous penetration of the cercariae7 and usually only lasts from minutes to hours. A history of such a reaction should be sought.

The next stage of the lifecycle is the tissue migration and maturation of the schistosomules. Acute schistosomiasis is thought to reflect a hypersensitivity reaction to the schistosomules, and symptoms typically occur two to six weeks after exposure (range one to 12 weeks). The most common symptoms are fever, abdominal pain, cough, headache, myalgia and an urticarial rash.

Symptoms may vary with the species (Table 1).

<table>
<thead>
<tr>
<th>Signs and symptoms</th>
<th>S. mansoni, % (n = 95)</th>
<th>S. haematobium, % (n = 34)</th>
<th>S. mekongi, % (n = 7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>54–100</td>
<td>93–94</td>
<td>86</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>33–93</td>
<td>0</td>
<td>42</td>
</tr>
<tr>
<td>Dry cough</td>
<td>17–91</td>
<td>44–86</td>
<td>71</td>
</tr>
<tr>
<td>Headache</td>
<td>33–87</td>
<td>31–93</td>
<td>86</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>25–81</td>
<td>14</td>
<td>28</td>
</tr>
<tr>
<td>Myalgia</td>
<td>50–74</td>
<td>14–69</td>
<td>28</td>
</tr>
<tr>
<td>Neck pain</td>
<td>64</td>
<td>71</td>
<td>No comment</td>
</tr>
<tr>
<td>Urticaria</td>
<td>8–17</td>
<td>13–57</td>
<td>71</td>
</tr>
</tbody>
</table>

The symptoms of acute schistosomiasis typically last from days to weeks, whereas the cough, in particular, can linger for up to six weeks. There is no specific diagnostic test available at this stage. Eosinophilia is often, but not universally, present8 and, furthermore, is often delayed by up to three weeks from the onset of symptoms.7 Ova production does not occur until the end of the maturation phase, so there is a delay of at least 30–50 days between exposure and egg production. Thus, a search for ova in the stool or urine at this stage is usually fruitless. Similarly, seroconversion is unlikely to
Figure 1. Schistosome lifecycle

Reproduced with permission from Gray DJ, Ross AG, Li YS, McManus DP. Diagnosis and management of schistosomiasis. BMJ 2011;342:d2651. Available at www.bmj.com/content/342/bmj.d2651 [Accessed 21 October 2015].
CASE 1

Acute schistosomiasis usually resolves spontaneously, but there have been case reports of serious acute complications, including myocarditis, pericarditis and neurological complications secondary to eosinophilia-induced cerebral vasculitis.\textsuperscript{7,9,10}

ANSWER 5

Acute schistosomiasis is increasingly being recognised in travellers returning from endemic countries and can occur with all species. In one study of 1800 febrile Belgian travellers, acute schistosomiasis was the third most common cause of fever in travellers from Africa, after malaria and rickettsial infections.\textsuperscript{12}

The vast majority of cases are found in travellers exposed in Africa, but in the Asian regions, cases have been reported from travellers to Laos, where \textit{S. mekongi} is prevalent. Traditionally, only southern Laos was considered an area of risk, yet one study found a small number of travellers with acute schistosomiasis whose only freshwater exposure was in northern Laos.\textsuperscript{13}

Awareness of acute schistosomiasis in the general practice setting has been shown to be low.\textsuperscript{14} A recent report of a cluster of 36 French patients exposed at the Lily Waterfalls in Madagascar found that 78% ultimately had positive serology. Of these, 82% had symptoms compatible with acute schistosomiasis and 70% of these travellers had seen their GP while sick. Acute schistosomiasis was not considered as a diagnosis in any of the patients – the diagnoses retained after the first consultation included viral infection (19%), invasive gastroenteritis (12%), pneumonia (6%) and typhoid (6%). Rather alarmingly, only 6% entertained the diagnosis of malaria.\textsuperscript{14}

The current edition of Therapeutic Guidelines – Antibiotics does not make specific comment on acute schistosomiasis. It is important not to treat acute schistosomiasis with praziquantel, as this is likely to cause a worsening of symptoms, which may even become life threatening.\textsuperscript{9,10} Corticosteroids may be indicated in severe cases,\textsuperscript{6} and such cases should be managed by an infectious diseases physician.

Chronic schistosomiasis remains a major public health issue in tropical countries. Transmission occurs in 78 countries and over 230 million people are estimated to be chronically infected.\textsuperscript{11} There are six species of schistosomiasis; the majority of cases are caused by \textit{Schistosoma haematobium}, \textit{S. mansoni} and \textit{S. japonicum} (Figure 2).

ANSWER 6

Periodic serological testing should be undertaken. It may take three to six months after exposure for serology to become positive.\textsuperscript{15} Serology does not allow for speciation, so it is worth collecting stool and urine samples to search for ova. Urine collected in the middle of the day is more likely to identify ova, but the yield is generally poor; one Australian study of 28 travellers identified eggs in only 7.8% of those diagnosed via positive serology.\textsuperscript{16}

Praziquantel is an effective treatment against the adult worm\textsuperscript{17,18} and must be prescribed only after sufficient time has passed to ensure the parasite is now mature. Three months post-exposure is
recommended, and the Therapeutic Guidelines recommend a dose of 40 mg/kg divided into two doses of 20 mg, given four hours apart for *S. mansoni* and *S. haematobium*, and 60 mg/kg in three divided doses for *S. mekongi* and *S. japonicum*. Serology tends to remain positive for long periods; only 45% of travellers have a four-fold decrease in serology after 12 months and 64% at 24 months post-treatment. Thus, it is not recommended to repeat serology as a ‘proof of cure’. One Danish study found a 20% treatment failure rate with single-dose praziquantel treatment on the basis of viable ova identified in tissue samples. The authors recommended consideration of a repeat dose of praziquantel after one to three months in all travellers; however, this is not reflected in current Australian guidelines. Yong and colleagues suggest repeat treatment should instead be confined to those with ongoing symptoms, ongoing eosinophilia or parasite identification.

**ANSWER 7**

All travellers to endemic areas who have had even a one-minute exposure to fresh water should be tested with serology three months post travel. Many cases of schistosomiasis in travellers will be asymptomatic, but there have been numerous case reports of late complications including infertility.

**ANSWER 8**

Travellers should be aware of the possibility of schistosomiasis transmission with exposures even as short as one minute. They should be aware of the potentially serious complications of acute schistosomiasis, including myocarditis, pericarditis and neurological manifestations including seizures, motor paralysis and ataxia. Furthermore, travellers should be advised that it is common practice for locals to tell them that a body of water is ‘safe’ when this is not the case. Travellers are often advised by locals to take a dose of praziquantel immediately after swimming — this is not only ineffective but has been shown to delay the detection of eggs by up to 11 months, and should thus be avoided. Unfortunately, warning people about schistosomiasis appears to be ineffective. In the group of French travellers previously described, about half reported that they were aware of the risk, yet 80% still swam in the waterfall. Of French travellers previously described, about half reported that they were aware of the risk, yet 80% still swam in the waterfall. Thus, travellers should be informed of the importance of attending follow-up three months post-travel for serological testing, even if they are asymptomatic.

**REFERENCES**


CASE 2

AMY PRESENTS WITH A DRY COUGH
It is January and Amy, aged 22 years, calls your practice requesting an appointment. She takes the last free appointment and comes in to see you. She says she is staying with one of your regular patients, a mother with two children, aged 3 and 6, who is pregnant with her third child. She complains that for the past three days, she has had ‘a horrible dry cough’, has been ‘feeling hot and tired’, and ‘just feels sore all over’.

QUESTION 1
How would you manage this consultation? What features of the history are you most interested in?

FURTHER INFORMATION
Amy is a healthy, active university student. She describes an abrupt onset of symptoms one day after arriving home from a recent overseas trip. She spent most of her time staying with friends in Tokyo, Japan who were also coughing and unwell. Amy also spent several days in Saudi Arabia visiting temples at the beginning of the trip five weeks ago. She is otherwise well and has no personal or family history of asthma or other respiratory conditions. She is a nonsmoker. She tells you that she has not had any vaccinations since she left high school.

On examination, Amy has a temperature of 38.5°C and looks flushed. She has a respiratory rate of 25 breaths/min with no respiratory distress. Her respiratory and cardiovascular examinations are unremarkable.

QUESTION 2
What is the most likely diagnosis?

FURTHER INFORMATION
Amy tells you that while she visited her grandmother at the local nursing home, the television news was reporting about Middle East respiratory syndrome (MERS). Amy is worried that she might have MERS.

QUESTION 3
Where would you look for information and support in management if you suspected MERS in the differential?
QUESTION 4
Would you consider doing any investigations? What is your rationale for this choice? Would you consider giving Amy any medication?

QUESTION 5
What is the risk for the pregnant mother if she acquires Amy’s illness? What is the benefit of vaccination for the mother?

FURTHER INFORMATION
Amy reminds you that she visited her elderly grandmother at the local nursing home while she was unwell. Her grandmother’s medical history includes hypertension, hyperlipidaemia and a past history of acute myocardial infarction one year ago.

QUESTION 6
What places Amy’s grandmother at higher risk? What is the benefit of vaccination for those in this risk group?

CASE 2 ANSWERS

CASE 2 ANSWERS

ANSWER 1
Transmission of infection
As Amy has presented with symptoms of a communicable disease, it is important to consider the risk of transmission both within your practice and with outside contacts. It would be reasonable to consider implementing transmission-based procedures (ie droplet and contact precautions).1–3 This could include offering the patient a surgical mask to wear when not in isolation, and practising hand hygiene and cough etiquette.

The use of signage in practices informs patients presenting with flu-like symptoms to immediately tell staff on arrival, to don a surgical mask (Grade C evidence), and perform hand hygiene (Grade B evidence) with use of alcohol-based hand rubs that contain 60–80% v/v ethanol or equivalent (Grade B evidence) or, if visibly dirty, using soap and water (Grade B evidence).1–4

History and examination
A full history is important in attaining a likely diagnosis. The onset, duration and severity of symptoms, as well as associated symptoms, will be important in guiding clinical management. Ask about associated symptoms including cough, dyspnoea, sore throat, myalgia, headaches and diarrhoea.5

Details of recent travel and vaccination status are vital in formulating a diagnosis of communicable disease. A history of contact with unwell individuals and a knowledge of the epidemiology of disease prevalence in the countries visited will help to rule out conditions such as malaria, and rule in others such as influenza. Websites such as CDC Travel have updated information available.6

A history of contact with animals (eg poultry or bats during travel in Asia) is useful in reference to possible contact with the H5N1 avian influenza or rabies.7

Exploring the patient’s comorbidities, including chronic conditions such as cardiovascular, respiratory, obesity, smoking, and pregnancy status, will assist in understanding the patient’s risk of developing serious illness.8

Identification of any potential contact at high risk of complications from an infectious disease is useful for early detection and treatment of others. Amy has had contact with a pregnant woman and her two children.

ANSWER 2
Considering that Amy was predominantly in Japan, potential risks include hepatitis A and B, Japanese encephalitis (JE), rabies, tick-borne encephalitis, H5N1 avian influenza and current seasonal influenza. Most of these can be excluded by her presenting symptoms and the fact she spent her time in the city. For example, she is not at high risk for JE as she was not in rural areas or in the peak season.6,9

The most likely diagnosis is seasonal influenza.

Influenza is the most common vaccine-preventable health risk for travellers.8 Hundreds of millions of people travel annually and 15–50% experience health problems. Respiratory tract infections, including pharyngitis, influenza and pneumonia, are the second most common cause of illness in travellers, and of fever.10,11
In particular, influenza is associated with travel to the Northern Hemisphere during the period of December through February. Travellers to tropical regions are at risk of influenza all year round. Amy was in Japan in January, the peak influenza season in the Northern Hemisphere. Amy also had other significant risk factors for influenza, including a trip duration of >30 days and “the reason for travel” being to visit friends and relatives. The latter alone increases the risk of acquiring influenza six-fold.

This knowledge allows targeting of higher risk individuals for pre-travel influenza vaccination, which should be given two weeks prior to travel to allow for the development of immunity. There is currently no evidence available to support re-vaccination before overseas travel in those who have already been vaccinated during the preceding influenza season, so re-vaccination is not recommended.

There are different vaccines available for northern and southern hemispheres. These are only available in the relevant hemispheres. There are different vaccines available for northern and southern hemispheres. The vaccines differ as the influenza viruses that become the predominant seasonal ‘flu’ vary over time and geographical regions. The influenza vaccines are revised after each season at the recommendation of WHO, which advises on the strains predicted to be circulating in the upcoming season in the particular geographical region. Currently, these vaccines contain three or four strains. Sometimes, the genetic code in a flu strain can drift, or mutate, within the six-month flu season to reduce the effectiveness of this vaccine. This occurred in the previous winter (2014–15) in the Northern Hemisphere, and the effectiveness of the vaccine was shown to be around 23%.

There is no pathognomonic symptom of influenza, so diagnosis based on symptoms and signs alone is limited and must be assisted by epidemiological data to support the clinical suspicion: in this case, the annual peak influenza season in Japan.

Several studies have shown that during influenza season, cough and fever >38°C have a positive predictive value of 79–96.8%, and a sensitivity of 77–85% with the inclusion of myalgias. Influenza viruses are single-stranded ribonucleic acid (RNA) orthomyxoviruses classified as A, B or C subtypes. The A and B subtypes can cause significant disease in humans. The incubation period is usually two to three days but can last up to one week. After an incubation period of one to three days, influenza often manifests as a sudden onset of systemic symptoms such as malaise, lethargy, headache, myalgia and anorexia, with fever particularly prominent. Sore throat, cough, nasal discharge and sneezing can also be present. Fevers and myalgias can last three to five days, and the cough may persist for longer than two weeks.

**Answer 3**

Amy was not in Saudi Arabia within the last 14 days, so her case does not fit the current case definition for MERS. She therefore does not fit the epidemiological criteria, and so is unlikely to have MERS (the recent MERS guidelines are available at www.health.gov.au/internet/main/publishing.nsf/Content/5691B039B3B59D8CA257BF0001ABE27/$File/MERS-CoV-Information-GPs-2015-09-14.pdf). Guidelines for general practitioners (GPs) on emerging infectious diseases including case definitions, investigations, treatment and management are available on the relevant state/territory and Commonwealth health websites. These guidelines are regularly updated.

Local Public Health Units (PHU) are available for consultation and advice in such situations, and should be alerted immediately to any potential threat. Infectious disease consultants at the local hospital are also a source of information and advice. Notification of such diseases to the local PHU is required under the Public Health Act 2010; MERS and influenza are currently notifiable diseases. Information and forms are available on state health websites. If you did suspect MERS as per the guidelines, you would isolate the patient in a single room using standard and transmission-based precautions, and immediately call the local PHU. Current advice is that you should not collect specimens for testing.

A returned traveller with a fever is a potential carrier of a new infectious disease across international borders. GPs involved with the Australian Sentinel Practices Research Network (ASPREN; www.aspren.com.au/index.html) are swabbing 25% of patients presenting with fever, cough and fatigue as part of frontline surveillance, but all GPs are a crucial part of the frontline surveillance. Early identification by GPs can assist in preventing the spread of the disease.

**Answer 4**

Influenza can be difficult to distinguish from respiratory illnesses caused by other pathogens on the basis of signs and symptoms alone. Diagnosis is usually made clinically on the basis of symptoms with consideration of the epidemiological context – for example, in a clinical illness consistent with uncomplicated influenza in an area where influenza virus is prevalent. There are many other organisms that can cause similar influenza-like illness, including respiratory syncytial virus, parainfluenza virus, adenovirus, rhinovirus and coronavirus; all are common causes of lower and upper respiratory tract infections.

In cases where a definite diagnosis would support clinical decision making and help define treatment choices, diagnostic testing such as nasopharyngeal swabs should be considered – for example, if:

- the condition was severe
- the results would change management
- there is a high risk of complications in the patient or contacts
- the epidemiological data did not support the diagnosis
- it was an institutional setting.

In this situation, as there are four contacts at high risk of complications (your regular patient and her two children, and Amy’s grandmother), performing a nasopharyngeal viral swab for culture could be indicated. Nasopharyngeal specimens usually have higher yield than nasal or throat swab specimens. Although viral culture will provide the most accurate method of diagnosis, a result is often available only in two to 10 days (see ‘Resources for Doctors’ for a guide on the collection of nasopharyngeal specimens). Note that laboratory-confirmed influenza is notifiable in Australia. The neuraminidase inhibitors (NAIs) currently available in Australia, oseltamivir (Tamiflu) and zanamivir (Relenza), are active against influenza A and B viruses. These antivirals work by preventing the release of the virus from infected cells to reduce spread. If the NAIs are taken within 48 hours of onset of symptoms, they have been shown to limit the duration of illness by one to three days, as well as...
The document discusses the risk of complications from influenza and the importance of timely vaccination. It highlights that pregnant women are at high risk of influenza complications and that vaccination during pregnancy is recommended. The text also mentions the use of antiviral medication for high-risk groups and the importance of early diagnosis and management. There is a focus on the management of influenza in different settings, including healthcare facilities and schools. The document references recent studies and guidelines, including the Royal Australian College of General Practitioners and the Australian Immunisation Guidelines. The text is structured to provide a comprehensive overview of the management of influenza, including the risk factors, vaccination strategies, and clinical interventions.
Centers for Disease Control and Prevention. Influenza signs and symptoms

Epperson S, Bresee J. Yellow book travelers’ health – Chapter 3: Infectious


Centers for Disease Control and Prevention (CDC) – Travelers’ health, wwwnc.cdc.gov/travel


REFERENCES


CASE 3

ELIZABETH VOLUNTEERS TO TRAVEL TO EAST TIMOR

Elizabeth, 52 years of age, is a general practitioner from Melbourne who is planning to travel to Timor-Leste (East Timor) to volunteer for one to two weeks in a medical clinic in the capital, Dili. She intends to travel there annually after this trip to volunteer for one to three weeks at a time. On her first trip, she will spend most of her time in Dili, but intends to visit some rural areas and work during the day with a mobile clinic, then stay in Dili at night. During future trips, she is likely to spend more time in rural areas, staying in simple accommodation. Elizabeth is up to date with her hepatitis A and B vaccines.

QUESTION 1

Which travel vaccines would you recommend for Elizabeth?

QUESTION 2

Would you recommend malaria prophylaxis? If so, which medication(s) would you recommend?

QUESTION 3

What other preventive measures would you advise? What are the other two main mosquito-borne infections to prevent?

FURTHER INFORMATION

Elizabeth asks about a recent case of Japanese encephalitis (JE) acquired in Bali.

QUESTION 4

Is Elizabeth at risk of acquiring JE? Would you advise Elizabeth to vaccinate against JE?

FURTHER INFORMATION

Elizabeth is leaving in two weeks and decides to be vaccinated against JE. She requests information about the vaccine(s) and timing of booster doses. She also asks about another doctor travelling with her, who has previously been vaccinated with JE-Vax.
QUESTION 5  
Which vaccine do you recommend for Elizabeth? What general advice can you give regarding JE vaccine boosters for her colleague?

FURTHER INFORMATION
Elizabeth is up to date for the MMR and influenza vaccines, and has natural varicella immunity. She will defer her rabies vaccine due to the lack of time. She decides to have the Imojev vaccine, but needs to have a typhoid vaccine and a tetanus, diphtheria, pertussis and polio vaccine on the same day.

QUESTION 6  
What do you advise?

CASE 3 ANSWERS

ANSWER 1
Elizabeth should be up to date with routine vaccinations, including measles, mumps and rubella (MMR); diphtheria, tetanus and pertussis (dTpa); varicella; polio and the annual influenza vaccine. She should also have a typhoid vaccine and consider vaccination for JE and rabies.

The incidence of tuberculosis (TB) in East Timor is >100 cases per 100,000 population, the highest risk category. However, the proportion of multidrug-resistant (MDR) TB is thought to be low, with only three laboratory-confirmed cases of MDR TB reported in 2014. TB infection control measures should be instituted at the clinic. Bacillus Calmette-Guérin (BCG) vaccine is not indicated unless the risk of exposure to multidrug-resistant TB is high, but tuberculin skin testing or quantiferon testing could be considered before and after travel.

ANSWER 2
The risk of exposure to malaria is high in rural areas of East Timor. The advice regarding malaria risk in Dili varies from low to very high, and is probably variable and seasonal. Although her trip is short, Elizabeth should be advised to take malaria prophylaxis. Local information can be helpful in this setting.

Malaria in East Timor is chloroquine-resistant. Of the malaria species, 50% are Plasmodium falciparum, nearly 50% are P. vivax, and <1% are P. ovale or P. malariae. The recommended antimalarial medications are either:

• doxycycline 100 mg once daily, starting one day before entering and continuing for four weeks after leaving the malarial area
• atovaquone 250 mg/proguanil 100 mg tablets (malarone), starting one to two days before and continuing for seven days after leaving the malarial area.

ANSWER 3
It is important to give advice on avoidance of mosquito bites by covering up with clothing such as long sleeves and trousers, especially after sunset (but also during the day, to prevent dengue fever); regularly applying DEET-containing insect repellents on exposed skin; and using insecticide-impregnated mosquito nets when necessary. Spray thin clothing with insect repellent or pre-impregnate with permethrin, and spray insecticide in the room or use pyrethroid mosquito coils. If travelling to high-risk malarious areas that are remote from medical facilities, carrying emergency malaria standby treatment may be considered, especially for trips that are three weeks or longer.

The other two main mosquito-borne infections to prevent are dengue fever, which is associated with urban areas and daytime mosquitoes, and JE. Chikungunya has also been reported in Timor.

ANSWER 4
JE is the leading cause of viral encephalitis in Asia and occurs in almost all Asian countries. It is a zoonosis that is transmitted
CASE 3

In an enzootic cycle between *Culex* mosquitoes and amplifying vertebrate hosts, mainly pigs and wading birds. Infection and illness in humans are incidental and there is no person-to-person transmission.14 *Culex* mosquitoes feed outdoors between dusk and dawn, and breed in flooded rice paddies and marshy environments.15 Approximately one in 250–1000 infections in susceptible humans hosts is symptomatic14,15 but in non-indigenous individuals, including travellers, this figure may be up to one in 25.7

JE occurs in rural areas, city peripheries and urban areas of most Asian countries, including East Timor (Figure 1), Papua New Guinea and in the outer Torres Strait Islands of Australia (including three cases on Badu Island, two of which were fatal). Nine cases of JE have been notified in Australia since 2001.15 Most recently, a traveller, 45 years of age, developed symptoms of encephalitis four days after returning from Indonesia, the first JE infection notified in Victoria.16 Transmission can occur in a seasonal or year-round pattern.1,14

Information regarding the risk of JE by country, with geographical and seasonal information, can be found on the Centers for Disease Control and Prevention (CDC) website (see ‘Resources for doctors’).

In Timor-Leste, sporadic cases of JE are reported and the disease is presumed to be endemic countrywide. The World Health Organization (WHO) considers Timor-Leste to be an area of high incidence with countrywide endemic areas.17 Transmission season has been reported to occur during the rice-growing seasons from September to December and February to May,14 although the CDC reports a lack of data regarding seasonal transmission.1 The risk is high on the Maliana Plain and data suggest that 65% of Dili’s population tested were seropositive for JE by enzyme-linked immunosorbent assay (ELISA).14

The estimated overall incidence of JE among travellers from non-endemic countries to Asia is less than one per one million travellers. This risk increases with risk factors and prolonged stays. Risk factors for JE infection include exposure to mosquitoes between dusk and dawn in rural areas (more likely in longer term visitors who spend time outdoors, including aid workers, students, missionaries, researchers, cyclists or hikers and expatriates).1,15

Other specific risk factors include age >50 years, JE infection in childhood, dual neurological infections (eg with mumps or neurocysticercosis), compromised blood–brain barrier (cochlear implants, shunts etc), pregnancy (miscarriage in first or second trimester), genetic susceptibility, and those with chronic conditions such as solid organ transplantation, cardiovascular disease, diabetes mellitus and renal disease.1,15

There is no specific antiviral treatment for patients with JE, and management is supportive.18

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**Figure 1. Geographic distribution of Japanese encephalitis virus**

Vaccination advice

Although Elizabeth’s current trip will be short and the risk of JE exposure is low, she will be spending the nights in an urban area (and Culex mosquitoes are active from dusk until dawn), she plans to travel to East Timor annually (with repeated risk of exposure) and plans to visit rural areas overnight in the future. Although JE vaccination remains optional for this trip, it will be useful for future travel and should be considered (Table 1). Elizabeth has also expressed concern about her risk of exposure given the recent case notified in Victoria.

Table 1. Vaccine recommendations for JE vaccination1,3,14

<table>
<thead>
<tr>
<th>Current NHMRC vaccine recommendations</th>
<th>Consider vaccination in these groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Travellers spending 1 month or more in rural/endemic areas of Asia or Papua New Guinea, especially during transmission season, including those based in urban areas but are likely to visit rural areas; and/or considerable outdoor activity, and/or staying in suboptimal accommodation, even in shorter-term travellers; or &lt;1 month in areas of epidemic transmission</td>
<td>Repeat travellers who are at risk of cumulative duration of exposure Any individual with prolonged duration of stay, regardless of itinerary Any traveller to rural areas Travellers visiting regions at risk of JE transmission who:</td>
</tr>
<tr>
<td>All other travellers spending 1 year or more in Asia, including urban areas (except Singapore, where cases have been reported but routine vaccination is not recommended). Up-to-date information on country-specific JE risk can be found at wwwnc.cdc.gov/travel/yellowbook/2016/infectious-diseases-related-to-travel/japanese-encephalitis#8880 Residents of the outer Torres Strait Islands Non-residents who will be working in the outer Torres Strait Islands for 30 days or more during the wet season (December to May). The risk is greatest from February to March All those who wish to minimise risk / request vaccination if fully informed of risks and benefits</td>
<td>have greater outdoor exposure are aged &gt;50 are aged &lt;10 (greater risk of mosquito bites) have chronic conditions such as hypertensions, diabetes mellitus, chronic renal disease have had solid organ transplant, cochlear implant or ventriculoperitoneal shunts are on anti-TNF therapy are known to have genetic predisposition to JE (eg CCR5Delta32 homozygosity) are pregnant (risk of miscarriage in first and second trimester)</td>
</tr>
</tbody>
</table>

Imojev has been shown to provide excellent protection if used as a booster vaccine in children two to five years of age, who were previously vaccinated with a mouse brain–derived vaccine.7 JEpect is a Vero cell–derived, inactivated vaccine based on an attenuated strain of the JE virus. Two doses are given 28 days apart. Data suggest that an accelerated course given on days one and seven provides a non-inferior immune response, but there are no clear recommendations regarding this in the Australian guidelines, and the length of protection is not known.7 A booster dose is recommended one to two years after the primary course in adults,1,7,14,20 but no firm recommendations have been given as yet for booster dosing in children. In adults, data indicate seroprotection for 10 years or longer after the first booster.20

JEpect is registered for use in those 18 years or older, but can be given to babies between two and nine months of age, as well as to older infants and children where an alternative is not available or if it is contraindicated. Infants and children under three years of age receive a half dose (0.25 ml) per dose. Pregnant women at risk of JE should be offered JEpect, as no adverse pregnancy outcomes have been attributed to JE vaccination, although there is a theoretical risk. Data regarding lactation and JE vaccine are lacking, but the vaccine should be offered if there is increased risk of acquiring JE.7

Data suggest that a single dose of JEpect can provide protective antibody levels for up to two years in adults previously vaccinated with a completed course of mouse brain–derived vaccine.7,20 Both Imojev and JEpect are generally well tolerated and lack the serious adverse events associated with JE-Vax. Local reactions and minor systemic reactions (headache, myalgia) are common to very common after vaccination. JE vaccines are contraindicated in individuals who have had anaphylaxis following a previous dose of any JE vaccine or any vaccine component.7

Given that Elizabeth is leaving in two weeks, the single-dose Imojev vaccine is the best option. If Elizabeth had contraindications to a live vaccine, a rapid course of JEpect on days one and seven could be considered, although no clear recommendations can be given. Alternatively, she could have her first JEpect dose now, travel this time with only partial protection, and have her second dose after this year’s trip on day 28 in preparation for future travel. Depending on the itinerary, it may be possible to complete a course of JEpect in Dili, where its availability was confirmed as of May 2015.7

Imojev is also preferable to JEpect because it will also provide longer lasting protection, without the need for a booster over the next five years.
Elizabeth’s previously vaccinated colleague could consider having a single dose of Imojev, but would also gain two years of protection from a single JEspec booster dose.

ANSWER 6

Data for the co-administration of Imojev with other vaccines, other than yellow fever vaccine and MMR vaccine – which can be given at the same time, using separate syringes and injection sites, or otherwise at least four weeks apart7 – are not available.

JEspec can be given at the same time as hepatitis A vaccine, quadrivalent meningococcal conjugate vaccine, and rabies vaccine. Co-administration with other vaccines (including yellow fever vaccine) has not been studied.

If other vaccines need to be given at the same time as either JE vaccine, injections should be given in separate limbs.7

For practical reasons, Elizabeth should receive all recommended vaccines during her visit, in separate limbs as advised.

Recommendations regarding the newer JE vaccines will be updated when suitable evidence becomes available.

RESOURCES FOR PATIENTS

- International Society of Travel Medicine, www.istm.org
- Fit for Travel, UK, www.fitfortravel.nhs.uk
- Travax, www.travax.nhs.uk
- IAMAT, www.iamat.org

RESOURCES FOR DOCTORS

- International Society for Infectious Diseases program for monitoring emerging diseases (ProMed), www.promedmail.org
- Centers for Disease Control and Prevention, wwwnc.cdc.gov/travel (with links to outbreak news and Yellow Book)
- Japanese encephalitis distribution map, www.cdc.gov/japanesencephalitis/maps

REFERENCES


19
CASE 4  
GERALD TRAVELS TO MOZAMBIQUE

Gerald, aged 54 years, is going to spend six months in Nacala in northern coastal Mozambique, working for a mining company there. There is a high risk for malaria throughout Mozambique.1–5 Gerald presented for a pre-travel medical consultation and you strongly advised him to take appropriate malarial chemoprophylaxis. Gerald declined, stating that ‘I have worked in these sorts of areas before and no one else took malaria tablets. I might get malaria anyway, and the tablets only mask the symptoms and they have lots of side effects. Besides, the locals get malaria most of the time and they are fine.’

QUESTION 1
What are the current guidelines for malaria chemoprophylaxis? What medications would you recommend?

QUESTION 2
How would you manage Gerald’s situation? What information can you provide to Gerald to give a balanced opinion on malaria prophylaxis in this situation?

FURTHER INFORMATION
Gerald became unwell on site in Mozambique. Figure 2 describes the evolution of his illness. It was unknown if he had

Figure 1. Mozambique map

Figure 2. Evolution of illness
a pre-deployment travel or medical assessment, if he had any underlying medical conditions, or if he had taken any malaria chemoprophylaxis.

He attended the onsite medical clinic in the mine site in Nacala. The medical practitioner correctly diagnosed malaria and commenced Gerald on a standby treatment course of artemether + lumefantrine. Gerald returned to his residence, but a few hours later was found unconscious on the floor in his room, with vomitus around his body. It was decided that he should be transferred to South Africa for further medical treatment as soon as possible. By the time the medevac company was contacted, one week after onset of illness, Gerald was comatose with malaria, pneumonia, renal failure and liver complications. The medical team from the air ambulance resuscitated him for seven hours to stabilise his medical conditions for the flight to South Africa.

QUESTION 3
What were some pitfalls in Gerald’s medical management while he was overseas?

QUESTION 4
If Gerald had been well while overseas but developed a fever and flu-like symptoms after returning to Australia, how would you manage his condition? Describe your differential diagnosis, history and examination, and symptoms you would be looking for?

QUESTION 5
What investigations would you order initially?

CASE 4 ANSWERS

ANSWER 1
Current guidelines for malaria chemoprophylaxis can be found on the Centers for Disease Control and Prevention (CDC), World Health Organization international travel and health and UK Travel Health Pro websites. Other useful references in the Australian context are the Manual of travel medicine and Therapeutic Guidelines. There are many factors that need to be taken into consideration when considering which malaria chemoprophylaxis to use. The above references discuss this well, particularly the Manual of travel medicine. In this case, we are considering chemoprophylaxis for a fly-in, fly-out worker, who has special considerations, many of which will be covered as we progress through this case.

Doxycycline is generally the most cost-effective choice for malaria chemoprophylaxis. Atovaquone+proguanil (Malarone) is far more expensive, but it is equally effective and has a favourable side-effect profile. Travellers can stop taking atovaquone+proguanil seven days after leaving a malaria-risk area. For doxycycline, treatment should continue for four weeks after leaving the area. Therefore, if there is no cost constraint, for fly-in, fly-out workers on a four-weeks-on, four-weeks-off roster, for example, atovaquone+proguanil is preferred to doxycycline. This means they are off their malaria medication for some time between rotations, which would not be the case with doxycycline.

Mefloquine is a further option for this area. According to the Therapeutic Guidelines, it should be started two to three weeks before the patient leaves so the patient can transition to an alternative chemoprophylaxis prior to travel if there are any concerning side effects. However, in the author’s experience it should be started two to three weeks before the first deployment; during subsequent visits, mefloquine can be taken weekly one to
two weeks before leaving, while at risk and four weeks after leaving the area. If a worker were on a four-week-on, four-week-off roster, as with doxycycline there would not be a break in medication between rotations. This medication has been associated with severe neuropsychiatric side effects, the incidence of which is 1/10,000. Milder neuropsychiatric effects, such as mood changes, nightmares and depression can occur in about 5–10%. They can also be an issue in those involved in tasks requiring delicate coordination and spatial discrimination. This combination of possible adverse events has made this medication less popular with many employers.

ANSWER 2
You could explain and emphasise the following points:

- **Malaria can be fatal, particularly in individuals infected with the more severe type of malaria (Plasmodium falciparum), especially when not taking appropriate anti-malarial medication or when there are delays in receiving proper treatment.**
- **The primary purpose of malarial chemoprophylaxis is to minimise the risk of dying from malaria when travelling to or residing in high-risk malaria areas.**
- **Although there is the risk of adverse reactions to anti-malarial medication, this is usually low with the medications currently used. On weighing up the pros and cons, taking appropriate anti-malarial medication is much preferred to contracting malaria (in high-risk malaria areas).**
- **Taking anti-malarial medication may make the diagnosis of malaria more difficult, which could delay the correct diagnosis and management.** However, in regions with poor health infrastructure and deficient access to high-quality medical facilities, the main role of anti-malarial medication is to enhance survival.
- **Malaria mortality mainly occurs in childhood. After surviving malaria a few times, usually in childhood, with continuous exposure to malaria, residents of areas where malaria is prevalent often develop partial immunity to malaria (semi-immune). They may tolerate a low-parasite load without becoming sick with malaria. Nevertheless, even local residents may die from malaria following their first infection. When the immune system is not being subjected to repeated infections of malaria, the partial immunity diminishes. Once the individual has been away from a malarious area for an extended period of time, they would be considered to have lost this partial immunity.**

In addition to recommending anti-malarial medication, you should also advise Gerald to take protective measures against insect bites (eg use of insect repellents and protective clothing). If he develops a fever, he should seek expert medical advice as soon as possible.

ANSWER 3
Healthcare workers in malaria-endemic regions, more so than in non-malaria–endemic countries, often do not consider malaria as the most important differential diagnosis in managing patients who present with fever. In Africa, unlike Australia, malaria is not generally thought of as a life-threatening disease. Many patients are treated as outpatients, often with undesirable outcomes. Severe malaria normally develops three to seven days after the onset of symptoms. The most common severe complications in travellers are cerebral malaria, acute renal failure and respiratory failure. If a person such as Gerald contracts falciparum malaria, without having taken malaria chemoprophylaxis, his medical condition often deteriorates significantly, and he may die within a few days if definitive treatment is not given as soon as possible in the illness process. In Gerald’s case, he did not present for medical treatment until day 6. Although he was commenced on treatment, he may not have taken the medication, or if he did take it, it is likely that he brought it up when he vomited. In a US study, mortality from P. falciparum is related to poor adherence to chemoprophylaxis, but a large number (66%) were due to medical errors such as failure to prescribe correct chemoprophylaxis, failure to diagnose patients correctly at presentation and failure to initiate treatment promptly at diagnosis. Any fever in a patient presenting unwell from a malarious area should be treated as malaria until proven otherwise. Warning signs for severe malaria include confusion, unconsciousness, respiratory distress, renal failure and acidosis. In a country such as Australia, all cases of falciparum malaria should be referred to an infectious disease physician for hospital admission.

ANSWER 4
If a returned traveller presents with a fever, up to at least one year after visiting a malaria-risk area, regardless of whether chemoprophylaxis was taken, malaria must always be considered as a differential diagnosis.

Malaria is the most common specific diagnosis in Australian and multinational travellers with febrile illnesses acquired overseas. Malaria is also the most common potentially life-threatening travel-related infection. Given his substantial risk of falciparum malaria if Gerald had returned to Australia and presented to a general practice with a fever, it would be best to refer him for assessment by an infectious diseases unit as soon as possible. A person with falciparum malaria should always be admitted to an experienced infectious diseases or tropical diseases unit for further management.

Other diagnoses, in decreasing order of frequency, are:

- respiratory illnesses
- gastrointestinal illness
- idiopathic
- dengue fever
- chikungunya
- enteric fever
- rickettsial infection.

A thorough history should be taken, including Gerald’s medical and travel history, and physical examination of all systems should be performed. The important clinical features to look for are:
- lymphadenopathy
- hepatomegaly
- splenomegaly
- jaundice
- anaemia
- wheeze
- rash or skin lesions
- muscle or joint involvement

- neck stiffness
- photophobia
- conjunctivitis
- neurological signs
- evidence of bleeding.

Routine urinalysis should be performed. Repeated physical examinations are often required to monitor the evolution of symptoms and signs, and response to therapy.\textsuperscript{17,18}

**Figure 3. Evaluation and initial management of fever in a returned traveller\textsuperscript{12}**

```
Suspected febrile illness in a returned traveller

Confirm fever

Severe sepsis
- (confusion, collapse, cyanosis, tachypnoea, hypotension, neck stiffness, peritonism or digital gangrene)

History: travel and fever onset (compare with typical incubation periods)
Pattern of fever: occasionally helpful (eg second-daily paroxysm in vivax malaria)
Focal features: neck stiffness, cellulitis, abdominal tenderness, pulmonary consolidation
Investigations: full blood count, liver function tests, blood cultures (two), chest X-ray, urine microscopy and culture, baseline serological tests, specific investigations for focal disease

No features of severe sepsis

Resuscitation if shocked, blood cultures, malaria films, penicillin or ceftriaxone (if meningococcal disease likely)

Malaria possible\textsuperscript{†}

Rash

Respiratory symptoms

Fever >7 days, malaria ruled out

Jaundice

Consider dengue or rickettsial disease
- Serological disease
- Consider empirical doxycycline for rickettsia

Consider enteric fever
- Blood, stool and urine cultures
- Consider empirical quinolone or third-generation cephalosporin

Consider unusual causes of pneumonia (eg Legionnaire’s disease, melioidosis)
- If severe, give empirical treatment, including macrolide or quinolone

Plasmodium vivax, ovale or malariae

Plasmodium falciparum

Urgent hospital transfer

PCR, polymerase chain reaction

*Evaluation should also include the differential diagnoses that would be considered in a non-traveller with fever

\textsuperscript{†}Travel to high-risk area, rural or prolonged travel, non-compliance with prophylaxis

ANSWER 5
Initial investigations should include: 17, 18

- full blood examination (FBE)
- kidney and liver function tests, C-reactive protein (CRP)
- blood cultures
- thick and thin blood smears for malaria (repeated examination may be required)
  - As a rule, pathology service providers in Australia routinely do rapid antigen detection testing (RADT) when thick and thin films are requested. They can also be used in areas where malaria diagnosis on slides is difficult or unavailable. Currently, there are issues with these test kits being widely used in the field, namely accuracy, cost and adverse field conditions. 19 Training can increase accuracy. 20
- Dengue and Chikungunya serology
- rickettsial serology
- stool examination if indicated (including multiplex PCR test)
- chest X-ray
- urine microscopy and culture.

Refer to Figure 3 for the general plan of management for a returned traveller with fever.

RESOURCES FOR DOCTORS

- fitfortravel by Health Protection Scotland – a division of NHS National Services Scotland, travel health information for people travelling abroad from the UK, www.fitfortravel.nhs.uk
- Centers for Disease Control and Prevention, Travelers' health, www.cdc.gov/travel
- Centers for Disease Control and Prevention, CDC health information for international travel 2016, wwwnc.cdc.gov/travel/page/yellowbook-home
- TravelHealthPro, National Travel Health Network and Centre (NaTHNaC), http://travelhealthpro.org.uk
- International Association for Medical Assistance to Travellers, a division of the Foundation for the Support of International Medical Training (FSIMT), www.iamat.org

REFERENCES


CASE 5

JEFF IS TIRED AND ANXIOUS

Jeff is a company director, 39 years of age, who returned from a business trip to Vietnam yesterday. He is generally well, but has been feeling tired and anxious since his return. Jeff admits that he spent the last night of his visit with a woman he had met at a nightclub at his hotel. He used a condom. Jeff wants to be tested for sexually transmissible infections (STIs) and wonders if he should take some antibiotics in case he has acquired an infection.

QUESTION 1

What information do you need from Jeff at this point in the consultation?

FURTHER INFORMATION

Jeff tells you that his local business associates had invited him to dinner at a restaurant, then to a club at his hotel to celebrate the successful conclusion of their business deal. They seemed keen for him to enjoy himself as much as possible. Later in the evening, he was introduced to one of several young women who had joined them. He had consumed a considerable amount of alcohol, but agrees that even at the time, he recognised that she was probably some sort of sex worker. Back in his hotel room, they had vaginal intercourse using condoms, but only after she performed oral sex on him, and he on her. This sexual encounter occurred approximately 36 hours before your consultation with him. Jeff has no symptoms, in particular, no discharge or dysuria. He is married and has three children. His wife has had a tubal ligation. They have not had any sexual contact since his return. He cannot recall his vaccination history. He is not taking any medication and, in particular, was not taking any antibiotic prophylaxis.

QUESTION 2

What STIs might Jeff be at risk of? How do you guide his investigation?

FURTHER INFORMATION

You give Jeff a dose of hepatitis B vaccination and order blood for HIV serology, hepatitis B core and surface antibody, syphilis serology, and a first-pass urine collection for Neisseria gonorrhoeae and Chlamydia trachomatis nucleic acid amplification test (NAAT). You advise him to avoid sex until further advice.

Jeff returns two days later complaining of a urethral discharge. He is upset that he was not given antibiotics at his initial presentation. On examination, you note a profuse creamy discharge.

QUESTION 3

What is the most likely cause of Jeff’s symptoms? How would you manage this change in the presentation?
QUESTION 4
What explanation can you give Jeff for withholding antibiotics at the initial presentation?

FURTHER INFORMATION
Jeff’s symptoms resolve quickly. The NAAT testing on his initial presentation indicates that *N. gonorrhoeae* was detected and *C. trachomatis* was not detected. The culture isolated *N. gonorrhoeae*, which was susceptible to ceftriaxone. The blood tests indicated that Jeff had received hepatitis B vaccination previously, which was confirmed by vaccination records from his previous general practitioner (GP). HIV and syphilis serology were negative.

QUESTION 5
What follow-up is required?

CASE 5 ANSWERS

ANSWER 1
You should ask Jeff for further details about the sexual exposure and its context. For example, it is relevant to know the nationality of the woman he had met and whether she was, or could have been, a sex worker. For the sexual contact that occurred in the hotel room, in addition to knowing that a condom was used, it is relevant whether any oral, vaginal, penile (or anal) sexual contact occurred while the condom was not being used.

You should also ask Jeff about his hepatitis B immunisation status and if he is taking any medication. If an individual presents with any sort of human blood or body fluid contact in South-East Asia or a country where hepatitis B is endemic, it is important to verify and record the history of hepatitis B vaccination.

ANSWER 2
Sexual risk taking is common in travellers, and STIs are a common travel presentation. Providing sexual entertainment for business partners is not uncommon in many parts of the world, and Jeff’s sexual partner for that night may well have been a commercial sex worker. The epidemiology of STIs is highly demographically and geographically specific, as are recommendations about their treatment. However, assessment of an asymptomatic individual with a sexual exposure in Europe, the Americas and Eastern Asia can be conducted without specialist consultation, as the most common conditions occurring will overlap with the Australian epidemiology. Many sexual health centres in capital cities in Australia operate a telephone specialist consultation service for GPs and would be able to provide a list of conditions to test for.

The consistent and correct use of condoms during vaginal or anal sex is effective as a barrier in the prevention of human immunodeficiency virus (HIV) infection and Jeff is not at risk. However, you could include HIV testing (at baseline and at six to 12 weeks) in this situation for the purposes of allaying the patient’s anxieties. Approximately 15% of the adult population in Vietnam carries the hepatitis B virus (HBV), a much more transmissible infection than HIV. Post-exposure vaccination reduces infection (ideally within 24 hours but acceptably within 14 days) and Jeff should be vaccinated while you establish his vaccination status. Hepatitis B surface antibody titre is often used to screen for prior vaccination in individuals who might in the future be exposed to HBV. However, vaccination records are even more useful as some patients lose measurable levels of surface antibody without losing the protective effect, which is considered to be cellular. Delaying the dose while waiting for evidence of prior vaccination might delay eventual vaccination and reduce its efficacy. On the other hand, vaccinating an already vaccinated individual, which occurs quite commonly, is quite harmless.

Oral sex without condoms does not represent a risk of HIV, but does have the potential to transmit other STIs. In particular, gonorrhoea is commonly transmitted by oral sex in men who have sex with men in Australia.
ANSWER 3
Gonorrhoea, chlamydia, syphilis, hepatitis B and HIV infection are more prevalent in sex workers in Vietnam than Australia, where they are uncommon.6 In Jeff’s case, gonorrhoea is the most likely presentation, on clinical and epidemiological grounds, as it is the only cause of urethral discharge commonly transmitted through oral sex. It is also common for patients with gonorrhoea to present with quite noticeable symptoms within two to three days of exposure.
NAAT is the most commonly used (and reliable) screening test. However, it is insufficient in a patient with symptomatic disease, particularly if the infection is acquired outside Australia. It is important to also collect a specimen for culture and antibiotic sensitivity testing. The type of testing is important in this case, as is the withholding of antibiotics (see Answer 4).
NAAT can use a first-void urine specimen in the case of urethral infection, and a throat swab, ensuring that the swab comes into contact with the posterior pharynx. The materials for these tests are commonly provided to general practices by the pathology provider as they are used for a range of purposes.
First-void urine samples avoid the need for intimate examination and uncomfortable testing procedures in well, asymptomatic patients presenting for screening. Testing recommendations for screening an asymptomatic individual who may have been exposed to infection, and possible sites of specimen collection, are summarised below:
- pharyngeal swab
- high vaginal or cervical swab or first void urine
- urethral swab or first void urine
- swab of anorectal canal.
- all swabs using the laboratory preferred swab type.
Symptomatic patients need to be examined, and the specimens (other than urine) taken by the clinician. Patients are often uncertain how best to describe genital symptoms and additional clinical signs are commonly present.
For laboratory culture, the specimen must contain live bacteria and it must be transported to the laboratory in a manner that preserves it. Neisseria gonorrhoeae has fastidious growth requirements, and the commonly used in-clinic culture swabs may not be adequate. Laboratories will provide, if asked, a swab tube transport medium specifically designed to keep organisms viable. Locally acquired symptomatic gonorrhoea urethritis is rising fairly steadily in much of Australia, and it is always advisable to take a specimen for culture before delivering treatment.
Gonococcal infection is treated with a single dose of 500 mg ceftriaxone diluted in 2 ml of 1% lignocaine and a single oral dose of 1000 mg (2 x 500 mg tablets) of azithromycin.7 A symptomatic patient should be offered this treatment immediately, but only after appropriate samples have been taken. The patient should be advised to avoid all sexual contact until the diagnosis, the appropriateness of the original treatment and, if necessary, proof of cure, have been confirmed. The patient should be requested to return after one week to discuss the results, the success of treatment, and when it is safe to recommence sexual activity.

ANSWER 4
You should explain to Jeff that ‘blind’ treatment at the initial presentation may not have prevented the infection that he has now developed. Furthermore, such treatment would have significantly complicated and obscured effective diagnosis and treatment at this stage.
Emergence of *N. gonorrhoeae* antibiotic resistance is a major public health surveillance concern in Australia. Thanks to the quality of these data, we can be confident that the recommended treatment for locally acquired gonorrhoea will cover known or likely strains of the bacteria. However, less information is available from South-East Asian countries where, in the past, drug-resistant strains have been first to emerge.9
Prophylactic or presumptive treatment relies on a good knowledge of the antibiotic sensitivities in commonly isolated bacterial strains. When it fails, it actively selects for the resistant organism, which the index patient, in this case Jeff, might continue to transmit in the mistaken belief that he is cured. Precisely this mechanism is likely to be an important step in the initial movement of drug-resistant gonorrhoea into Australia.9 Concern is rising about the possibility of ceftriaxone-resistant gonorrhoea becoming established in Australia, which has the potential for very serious public health consequences. So, in an asymptomatic patient, we would only recommend prophylactic treatment in a known exposure in the setting of well-documented epidemiology. For a symptomatic patient, specimens for culture must be taken before treatment is delivered so that the results are collated in surveillance and it can be confirmed that the individual has received the appropriate treatment.

The advent of NAAT has certainly simplified the diagnosis of bacterial STIs in men. However, only culture will give information about antibiotic sensitivity for *N. gonorrhoeae*, which varies significantly worldwide.9 In particular, there are no oral antibiotics available in Australia that reliably treat the commonly found strains of *N. gonorrhoeae*. More seriously, ceftriaxone-resistant *N. gonorrhoeae* strains are being reported10 and their prevalence in countries without reliable public health monitoring of gonorrhoea drug susceptibility, such as Vietnam, is unknown.9 A negative gonorrhoea NAAT result effectively excludes the possibility of infection, but only a culture will confirm that the treatment given is effective.

ANSWER 5
The minimum time between exposure and testing for *N. gonorrhoeae* or *C. trachomatis* on NAAT has not been established, although it is characteristically very short. It would be entirely plausible for a positive test to precede the development of symptoms. Jeff should have a repeat gonorrhoea NAAT test at least four weeks after he received treatment.
Gonorrhoea is a notifiable disease and it is a common practice for laboratories to send general practitioners a notification form with the microbiology result. The usual practice is to contact sexual partners to suggest that they receive testing and treatment. Tracing the Vietnamese sex worker in this case is unlikely to be successful. Jeff has had no sexual partners since the exposure and no further contact tracing is required.¹¹

CONCLUSION

Jeff decides that he would prefer not to discuss this STI with his wife, nor is he prepared to expose her to the low risk of HIV or syphilis exposure that he might have encountered. He decides to use condoms or avoid sex until follow-up serology indicates that he is uninfected.

RESOURCES FOR DOCTORS

- State capital sexual health centres operate an information line to provide telephone advice to GPs.

REFERENCES

CASE – LUCAS AND JONAS

Lucas, 28 years of age, comes to see you for travel advice. Lucas is a nurse at an aged care facility and has taken leave for an overseas trip during the summer with his twin brother Jonas. First they will go to South Africa for a one-week cross-country cycling tour and then travel up the eastern coast of Africa as far as Egypt over the next three weeks. From there they will fly to Crete, where they will stay for two days, then to Turkey for five days, trekking in Nepal for five days, then to Chiang Mai, Thailand, for three days and back to Australia via Bangkok where they will spend two nights. During the consultation you discuss measures for preventing malaria, schistosomiasis, Japanese encephalitis (JE) and other infectious diseases of relevance to the areas that Lucas and Jonas will be visiting.

QUESTION 1

The current recommendation for malaria chemoprophylaxis is:

A. doxycycline 100 mg, starting one day before and continuing for seven days after leaving a malarious area
B. atovaquone+proguanil (Malarone) 250+100 mg tablets, starting one to two days before and continuing for seven days after leaving a malarious area
C. atovaquone+proguanil (Malarone) 250+100 mg tablets, starting one to two days before and continuing for four weeks after leaving a malarious area
D. mefloquine 100 mg, starting one to two days before and continuing for seven days after leaving a malarious area.

QUESTION 2

What advice should you give Lucas regarding schistosomiasis?

A. Schistosomiasis transmission requires exposure to fresh water for at least five minutes.
B. In the event of exposure, a dose of praziquantel should be taken immediately to prevent infection.
C. Acute schistosomiasis usually resolves spontaneously and serological testing at 12 months after exposure is recommended as a proof of cure.
D. Serological testing is recommended at three months post-travel even if asymptomatic.

QUESTION 3

Which of the following poses the greatest risk for Lucas of contracting JE?

A. Lucas’s age
B. Cycling in Bangkok in the morning and early afternoon
C. Spending time outdoors at night in Chiang Mai
D. Not being exposed to JE in the past

QUESTION 4

What factors should you consider when advising Lucas about JE vaccines?

A. Lucas does not need to be vaccinated against JE as he will be in an endemic area for a brief period of time.
B. Jespect cannot be given at the same time as hepatitis A and rabies vaccines.
C. Imojev can be administered in the same syringe as other vaccines.
D. Lucas would only need a single dose of Imojev.

FURTHER INFORMATION

Jonas is an aid worker and travels regularly to Asia for work. He has previously had a vaccination for JE and advised Lucas to enquire about having this vaccine along with his other travel vaccines. They are leaving in three weeks.

FURTHER INFORMATION

Lucas decides to have the Imojev vaccine, as well as hepatitis A, rabies, typhoid and cholera vaccines. He is up to date with vaccinations for measles, mumps and rubella (MMR); diphtheria, tetanus and pertussis (dTpa); tuberculosis; and polio. He also had the seasonal influenza vaccine through work. He takes malaria chemoprophylaxis as directed.
FURTHER INFORMATION

Two days after returning from their trip, Lucas’s brother Jonas comes to see you because he is worried that he may have contracted a sexually transmissible infection (STI). On the last night of their trip, Jonas had unprotected sex with a woman he met in a bar in Bangkok. He noticed a urethral discharge last night. After taking a more thorough history and examining Jonas you suspect that he has gonorrhoea.

QUESTION 5

What should you do next?
A. Ask Jonas to provide a first-void urine sample to do a nucleic acid amplification test (NAAT) for gonorrhoea.
B. Take pharyngeal, urethral and anorectal swabs for NAAT.
C. Collect specimens for culture and antibiotic sensitivity before prescribing antibiotics.
D. Prescribe a single dose of 500 mg ceftriaxone immediately.

QUESTION 6

How would you manage Jonas’s infection?
A. Treat the infection with 500 mg ceftriaxone or 1000 mg of azithromycin.
B. Ask Jonas to see you one week after treatment to assess symptom resolution.
C. Advise Jonas to see you only if his symptoms persist.
D. Repeat the NAAT one week after treatment.

FURTHER INFORMATION

Lucas went back to work the day after returning from his trip. Two days later, he presents complaining of fatigue, headache and muscle aches. He has a cough and on examination, you find that his temperature is 38.5°C. He is concerned about taking more time off work.

QUESTION 7

Which of the following statements is true?
A. A diagnosis of dengue fever is possible as the incubation period is three to 10 days.
B. A diagnosis of malaria can be excluded as Lucas had taken malaria chemoprophylaxis.
C. A diagnosis of acute schistosomiasis can be excluded as symptoms occur within two weeks of exposure to the parasite.
D. A diagnosis of influenza is unlikely, as Lucas had been vaccinated prior to travel.
Independent learning program for GPs