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TRAVEL MEDICINE (2) Practical issues for the Traveller

- ☞ Travellers should seek medical advice at least 4-6 weeks before travelling to developing countries
- ☞ Travel vaccines protect against many travel-related diseases, however few offer 100% protection
- ☞ Travellers should take general precautions to reduce risk of exposure to infectious agents
- ☞ Some illnesses in the returned traveller require urgent medical attention

Travellers to tropical locations and/or developing countries will generally attend for pre-travel medical review⁽¹⁾. This bulletin will deal with frequently asked questions regarding pre-travel medical advice and also discuss the problem of illness in the returned traveller.

VACCINATION

Advice on vaccination is the commonest reason for medical attendance prior to travel. However this is an important opportunity to remind travellers that the majority of health problems abroad occur as a result of contact with contaminated food / water or due to insect bites. Moreover for many of the diseases encountered, a vaccine does not exist e.g. diarrhoea, dengue fever, **therefore travellers must be reminded to exercise vigilance against contact with possible environmental pathogens.**

Vaccines are a highly effective way of preventing disease and are generally safe and effective⁽²⁾. It is important to remind the traveller that few travel vaccines offer 100% protection and additional precautions against disease should also be followed⁽¹⁾. Additional preventive advice, which needs to be individualised for each traveller is included in table 1. Table 2 outlines the factors used to determine vaccination requirements in an individual seeking pre-travel advice.

Table 1: Important preventive advice for the individual traveller*⁽³⁾

- Traveller's diarrhoea prevention and self-treatment
- Malaria prevention
- Other vector-borne and water-borne disease e.g. dengue fever, typhoid fever
- Personal safety and behaviour
- Environmental illness – altitude, heat, cold
- Animal bites and rabies avoidance
- The need to ensure adequate supply of prescribed medicines
- Consideration of travel medical kits
- Travel health and medical insurance

*Nature of advice depends on travel itinerary

Table 2: Factors determining individual vaccination requirements⁽⁶⁾

- The country/countries being visited
- The style of travel: adventure travel or luxury tour, duration, time of year, type of accommodation,
- Purpose of travel: tourism, work, visiting friends or relatives
- Vaccinations officially required for entry e.g. yellow fever
- Individual contraindications to vaccinations including: hypersensitivity, concomitant disease, medical history, pregnancy, medication
- Personal history of immunisations including: primary and booster doses of routine and travel vaccinations
- Cost/benefit of vaccinations

Immunisations should be **commenced several weeks before the date of travelling** (ideally 4-6 weeks) but longer periods (6 months) may be required for those at higher risk (e.g. due to trekking) or those planning to live overseas⁽⁴⁾. A common scenario is that travellers do not give themselves enough time to have the full vaccination course. An accelerated course for some vaccinations can be given, although immunity is usually delayed for between 10-14 days for most vaccines and travellers must be aware that their susceptibility to infection during this period is the same as if they are not vaccinated⁽¹⁾.

Multiple vaccines can be administered at different sites on the same day; some combination vaccines are available which reduce the number of injections required⁽²⁾. However there are some vaccines (in particular aluminium-containing), which may cause accentuated reactions if a number of vaccines are given simultaneously⁽²⁾. In general inactivated vaccines will not interfere with each other or with live vaccines, and can be administered at one appointment⁽⁵⁾. Live vaccines can be given together but at different sites or on separate occasions three weeks apart⁽⁵⁾.

Information on the specific vaccination requirements for the individual countries should be sought from reliable sources – see Volume 13, No 1, table 4 for a list of useful websites. Regulations regarding entry requirements of each country can be obtained from travel agencies and the relevant Embassies, Diplomatic or Consular Missions⁽⁴⁾.

The vaccination requirements for a traveller can be split into three categories: **required, routine and recommended**⁽⁷⁾.

Required vaccines: The only vaccine currently regulated by the WHO is the yellow fever vaccine, which is required for all travellers going to endemic countries. In addition many countries outside this zone require proof of vaccination of travellers arriving from or via an infected country⁽⁶⁾. Saudi Arabia requires proof of vaccination with the quadrivalent meningococcal vaccine (ACW135Y) for pilgrims travelling to the Hajj⁽⁸⁾ (*The Hajj commences on 18th December in 2007*).

Routine vaccines: Each traveller should be up to date with their childhood immunisations and have received the appropriate booster doses⁽⁷⁾. Adults may require boosters against certain diseases including diphtheria (children >10 years and adults should not be given the higher strength childhood vaccine due to an increased risk of adverse events), tetanus and polio⁽²⁾. Some travellers may require additional vaccines including influenza and pneumococcal vaccines⁽²⁾.

Recommended vaccines: These are vaccines, which depend on a number of factors including the area visited, the time of year, the type of travel, the age and health of the traveller, and previous vaccination history⁽²⁾. For most tropical countries hepatitis A and typhoid are recommended⁽¹⁾. Other recommended vaccines include hepatitis B, rabies, Japanese encephalitis, tick-borne encephalitis and cholera.

Adverse effects: Vaccine associated side-effects are usually mild. On average, 5-10% of individuals experience side-effects including local (redness, swelling and pain of the limb), or systemic (fever, headache) in nature, occurring shortly after vaccination ⁽⁶⁾. The individual Summary of Product Characteristics (SPC) should be consulted for each vaccine. As for all vaccines, **although anaphylactic reactions are rare events, facilities must be on site for treating such emergencies** ⁽⁶⁾. A record must be kept of the brand name of vaccine, manufacturing company, site of administration, method of administration, dose and batch number.

Live vaccines should be avoided in pregnancy and breast-feeding, however if travel to high-risk areas cannot be avoided the benefits of immunisation should be weighed up against the risks ^(4,5). Live vaccines should also be avoided in people who are immunosuppressed ⁽⁵⁾. Vaccination of people with fevers should be deferred due to the possibility of a reduced immune response and it may be difficult to distinguish vaccine side effects from symptoms of fever ⁽⁵⁾.

TRAVEL VACCINES

Table 3 below describes some of the commonly used travel vaccines. It is beyond the scope of this bulletin to give full prescribing information for individual vaccines therefore the Summary of Product Characteristics (SPC) for individual vaccines should be consulted

at www.medicines.ie or www.imb.ie

Table 3: Common travel vaccines

Vaccine	Risk	Administration
<p>HEPATITIS A ^(9, 10)</p> <p>[Combination vaccines of hepatitis A & typhoid and hepatitis A & B available]</p>	<p>One of the most common vaccine-preventable illness acquired by international travellers ⁽⁷⁾</p> <p>Risk is highest in developing countries with poor sanitation and hygiene</p> <p>Backpackers who travel for prolonged periods and travellers who visit friends and relatives are particularly at risk ⁽¹¹⁾</p>	<p>Administered at least 2 or more weeks before the planned trip</p> <p>Single intramuscular (IM) injection into the deltoid region</p> <p>Booster ideally given 6-12 months later, which provides long term protection</p>
<p>TYPHOID FEVER ^(12, 13)</p> <p>(Even if vaccinated, travellers should ensure that food and water precautions are followed)</p> <p>[Combination vaccine with hepatitis A available]</p>	<p>Associated with poor sanitation and contaminated food and water. Prevalent worldwide and endemic in South Asia and parts of South-East Asia, the Middle East, Central and South America and Africa ⁽⁵⁾</p> <p>Vaccination recommended for travellers going to endemic countries, the risk of acquiring the disease varies with the type of travel, duration, and contact with local populations</p>	<p>Administered at least two weeks before the risk of exposure</p> <p>Single IM injection</p> <p>Revaccination recommended every 3 years for those who remain at risk of infection ⁽²⁾</p>
<p>HEPATITIS B ^(14, 15)</p> <p>[Combination vaccine with hepatitis A available]</p>	<p>Not recommended routinely for travellers</p> <p>Should be considered for those working abroad, travelling long term or likely to be at risk for some other reason including exposure to blood or body excretions and unprotected sexual exposure ^(1,7)</p>	<p>1.0 ml given IM at 0,1 and 6 months or an accelerated schedule of 0,1 and 2 months with 4th dose at 12 months *</p> <p>A booster may be required after 5 years ⁽¹⁶⁾ (0.5ml paediatric dose available)</p>
<p>MENINGOCOCCAL VACCINE</p> <p>The quadrivalent ACWY vaccine (unlicensed) is the recommended meningococcal vaccine for travellers ^(2, 17)</p> <p>[The meningitis C vaccine used routinely in Ireland is not suitable for travel to areas where Group A is predominant]</p>	<p>Risk of acquiring meningococcal infection is very high in areas including the meningitis belt of Africa (epidemics of Group A infection occur in the dry season), Nepal, Mecca and areas of New Delhi</p> <p>Outbreaks of meningococcal A and W135 have occurred in Saudi Arabia and the ACWY vaccine is required for entry to Saudi Arabia during the Hajj festivities ^(2, 4)</p>	<p>Given by deep subcutaneous (S/C) injection as a single dose for individuals ≥ 2 years ⁽¹⁸⁾</p> <p>Immunity will persist for up to 5 years in adults and children > 5 years. Children < 5 years should be considered for revaccination after 2-3 years if they remain at high risk ⁽¹⁷⁾</p>
<p>YELLOW FEVER ⁽¹⁹⁾</p> <p>A live vaccine required for those travelling to or through an endemic area</p>	<p>Spread by infected mosquitoes and occurs in tropical Africa and South America ⁽²⁰⁾</p> <p>Presents with haemorrhage and jaundice in severe cases</p> <p>Special Precautions: Yellow fever vaccine should not be given to pregnant women; however if travel to a high-risk area is unavoidable the risk from the disease and theoretical risk to the foetus have to be assessed on an individual basis ⁽¹⁵⁾</p>	<p>Administered at least 10 days prior to planned date of entry to country at an approved Yellow Fever Vaccination Centre ⁽⁷⁾</p> <p>Single dose of 0.5ml S/C is approved for individuals > 9 months ^(19, 20)</p> <p>Booster dose recommended every 10 years for those at continued risk of exposure</p>
<p>RABIES ⁽²¹⁾</p> <p>Worldwide there are up to 50,000 cases of rabies each year of which the vast majority result from the bite of a rabid dog ⁽²²⁾</p> <p>Travellers must be aware that they must seek immediate medical advice and treatment if bitten by a potentially rabid animal and will require post-exposure treatment even if they have had pre-exposure</p>	<p>Causes viral encephalomyelitis in many parts of the world</p> <p>Incubation period ~ 3-12 weeks</p> <p>High-risk countries include India, Nepal, parts of Mexico, Thailand and Vietnam</p> <p>Vaccination should be considered for travellers</p> <p>a) who are planning to live or travel in a rabies-zoonotic area for > 1 month unless there is reliable access to prompt, safe medical care or</p> <p>b) for those travelling < 1 month who may be exposed to rabies because of their travel activities e.g. hikers, runners</p>	<p>3 doses of 1.0 ml IM given on days 0,7 and 28 days. The third dose can be given from day 21 if insufficient time before travel</p> <p>Booster dose recommended 2-3 years in those at continued risk</p> <p>The vaccinee should keep a record of the vaccine and regimen received</p>
<p>JAPANESE ENCEPHALITIS (JE) ⁽²³⁾</p> <p>Special Precautions: Due to a risk of allergic reactions, the vaccine should be used cautiously in person with a history of urticaria, asthma, allergic rhinitis, multiple allergies and allergies to bee stings. It has been associated with delayed hypersensitivity reactions therefore the course should be completed at least 10 days before departure. Vaccine recipients should be warned of this risk.</p>	<p>Mosquito-transmitted infection, endemic in Asia, mainly rural areas</p> <p>Transmission season extends from April to November in temperate regions and all year round in tropical areas.</p> <p>Requires careful risk assessment to decide if JE vaccine is required</p> <p>Factors to consider include: duration of stay, extent of outdoor activities. Expatriates and travellers planning to spend > 30 days in areas at risk including rural parts of Asia and those spending a short time in rice fields (where the mosquitoes breed) or close to pig farming (a host for the virus) should be considered for vaccination. The average short-term travellers risk of acquiring JE is low ⁽⁷⁾</p>	<p>Vaccine unlicensed in Ireland</p> <p>Given by SC injection on days 0, 7-14 days and 28-30 days ⁽²³⁾ *</p>
<p>TICK-BORNE ENCEPHALITIS ⁽²⁴⁾</p>	<p>Occurs in Europe, the Far East and Siberia</p> <p>Disease transmitted by infected ticks or from unpasteurised milk from infected animals and has a case fatality from 1% in Europe to 20% in the Far East ⁽²⁴⁾</p> <p>Incidence peaks in early spring and summer. Vaccination should be considered in those travellers planning to camp or trekking through forests</p>	<p>Vaccine unlicensed in Ireland</p> <p>Given IM in a dose schedule of 0, 1-3 months and 5-12 months after the second dose *</p>
<p>CHOLERA ⁽²⁵⁾</p> <p>(Even if vaccinated, recipients should ensure that food and water precautions are followed)</p>	<p>Occurs in poor countries where there is poor sanitation</p> <p>Risk for most travellers is very low and simple precautions are usually sufficient for most short-term travellers. Workers in disaster areas and refugee camps are most at risk for whom cholera vaccination may be recommended ⁽²⁾</p>	<p>Oral vaccine licensed against disease caused by <i>Vibrio Cholerae serogroup O1</i></p>

* In exceptional circumstances an accelerated schedule may be considered

TRAVEL RELATED THROMBOEMBOLISM

This form of venous thromboembolism has generated much interest in recent times. While good quality randomised controlled trials are lacking, it is recognised as a potentially important health problem to many long-distance air travellers including those without recognised risk factors⁽²⁶⁻²⁸⁾.

The risk of travel-related thrombosis appears to be related to the distance travelled, with **travel over 5,000 km being associated with the highest risk**^(26,29). The true incidence of travel-related thrombosis is unknown but is probably in the region of 2-4% with symptomatic venous thromboembolism rates being considerably lower⁽³⁰⁾.

Risk factors for the development of travel-related thromboembolism can be divided into environmental (immobility, compression of the popliteal vein due to cramped seating condition, dehydration and lower partial oxygen pressure in airline cabin) and individual (previous venous thromboembolism, recent surgery or trauma, active malignancy, advanced age, pregnancy, hormonal medication and obesity)^(26, 27, 31, 32).

There are conflicting views on thromboprophylaxis for travel and an assessment of the increased risk of venous thromboembolism must be made on an individual basis. All patients travelling on long-distance flights (>5000km or >6-8 hours' duration) should be encouraged to **avoid constrictive clothing, ensure good hydration, restrict alcohol and coffee intake, undertake regular leg exercising and occasional walks during travel**^(26, 27, 31). A number of studies have looked at the use of **graduated elastic compression stockings (GECS)** and reported a reduction in symptomless DVT compared to control groups⁽³³⁾. This intervention should be encouraged in patients perceived to be at intermediate risk of thrombosis⁽³⁴⁾. There is little evidence to support the use of **aspirin** for the prevention of travel related thrombosis. The LONFLIT 3 study (n=300) looked at the use of aspirin 400mg a day twelve hours before flight for three days and found it to have limited efficacy⁽³⁵⁾. In addition, because of the risk of adverse gastrointestinal effects, its use is not recommended^(26, 29). The LONFLIT 3 study also investigated the use of **low molecular weight heparin (LMWH)** for travel related thrombosis. A single dose of enoxaparin 100U/kg was administered 2-4 hours before travel and demonstrated a significant reduction in the prevalence of deep vein thrombosis as determined by Doppler sonography⁽³⁵⁾. However given the small numbers of patients involved further studies are needed to prove that it is safe and cost-effective. Consideration could be given to its use in high-risk patients (e.g. previous VTE, cancer, thrombophilia) in addition to GECS and other measures^(26, 34). Similar to other medication which should not be frozen, travellers who are prescribed LMWH should be reminded that it should be carried as hand luggage and not put in the aircraft hold, and may require a doctor's letter for the airline.

PREVENTING MOSQUITO BITES

Effective **bite prevention** should be the first line of defence against malarial infection⁽³⁶⁾ and other diseases spread by mosquitoes. Biting time varies between species and protection in bed is especially important⁽³⁶⁾.

Insect Repellents are substances applied to the skin to reduce the attractiveness of humans to mosquitoes and other arthropods⁽³⁷⁾. There are many brands of repellent available but most evidence indicates that N, N-diethyl-m-toluamide (**DEET**) based repellents, which have been in use for more than 50 years, are the most effective^(36,39). DEET is available in a variety of concentrations (20-50%) as lotions, sprays or roll-on formulations⁽⁴⁰⁾. DEET 50% has the longest duration of action and needs fewer applications⁽³⁶⁾. It can reduce the efficacy of sunscreen and when both are required, DEET should be applied afterwards⁽³⁶⁾. Sweat-off time varies with activity. The interval between applications depends on this as well as the DEET formulation and concentration used⁽³⁶⁾. DEET should be applied to exposed skin areas only and the manufacturer's instructions and directions followed carefully^(36, 41, 42). DEET can damage clothes made from synthetic fibres, and some plastic watch straps, watch 'glasses' and plastic jewellery; these items should not be allowed to come into contact with DEET^(36, 41).

Other repellents: p-menthane 3,8 diol (PMD) (**lemon eucalyptus**) gives about the same amount of protection afforded by 15% DEET but is reported to provide a shorter period of protection than extended duration DEET⁽³⁶⁾. **Picardin** (Icaridin) is reported to have repellent properties comparable to those of DEET and it is recommended to use a 20% preparation for mosquito bite prevention⁽³⁶⁾. Therapies which have **not** shown to be effective mosquito repellents include: homeopathic, buzzers, vitamin B1, garlic, savoury yeast extract spread, tea tree oil and bath oils^(36,38).

Insecticides: such as **permethrin** and other synthetic pyrethroids have a rapid knock-down effect on mosquitoes and are used to kill resting mosquitoes in a room^(36,38). Mosquito nets (free of tears and tucked under the mattress) impregnated with permethrin provide the most effective barrier protection against insects⁽⁴⁰⁾. Nets need to be re-impregnated every 6 to 12 months (depending on how frequently the net is washed) to remain effective, although there are long-lasting nets available^(36,38). Insecticides should be used before retiring for the night to rid sleeping areas of insects^(36,38). Coils, mats, sprays and vapourised insecticides are also useful^(36,40,43). Air conditioning and the use of insect-proof screens on doors and windows also reduce the likelihood of bites^(36,37).

Pregnant women, infants and young children are advised to avoid travel to malarious areas^(36,43,44). Avoidance of mosquito bites is extremely important in pregnancy and strict adherence to bite precautions is important⁽³⁶⁾. Some sources suggest that DEET (at a concentration of not more than 50%) can be used in pregnancy^(36,40). Use of 20% DEET in the second and third trimesters of pregnancy was not associated with adverse effects on infants from those pregnancies followed for up to 12 months after birth⁽³⁶⁾. However, pregnant women should be advised against using DEET over large areas of the body over a long period of time without a strong indication⁽⁴²⁾. Other experts recommend that preparations containing a citronella/ eucalyptus oil base are preferred to DEET preparations⁽⁴⁵⁾. In the absence of severe maternal toxicity it is most unlikely that exposure to permethrin-based insecticides would cause fetal damage⁽⁴⁵⁾. DEET has a good safety record in children but is not recommended for infants below the age of 2 months^(36,38,40). Particular care should be taken with children to ensure the repellent is not ingested, and does not come into contact with their eyes or mouth^(36,39).

Clothing: Within the limits of practicality it is recommended to wear long-sleeved loose-fitting clothing (mosquitoes can bite through tight clothing), long trousers and socks when outdoors after sunset^(36,38,40,43). Clothing may be sprayed or impregnated with permethrin, or cotton clothing can be sprayed with DEET⁽³⁶⁾.

PROPHYLAXIS OF ACUTE MOUNTAIN SICKNESS

There are three forms of illness due to hypoxia of altitude: Acute Mountain Sickness (AMS), High Altitude Cerebral Oedema (HACE) and High Altitude Pulmonary Oedema (HAPE)⁽⁴⁶⁾. AMS is defined as headache in an un-acclimatised person who has recently ascended above 2500m with at least one of the following: loss of appetite, nausea, vomiting, insomnia, dizziness or fatigue⁽⁴⁷⁾. Below 2500m AMS is unusual and although unpleasant, a self-limiting condition⁽⁴⁷⁾.

A slow rate of ascent is the best way to prevent AMS, however this is not always possible or practicable⁽⁴⁶⁾.

Acetazolamide: Although acetazolamide is not licensed for prophylaxis of acute mountain sickness in Ireland or the UK, the NMIC has received several queries regarding this use^(47,48). In the US acetazolamide has been designated an orphan drug by the FDA for this use⁽⁴⁹⁾. Debate surrounds the minimum prophylactic dose and duration for acetazolamide⁽⁴⁷⁾. A recent paper states that the dose used in trials has usually been 250mg 8 hourly but 250mg or even 125mg twice daily is usually recommended now⁽⁴⁶⁾. The British Mountaineering Council and other researchers recommend 125mg to 250mg twice daily one to two days before ascent and continued for at least 48 hours after arrival at altitude⁽⁴⁷⁾. In some sources higher doses are mentioned of up to 1000mg day⁽⁴⁷⁾.

Adverse effects of acetazolamide include a mild diuresis, which tends to diminish if the drug is continued. Paraesthesia of the fingers and toes is almost universal. Flushing, thirst, headache, rash and blood dyscrasias are mentioned but are rare. Acetazolamide is a sulphonamide and should be avoided in people with a known allergy to sulphonamides⁽⁴⁶⁾.

ILLNESS IN THE RETURNED TRAVELLER

As international travel exposes people to more exotic and remote areas, especially in developing countries, the traveller is increasingly likely to come into contact with diseases, for which he/she has no prior contact and therefore no immunity⁽⁵¹⁾. It has been estimated that for every 100,000 who travel to developing countries for one month, 50,000 will have a health problem during their trip, 8,000 will seek medical care, 5,000 will be confined to bed, 1,100 will be incapacitated in their activities either abroad or on their return, 300 will require hospitalisation either during or after the trip, 50 will require emergency transport home and one will die⁽⁵²⁾. Although there are many possible causes of illness in the returned traveller, it is important for the clinician to be aware of the commonest and therefore more likely conditions as well as those posing the greatest risk to the individual (and to public health via person-to-person transmission) in terms of morbidity and potential for fatal outcome⁽⁵³⁾.

General principles of evaluation: When reviewing a sick returned traveller, it is vital to be able to identify a potentially life-threatening illness so that this can be dealt with as an emergency. If in doubt, advice from a specialist travel unit should be sought. It is important to document the travel itinerary, including all areas visited, even stop-overs in airports / train stations^(54,55). The history should also include: type of holiday undertaken (structured itinerary, back-packing), type of accommodation (luxurious, hostel, visiting friends or family (latter involves greater exposure to local diseases)); activities pursued while on holiday (e.g. contact with water, type of terrain visited, sexual behaviour); contact with ill people (either local or fellow travellers) or with animals during the trip; vaccinations / prophylactic measures followed during the holiday and their suitability for the areas visited; history of bites (animals and insects), abrasions, or symptoms encountered during the holiday period⁽⁵³⁾. Exact dates that each site was visited should be noted to identify incubation periods and possible infectious causes (some diseases display seasonality). Table 4 outlines some possible consequences of specific exposures while travelling.

Table 4: Some potential tropical infections linked with specific exposure types^(51, 56)

Exposure	Illness outcome
Raw / undercooked / exotic foods	Enteric infections, hepatitis, E. trichinosis
Ingesting untreated water, milk, cheese	Salmonellosis, shigellosis
Freshwater swimming	Schistosomiasis, leptospirosis
Insect bites	- <i>Mosquito</i> : malaria, dengue - <i>Tick</i> : borreliosis, certain haemorrhagic fevers, rickettsial infections - <i>Tsetse fly</i> : African trypanosomiasis (sleeping sickness) - <i>Reduviid bug</i> : Chagas disease - <i>Sandfly</i> : Schistosomiasis (Bilharzia)
Animal exposure / bites	Rabies, Q fever, borreliosis, plague, certain haemorrhagic fevers, avian influenza
Exposure to infected persons	Lassa, Marburg, Ebola viruses, SARS, hepatitis, typhoid

Table 5: Reported Causes of Fever in hospitalised adults returned from travel to Tropical areas^(53, 56)

Cause	Percentage (range) of cases
Malaria	32-42
Undiagnosed	25*
Respiratory	2-11
Diarrhoeal illness	4-6
Hepatitis	3-6
Dengue	2-6
Urinary tract infection	2-4
Enteric fever	2
Pharyngitis or Epstein-Barr virus each	1-2
Amoebic liver abscess or tuberculosis or]	1
Meningitis or acute HIV – each]	

*includes presumed viral and non-specific infections

Patients with Fever: The majority of serious imported infections will present with fever as the major symptom⁽⁵³⁾. Table 5 outlines the results from studies undertaken in hospitalised patients in the 1990s, which showed that malaria was the diagnosis in one third of patients. However, a quarter of cases never got a formal diagnosis.

Investigation of Fever in the Returned Traveller: The initial emphasis should be on excluding malaria, meningitis, septicaemia and serious infections of chest, gastrointestinal or urinary tract^(53,55). **Physical examination, in association with the travel history**, may give a clue to the diagnosis^(53,54) (e.g. jaundice associated with hepatitis, leptospirosis, malaria; lymphadenopathy in dengue fever, glandular fever or rickettsial infections; skin tracks with hookworms). **Baseline Laboratory Tests** are vital in the differential diagnosis; they include full blood count (and blood films) serum electrolytes, liver functions tests, blood cultures, urinalysis and urine and stool cultures. Directed serological analysis should be undertaken or blood stored for such analysis at a later date, when there are more data to suggest a diagnosis. Other investigations, including radiological, should be determined by the travel history and examination. **Neutrophil leucocytosis** is seen with several infections, including bacterial, amoebic abscess or leptospirosis. **Low platelets** may point to a diagnosis of malaria, dengue or may be part of a viral or parasite infection. **Eosinophilia** usually suggests a helminth infection (but check that the patient is not atopic)^(53,55). The more commonly encountered helminths include the following: nematodes such as hookworms, (anaemia), strongyloides (abdominal and skin infection which can persist for decades) and ascaris (abdominal infection with / without respiratory symptoms; visible worms in the faeces): trematodes such as schistosoma species which may cause mild swimmer's itch, or "Katayama fever" with fever, transient urticarial rash, headache, haematuria, dry cough and malaise, with / without hepatosplenomegaly⁽⁵⁷⁾. Stool microscopy for ova, cysts, parasites and specific cultures according to suspicion of disease, may be helpful as part of the overall assessment of eosinophilia. **Blood films** may be useful in excluding several diseases such as borreliosis, filariasis, in addition to malaria. Frequently, a definitive diagnosis may only be possible by checking "convalescent" serology, at least 2 weeks after the initial presentation.

Risk of Person-to-Person Transmission: The possibility of transmission of disease from the patient to the healthcare worker is small overall but must be borne in mind when managing an ill returned traveller with an undiagnosed fever. Isolation is needed if certain diseases are suspected such as diphtheria, SARS and suspected viral haemorrhagic fevers. In addition, follow-up of the patient's contacts in these cases may be required – immediate advice should be sought from local public health specialists in this regard⁽⁵³⁾.

Practical Advice for the Primary Care Physician: Currently, there are many possible travel destinations, each with its own risk for the traveller, therefore it may not be possible to identify the cause of illness in the returned traveller without the aid of a specialist travel medicine unit. However, since the primary care physician may be the first to examine the ill traveller, it is vital that his/her **examination should be focused on identifying potentially life-threatening conditions requiring urgent hospitalisation**. Most of these conditions will present with fever and the history may identify potential causes such as malaria, dengue fever, rabies. **If in doubt seek urgent specialist advice**. For patients presenting with more indolent illness the approach as outlined above may enable a diagnosis to be made and appropriate treatment to be given as an outpatient. But it is important to remember that up to 25% of returned travellers presenting with an illness may never get a definitive diagnosis.