

FEVER IN THE RETURNED TRAVELLER



“A Tropical Moonlight”, oil on canvas, Fredrick Edwin Church, 1874.

“I Bernal Diaz Del Castillo, citizen and governor of the most loyal city of Santiago de Guatemala, one of the first discoverers and conquerors of New Spain and its provinces... tell you the story of myself and my comrades; all true conquerors, who served his Majesty in the discovery, conquest, pacification, and settlement of the provinces of New Spain...

...One of our Cempoalan allies was killed that night, two more and a horse were seriously wounded, and we took four of the enemy. After thanking God for delivering us, and burying our dead friend and tending our wounded, we set our guard and slept for the rest of the night. But on waking next morning we realized our sad plight. We were all weary and wounded, some with two or three wounds, many of us were ragged and sick, and Xicotenga was still on our heels. We had lost forty five men in all, in battle or from disease and chills, while another dozen were sick from fever, among them Cortes... Cortes led the expedition though he was still suffering from tertian fever...

We saw them beginning to surround us. Our horsemen charging in bands of five, broke their ranks. And then commending ourselves most heartily to God and the Blessed Mary, and calling on the name of our patron St. James, we charged them all together...

I will describe the whole of the battle. We were struck by the tenacity of their fighting, which was beyond description. Neither cannon, muskets nor crossbows were of any avail, nor hand to hand combat, nor the slaughter of thirty or forty of them every time we charged. They fought on bravely and with more vigour than before...

...Here Cortes showed himself the brave man he was! The battle was fierce and fighting intense. It was a memorable sight to see us all streaming with blood and covered with wounds; and some of us were slain. It pleased our Lord that we should reach the place where the image of our Lady used to stand, but we did not find it there. It appears, as we afterwards learnt, that the great Montezuma paid devotion to it, and he had ordered it to be kept safe. We set fire to their idols...

Now we saw our forces diminishing every day, and the Mexicans increasing in numbers. Many of our men had died, and all of the rest were wounded. Though we fought most valiantly, we could not drive back the many bands which attacked us by night and day, or force them to a standstill. We became short of powder, and then of food and water. We had sent to ask them for a truce, but because of Montezuma's death they would not leave us in peace. In fact we stared death in the face....Those of us who escaped only did so by the grace of God...

As we were retreating, we heard the sound of trumpets from the great cue of Huichilobos and Tezcatlipoca, which dominates their whole city, and the beating of a drum, a very sad sound, as of some devilish instrument, which could be heard six miles away; and with came the noise of many kettle drums, conches, horns, and whistles. At that moment, as we afterwards learnt, they were offering the hearts and blood of ten of our comrades to these two idols...

Some of our crossbowmen and musketeers shot while others were loading, the horsemen made charges, and Pedro Moreno loaded and fired his cannon. Yet despite the number of Mexicans that were swept away by this shot we could not keep them at bay....

When we had retired almost to our quarters, across a great opening full of water, their arrows, darts and stones, could no longer reach us...the dismal drum of Huichilobos sounded again, accompanied by conches, horns, and trumpet like instruments. It was a terrifying sound, and when we looked at the tall cue from which it came we saw our comrades who had been captured in Cortes's defeat being dragged up the steps to be sacrificed. When they had hauled them up to a small platform in front of the shrine were they kept their accursed idols we saw them put plumes on the heads of many of them; and then they made them dance a sort of fan in front of Huichilobos. Then after they had danced the papas laid them down on some narrow stones of sacrifice and cutting open their chests, drew out their palpitating hearts, which they offered to the idols before them..."

Bernal Diaz, Memoires of the "The History of the Conquest of New Spain", 1568.

One of the great intellectual debates of the 18th Century concerned the innate good or evil of humanity. Jean-Jacques Rousseau believed that all people were born good, and that society was then responsible for them becoming evil. The more advanced the society, the more selfish and evil it would make people. Conversely the more primitive the society the closer to nature it was and the more pure would be its people. Many of his more illustrious Philosophers however disagreed with him, notably Voltaire who sarcastically rebuked Rousseau's notion of the primitive idyll by claiming he had "given up the habit of walking on all fours". Diderot remarked, "I don't care for acorns and dens and hollow oaks. I require a carriage, a convenient apartment, fine linen and a perfumed girl, and after that I would gladly accommodate to all the other curses of our civilized state" - perhaps proving Rousseau's point! One only needed to look to history. The clash of the "civilized" old world Conquistadors, and the fantastic Neolithic society of the new world in the Sixteenth century. The Aztecs by Rousseau's reasoning should have been more "pure" than the old world invaders, in view of their supposed closer proximity to the primal state. The horrific descriptions of Diaz concerning the barbaric practices of Aztec human sacrifice however quickly lays to rest this reasoning. Both sides slaughtered each other in the name of their deities. Spinoza had insisted that human nature was always and everywhere the same, evil and self-interested - perhaps he was closest to the truth.

The Sixteenth century Spanish Conquistadors had not the least doubt that they overcame a vastly numerically superior empire because of the justness of their cause which was preordained by God. The Pulitzer Prize winning author, Jared Diamond, has argued convincingly that the reason for the stunning victory was not only by dint of superior technology, (guns and steel), but also by, and most tellingly, germs - the microorganisms, that brought measles and smallpox to a population that had never before encountered them. The result for the native Indians was a disaster on a scale comparable to the European Black Death of the Fourteenth century. In fact this was possibly the single greatest factor that brought about the fall of the Aztec Empire.

Today the native populations of South America are far more immune to the Old World microorganisms such as measles that decimated their ancestors. Those travellers from the old world to the new however remain at substantial risk from many new world microorganisms, such as malaria and yellow fever.

FEVER IN THE RETURNED TRAVELLER

Introduction

Fever in the returned traveller should always be taken seriously.

A wide range of infectious diseases are possible in returned travellers, a number of which can be **lethal** if missed.

Note that a fever may *not* invariably be present, and so any patient *unwell* enough to present to an Emergency Department should still prompt a *high index of suspicion* for a possible serious underlying infectious disease.

Fever may be absent for an number of reasons including:

- It may be intermittent (as *may* be seen in malaria)
- The patient may be taking antibiotics
- The patient may have suppressed immunity, blunting the febrile response, (elderly patients for example).

Initial investigation and management will be guided by the clinical presentation, including the important board aspects of:

- The history
- The examination
- The regions of travel
- Possible incubation periods

In addition to the risk factor of overseas travel, the usual “red flags” of any patient who presents with a PUO must also be taken into account, (see also separate guidelines on **Pyrexia of Unknown Origin in Adults**).

Note that more than one infectious disease can be present in a returned traveller.

Empirical treatment will often be required for patients who are unwell, or have particularly high risk profiles

The threshold for a period of admission for investigation and observation must be low.

There should always be close consultation with the ID Unit

See also separate clinical guidelines for specific individual diseases.

Epidemiology

Useful Information Resources:

For travel related warnings on infectious diseases appropriate to travel history:

- <http://wwwnc.cdc.gov/travel/default.aspx>

For international disease outbreak news:

- <http://www.who.int/csr/don/en/>

Pathology

A wide range of infectious diseases are possible in returned travellers, a number of which can be **rapidly lethal** if missed.

Among the most important in this regard are:

- Highly pathogenic influenza strains/ SARS
- Malaria, (falciparum and knowlesi)
- Typhoid
- Haemorrhagic dengue fever
- African viral haemorrhagic fevers
- Arbovirus encephalitides
- Rabies
- Cholera

See also separate guidelines for each of these conditions.

Clinical assessment

Any patient suspected of having a potentially serious infectious disease must be assessed and management in an appropriately timely manner.

The more common potentially lethal diseases must always be specifically borne in mind, particularly:

- **Falciparum malaria**, must always be considered.

- Typhoid
- Dengue fever, (haemorrhagic).

Localizing signs as a general rule tend to fall into 4 broad groups - diarrhoea, neurological, respiratory and a hepatic picture.

However:

- **It is important to note that many diseases may present without clear localizing signs, despite their textbook descriptions.**
- **Similarly many can have “false localizing signs”.**

Note also that more than one infectious disease can be present in a returned traveller.

(Occam’s razor is an instrument with which many clinicians eventually slit their own throats!).

Important points of history:

Important aspects include:

1. Travel itinerary:
 - **This should be as precise as possible**
2. Note the *type* of potential exposure:
 - The type of exposure should be documented. The type of accommodation, mode of transport, activities undertaken particularly if water related, the level of hygiene, type of food, consumption of unpasteurised milk, exposure to insects/animals and sexual practices and acquisition of body art can all be important clues to diagnosis.
3. Note the incubation period:
 - This is the time from exposure to the development of clinical symptoms, and can help in the assessment of the probability of many specific diseases.
 - Most travellers will present relatively soon after arrival home, with over 90% of infections related to short term travel manifesting within *6 months* of return. It is rare for illness related to short term travel to develop more than *one year* later. ¹

Diseases that usually only occur after prolonged or repeated exposures are *rare in short term* travellers. ¹

4. Prophylaxis:

- Note any pre-travel immunizations or chemoprophylaxis (as well as compliance) taken by the patient.
- Note also any antibiotic treatment in general a patient may be taking, which may *attenuate* the clinical picture.

5. Symptoms of possible serious sepsis:

Note also the presence of any of the well recognized presenting symptoms of possible serious infection including:

- Rigors
- Severe myalgias
- Altered conscious state
- Vomiting particularly with headache or abdominal pain
- Unexplained rash and jaundice.
- *A rapid evolution* of the disease process can also be a sign of serious infection.

Important points of examination:

Important aspects include:

1. Vital signs:

- Note that the absence of fever does not necessarily rule out a potentially serious infection.
- Look for signs of shock, including haemodynamic parameters and capillary refill times, as one indication of disease severity.

2. Conscious state:

- This may indicate cerebral pathology, but it can also be a non-specific sign of disease severity of *virtually any* cause.

3. Hydration status:

4. Rash:
 - This is an important but unfortunately very non-specific sign.
 - Purpuric rashes should always prompt consideration of serious bacterial infection such as meningococcus.
 - Rickettsia, typhoid, haemorrhagic fevers, and dengue are also considerations, however absence of rash does not rule these out.
5. Respiratory distress:
 - The Influenzas should be considered *throughout* the year because of international travel.
 - Legionella is more common *outside* Australasia.
6. Jaundice:
 - Jaundice can be due to hepatitis but can also be an ominous sign of overwhelming sepsis in general, including severe malaria.
 - Remember that a patient may also present with liver infection before jaundice becomes apparent.
 - It is important in patients with fever and jaundice to also consider the possibility of a **surgical** cause of **cholangitis**

Investigations

As a general rule all returned travellers suspected of having an infectious disease should have:

1. FBE:
 - Anaemia:
 - ♥ Significant anaemia may be associated with severe malaria
 - WCC:
 - ♥ If elevated raises suspicion for infection, but if not does not, of course, rule infection out.
 - Eosinophilia:
 - ♥ The higher the grade of eosinophilia, the more likely a travel-related diagnosis, particularly helminth infestation (e.g.

strongyloidiasis, filariasis, hookworm, schistosomiasis, cutaneous larva migrans and ascariasis).²

♥ The absence of eosinophilia however does not exclude parasites, as eosinophilia generally occurs only during the tissue invasive stages of worm development.

- Thrombocytopenia:

- ♥ Can be associated with severe malaria

2. CRP:

- If elevated will raise suspicion for infection.
- May be elevated even in the presence of a normal WCC.
- If normal, again does **not** rule out the possibility of early serious infection.

3. U&Es/ glucose

4. LFTs

5. Blood cultures:

- These will be particularly important for typhoid.

6. CXR:

- Unsuspected pneumonia and Tuberculosis

7. MSU:

- Microscopy, culture and sensitivity.
- Consider also legionella Ag testing.
- PCR testing may also be available for some organisms.

8. Coagulation profile, (when liver disease and/ or a coagulopathy is suspected).

Further investigations will then be guided by the degree of the index of suspicion for any particular disease.

*The following is not exhaustive, but important **considerations** will include:*

9. **Malaria screen:**

- **All travellers to malaria endemic regions should be tested for malaria**
- **For practical purposes all malarial regions have falciparum**
- **Three thick and thin films are done as well as an ICT**

See also separate specific guidelines for malaria.

10. Faecal sampling:

- For microscopy, culture and sensitivities.
 - ♥ For bacteria, ova and parasites.
 - ♥ If a particular organism is suspected, this should be indicated to the laboratory.
- Antigen testing is available for a number of specific organisms.
- **PCR:**
 - ♥ For enteroviruses, and many other organisms.

11. Serological testing:

- **Hepatitis serology:**
 - ♥ Hepatitis A, B, C, D and E (if from the Indian subcontinent).
 - ♥ CMV/EBV
- **Dengue serology**
- **HIV**
- Infection with vaccine preventable infections such as measles and mumps should not be forgotten!

Specific serology should be considered especially when vaccination status is uncertain and the clinical picture is suggestive.

Many other diseases have specific serological tests available, and these can be done according to clinical suspicion.

12. PCR blood testing:

- **Many diseases have specific PCR tests available, and these can be done according to clinical suspicion.**
13. Respiratory symptoms:
- **Nasal/ pharyngeal swabs** for virology studies including **PCR** testing.
14. Ultrasound:
- For jaundiced patients, may be considered for:
- Ruling out possible surgical causes of jaundice.
 - Delineating possible liver abscess.
15. CT scan:
- Cerebral CT scan should be considered for any patient with confusion or altered conscious state.
16. MRI:
- *Once patients are stabilized* this is an excellent investigation for patients with suspected encephalitis, especially in whom a CT scan has not provided a clear diagnosis.
17. LP:
- This is done to diagnose meningitis or encephalitis. The usual precautions of avoiding this investigation in patients suspected of having raised intracranial pressure or coagulopathy should be kept in mind.
 - Empiric treatment should not be delayed by the LP in unwell patients.
 - Microscopy, culture and **PCR studies** can be done for specific diseases.

Management

There should always be close consultation with the ID Unit for any returned traveller who presents to the ED with a fever.

Most cases will require admission, particularly if the patient appears unwell and/ or there is diagnostic uncertainty.

1. Initial resuscitation:
- As with any unwell patient the first priority will be the initial resuscitation, as clinically indicated.

- Ongoing supportive treatments are provided as clinically indicated.
2. Empirical antibiotic treatment:
- Unwell and/ or seriously at risk patients will often require urgent empirical treatment before a definitive diagnosis can be made.
 - The treatment given will be guided by how unwell the patient is as well as the index of suspicion for a particular disease.
3. Isolation precautions:
- These will mainly be necessary in cases of:
- Respiratory disease
 - Gastrointestinal disease
 - Patients with significant immunocompromise.

Health Department Notifications

Many infectious diseases contracted outside of Australia will have important public health considerations.

Reporting to and close consultation with the Health Department will also be an important part of the management of these patients.

Appendix 1

Incubation periods of some important imported infections: ¹

< 10 days	< 21 days	> 21 days
Dengue	Malaria	Malaria
Influenza	VHF	Viral hepatitis
Plague	Rickettsial disease	HIV
Paratyphoid fevers	Typhoid fever	Rabies
Sandfly fever	African Trypanosomiasis	Tb
Legionella	Brucellosis	Q fever
	Q fever	Parasitic diseases:
	Relapsing fever	● Acute Schistosomiasis
	Measles	● Visceral leishmaniasis
	Mumps	● Amoebic liver abscess
		● Filariasis

References

1. Leder K et al, "Infections in Returned Travellers and Immigrants", in Yung A et al, Infectious Diseases; a clinical approach, 2nd ed 2005.
2. Looke et al. "Infections in the Returned Traveler", MJA: 2002 177 (4) 212-219.

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