What infections do returned travellers bring back to Australia?

Sarah McGuinness (sarah.mcguinness@monash.edu) MBBS, DTMH, MPH&TM, FRACP
Infectious Diseases Physician, Alfred Hospital
PhD candidate, Infectious Diseases Epidemiology Unit, Monash University
How often & why do Australians travel?

Short-term departures by Australian residents (a)

9.2 million
2014-2015
(25% Victorians)

<table>
<thead>
<tr>
<th>Reason for Travel 2014-2015</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Holiday</td>
<td>59%</td>
</tr>
<tr>
<td>Visiting friends and relatives</td>
<td>24%</td>
</tr>
<tr>
<td>Business</td>
<td>10%</td>
</tr>
</tbody>
</table>

(a) Year ending June.
Source: ABS 1990-2010 Overseas Arrivals and Departures collection

Source: Australian Bureau of Statistics (www.abs.gov.au)

NB: short-term defined as intended absence from Australia of less than one year
## Where do Australians Travel?

**SHORT-TERM RESIDENT DEPARTURES, Australia - Financial Years, Trend Series**

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>New Zealand</td>
<td>832.3 '000</td>
<td>1,237.5 '000</td>
<td>48.7 % change</td>
</tr>
<tr>
<td>UK, CIs &amp; IOM(c)</td>
<td>402.2 '000</td>
<td>1,118.7 '000</td>
<td>223.0 % change</td>
</tr>
<tr>
<td>United States of America</td>
<td>396.3 '000</td>
<td>980.8 '000</td>
<td>147.5 % change</td>
</tr>
<tr>
<td>Indonesia</td>
<td>346.4 '000</td>
<td>552.6 '000</td>
<td>37.4 % change</td>
</tr>
<tr>
<td>China</td>
<td>214.5 '000</td>
<td>549.5 '000</td>
<td>194.0 % change</td>
</tr>
<tr>
<td>Fiji</td>
<td>190.3 '000</td>
<td>413.2 '000</td>
<td>92.6 % change</td>
</tr>
<tr>
<td>Thailand</td>
<td>186.9 '000</td>
<td>361.7 '000</td>
<td>112.7 % change</td>
</tr>
<tr>
<td>Singapore</td>
<td>170.0 '000</td>
<td>335.5 '000</td>
<td>76.3 % change</td>
</tr>
<tr>
<td>Hong Kong</td>
<td>169.3 '000</td>
<td>280.7 '000</td>
<td>228.5 % change</td>
</tr>
<tr>
<td>Malaysia</td>
<td>155.4 '000</td>
<td>268.3 '000</td>
<td>177.3 % change</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>4,576.9</strong></td>
<td><strong>9,221.5</strong></td>
<td><strong>125.7</strong> % change</td>
</tr>
</tbody>
</table>

(a) Top 10 destination countries based on trend estimates for 2004-05.

(b) Top 10 destination countries based on trend estimates for 2014-15.

(c) United Kingdom, Channel Islands and Isle of Man.
Illness in travellers

- Up to 50% develop a health problem
- Up to 8% sufficiently ill to seek health care while abroad or after returning home
Infections in Returned Travellers

Most common syndromes:
- Travellers’ diarrhoea
- Respiratory tract infections
- Skin problems: infections, rash, bites
- Febrile illnesses

Most life-threatening illnesses (febrile):
- Malaria (P. falciparum)
- Bacterial sepsis (e.g. meningococcal disease)
- Viral haemorrhagic fevers (e.g. Ebola)
Infections in the returned traveller

Timing of illness in relation to travel (incubation)

Travel itinerary (epidemiology)

Traveller characteristics e.g. VFR travellers, immunosuppression, pregnancy (increased risk of or susceptibility to infection)

Exposure history e.g. animal contact, body fluid exposure, fresh water exposure, mosquito bites (add to DDx)
<table>
<thead>
<tr>
<th>Timing of illness in relation to travel</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Short (&lt;2 weeks)</strong></td>
</tr>
<tr>
<td>------------------------</td>
</tr>
<tr>
<td>Malaria (most 7-30d)</td>
</tr>
<tr>
<td>Influenza (1-3 days)</td>
</tr>
<tr>
<td>Bacterial gastroenteritis (TD) (most 1-3 days)</td>
</tr>
<tr>
<td>Arboviruses: dengue, zika, chikungunya (2-12 days)</td>
</tr>
<tr>
<td>Spotted-fever rickettsiae &amp; typhus (2-20 days)</td>
</tr>
<tr>
<td>Leptospirosis (7-24 days)</td>
</tr>
<tr>
<td>Typhoid and paratyphoid fever (7-21 days)</td>
</tr>
<tr>
<td>Viral haemorrhagic fevers including Ebola (2-21 days)</td>
</tr>
</tbody>
</table>
Travel Itinerary

- Countries vary greatly in disease patterns
- Variation within countries based on season, altitude, climate, urbanisation, vectors etc
- Longer trips are associated with increased risk of travel related illness
<table>
<thead>
<tr>
<th>Type of exposure</th>
<th>Related illnesses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fresh water exposure</td>
<td>Schistosomiasis, leptospirosis</td>
</tr>
<tr>
<td>Raw or undercooked food</td>
<td>Food-borne viruses and bacteria, intestinal parasites, listeriosis, cholera</td>
</tr>
<tr>
<td>Unpasteurised dairy products</td>
<td>Brucellosis, Listeriosis, Campylobacter,</td>
</tr>
<tr>
<td>Animal bites</td>
<td>Rabies, rat-bite fever, wound infections</td>
</tr>
<tr>
<td>Bird contact</td>
<td>Psittacosis, avian influenza</td>
</tr>
<tr>
<td>Mosquito bites</td>
<td>Malaria, dengue, chikungunya, zika, viral encephalitis, yellow fever, filariasis</td>
</tr>
<tr>
<td>Fly bites</td>
<td>African trypanosomiasis, onchocerciasis, leishmaniasis, loa loa</td>
</tr>
<tr>
<td>Flea bites</td>
<td>Murine typhus, plague, tungiasis</td>
</tr>
<tr>
<td>Tick bites</td>
<td>Rickettsial infections, tick-borne encephalitis</td>
</tr>
<tr>
<td>Soil-skin contact (bare feet)</td>
<td>Cutaneous larva migrans, hookworm, strongyloides</td>
</tr>
<tr>
<td>Sexual contact</td>
<td>HIV, hepatitis B and C, STIs</td>
</tr>
</tbody>
</table>
**Traveller characteristics:**

**reason for travel**

*Figure 3. Top 10 specific diagnoses, by main reasons for travel.*
GeoSentinel Surveillance of Illness in Returned Travelers, 2007–2011

Karin Leder, MBBS, MPH, PhD; Joseph Torresi, MBBS, PhD; Michael D. Libman, MD; Jakob P. Cramer, MD, MSc; Francesco Castelli, MD, PhD; Patricia Schlagenhauf, PhD; Annelies Wilder-Smith, MD, PhD, MIH; Mary E. Wilson, MD; Jay S. Keystone, MD, MSc; Eli Schwartz, MD; Elizabeth D. Barnett, MD; Frank von Sonnenburg, MD, PhD; John S. Brownstein, PhD; Allen C. Cheng, MBBS, PhD, MPH; Mark J. Sotir, PhD, MPH; Douglas H. Esposito, MD, MPH; and David O. Freedman, MD, for the GeoSentinel Surveillance Network*

- 5 years of data
- >40,000 ill returned travellers
- 34% gastrointestinal
- 23% febrile illness
- 20% dermatologic
- 10% respiratory
- 13% other
Gastrointestinal illnesses

- GI illnesses are common in travellers
- More than 25% of those who seek medical care during or after travel present with GI symptoms
- Up to 50% of people who travel to a developing country develop diarrhoea
Traveller’s diarrhoea (TD)

- TD definition: passage of 3 or more unformed stools over 24h during or shortly after a period of foreign travel

- Attack rate of 20-50%, depending on:
  - Destination country
  - Season (peak in summer in subtropical climes)
  - Style of travel (cruise ships = high risk of viral gastroenteritis outbreaks & foodborne outbreaks)
  - Food and drink choices
  - Host risk factors (e.g. PPI, immunosuppression)
Causal pathogen found in 40-60% of patients (85% bacteria)

<table>
<thead>
<tr>
<th>Bacterial</th>
<th>Asia</th>
<th>Latin America</th>
<th>Africa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enterotoxigenic E coli</td>
<td>6-37%</td>
<td>17-70%</td>
<td>8-42%</td>
</tr>
<tr>
<td>Other E coli</td>
<td>3-4%</td>
<td>7-22%</td>
<td>2-9%</td>
</tr>
<tr>
<td>Campylobacter jejuni</td>
<td>9-39%</td>
<td>1-5%</td>
<td>1-28%</td>
</tr>
<tr>
<td>Salmonella spp</td>
<td>1-33%</td>
<td>1-16%</td>
<td>4-25%</td>
</tr>
<tr>
<td>Shigella spp</td>
<td>0-17%</td>
<td>2-30%</td>
<td>0-9%</td>
</tr>
<tr>
<td>Plesiomonas shigelloides</td>
<td>3-13%</td>
<td>0-6%</td>
<td>3-5%</td>
</tr>
<tr>
<td>Aeromonas spp</td>
<td>1-57%</td>
<td>1-5%</td>
<td>0-9%</td>
</tr>
<tr>
<td>Viral</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rotavirus</td>
<td>1-8%</td>
<td>0-6%</td>
<td>0-36%</td>
</tr>
<tr>
<td>Parasitic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Entamoeba histolytica</td>
<td>5-11%</td>
<td>&lt;1%</td>
<td>2-9%</td>
</tr>
<tr>
<td>Giardia lamblia</td>
<td>1-12%</td>
<td>1-2%</td>
<td>0-1%</td>
</tr>
<tr>
<td>Cryptosporidium spp</td>
<td>1-5%</td>
<td>&lt;1%</td>
<td>2%</td>
</tr>
<tr>
<td>Cyclospora cayetanensis</td>
<td>1-5%?</td>
<td>&lt;1%?</td>
<td>&lt;1%?</td>
</tr>
<tr>
<td>No pathogen identified</td>
<td>10-56%</td>
<td>24-62%</td>
<td>15-53%</td>
</tr>
</tbody>
</table>

Adapted from Ansdell and Ericsson, with permission of the authors.

Table 1: Regional distribution of the most common pathogens that cause traveller’s diarrhoea
Gastrointestinal Pathogens

Enteropathogens and Chronic Illness in Returning Travelers

Chronic diarrhoea

- ~1% of travellers with acute diarrhoea develop chronic diarrhoeal symptoms

- Parasitic pathogens found in up to 30%
  - Giardia most common (reasonable to treat empirically)
  - Entamoeba & others (e.g. cryptosporidium)

- In many patients no pathogen identified

- Post-infectious irritable bowel syndrome (IBS) may affect >10% of travellers who experience TD
### Dermatological Diagnoses (n = 9669)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Cases, n</th>
<th>Median Age, y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin or soft-tissue infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rash or itch</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insect bite or sting</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Animal bite or scratch</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dermatologic diagnosis, specific cause identified*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rabies PEP after bite or scratch</td>
<td>1249</td>
<td>31</td>
</tr>
<tr>
<td>Cutaneous larva migrans</td>
<td>806</td>
<td>30</td>
</tr>
<tr>
<td>Leishmaniasis (cutaneous or mucocutaneous)</td>
<td>264</td>
<td>23</td>
</tr>
<tr>
<td>Myiasis</td>
<td>174</td>
<td>36</td>
</tr>
<tr>
<td>Tungiasis</td>
<td>87</td>
<td>30</td>
</tr>
<tr>
<td>Gnathostomiasis</td>
<td>12</td>
<td>26.1</td>
</tr>
<tr>
<td>Leprosy</td>
<td>11</td>
<td>44</td>
</tr>
<tr>
<td>Cutaneous atypical mycobacteria</td>
<td>6</td>
<td>36.5</td>
</tr>
<tr>
<td>Sporotrichosis</td>
<td>1</td>
<td>14</td>
</tr>
<tr>
<td>Yaws</td>
<td>1</td>
<td>67</td>
</tr>
</tbody>
</table>
Other skin manifestations

Localised furuncular myiasis
- Ectoparasitic infection by fly larvae
- Acquired in Latin America (*D. hominis*)
  - > Africa (*Cordylobia anthropophaga*)
- Mostly managed by manual extraction

*Dermatobia hominis*
Human botfly

Creeping eruption of cutaneous larva migrans (CLM)
- Superficial migration of animal hookworm larvae through skin
- Treat with ivermectin or albendazole
Other skin manifestations

Sporotrichosis

Cutaneous leishmaniasis

Buruli ulcer (*Mycobacterium ulcerans*)
Respiratory Infections

Respiratory Diagnoses (n = 4851)
- Upper respiratory tract infection
- ILI
- Bronchitis
- Pneumonia
- Pharyngitis, tonsillitis, or laryngitis
- Sinusitis
- Otitis

Respiratory diagnosis, specific cause identified:
- Influenza
- H1N1
- Influenza A or B
- TB
- MDR or XDR pulmonary TB
- Legionellosis
- Pulmonary atypical mycobacteria
- Pertussis
- Diphtheria

Cases, n
- Influenza: 367
- H1N1: 176
- Influenza A or B: 191
- TB: 170
- MDR or XDR pulmonary TB: 3
- Legionellosis: 35
- Pulmonary atypical mycobacteria: 35
- Pertussis: 30
- Diphtheria: 2

Median Age, y
- Influenza, H1N1: 16
- Influenza A or B: 36
- TB: 35
- MDR or XDR pulmonary TB: 35
- Legionellosis: 59
- Pulmonary atypical mycobacteria: 62
- Pertussis: 42
- Diphtheria: 20.5

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Fever in the returned traveller

- Systemic febrile illness
- Fever plus focal symptoms
  - Respiratory
  - Dermal
  - Neurological
  - Gastrointestinal
- Unrelated to travel
- “Non-exotic” travel associated
- “Exotic” travel associated
Unrelated to travel

Systemic febrile illness:
- Fever plus focal symptoms
  - Respiratory
  - Dermal
  - GI
  - Neurological
- Life-threatening bacterial sepsis
  - Staphylococcal
  - Pneumococcal
  - Meningococcal
  - Gram negative
- Common local diseases
  - Viral illnesses (e.g. influenza)
  - UTI
  - STI
- Complications of pre-existing conditions
“Non-exotic” travel-associated

- Systemic febrile illness:
  - Life-threatening bacterial sepsis
    - Staphylococcal
    - Pneumococcal
    - Meningococcal
    - Gram negative

- Fever plus focal symptoms
  - Respiratory
  - Dermal
  - GI
  - Neurological

- Common local diseases
  - Viral illnesses (e.g. influenza)
  - UTI
  - STI
“Exotic” travel-associated

- Systemic febrile illness:
  - Malaria
  - Dengue
  - Enteric fever
  - Rickettsial disease
  - Leptospirosis… etc

- Fever plus focal symptoms
  - Respiratory
  - Dermal
  - GI
  - Neurological

- Fever with rash
- Fever with jaundice
- Fever with altered conscious state
Systemic febrile illnesses

- Up to 50% - no diagnosis is identified

- Leading causes:
  - Malaria
  - Dengue
  - Enteric fever
  - Rickettsial infections

- Life-threatening illnesses
  - Malaria
  - Meningococcal infection (& other forms of sepsis)
  - Viral haemorrhagic fevers (VHF)

- Diseases with public health implications:
  - Measles
  - Hepatitis A
  - VHF
Table 2. Summary of diagnosis groups and selected specific diagnoses in febrile patients after travel (6957 patients with fever among 24,920 ill returned travelers).

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. (%) of ill returned travelers with fever</th>
<th>Percentage of patients hospitalized</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic febrile illness&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>2451 (35)</td>
<td>46</td>
</tr>
<tr>
<td>Malaria</td>
<td>1454 (21)</td>
<td>52</td>
</tr>
<tr>
<td>Malaria due to <em>Plasmodium falciparum</em></td>
<td>964 (14)</td>
<td>56</td>
</tr>
<tr>
<td>Malaria due to <em>Plasmodium vivax</em></td>
<td>388 (6)</td>
<td>51</td>
</tr>
<tr>
<td>Malaria due to other species</td>
<td>129 (2)</td>
<td>27</td>
</tr>
<tr>
<td>Dengue</td>
<td>430 (6)</td>
<td>29</td>
</tr>
<tr>
<td><em>Salmonella enterica</em> serovar Typhi or Paratyphi infection</td>
<td>141 (2)</td>
<td>57</td>
</tr>
<tr>
<td>Rickettsia</td>
<td>113 (2)</td>
<td>20</td>
</tr>
</tbody>
</table>
### Table 4. Cases of malaria and regions visited in a study of malaria in travelers, 2000–2002.

<table>
<thead>
<tr>
<th>Region visited</th>
<th>No. of cases of malaria</th>
<th>No. of travelers visiting region, in millions&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Risk per 10 million travelers of presenting to a GeoSentinel clinic with malaria</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very low-risk area&lt;sup&gt;b&lt;/sup&gt;</td>
<td>83</td>
<td>1766.9</td>
<td>0.5</td>
<td>1 (0.7–1.4)</td>
</tr>
<tr>
<td>Caribbean</td>
<td>9</td>
<td>50.5</td>
<td>1.8</td>
<td>3.8 (1.9–7.5)</td>
</tr>
<tr>
<td>North Africa</td>
<td>10</td>
<td>30.8</td>
<td>3.2</td>
<td>6.9 (3.6–13.3)</td>
</tr>
<tr>
<td>South America</td>
<td>17</td>
<td>43.8</td>
<td>3.9</td>
<td>8.3 (4.9–13.9)</td>
</tr>
<tr>
<td>Southeast Asia</td>
<td>64</td>
<td>118.8</td>
<td>5.4</td>
<td>11.5 (8.3–15.9)</td>
</tr>
<tr>
<td>Central America</td>
<td>24</td>
<td>13.5</td>
<td>17.8</td>
<td>37.8 (24.0–59.6)</td>
</tr>
<tr>
<td>South Asia</td>
<td>45</td>
<td>17.8</td>
<td>25.3</td>
<td>53.8 (37.4–77.4)</td>
</tr>
<tr>
<td>Oceania</td>
<td>31</td>
<td>8.6</td>
<td>36</td>
<td>76.7 (50.8–115.9)</td>
</tr>
<tr>
<td>Sub-Saharan Africa</td>
<td>514</td>
<td>52.7</td>
<td>97.5</td>
<td>207.6 (164.7–261.8)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Estimated from World Travel Organization data.

<sup>b</sup> Nonrisk/very low-risk areas were Europe, Northeast Asia, Australia/New Zealand, North America, and the Middle East.
<table>
<thead>
<tr>
<th>Disease</th>
<th>Total cases</th>
<th>Cases acquired O/S</th>
<th>Victorian cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dengue</td>
<td>1841</td>
<td>1591 (86%)</td>
<td>414</td>
</tr>
<tr>
<td>Malaria</td>
<td>414</td>
<td>413 (&gt;99%)</td>
<td>88</td>
</tr>
<tr>
<td>Shigellosis</td>
<td>556</td>
<td>216 (39%)</td>
<td>115</td>
</tr>
<tr>
<td>Enteric fever</td>
<td>150</td>
<td>141 (94%)</td>
<td>44</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>189</td>
<td>116 (61%)</td>
<td>53</td>
</tr>
<tr>
<td>Measles</td>
<td>158</td>
<td>52 (33%)</td>
<td>41</td>
</tr>
<tr>
<td>Hepatitis E</td>
<td>31</td>
<td>27 (87%)</td>
<td>8</td>
</tr>
</tbody>
</table>
Maculopapular rash:
- Dengue fever
- Measles
- Acute HIV, EBV, CMV
- Alphaviruses (RRV, BFV, Chikungunya)
- Rickettsial infection (spotted & typhus)
- Leptospirosis

Rose spots:
- Enteric fever

Eschar
- Rickettsial infection (spotted & typhus)

Petechial rash:
- Meningococcal disease
- Leptospirosis
- Rickettsial diseases
Fever and Jaundice

- Malaria
- Leptospirosis
- Hepatitis A, B, C, E (but not concurrent)
- CMV, EBV, Dengue
- Rickettsial diseases
- Yellow fever
- Amoebic liver abscess
- Fascioliasis, clonorchiasis, opisthorchiasis
Fever and altered mental state

- Cerebral malaria
- Meningoencephalitis
  - Viral: Japanese encephalitis, TBE
  - Bacterial: meningococcal
- Scrub typhus
- Leptospirosis
- Typhoid fever
- African trypanosomiasis
- Rabies
Relative risks of infections for travellers

- High risk:
  - Acute viral or bacterial gastroenteritis
  - Upper respiratory tract infections

- Moderate risk:
  - Dengue
  - Malaria
  - Giardia
  - Animal bite/scratch requiring rabies PEP
  - STIs
  - Influenza
  - Enteric fever (VFRs, travel to Indian subcontinent)

- Low risk:
  - Enteric fever (other travelers)
  - Rickettsial diseases
  - Chikungunya
  - Leptospirosis
  - Schistosomiasis
  - Tuberculosis
  - Cholera
  - Measles
  - Hepatitis A
  - Leishmaniasis
  - Cutaneous larva migrans (CLM)

- Very low risk: Yellow fever, rabies, anthrax, plague, VHF, trypanosomiasis, filariasis, poliomyelitis
Resources

- http://www.fevertravel.ch/

Example case:
- Traveller to Indonesia (Bali) who presents for evaluation on 22/3/16
- Travel from 4 – 18/3/16 March (2 weeks), symptoms started 19/3/16

Do not forget

- To request a malaria test and a full blood count in all patients returning from an endemic area with fever
- To perform an HIV test in all patients
- To enter in the differential diagnosis the autochthonous diseases that you would consider in a non-traveler