Leptospirosis and Ciguatera

Destination Oceania Workshop
ICTMM, Brisbane, September 2016

Colleen Lau
MBBS (UWA), MPH&TM (JCU), PhD (UQ), FRACGP, FACTM
NHMRC Fellow, Research School of Population Health, ANU
Travel Medicine Doctor, Travel Medicine Alliance Australia

Leptospirosis
- One of the most common bacterial zoonoses worldwide
- >1 million cases and 60,000 deaths per year
- Identified as a Neglected Zoonotic Disease by WHO
- Genus Leptospira: >20 species, >250 serovars
- Can infect any mammal species, cause chronic renal infection and urinary excretion of leptospires
- Leptospires can survive in environment for weeks or months depending on environmental conditions


Risk Factors

<table>
<thead>
<tr>
<th>Variables</th>
<th>Drivers of transmission &amp; emergence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individual behaviour</td>
<td>Occupation – farming, abattoirs, veterinary, military, sewage, outdoor work Recreational – swimming, rafting, caving, ecotourism, travel</td>
</tr>
<tr>
<td>Culture &amp; Lifestyle</td>
<td></td>
</tr>
<tr>
<td>Natural environment</td>
<td>Tropics, subtropics Rainfall, flooding, cyclones, extreme weather events Hydrology Environmental degradation Islands</td>
</tr>
<tr>
<td>Anthropogenic environment</td>
<td>Land use, e.g. farming Urbanisation, urban slums Poor sanitation and hygiene Poverty</td>
</tr>
<tr>
<td>Animals</td>
<td>Species Biodiversity Farming practices – subsistence livestock International transport – livestock, rodents</td>
</tr>
</tbody>
</table>

Risk Factors – Australia

<table>
<thead>
<tr>
<th>Variables</th>
<th>Drivers of transmission &amp; emergence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individual behaviour</td>
<td>Occupation – farming, abattoirs, veterinary, military, sewage, outdoor work Recreational – swimming, rafting, caving, ecotourism, travel</td>
</tr>
<tr>
<td>Culture &amp; Lifestyle</td>
<td></td>
</tr>
<tr>
<td>Natural environment</td>
<td>Tropics, subtropics Rainfall, flooding, cyclones, extreme weather events Hydrology Environmental degradation Islands</td>
</tr>
<tr>
<td>Anthropogenic environment</td>
<td>Land use, e.g. farming Urbanisation, urban slums Poor sanitation and hygiene Poverty</td>
</tr>
<tr>
<td>Animals</td>
<td>Species Biodiversity Farming practices – subsistence livestock International transport – livestock, rodents</td>
</tr>
</tbody>
</table>
Risk Factors – Pacific Islands

Variables

Drivers of transmission & emergence

Individual behaviour
Occupation – farming, abattoirs, veterinary, military, sewage, outdoor work
Recreation – swimming, rafting, caving, ecotourism, travel

Natural environment
Tropics, subtropics
Rainfall, flooding, cyclones, extreme weather events

Anthropogenic environment
Land use, e.g. farming
Urbanisation, urban slums

Animals
Species
Biodiversity
Farming practices – subsistence livestock
International transport – livestock, rodents

Morbidity & Mortality by Region

<table>
<thead>
<tr>
<th>Region/Country</th>
<th>Morbidity</th>
<th>Cases</th>
<th>Mortality</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Global</td>
<td>14.8</td>
<td>1,030,000</td>
<td>0.8</td>
<td>58,900</td>
</tr>
<tr>
<td>North America</td>
<td>3.6</td>
<td>12,800</td>
<td>0.2</td>
<td>600</td>
</tr>
<tr>
<td>Western Europe</td>
<td>3.9</td>
<td>16,300</td>
<td>0.2</td>
<td>800</td>
</tr>
<tr>
<td>High-income Asia Pacific</td>
<td>7.0</td>
<td>14,800</td>
<td>0.3</td>
<td>700</td>
</tr>
<tr>
<td>East Asia</td>
<td>10.3</td>
<td>142,000</td>
<td>0.5</td>
<td>6,900</td>
</tr>
<tr>
<td>South Asia</td>
<td>18.0</td>
<td>289,000</td>
<td>1.0</td>
<td>16,500</td>
</tr>
<tr>
<td>South-East Asia</td>
<td>55.5</td>
<td>266,000</td>
<td>3.0</td>
<td>14,200</td>
</tr>
<tr>
<td>Oceania</td>
<td>150.7</td>
<td>16,700</td>
<td>9.6</td>
<td>1,100</td>
</tr>
</tbody>
</table>

Morbidity and mortality cases/100,000/year


Global Environmental Change & Leptospirosis

- Climate change and extreme weather events – flooding
- Floodwaters disseminate bacteria in the environment
- People displaced from homes
- Animals displaced from habitats
- Sanitation and infrastructure disrupted
- High intensity contact between humans, animals, and pathogens in a highly contaminated environment
- Population growth – urbanisation, urban slums, poverty
- Poor sanitation, high flooding risk, overcrowding, rodents+++ 
- Agricultural intensification
- Both commercial and subsistence livestock
- Environmental degradation and biodiversity loss
- Invasive species (e.g. rodents) more easily established

Queensland 2011

The emergence of Leptospira borgpetersenii sewage strains as the dominant infecting serovar following the summer of natural disasters in Queensland, Australia 2011

Queensland 2011: the emergence of Leptospira borgpetersenii strains as the dominant infecting serovar following the summer of natural disasters in Queensland, Australia 2011

Wynwood et al. Tropical Biomedicine 2014.
Examples of Outbreaks related to Flooding

<table>
<thead>
<tr>
<th>Place</th>
<th>Outbreak</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fiji 2012</td>
<td>525 cases</td>
<td>Cyclone and flooding</td>
</tr>
<tr>
<td>New Caledonia</td>
<td>15 severe cases</td>
<td>Cyclone and flooding</td>
</tr>
<tr>
<td>January 2011</td>
<td>2 deaths</td>
<td></td>
</tr>
<tr>
<td>New Caledonia</td>
<td>135 cases</td>
<td>La Nina, heavy rainfall and</td>
</tr>
<tr>
<td>2009</td>
<td>5 deaths</td>
<td>flooding</td>
</tr>
<tr>
<td>Guam 2002</td>
<td>21 of 105</td>
<td>&quot;Extreme adventure&quot; outdoor</td>
</tr>
<tr>
<td>Philippines</td>
<td>&gt; 2000 cases</td>
<td>Severe flooding</td>
</tr>
<tr>
<td>2009</td>
<td>167 deaths</td>
<td></td>
</tr>
<tr>
<td>Queensland, Australia 2011</td>
<td>&gt; 100 cases</td>
<td>Severe flooding</td>
</tr>
<tr>
<td></td>
<td>No deaths</td>
<td></td>
</tr>
</tbody>
</table>

Outbreaks Related to Recreational Activities

<table>
<thead>
<tr>
<th>Place</th>
<th>Event</th>
<th>Outbreak</th>
</tr>
</thead>
<tbody>
<tr>
<td>Illinois 1998</td>
<td>Triathlon, 876 participants</td>
<td>11% of 474 athletes seropositive</td>
</tr>
<tr>
<td>Biomeo 2000</td>
<td>10-day-end challenge event involving jungle trekking, canoeing, outrigger sailing, kayaking, archery, mountain biking</td>
<td>42% attack rate among 189 intertropical athletes</td>
</tr>
<tr>
<td>Guam 2002</td>
<td>&quot;Extreme adventure&quot; outdoor event</td>
<td>21 of 105 participants</td>
</tr>
<tr>
<td>Martinique 2011</td>
<td>Canyoning, 45 participants</td>
<td>8 met case definition 7 confirmed by PCR</td>
</tr>
<tr>
<td>Sri Lanka 2012</td>
<td>Whitewater rafting, 20 office workers</td>
<td>6 developed fever 15/19 seropositive</td>
</tr>
<tr>
<td>Reunion 2013</td>
<td>Triathlon, 190 participants</td>
<td>Attack rate: 6.1% Adult swimmers: 23.1% Lower risk in those who wore neoprene suits</td>
</tr>
</tbody>
</table>

Leptospirosis in Travellers

<table>
<thead>
<tr>
<th>Place</th>
<th>Event</th>
<th>Outbreak</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>35% from recreation/travel, 19% overseas</td>
<td></td>
</tr>
<tr>
<td>Hawaii</td>
<td>0% in 1970s, to 50% in 1990s from recreation</td>
<td></td>
</tr>
<tr>
<td>California</td>
<td>85% from recreation</td>
<td></td>
</tr>
<tr>
<td>UK</td>
<td>&gt;50% from travel</td>
<td></td>
</tr>
<tr>
<td>Israel</td>
<td>42% from travel</td>
<td></td>
</tr>
</tbody>
</table>

Emerging Disease in Travel and Recreation

- Australia: 35% from recreation/travel, 19% overseas
- Hawaii: 0% in 1970s, to 50% in 1990s from recreation
- California: 85% from recreation
- UK: >50% from travel
- Israel: 42% from travel

Clinical Presentation – Early Phase

- Incubation 5 to 14 days (range 1 to 30 days)
- Acute onset of fever and chills
- Headache
- Myalgia, especially calf tenderness
- Jaundice
- Conjunctival suffusion
- Rash – macular, papular, urticariform
- Nausea, vomiting, abdominal pain
- Dizziness, lethargy, malaise
- Eye pain, photophobia
- Many have asymptomatic or mild infections
Complications in the Late Phase

- Acute lung injury, including pulmonary haemorrhage, ARDS
- Acute renal failure
- Acute liver failure
- Myocarditis, pericarditis, cardiac arrhythmias
- Coagulopathy and haemorrhage
- Neurological complications (aseptic meningitis, encephalitis, convulsions, Guillain-Barré Syndrome, transverse myelitis)
- Uveitis
- Case fatality rate of up to 30%
- Patients with suspected leptospirosis and any symptoms or signs suggestive of the above complications should be treated immediately and urgently referred if required

Laboratory Diagnosis

- First 7 to 10 days – Blood cultures or PCR
- After first week – Serology
- Might need to repeat serology for rising titres

Biphasic illness

Treatment

Early phase

- Antibiotics to shorten duration of illness, reduce mortality & complications
  - Oral: Amoxicillin or Doxycycline (Alternatives: Erythromycin, Azithromycin, Clarithromycin)
  - IV: Crystalline Penicillin G (Alternatives: Ampicillin, Ceftriaxone or other 3G cephalosporins, Erythromycin)

Late phase complications

- Supportive treatment, e.g. ventilation, haemodialysis, management of arrhythmias, coagulopathies, shock
- Steroids controversial – no robust evidence to support the routine use of high dose steroids. One study showed higher risk of nosocomial infections

Preventive Strategies for Travellers

- Avoid swimming in polluted rivers and streams
- Avoid swimming and contact with flood waters
- Avoid walking barefoot
- Cover up open cuts and wounds
- Use personal protection (gloves, boots, neoprene suits) during high-risk activities, especially direct contact with freshwater and/or animals
- High-risk travellers: intense environmental exposure, disaster response, post-flooding, ecotourism, working with animals

Preventive Strategies – Travellers

Prophylactic antibiotics:

- Little evidence on effectiveness, and routine use is not recommended
- Pre-exposure prophylaxis for short-term intense exposures, e.g. recreational, military, disaster response
  - Doxycycline 200mg weekly, starting 1-2 days before exposure and continue during exposure
- Post-exposure prophylaxis after high-risk exposure, e.g. contact with flood waters with open wounds in a high risk area
  - Doxycycline 200mg daily for 3 to 5 days

Misdiagnosis and Under-diagnosis

Common because of

- Non-specific clinical presentation, overlapping clinical features with other infections
- Low index of suspicion by clinicians
- Concurrent outbreaks of leptospirosis and other infections
- Poor availability of diagnostic tests
- Variable sensitivity and specificity of RDTs and ELISA
- ‘Wrong’ serovars in MAT panel

Preventive Strategies – Travellers

Prophylactic antibiotics:

- Little evidence on effectiveness, and routine use is not recommended
- Pre-exposure prophylaxis for short-term intense exposures, e.g. recreational, military, disaster response
  - Doxycycline 200mg weekly, starting 1-2 days before exposure and continue during exposure
- Post-exposure prophylaxis after high-risk exposure, e.g. contact with flood waters with open wounds in a high risk area
  - Doxycycline 200mg daily for 3 to 5 days
Preventive Strategies – Community

- Management of livestock
- Rodent control
- Keep streams and beaches clean
- Improve sanitation and hygiene
- Reduce flooding risk
- Improve drainage systems
- Reduce litter and garbage – block drains and attract rodents
- Improve community awareness and knowledge
- Warming signs in high-risk areas

Preventive Strategies – Need to Think Bigger

- Population growth + urbanization + agricultural intensification + climate change – May independently or potentially synergistically increase leptospirosis risk
- Many risk factors are not within the control of individuals and small communities – therefore importance of public health and environmental health

Ciguatera Fish Poisoning

- Most common marine poisoning in the world
- Occurs globally in coastal tropical waters, especially common in Pacific Islands
- Associated with high sea surface temperatures (>28°C) and degradation of coastal marine environments
- Ciguatoxin produced by dinoflagellates (microalgae) and cyanobacteria
- Toxin is lipid soluble and bioaccumulate up the food chain – large carnivorous fish are highest risk

Global Distribution of Ciguatera Fish Poisoning

<table>
<thead>
<tr>
<th>Country or Territory</th>
<th>Incidence/100,000: 1998-2008</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tokelau</td>
<td>1,576</td>
</tr>
<tr>
<td>Cook Islands</td>
<td>1,436</td>
</tr>
<tr>
<td>Marshall Islands</td>
<td>416</td>
</tr>
<tr>
<td>Vanuatu</td>
<td>397</td>
</tr>
<tr>
<td>French Polynesia</td>
<td>329</td>
</tr>
<tr>
<td>Fiji</td>
<td>144</td>
</tr>
<tr>
<td>Tonga</td>
<td>29</td>
</tr>
<tr>
<td>New Caledonia</td>
<td>9</td>
</tr>
<tr>
<td>Hawaii</td>
<td>3</td>
</tr>
<tr>
<td>Samoa</td>
<td>2</td>
</tr>
</tbody>
</table>

Australia

Nine victims of Ciguatera poisoning from fish caught off Scotts Head

More than 30 patients poisoned by toxic fish in Townsville

Townsville has recorded more than 30 cases of fish poisoning from Spanish mackerel this year.
Symptoms
- Onset <1 to 48 hours after eating fish
- Gastrointestinal – usually within 12 hours
  - Diarrhoea, abdominal pain, nausea, vomiting
- Neurological – usually develop over 24 hours
  - Parasthesia – perioral, glove-stocking
  - Myalgia, fatigue, pruritis, numbness
  - Temperature reversal
- Most resolve over days but can persist for years
- Cardiovascular – rarely bradycardia, hypotension

Diagnosis
- Clinical diagnosis – gastrointestinal and neurological symptoms after eating fish
- No blood tests available to confirm diagnosis
- Fish remnants can be tested for ciguatoxin

Management
- Supportive
- Mannitol
- Many local herbal remedies used throughout Pacific

Minimising the Risk
- Avoid eating large reef fish (>6kg), but any size fish can have ciguatoxin
- Avoid eating liver, brain, head, roe, or visera of reef fish
- Be aware that ciguatoxin is odourless, tasteless, and colourless – not affected by food storage or preparation
- Avoid catching fish from known ciguatera risk areas
| Questions & Comments |