Leptospirosis - a zoonotic disease with global impact

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Leptospirosis

- One of the most common zoonotic diseases known
- World-wide distribution
- Disease incidence is significantly underestimated
  - Broad diversity of symptoms
  - Limited diagnostics
  - Need for improved health education
- High incidence of mortality in humans
- Many animal species become chronic carriers of disease
Typical spirochete morphology

- EM of *Leptospira*
  - Note hooked and spiral ends
  - Morphology and cellular structure enable unique mode of motility
    - Penetrate large variety of tissues

Disease maintenance and transmission

• Pathogenic *Leptospira* reside in maintenance hosts
• Humans are accidental hosts
• Animals may also be accidental hosts
• Transmission is often a result of exposure to urine contaminated water or by direct contact with blood

Disease

• Gain entry through mucous membranes or abraded skin
• Localize in kidney
• Pass to bladder then urine
• Enter water to potentially infect new hosts
• Colonization of liver may indicate potential for severe infection
• Not all species tolerate water (host to host)
Specific maintenance host relationships

- >200 serovars
- Specific host-serovar relationship
  - Difficult to identify source of infection in areas rich with diversity
- Maintenance hosts have chronic infection with little sign of disease
- Accidental hosts (humans other non-maintenance hosts) often suffer acute infection with significant mortality rates
Emerging problem in urban slums

- Sharp increase in annual epidemics in urban slums
- Epidemics correspond with annual rainfall
  - Heavy rainfall = urban flooding = human infection
- Common sources of infection are domestic rat (#1) and dogs
- “The only epidemic-prone infection which can be transmitted directly from contaminated water is leptospirosis, a zoonotic bacterial disease.”*

*WHO Health action in crises fact sheet
http://www.who.int/hac/techguidance/em/flood_cds/en/#

Comparison of human leptospirosis, dengue, and hantavirus infections (2002)

<table>
<thead>
<tr>
<th>Disease</th>
<th>Leptospirosis</th>
<th>Dengue</th>
<th>Hantavirus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cases</td>
<td>Unknown</td>
<td>~50,000,000</td>
<td>Unknown</td>
</tr>
<tr>
<td>Severe infection</td>
<td>300,000 – 500,000</td>
<td>400,000</td>
<td>150,000 – 200,000</td>
</tr>
<tr>
<td>Mortality rate</td>
<td>5-20%</td>
<td>5-15%</td>
<td>3-10%</td>
</tr>
</tbody>
</table>

Source: Rudy Hartskeerl
WHO Collaborative Laboratory
Royal Tropical Institute
Amsterdam, The Netherlands
Pattern of infection – temperate regions

- Veterinarians, abattoir workers, animal workers
- Recreational exposure
  - Swimming, kayaking
- Travel
- Pets
Leptospira colonize many tissues during severe infection
Innate vs. Adaptive Immunity

• In maintenance hosts (cattle as a model) interaction with cells associated with innate immunity or that bridge innate and adaptive immune systems may be critical for establishing chronic infections
  – Neutrophils
  – NK cells*
  – Gamma delta T cells*

Animal migration and leptospirosis
Impact on protected animal species

• California sea lion
  – Rookeries on islands off the So. California coast
  – Hunted to near extinction
  – Now protected and numbers rebounded
  – 1970 severe leptospirosis epidemic
  – Continued every few years
  – *L. interrogans* serovar Pomona
  – Current season is one of the worst on record

• 2004 outbreak
• Sick animals (males) found as far north as British Columbia and Puget Sound
• Infection was dispersed over 2000 km north
  – Potential for equivalent dispersal south to Gulf of California (females)
Sea lion isolates form a unique group

- VNTR analysis
  - PCR regions that differ in the number of repeats
  - Run samples on gel and compare sizes

Changes in relationship

- New studies suggest that a maintenance host relationship is developing between serovar Pomona and California sea lions
- Broader impact
  - Sick animals haul out near freshwater outlets
    - Interaction between terrestrial and marine mammals
      - Potential for transmission to humans
  - The same genetic subgroup of Pomona has been isolated from terrestrial animals on the islands in the rookeries
Impact of human encroachment

• Channel Islands
  – Rookeries for California sea lions
  – Previously used for swine production
    • Introduced pigs destroyed normal flora
      – Affected ground cover of small mammals (e.g. Channel island foxes and spotted skunks)
  – DDT use impacted bald eagle population
    • Golden eagles replaced bald eagles in region
      – Hunt small mammals
  – Channel island foxes and spotted skunks are now maintenance hosts for leptospirosis
    • These animals are under pressure from new predator, lack adequate protection from flora, and now have chronic infections affecting reproduction
    • Both species are either listed as endangered or of special concern
**Bacterial genera with potential for zoonotic diseases – migratory animals**

<table>
<thead>
<tr>
<th>Marine Mammals</th>
<th>Birds</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Brucella</td>
<td>• Anaplasma</td>
</tr>
<tr>
<td>• Clostridia</td>
<td>• Borrelia</td>
</tr>
<tr>
<td>• Coxiella</td>
<td>• Brachyspira</td>
</tr>
<tr>
<td>• Leptospira</td>
<td>• Campylobacter</td>
</tr>
<tr>
<td>• Mycobacteria</td>
<td>• Rickettsia</td>
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<tr>
<td>• Vibrio</td>
<td>• Salmonella</td>
</tr>
</tbody>
</table>

**Future concerns**

- The role of environmental contaminants, e.g. PCB’s, can have an immunosuppressive affect on wildlife
- Changing climate may
  - Alter migration patterns of animal species
  - May alter northern environments to assure pathogen survival
A better understanding of human activity and impact on the environment combined with disease surveillance are essential to limit encroachment of diseases into new regions.