Leptospirosis: Public Health Perspectives

Marta Guerra, DVM, MPH, PhD, Dipl. ACVPM
Veterinary Officer, USPHS
Bacterial Special Pathogens Branch
Centers for Disease Control and Prevention

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History

- First recognized as an occupational disease of sewer workers in 1883
- In 1886, Weil described the syndrome – icteric leptospirosis with renal involvement
- Inada et al identified the causal agent in Japan in 1915
- German physicians also identified spirochetes in soldiers during WWI
- Rodents first identified as source of human exposure, followed by dogs and livestock
- Considered an occupational disease – agriculture, animal husbandry
Global Epidemiology

- Most widespread zoonosis in the world
- Incidence: estimated at 10 to 100 per 100,000 population in tropical regions
- > 500,000 cases yearly
- Vulnerable populations affected disproportionately
- Incidence highest in tropical regions – can occur year-round
- In temperate regions - seasonal occurrence - highest during warmer months
Epidemiology

- **Factors associated with endemic leptospirosis include:**
  - Tropical climate, stagnant waters
  - Levels of sanitation
  - Occupational or recreational exposure
  - Proximity of potential mammalian reservoirs to human populations

- **Factors associated with epidemics:**
  - Flooding events associated with excessive rains or natural disasters - hurricanes, typhoons, earthquakes, etc.
  - Highest incidence of cases occurs during the rainy season
Epidemiology in the United States

- 100-200 human cases of leptospirosis reported annually through 1994
- 1995 - ceased to be a nationally notifiable condition
- Remained reportable disease in 36 states and territories
- Higher incidence in states with tropical or semi-tropical climates – e.g. Hawaii, Texas, California, Puerto Rico
Current Situation in the United States

- Indications that incidence is increasing and exposure shifting from occupational to recreational
  - 2001 Study in Hawaii

- Recent recreational exposures
  - Illinois triathletes, 1998
  - Eco-challenge participants, Borneo, 2000
  - Florida Adventure Race, 2005

- 2012 – Council of State and Territorial Epidemiologists (CSTE) voted to reinstate leptospirosis as Nationally Notifiable Condition
  - Collect incidence data nationally and systematically
  - Case Report Form – assess risk factors and trends
Factors for Emerging Zoonotic Diseases

- **Increased contact between animals and humans**
  - Human population explosion
  - Human encroachment into wildlife habitat
  - Petting zoos

- **Transport of animals and humans into new areas**
  - Wildlife and exotic pet trade
  - Ecotourism

- **Climate change**
  - Rainy seasons
    - Increasing duration and severity
  - Hurricanes, earthquakes, flooding
    - Increasing frequency of natural events
Climate Change and Distribution

Leptospirosis in Humans

Photos courtesy of Dr. Eric Stern, BZB, CDC
Clinical Diagnostic Challenges

- Variable incubation period – 5–14 days (range 2-30 days)
- Majority of infections are sub-clinical or mild
- Initial presentation- acute febrile illness-nonspecific
  - similar to dengue, influenza, rickettsial diseases
- Illness is sometimes biphasic with potentially complicated second phase characterized by:
  - jaundice
  - renal dysfunction
  - pulmonary dysfunction
  - hemorrhagic manifestations
- Mortality rate of 5-15%, most with icteric disease
Clinical Diagnostic Challenges

- Severe disease manifestations may occur early during the disease course
- MMWR Notes from the Field: Investigation of Leptospirosis Underreporting — Puerto Rico, 2010
  - Analyzing 25 fatal lepto cases detected through dengue surveillance
  - Differentiate between dengue and leptospirosis early
  - Recognize potentially severe case by risk factors, clinical parameters
- Early recognition and treatment crucial to decrease morbidity and mortality

http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6122a5.htm
Laboratory Diagnostic Challenges

- Culture of spirochetes difficult – rely on serology
- Patients with leptospirosis may produce antibodies that react with several serogroups
- Serology (i.e. Micro Agglutination Test) does not identify the specific infecting serogroup or serovar
- High titer indicative of current or recent infection
- Low titer on single serum sample difficult to interpret
- Antibodies often persist for years
Prevention and Treatment Challenges

- To improve detection of leptospirosis cases - requires surveillance for acute febrile illness

- Early detection of cases leads to early treatment
  - Early treatment reduces duration and severity of illness
  - For ill patients with compatible illness, early antibiotic treatment should be strongly considered regardless of testing availability or results

- For outbreak management - may consider targeted mass prophylaxis in areas with high numbers of cases
  - Logistics of delivery
  - Compliance issues
  - Cost

- Vaccine development
Economic Analyses

- **WHO Burden of Illness Study – awaiting final report**
  - Incidence underestimated because of misdiagnosis
  - Use summary measure of mortality and disability – disability-adjusted life year (DALY)

- **Leptospirosis Hospitalizations in the United States**
  - CDC study
  - Nationwide Inpatient Sample (NIS) - database
  - Hospital discharge records from 1998-2008
  - 380 leptospirosis-associated hospitalizations
  - Identified through ICD-9 codes
Leptospirosis-Associated Hospitalization Rates by US Census Region, 1998-2008

Leptospirosis hospitalizations per 1,000,000 persons (95% CI)
# Leptospirosis vs Non-Leptospirosis Infectious Disease Hospitalizations in the US, 1998-2008

<table>
<thead>
<tr>
<th></th>
<th>Leptospirosis – Associated Hospitalizations</th>
<th>Non-Leptospirosis Infectious Disease-Associated Hospitalizations</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>43.0 (1.1)</td>
<td>51.9 (0.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Length of Stay (days)</strong></td>
<td>7.1 (0.4)</td>
<td>5.6 (0.01)</td>
<td>0.0003</td>
</tr>
<tr>
<td><strong>Charges</strong></td>
<td>$38,521 (3,622)</td>
<td>$25,302 (193)</td>
<td>0.0003</td>
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</tbody>
</table>
Accomplishments

- WHO Leptospirosis Burden of Illness Study
- WHO - Global Outbreak Alert and Response Network - report outbreaks to international community
- Reinstatement of national surveillance for leptospirosis in ~2013 in the United States
- New Case Report Form being developed to capture risk factors and trends
- Development of assays that can detect IgM antibody response in acutely ill patients 4-7 days after symptom onset
- PCR assay being validated - may provide earlier diagnosis

http://www.who.int/csr/outbreaknetwork/en/
Challenges

- International surveillance – limited case and outbreak detection at local level
- Lack of point-of-care diagnostics
- Feasibility of human vaccine – vulnerable populations
- Lack of long-term studies
  - Assess outcome of interventions
  - Develop predictive models
- ‘One Health’ concept – coordination of human and animal surveillance, investigations with goal of prevention and control
Acknowledgments

- MI Depts of Community Health and Agriculture
- PR Dept of Health
- Dengue Branch CDC
- Infectious Disease Pathology Branch CDC
- Bacterial Special Pathogens Branch CDC
  - Rita Traxler
  - Mark Lehman
  - Sean Shadomy
References

- PAHO Epidemiological Bulletin *Case definitions-Dengue and Leptospirosis*. 2000, 21 (2). [http://www.paho.org/English/SHA/be_v21n2-cases.htm#leptospirosis](http://www.paho.org/English/SHA/be_v21n2-cases.htm#leptospirosis)
Surveillance for Leptospirosis – Uses of Data

- Assess the magnitude of the problem in different areas and risk factors (groups/areas/conditions)
- Identify outbreaks
- Identify potential animal reservoirs of infection for further investigation
- Monitor for emergence of leptospirosis in new areas and new risk (occupational) groups
- Design rational control or prevention methods
- Identify new serovars and their distribution
- Inform on locally occurring serovars for a representative range in the MAT (Microscopic Agglutination Test)