

Leptospirosis: Public Health Perspectives

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

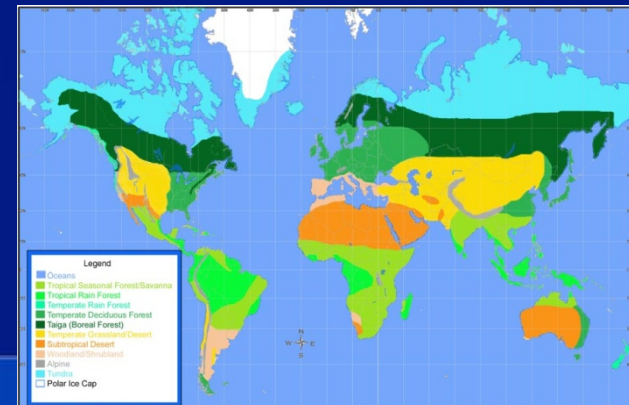
International Workshop on Alternative Methods for *Leptospira* Vaccine Potency
Testing: State of the Science and the Way Forward
Ames, Iowa
September 19-21, 2012

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 : estimate d 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

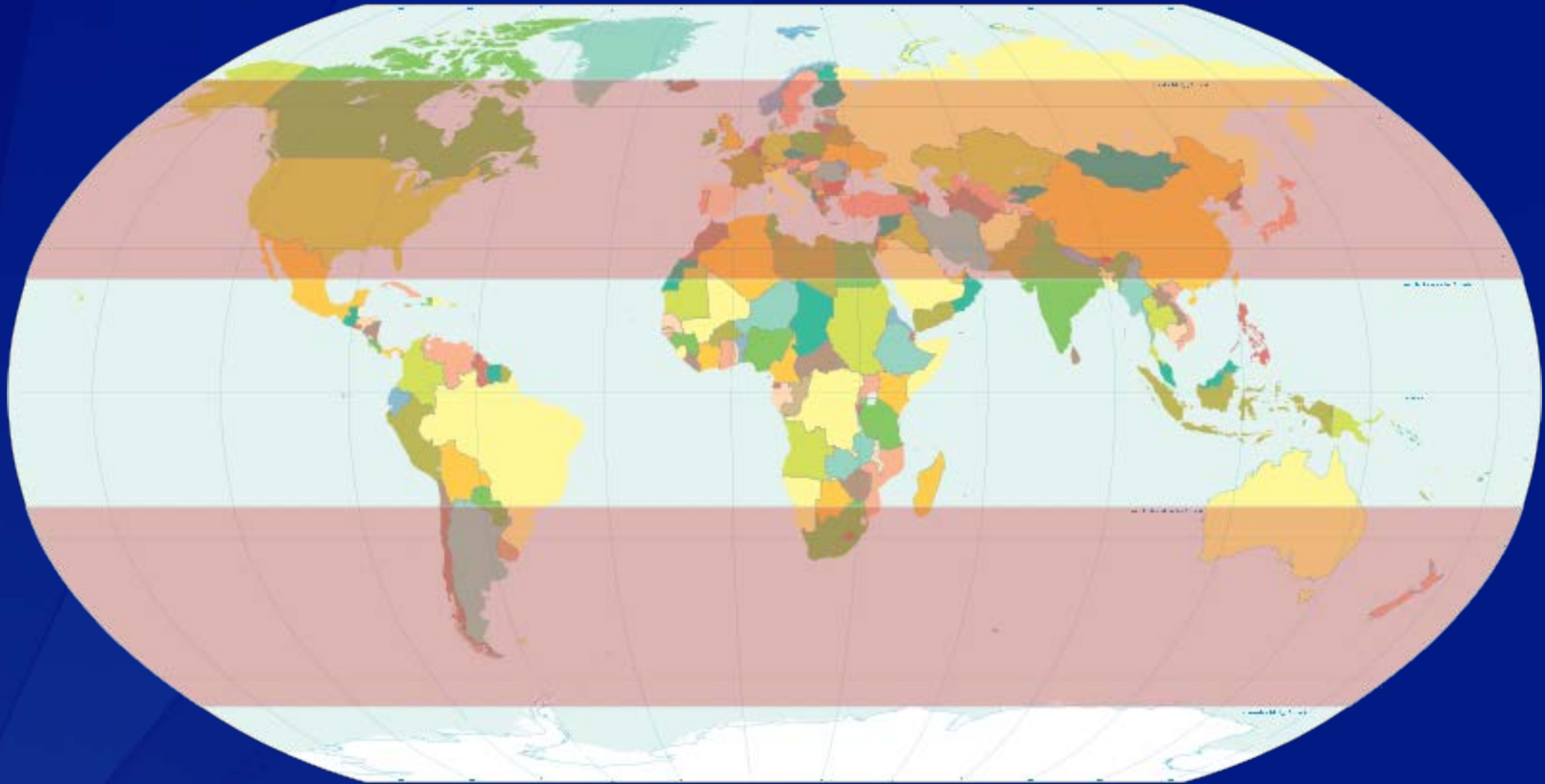
- ❑ **Indications that incidence is increasing and exposure shifting from occupational to recreational**
 - 2001 Study in Hawaii
- ❑ **Recent recreational exposures**
 - Illinois triathletes, 1998
 - Eco-challenge participants, Borneo, 2000
 - Florida Adventure Race, 2005
- ❑ **2012 – Council of State 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



<http://ihrrblog.org/2011/08/24/climate-change-causes-species-to-move-north-and-to-higher-elevations/>

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**

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

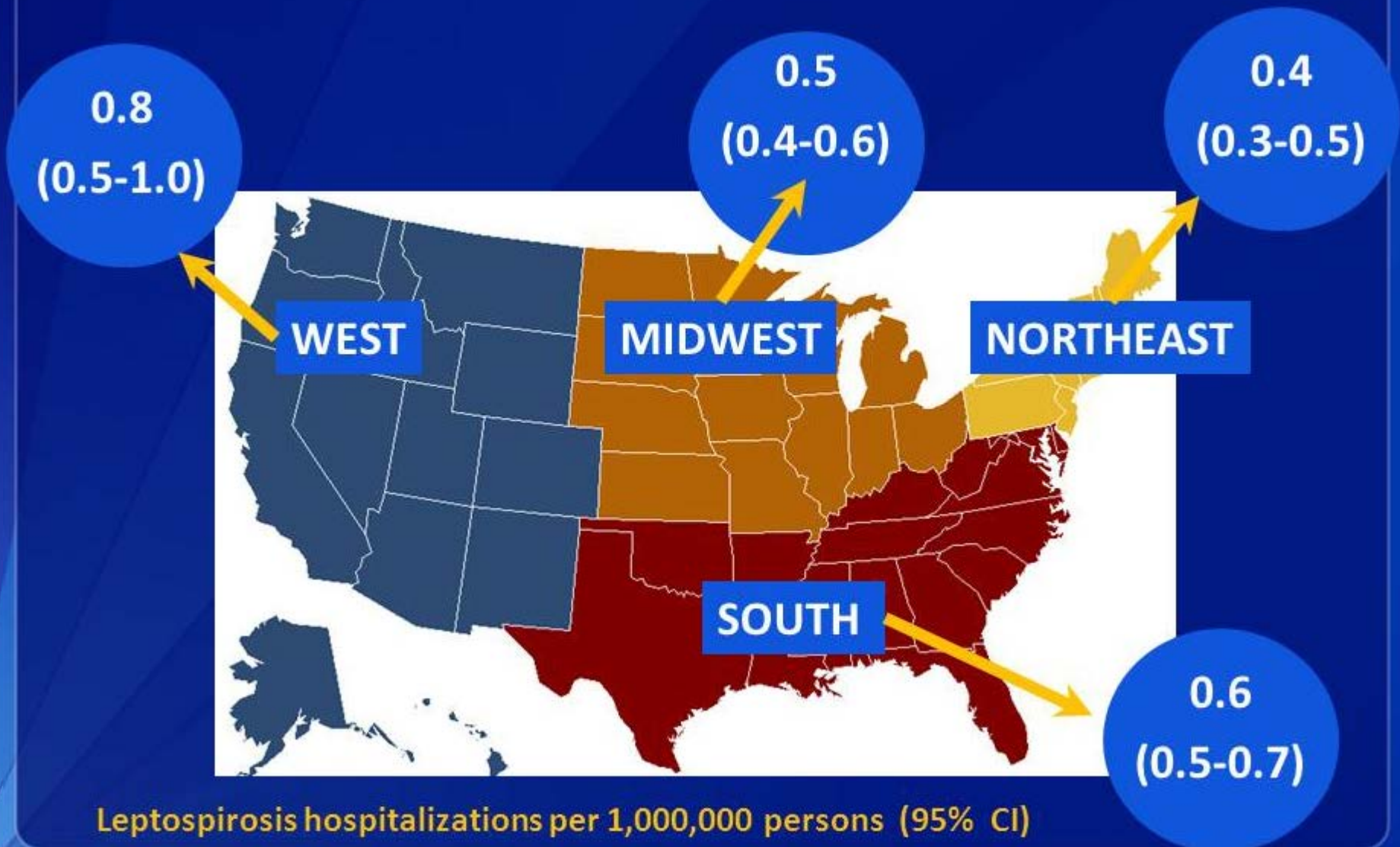
❑ **WHO Burden of Illness Study – awaiting final report**

- 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 vs Non-Leptospirosis Infectious Disease Hospitalizations in the US, 1998-2008

	Leptospirosis – Associated Hospitalizations	Non-Leptospirosis Infectious Disease- Associated Hospitalizations	p-value
	Mean (SE)	Mean (SE)	
Age	43.0 (1.1)	51.9 (0.2)	<0.0001
Length of Stay (days)	7.1 (0.4)	5.6 (0.01)	0.0003
Charges	\$38,521 (3,622)	\$25,302 (193)	0.0003

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**

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**

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 - Sean Shadomy

Questions?



For more information please contact Centers for Disease Control and Prevention

1600 Clifton Road NE, Atlanta, GA 30333

Telephone, 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348

E-mail: cdcinfo@cdc.gov Web: www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

National Center for Emerging and Zoonotic Infectious Diseases
Division of High-Consequence Pathogens and Pathology



References

- ❑ World Health Organization. *Human leptospirosis: guidance for diagnosis, surveillance and control*. 2003.
http://whqlibdoc.who.int/hq/2003/WHO_CDS_CSR_EPH_2002.23.pdf
- ❑ PAHO Epidemiological Bulletin *Case definitions-Dengue and Leptospirosis*. 2000, 21 (2). http://www.paho.org/English/SHA/be_v21n2-cases.htmleptospirosis
- ❑ Guerra MA. *J Am Vet Med Assoc*. 2009;234(4):472-478.
- ❑ Levett, PN. Leptospirosis. *Clinical Microbiological Reviews*. 2001; 14:296-326.
- ❑ Sehgal SC, Sugunan AP, Murhekar MV et al.. Randomized controlled trial of doxycycline prophylaxis against leptospirosis in an endemic area. *Int J Antimicrob Agents*. 2000 ;3(4):249-55.
- ❑ Takafuji ET, Kirkpatrick JW, Miller RN et al. An efficacy trial of doxycycline prophylaxis against leptospirosis. *NEJM*. 1984;310:497-500

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)**