Leptospirosis Through a One Health Lens

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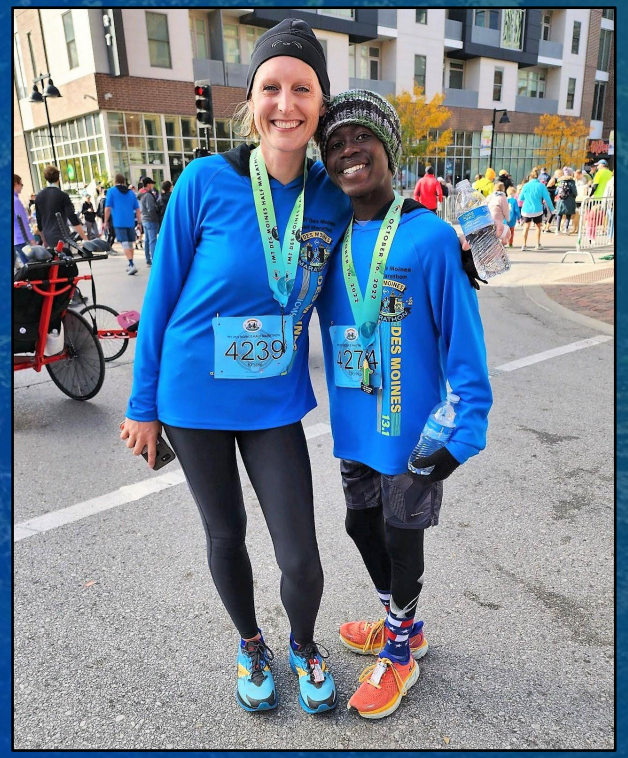
Introduction



OUTLINE

- A One Health Challenge
- Disease in Humans
- Disease in Animals
- Pathogen, Host, and Environmental Interactions
- Prevention Strategies
- Conclusion
- Case Study

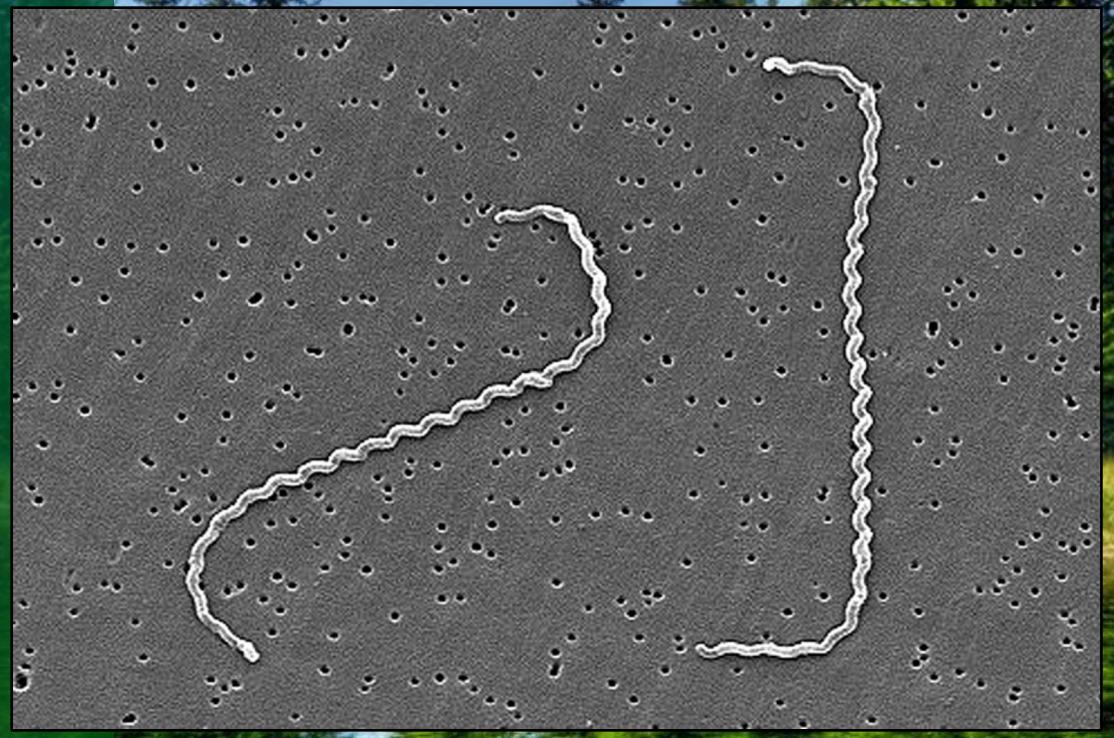
A ONE HEALTH CHALLENGE

Leptospirosis incorporates facets of humans, animals, and the environment

LEPTOSPIROSIS

Zoonotic bacterial infection of humans and animals

- Caused by *Leptospira* spp.
- Intra- and interspecies transmission is dependent on human-animal-environment interactions



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Leptospira spp.

Over 300 pathogenic serovars have been identified

- Strains are also classified based on DNA sequence composition
- 64 known species are grouped into:
  - 2 pathogenic subclades
    - P1 – pathogenic species
    - P2 – intermediately pathogenic species
  - 2 saprophytic subclades
    - Live in environment
    - Poorly associated with mammalian host species

Leptospira spp.

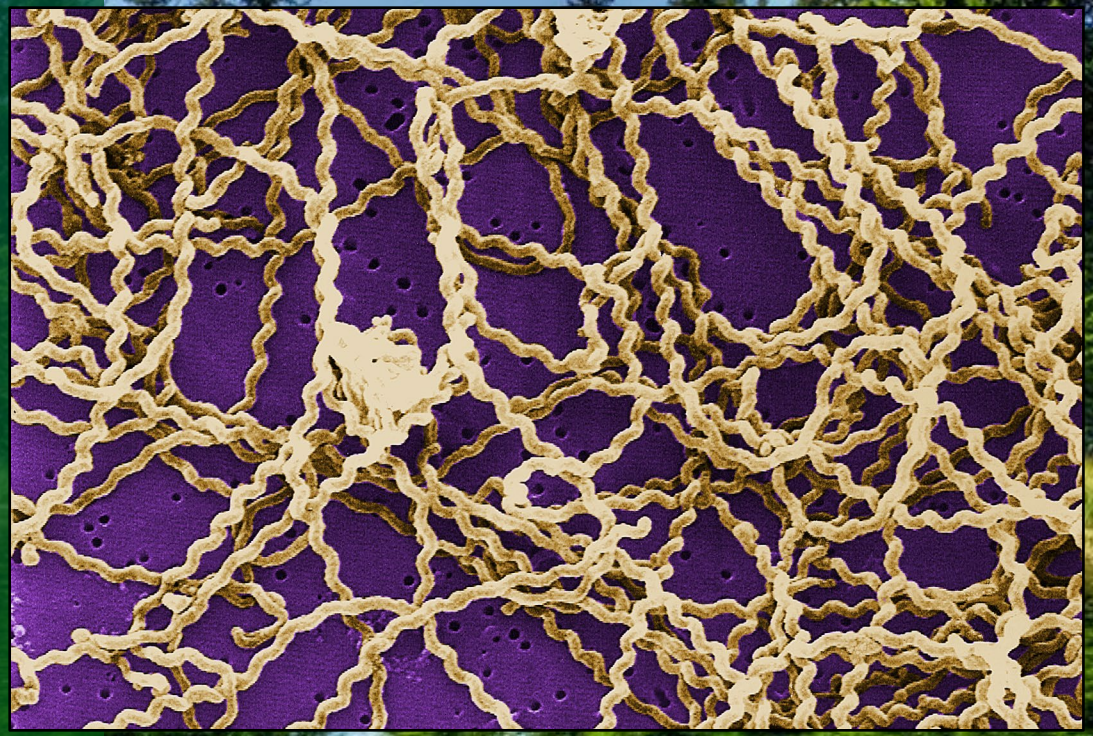
P1 and P2 subclades

- P1 virulent spp. are responsible for most leptospirosis infections in humans and animals – e.g.:
  - *L. interrogans*
  - *L. kirschneri*
  - *L. noguchii*
- P2 spp. have also been recognized as a cause of severe disease in some cases

LEPTOSPIROSIS

Pathogenic spirochetes contaminate soil and water

- Shed from the renal tubules of infected reservoir hosts
- Persist in the environment for weeks to months under optimal conditions
- Enter the body through exposure of abraded skin or mucous membranes or through ingestion of contaminated water



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A WORLDWIDE ISSUE

Leptospirosis has a global distribution

Developing Countries

- Occupational risk
  - Agriculture, animal husbandry, sewer maintenance
  - Sri Lanka has highest incidence worldwide (rice paddy work)
- Inadequate housing
  - Exposure to infected rodents and free-roaming dog populations

Developed Countries

- Occupational activities involving exposure to water or animal reservoir hosts
  - Veterinarians working with livestock
  - Water-intensive crop farming
  - Wildlife trapping
- Recreational activities involving water
  - Canoeing and kayaking
  - Open-water swimming
- Has also emerged following natural disasters and other crises due to flooding and housing insecurity

AN EMERGING ZOONOSIS

Considered the most widespread zoonosis in the world

- Global incidence is increasing with higher incidence in the tropics and subtropics
- Human encroachment into wildlife habitat and resulting increase in contact between animals and humans is a risk factor
- Nationally notifiable disease in the U.S.

DISEASE IN HUMANS

GLOBAL BURDEN OF DISEASE

- 1.03 million cases annually
- 58,900 deaths
- Highest morbidity and mortality:
  - South and Southeast Asia
  - Oceania
  - Caribbean
  - Andean, Central, & Tropical Latin America
  - Eastern Sub-Saharan Africa

SIGNS & SYMPTOMS

A nonspecific illness that can be mistaken for other diseases

- Most human infections are self-limiting and/or subclinical
- Symptoms can range from mild, febrile, flu-like illness to severe, multisystemic disease and even death
  - Acute renal failure
  - Hepatic injury
  - Pulmonary hemorrhage
  - Meningitis
  - Pancreatitis
- Vast majority of cases likely go unrecognized

SIGNS & SYMPTOMS

- Symptoms may include:
  - High fever
  - Headache
  - Malaise
  - Vomiting
  - Jaundice
  - Conjunctivitis
  - Abdominal pain
  - Diarrhea
  - Rash

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ILLNESS

Incubation period ranges from 2 days to 4 weeks

- Illness may occur in 2 phases:
  - Phase 1: abrupt onset of fever, chills, headache, vomiting, diarrhea
  - Patient may recover for a time but become ill again
  - Phase 2: If occurs, more severe – kidney or liver failure, meningitis
  - May last from a few days to 3 weeks or longer

DIAGNOSIS

Diagnosis is challenging and relies on serology

- Culture & isolation difficult due to fastidious requirements for growth
- Microscopic agglutination test (MAT) is considered gold standard
  - Requires paired serum samples to detect seroconversion
  - Cannot distinguish between IgM Abs indicative of present infection & IgG Abs indicative of past infection

TREATMENT

Treated with antibiotics

- Typically doxycycline or penicillin
- Should be given early in the course of disease
- Intravenous antibiotics may be required for more severe symptoms

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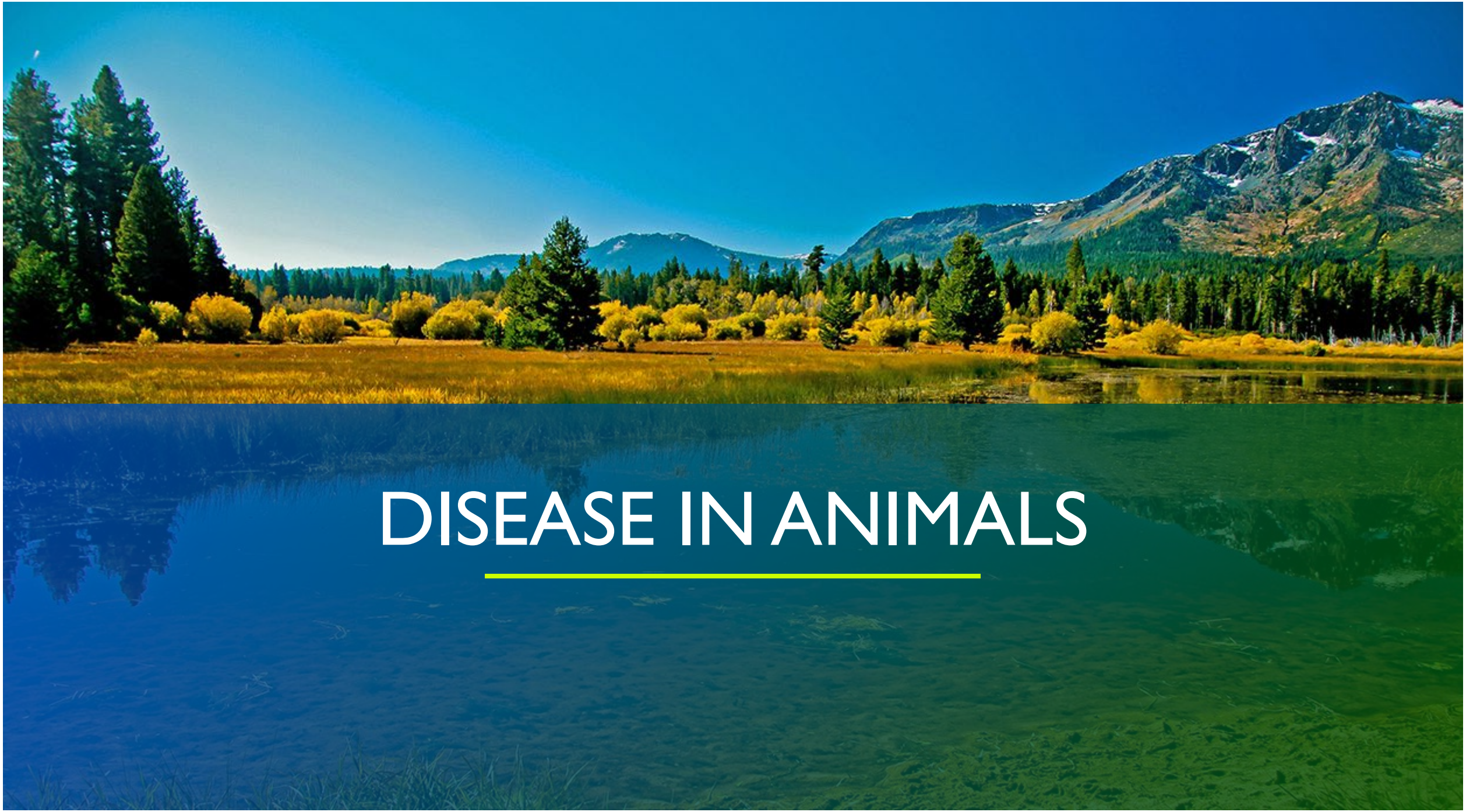

DISEASE IN ANIMALS

LEPTOSPIROSIS IN ANIMALS

Infects a wide range of species

- Widespread subclinical infection in a large variety of animal reservoir hosts:
  - Rodents and other species
- Pathogenic strains cause disease in:
  - Dogs
  - Cattle
  - Horses
  - Pigs
  - Camelids
  - Small ruminants
  - Wildlife species

DOGS

- Clinical picture resembles humans
- Most infections are subclinical
- When disease occurs, clinical signs include:
  - Lethargy
  - Fever
  - Inappetence
  - Polyuria/polydipsia
- Can lead to multiorgan dysfunction:
  - Acute kidney injury
  - Cholestatic hepatic dysfunction
  - Pancreatitis
  - Pulmonary hemorrhage
  - Myositis
  - Uveitis

CATTLE

- Major cause of abortion, neonatal illness, and production loss worldwide
- Most disease attributed to:
  - *L. borgpetersenii* serovar Hardjo
  - *L. interrogans* serovar Pomona
- When multisystemic disease occurs, usually in calves
- Risk factors:
  - Open herds
  - Access to contaminated water sources
  - Co-grazing with sheep
  - Use of natural service
- Subclinical infection can result in continued transmission throughout the herd and shedding can occur intermittently for months

HORSES

- Associated with febrile illness, reproductive losses, & neonatal illness
- Foals may develop acute kidney injury
- Recurring uveitis can follow infection in adult horses
  - Leptospirosis estimated to account for 50% of recurrent uveitis cases in North American horses
- Serovars and strains vary geographically
  - *L. interrogans* serovar Pomona is main species in North America

PIGS

- Well recognized globally as major cause of reproductive failure
- Also causes production losses, abortions, stillbirths, neonatal illness
- Incidental infections associated with hemorrhagic disease, hematuria, icterus, & acute kidney injury
- Predominating serogroups:
  - Tarassovi
  - Pomona
  - Australis
- Indoor housing reduces incidence of disease

CAMELIDS & SMALL RUMINANTS

- Causes reproductive issues:
  - Abortions
  - Infertility
  - Stillbirths
- Diagnosed as one of the major causes of abortions in llamas & alpacas
- May also result in liver failure or kidney failure

WILDLIFE SPECIES

- Isolated cases and outbreaks have been uncommonly described in both captive and free-ranging wildlife spp.
- Almost all mammals are susceptible
- Clinical syndromes are well known in seals, sea lions, and black rhinoceros
- Disease is typically self-limiting but kidney or liver damage and reproductive tract dysfunction can occur

DIAGNOSIS

Diagnosis is best made by a combination of serologic testing & PCR assay

- Microscopic agglutination test (MAT) is the most frequently used serologic test
- Culture, followed by molecular typing, is the only method to definitively identify the infecting serovar but is of little value to clinicians due to poor and slow growth

TREATMENT

Treatment is with antibiotics

- Antimicrobial therapy is usually effective
- Organ damage can be permanent

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PATHOGEN, HOST, AND ENVIRONMENTAL INTERACTIONS

Maintenance of Transmission

PATHOGEN FACTORS

- Organism virulence factors and an individual host's immune response impact outcome of infection
- Organism forms biofilms within renal tubules which may contribute to persistence despite treatment
- Incidental hosts typically exhibit more severe disease; however, reservoir hosts can also become ill
- Pathogen strain variation and host immunosuppression may impact disease expression
    - E.g., Cyclical outbreaks in yearling California sea lions followed by continuous subclinical infections and shedding in adult sea lion populations for up to 154 days after infection

STRAIN/HOST ADAPTATION

- Duration of urinary shedding depends upon degree of adaptation between the leptospiral strain and the specific reservoir host involved
- Globally, rodents are most important reservoir host due to:
  - High prevalence of infection in some rodent populations (up to 90%)
  - High concentration of spirochetes in rodent urine compared to other species
- Exposure to rodents is a well-established risk factor for both humans and animals
- Predation of rodents also a risk factor for animals
- Venereal and transplacental transmission also possible - could maintain transmission when environmental conditions don't favor survival of organism outside host

ENVIRONMENTAL CONDITIONS

- Once thought that pathogenic leptospires could only replicate inside infected hosts and not in the environment
- 2022 study found that organism could replicate in waterlogged soil but not soil or water alone
- May explain why outbreaks of leptospirosis follow flooding after a lag time, usually 1 to 3 months
- Increased flooding events across the globe have increased concern for risk of leptospirosis

PREVENTION STRATEGIES

VACCINES

- Whole bacterin vaccines available for dogs, cattle, pigs, and horses (U.S. only)
- Take time to educate clients about the importance of vaccination
- Dogs:
  - Bivalent vaccines (*L. interrogans* serovars Icterohemorrhagiae and Canicola) available since 1970s
  - Continued appearance of disease led to addition of 2 additional serovars in U.S. and Europe (Pomona and Grippotyphosa in U.S.; Grippotyphosa and Australis or Bratislava in other countries)

VACCINES

- Also used to protect humans in response to outbreaks in some countries (China, Japan, Korea, France)
- Immunity is serogroup-specific and efforts continue toward developing more protective, cost-effectives vaccines
- Vaccination programs are likely to be most effective when there is a thorough understanding of the *Leptospira* spp. and serovars circulating in reservoir hosts in the area of interest

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VACCINES

- If goal of vaccinating a particular animal host is to both:
    1. Prevent disease in the vaccinated host AND
    2. Prevent disease in exposed humans;

To be successful, the design of serovar-specific vaccines must depend on knowledge of both:

1. Regionally important serovars shed by host that cause disease in humans but may not cause disease in the host (common in reservoir hosts)
2. Regionally important serovars likely to cause disease in the host

EDUCATION

- Targeted education for those at risk regarding preventive measures may reduce the incidence of disease
- Education may include:
  - Wear protective clothing and/or footwear if exposed to potentially contaminated water or soil through work or recreational activities
  - Avoid swimming or bathing in water that may be contaminated with animal urine
  - Wash hands before eating and after interacting with animals
  - Implement rodent control
  - Minimize or avoid contact with potentially infected animals
  - Practice infection control guidelines if regularly in contact with potentially infected animals

PROPHYLACTIC TREATMENT

- Prophylactic doxycycline treatment has been used successfully for people who are at increased risk due to work or recreational activities
- Compliance has been low overall due to lack of perceived immunity or concerns about adverse effects
- May increase risk for selection of antimicrobial-resistant bacteria
- To date, there have been no reports of acquired antimicrobial resistance within *Leptospira* spp.

CONCLUSION

REQUIRES A ONE HEALTH APPROACH

PATHOGEN, HOST, AND ENVIRONMENTAL INTERACTIONS MUST BE WELL UNDERSTOOD

- Factors vary geographically and over time
- Treatment and prevention improvements will require advancements in diagnostics, surveillance techniques, ongoing education, and improved vaccine development

CASE STUDY

CASE STUDY

- 52-year-old male small animal veterinarian
- Sought treatment at an emergency department of a Washington State medical center on 30 January 2007
- Two day history of anorexia, fever, arthralgia, malaise, nausea, and vomiting

- Diagnosed with a viral syndrome and released

CASE STUDY

- Returned to the ER 2 days later with same symptoms and dehydration
- Given IV fluids and released

- February 2: Directly admitted to hospital for progressive symptoms including fever, dizziness, blurred vision, dehydration, mild cough

CASE STUDY

- First 3 days of hospitalization: spiking fever up to 105°F, chills, myalgias, and arthralgias
- Clinical course worsened and developed diffuse pneumonitis requiring intubation, progressive renal failure, and septic shock
- Admitted to intensive care

CASE STUDY

- Interview with patient revealed:
  - Occupation as a veterinarian
  - Handled a pet Norway rat for examination of fleas approximately 10 days prior to onset of his illness
  - Rat urinated while being handled during the exam
  - Patient had minor abrasions on his hands and gloves were not worn during the exam
  - Routine hand washing was performed after exam was completed
- Based on history, leptospirosis was named as the primary differential

CASE STUDY

- Leptospirosis testing was conducted at CDC in Atlanta, Georgia, using a microscopic agglutination test (MAT)
- Serum drawn 7 days after the patient's onset of illness was negative for *L. interrogans* antibodies and serum drawn 32 days post-onset was positive
- Serovar with the highest titer was Icterohaemorrhagiae demonstrating a greater than 4-fold rise, confirming Leptospirosis

- Pet owner was contacted and rat was brought for testing
- Rat was PCR positive for *Leptospira* spp. in the urine
- MAT confirmed *L. interrogans* serovar Icterohaemorrhagiae

CASE STUDY

- Patient was prescribed IV penicillin Feb. 4-13, amoxicillin Feb. 4-18, ceftriaxone Feb. 5-13, and levofloxacin Feb. 6-10
- Placed in ICU and given supportive treatment until pneumonitis resolved and extubation was successful
- Discharged 12 days after admission
- Patient lost 65 lbs. (25% of body weight)
- After physical therapy, patient returned to work part-time one month after episode
- Two months after episode, patient was fully recovered and returned to work full-time

CASE STUDY: PEARL OF WISDOM

FOLLOW INFECTION CONTROL GUIDELINES

IN CLOSING


WHAT DOES A THESAURUS EAT FOR BREAKFAST?
A SYNONYM ROLL.
martymousehouse.com

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THANK YOU!

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