

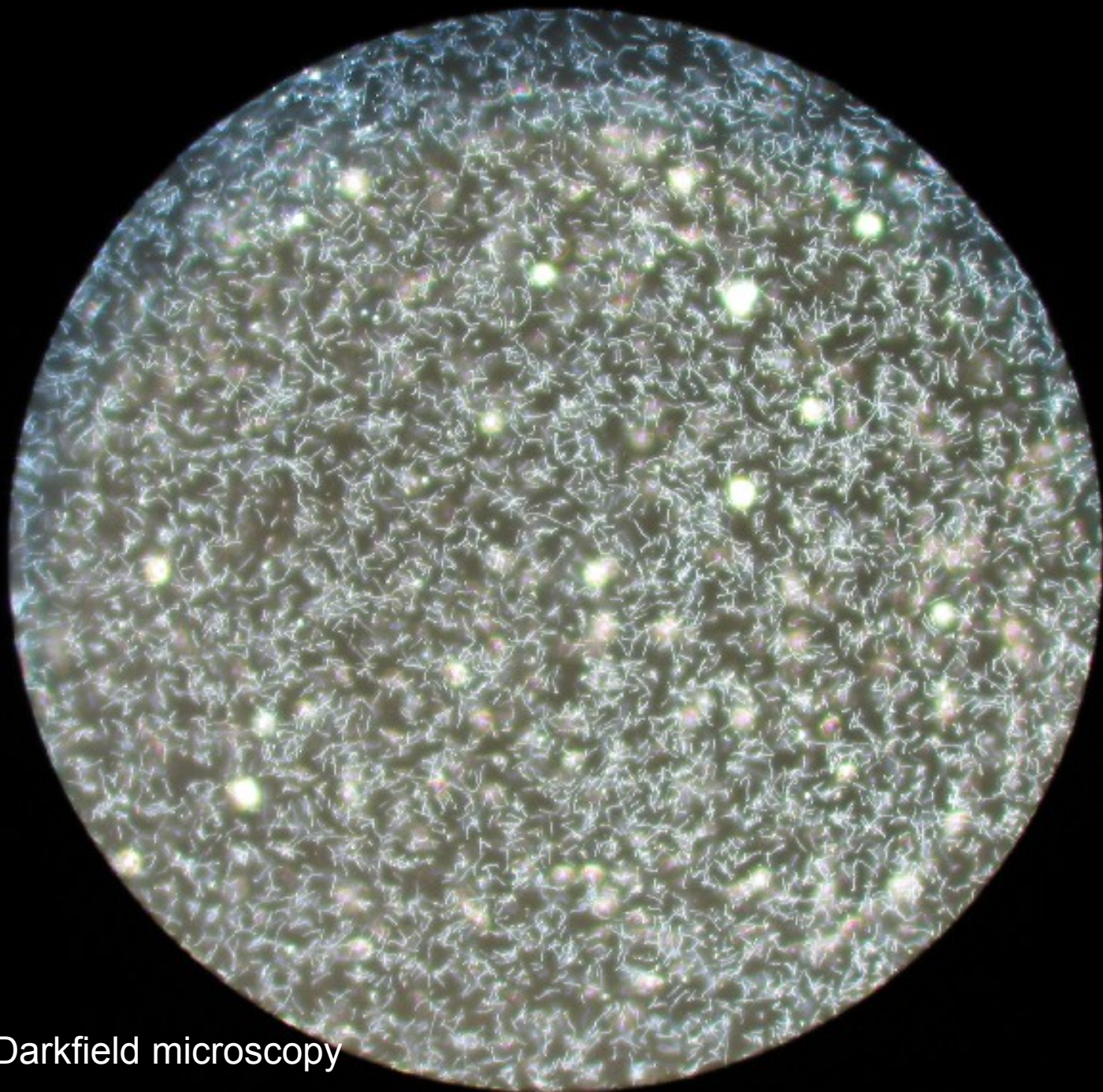
Swiss TPH Winter Symposium 2018

**One Health: Zoonoses Control in Humans and Animals
– Taking Stock and Future Priorities**

Leptospirosis and its complex ecology

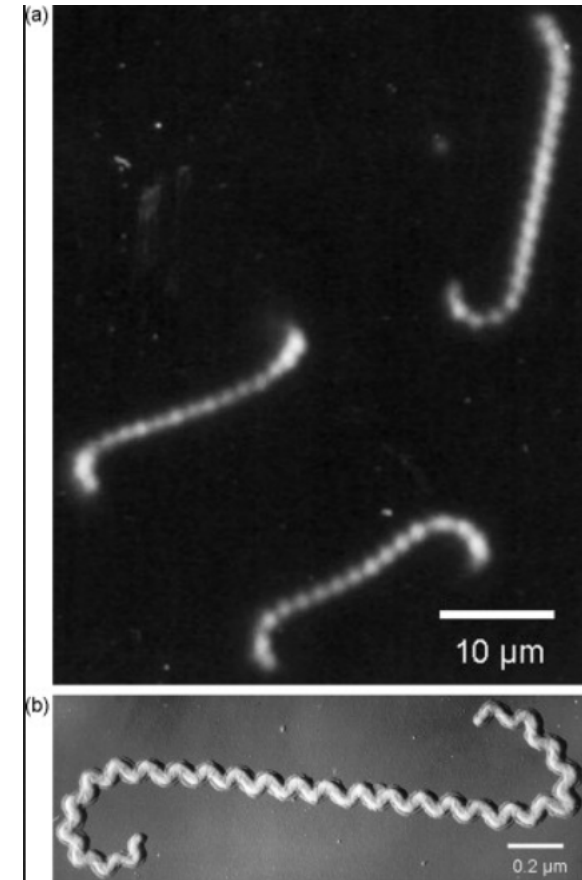






Leptospirosis

- Bacterium:
 - Order Spirochaetales
 - Family Leptospiraceae
 - Genus *Leptospira*
- Zoonotic disease of most mammals
- Survive in humid, warm & perish in dry environments
- Enter through damaged skin or mucosal membranes
- Persist in proximal tubules of kidneys in carrier animals
- Excreted with urine for months or years



Dark field (a) and shadowed electron (b) photomicrographs of *Leptospira* spp..
Ref: Leptospira and leptospirosis, Adler & Moctezuma

Leptospirosis Burden

Diseases	DALYs [*] per 100,000 per annum
Malaria	1,200 (921-1,594)
Cholera	65 (49-84)
Leishmaniosis	48 (32-71)
Schistosomiasis	48 (25-91)
Leptospirosis	42 (18-66)
Lymphatic filariasis	40 (26-58)
Rabies	21 (12-39)

*Disability adjusted life years

Ref: Global Burden of Leptospirosis: Estimated in Terms of Disability Adjusted Life Years, Torgerson et al. 2015

NTD list WHO

Buruli ulcer

Chagas disease

Dengue and Chikungunya

Dracunculiasis (guinea-worm disease)

Echinococcosis

Foodborne trematodiasis

Human African trypanosomiasis (sleeping sickness)

Leishmaniasis

Leprosy (Hansen's disease)

Lymphatic filariasis

Mycetoma, chromoblastomycosis and other deep mycoses

Onchocerciasis (river blindness)

Rabies

Scabies and other ectoparasites

Schistosomiasis

Soil-transmitted helminthiasis

Snakebite envenoming

Taeniasis/Cysticercosis

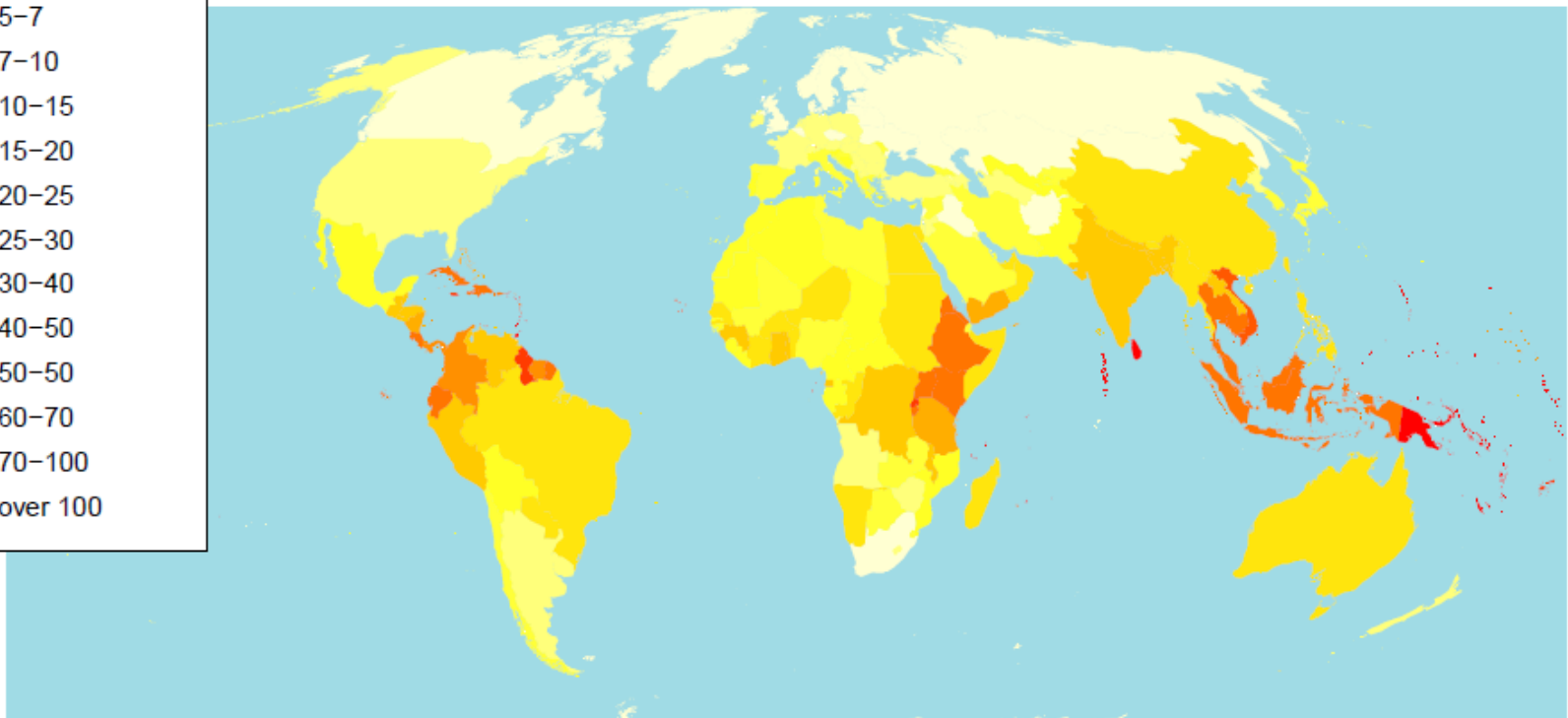
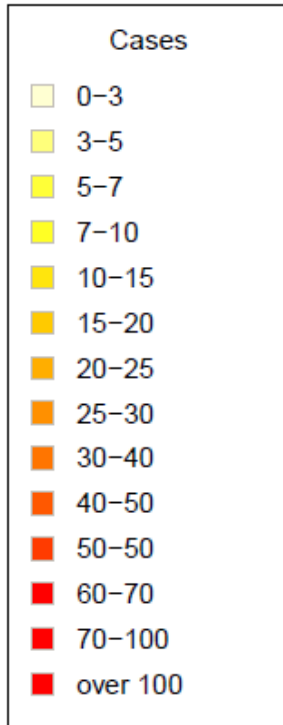
Trachoma

Yaws (Endemic treponematoses)

What about Leptospirosis?

Cases per 100,000 per annum

1,000,000 cases / 60,000 deaths annually
in some areas as high as 975 cases per 100 000



The Lancet. Global Morbidity and Mortality of Leptospirosis: A Systematic Review. F. Costa; J. E. Hagan; J. Calcagno; et al.

Taxonomy

Based on either serological (*sensu lato*) or molecular classification (*sensu stricto*)

Serological taxonomy divides *Leptospira* into two species

- *L. biflexa* (non-pathogenic),
- *L. interrogans* (pathogenic) and
 - > fifty serogroups and
 - > 250 serovars on the basis of surface antigens

Molecular classification system groups leptospires depending on DNA relatedness in 21 genomospecies

- pathogenic,
- non-pathogenic or
- opportunistic

Table 3. Typical reservoir hosts of common leptospiral serovars

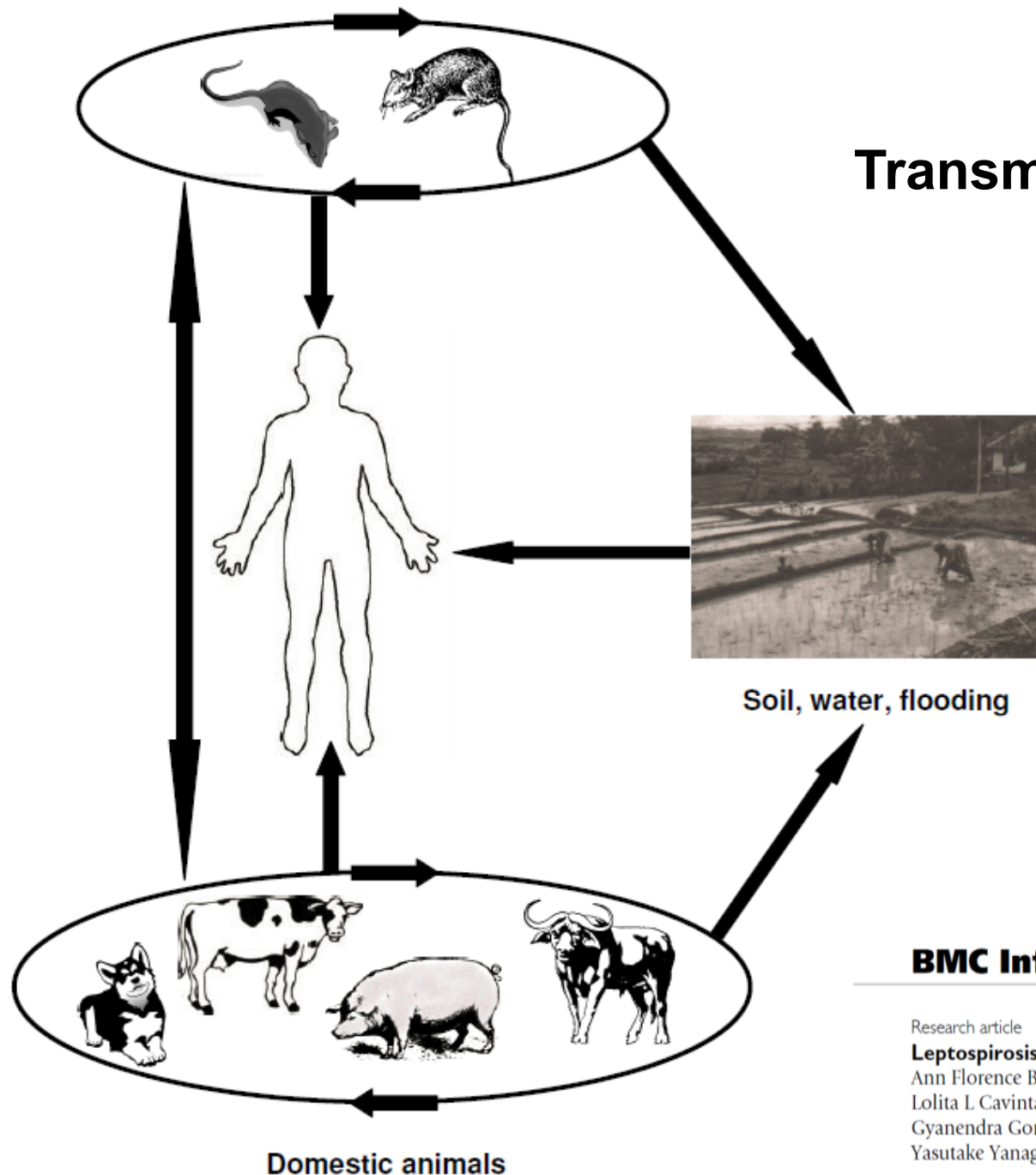
Reservoir host	Serovar(s)
Pigs	<i>pomona, tarassovi</i>
Cattle	<i>hardjo, pomona</i>
Horses	<i>bratislava</i>
Dogs	<i>canicola</i>
Sheep	<i>hardjo</i>
Racoon	<i>grippotyphosa</i>
Rats	<i>icterohaemorrhagiae, copenhageni</i>
Mice	<i>ballum, arborea, bim</i>
Marsupials	<i>grippotyphosa</i>
Bats	<i>cynopteri, wolffi</i>

Leptospirosis: a zoonotic disease of global importance

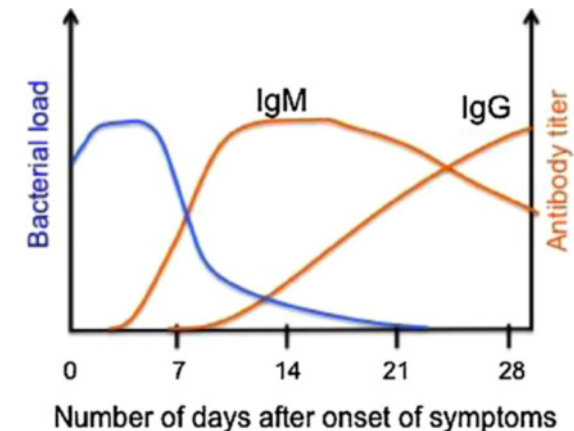
Ajay R Bharti, Jarlath E Nally, Jessica N Ricaldi, Michael A Matthias, Monica M Diaz, Michael A Lovett, Paul N Levett, Robert H Gilman, Michael R Willig, Eduardo Gotuzzo, and Joseph M Vinetz, on behalf of the Peru-United States Leptospirosis Consortium

THE LANCET Infectious Diseases Vol 3 December 2003

Transmission cycle



Photograph by S. Faine



Ref: From «Diagnosis and epidemiology of leptospirosis», M. Picardeau

BMC Infectious Diseases

Research article

Leptospirosis in the Asia Pacific region

Ann Florence B Victoriano¹, Lee D Smythe², Nina Gloriani-Barzaga¹, Lolita L Cavinta¹, Takeshi Kasai³, Khanchit Limpakarnjanarat⁴, Bee Lee Ong³, Gyanendra Gongal⁴, Julie Hall³, Caroline Anne Coulombe³, Yasutake Yanagihara⁵, Shin-ichi Yoshida⁵ and Ben Adler^{*6}

Clinical symptoms

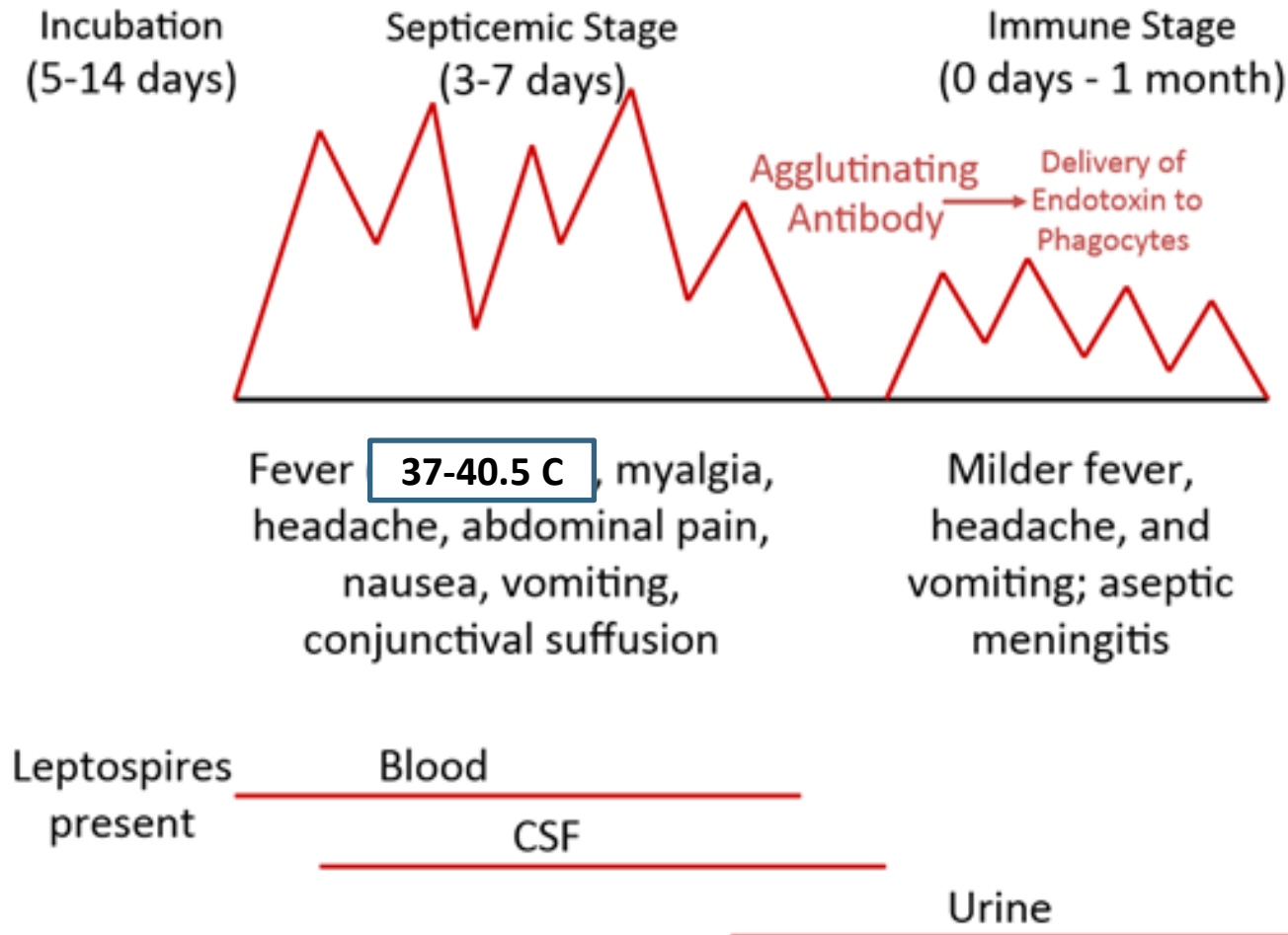
Serovar non-adapted host (“accidental host”)

- Mild to severe disease
- Humans: anicteric or icteric leptospirosis
- Livestock: abortion in adult, mortality in young

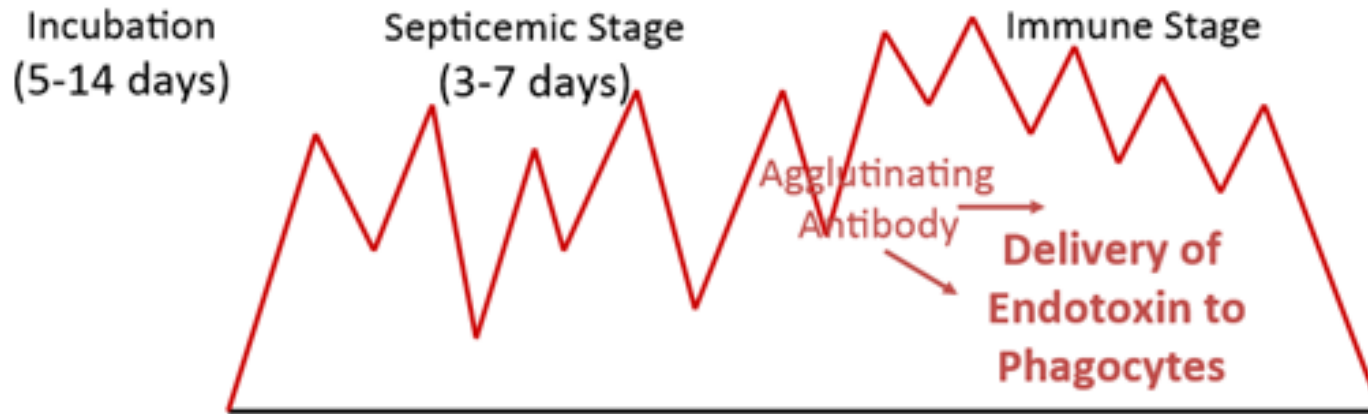
Serovar adapted host (“maintenance host”)

- Carriers & “silent” shedders
- Subclinical symptoms: reduced growth, milk yield, reproduction
- Economic impact, food security

Anicteric Leptospirosis



Icteric Leptospirosis (Weil's Syndrome)



Fever (37-40.5 C), myalgia,
headache, abdominal pain,
nausea, vomiting,
conjunctival suffusion

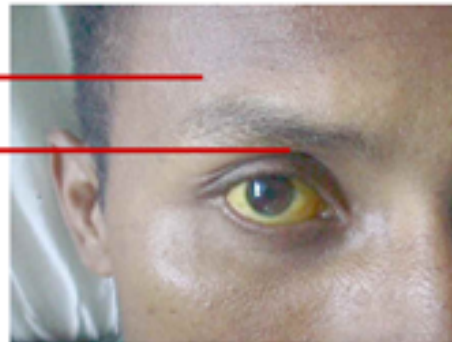
Jaundice, renal failure,
hypotension,
hemorrhagic
pneumonitis

Mortality rate 5-40%

Leptospires
present

Blood

CSF



Clinical symptoms humans

- **fever**
- **severe headache**
- **myalgia**
- **conjunctival suffusion**
- **jaundice**
- general malaise
- stiff neck
- chills
- abdominal pain
- arthralgia
- anorexia
- nausea
- vomiting
- abortion
- diarrhea
- oliguria/anuria
- hemorrhages
- skin rash
- **photophobia**
- cough
- cardiac arrhythmia
- hypotension
- mental confusion
- psychosis
- Delirium
-

Specific clinical case definition difficult!

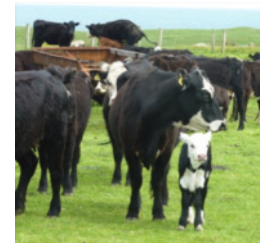
Treatment

Humans:

- Penicillin and Doxycycline are widely used
- Treatment with antibiotics as soon leptospirosis is suspected and preferably before fifth day after the onset of illness (bacteremic phase)
- Supportive treatments such as fluid therapy and dialysis are needed with acute, severe forms

Animals:

- Dihydrostreptomycin and Oxytetracycline.
- Dihydrostreptomycin has been shown to be able to eliminate leptospires from animals ([Hartskeerl et al., 2011](#)).

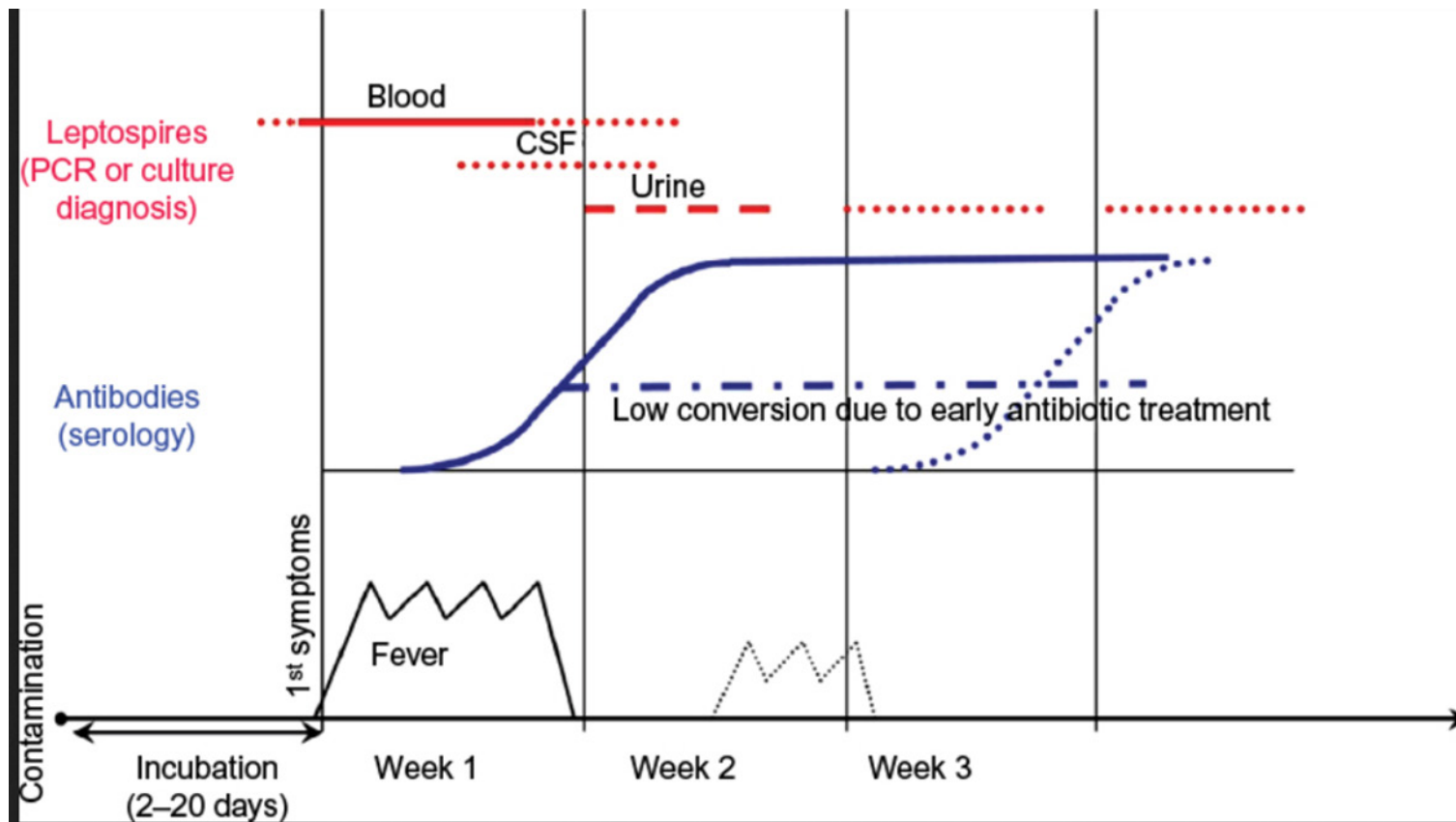


Human Leptospirosis

Incubation period: usually 5–14 days, range 2–20 days

Seroconversion 5–10 days after onset of disease or longer

IgM and IgG class antibodies remain detectable for months or years (at low titre)



Diagnostics

Detection of *Leptospira*

Real-time PCR

- sensitive
- differentiates between pathogenic and non-pathogenic, but not serovars
- detection at earlier stage than antibodies, so **ideal for the diagnosis of acute disease**

Molecular typing

- DNA hybridisation
- Multi locus sequence typing (MLST)
- Transmission studies

Dark-field microscopy with clinical samples and culture

- poor sensitivity and specificity

Diagnostics

Serological tests

Microscopic Agglutination Test (MAT): reference test

- Sensitivity & specificity*
 - Acute serum: 12% & 93%
 - Convalescent serum: 88% & 90%
- Expertise required
- Maintenance of *Leptospira* culture tedious - not cost effective
- Serovar/serogroup specific

Diagnostics

IgG/IgM detection assays

- Limited usefulness in acute serum
- Effective in convalescent sera
- ELISA tests often used to pre-screen before MAT – not always very sensitive
- Can be serovar specific



Leptospirosis in humans – 3 patterns

Urban areas (“slums”)

- rodent transmission
- poor hygiene
- outbreaks with inundations

Moist tropical regions (water surface)

- large variety of serovars and hosts
- occupational and residential exposure
- all year
- heavy rainfalls

Temperate regions

- few serovars
- occupational exposure to domestic animals, watersports
- Seasonal (flooding in Summer)



Potable water Peru



Santa Fe, Argentina – May 2003 human leptospirosis after a flood

Occurrence and pattern of leptospirosis

Typical risk factors: abattoir work, sewage work, dairy farmer, rice paddy/straw berry/sugar cane field worker, slum dweller, inundations, water sports in rivers and lakes (also Switzerland!)...

depends on:

- environmental factors such as climate and rainfall,
- the socio-economic situation (housing, hygiene, rodent control),
- prevalence and density of domestic and feral hosts,
- occupation (farming, meat industry etc.),
- farm management (vaccination policy, effluent control)
- recreational activities (water sports),
- surveillance systems (notification system, diagnostics)

Prevention and Control

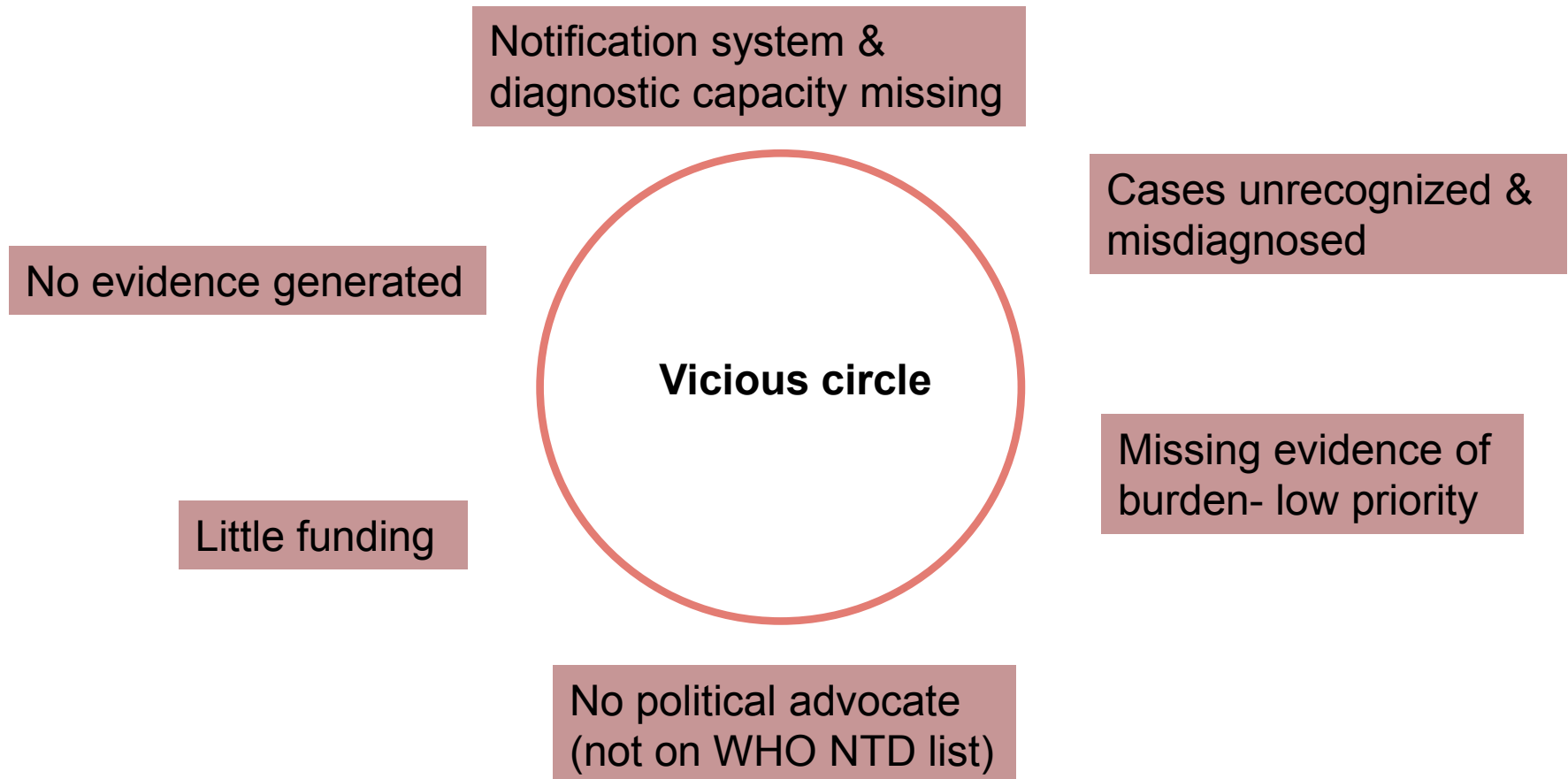
Varies depending on the source!

- Find out source!
 - epidemiological studies
 - surveillance systems in humans and animals (mandatory reporting with exposure data)
 - diagnostic capacity (reference center)
- Vaccination
 - restricted availability, annual booster needed
 - only few serovars in human vaccine (rodent associated)
 - useful in humans and animals depending on setting (risk groups)
 - administration tricky (short window)
- Antibiotic treatment of livestock (herd level)
 - Combined with vaccination
- Rodent control
 - traps
 - garbage removal etc.

Prevention and Control

- Protection of water source
 - fences, pipes, effluent control
- Behavior
 - prevent contact with urine
- Protective equipment (gloves, face shields, gum boots)
 - prevent urine splashes or contact with contaminated surfaces
- Avoid contaminated rivers, inundated areas
 - warnings
 - test water before sports event?
- Prophylactic antibiotic treatment (humans)
 - efficacy not proven
 - low compliance (side effects)
 - not concurrent with AMR policy

Prevention and Control



Where to go?

- Change political will: needs to be on NTD list of WHO!
- Epidemiological studies to prove burden and global economic impact (food security)
- One Health approach
- Make it a «tool-ready» disease
 - develop vaccine with cross-protection between serovars (pan-genome analysis)
 - accurate and affordable point of care diagnostic tests
- Clinical management
 - awareness
 - diagnostic procedures with algorithms
 - include risk factors
- Recommended literature:
 - Pereira, M.M., et al., A road map for leptospirosis research and health policies based on country needs in Latin America. Rev Panam Salud Publica, 2018. 41: p. e131