Waterborne disease (Leptospirosis) and Water Surveillance

Tracking *Leptospira* sources following human leptospirosis occurrences

July 22, 2024

Presentation

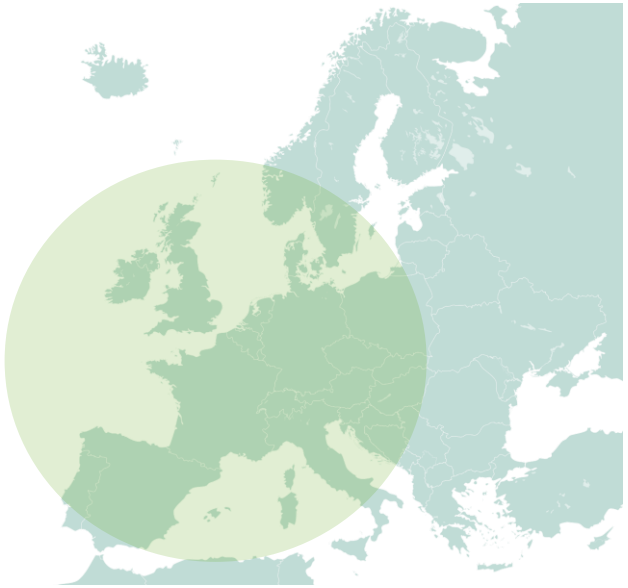
Florence Ayral, DVM
Infectious Diseases, Epidemiology

Veterinary Public Health

One Health Concept

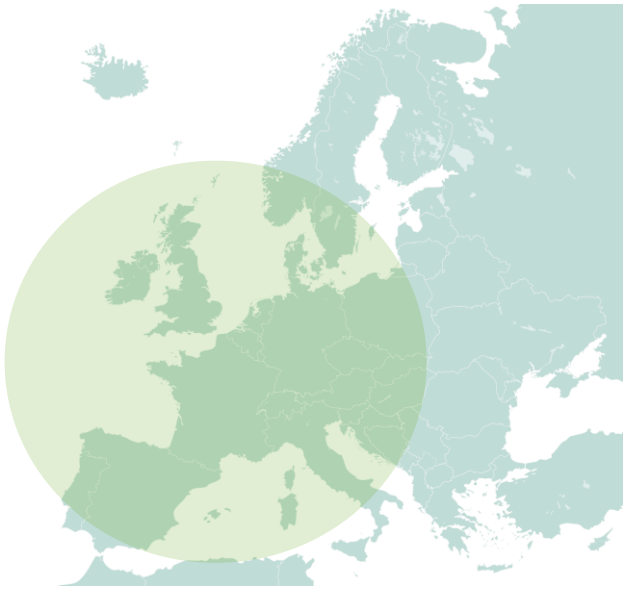
- Diagnostic lab incl. Micro agglutination Test
- Wild rodents, Heath Risk Population Management
- Wildlife expertise division

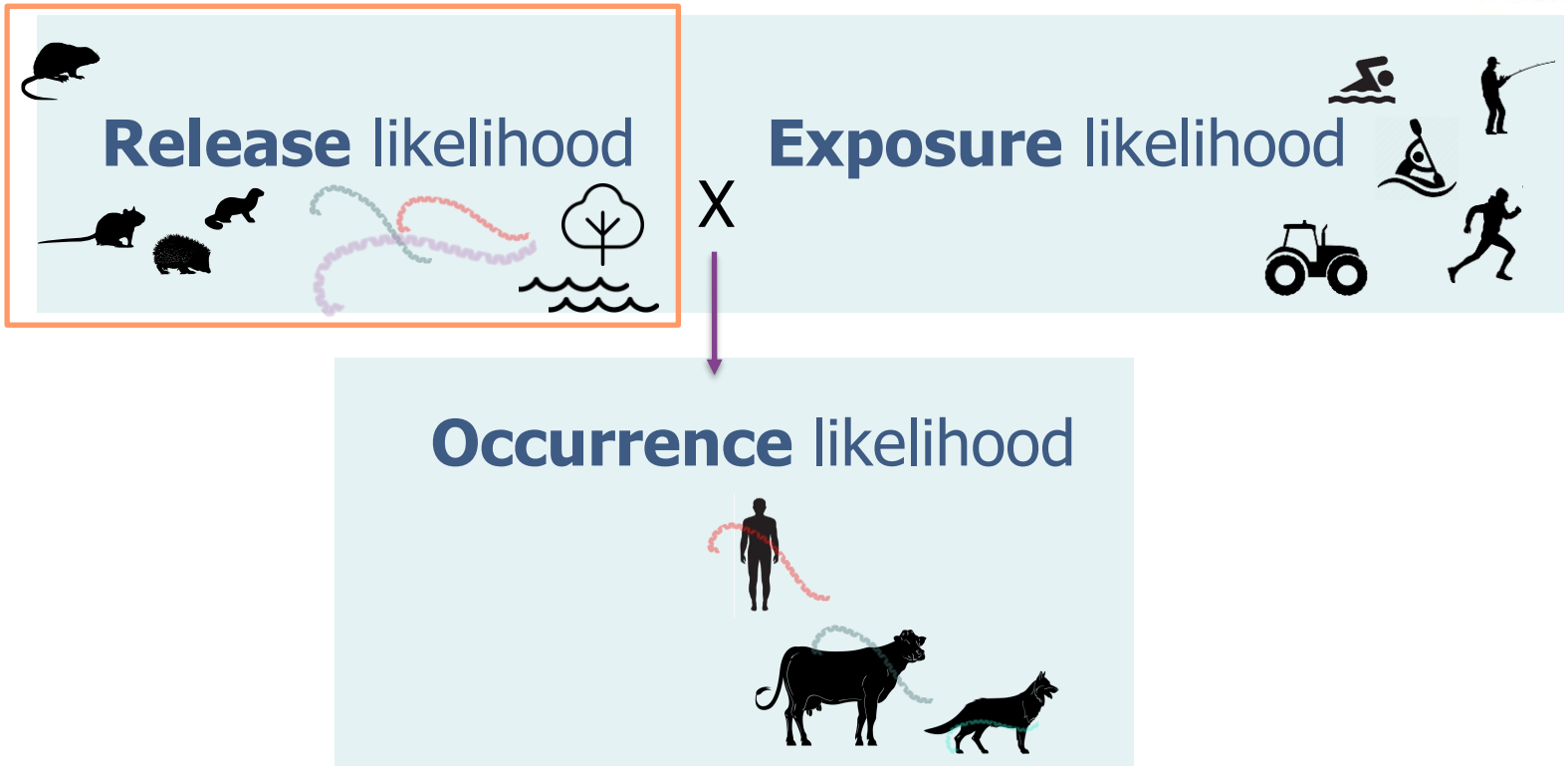
Context



In temperate climate countries, we don’t know why leptospirosis occurrences are observed in a given time and place.

Context





The final goal of tracking *Leptospira* sources is to gain knowledge on the release likelihood and improve leptospirosis risk management

Tracking *Leptospira* sources

Specific objectives of this session:

1. Explain what is a maintenance community of *Leptospira*

2. Conduct analysis of the maintenance community of *Leptospira* in a natural ecosystem
   - Describe the diversity of *Leptospira* hosts
   - Explain how to find relevant data on *Leptospira* infections in animals

Outline

This session consists of the following elements

1. Introduction to *Leptospira* Maintenance Community

2. Diversity of animal leptospirosis / infections and data available

3. Case study integrating the analysis of the maintenance community in a natural ecosystem

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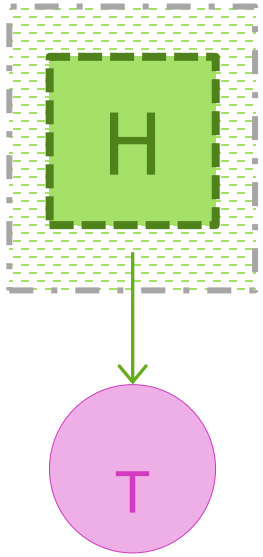
Definitions

- **Reservoir**: populations and/or environments in which the pathogen agent persists over prolonged periods and from which a target population can become infected.

Haydon *et al.*, 2002



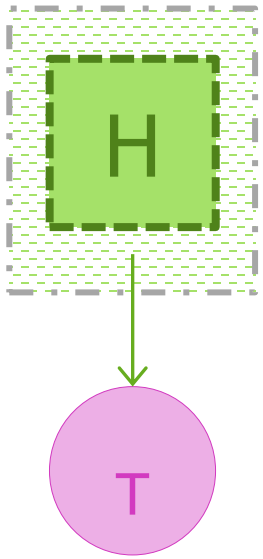
Definitions

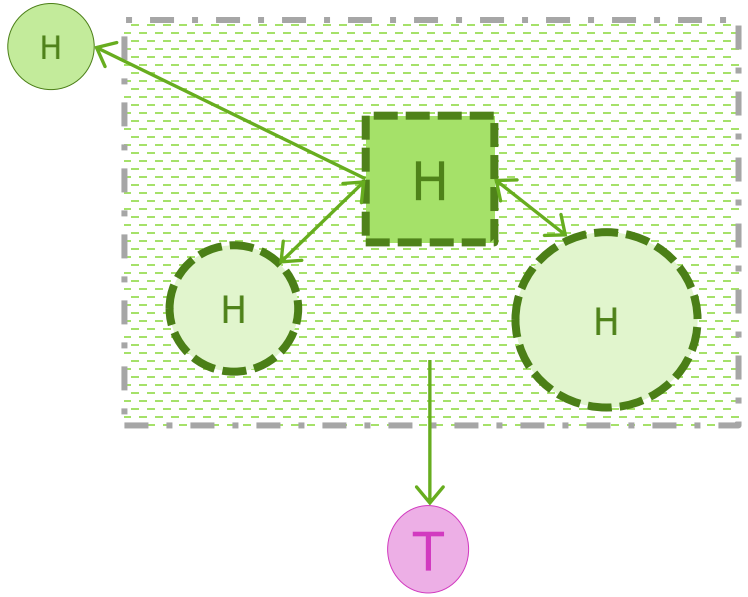
- **Reservoir**: populations and/or environments in which the pathogen agent persists over prolonged periods and from which a target population can become infected.

Haydon *et al.*, 2002

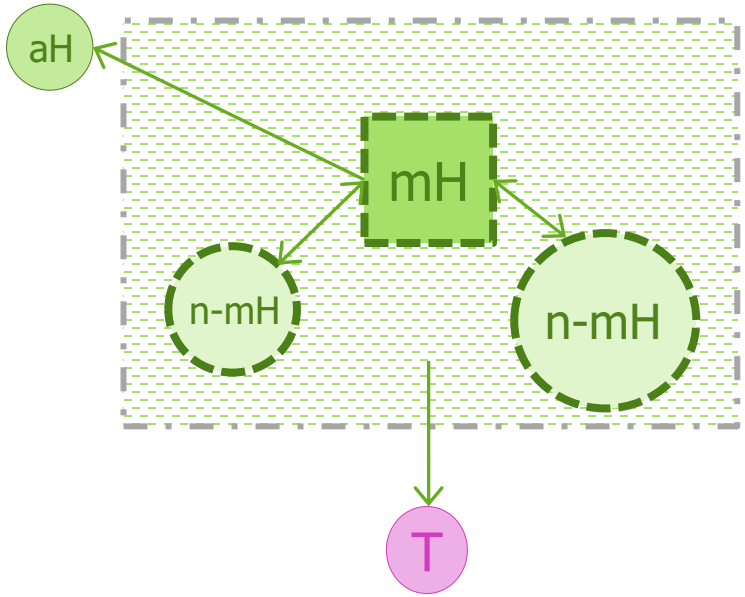
- **Maintenance community**: connected host populations that together help to maintain a pathogen agent over the long term.

Viana *et al.*, 2014





Definitions – epidemiological roles



- **Maintenance host**: host population able to maintain the pathogen agent over prolonged periods.
- **Non-maintenance host**: host population not able to maintain it over prolonged periods however may contribute to the maintenance with other connected host populations.
- **Accidental host**: host population that is susceptible to infection however does not contribute to the maintenance.

Leptospira maintenance hosts

First host reported and studied

Main source of human leptospirosis

Leptospira carriage varies, around 20%

Rattus norvegicus

Leptospira maintenance hosts

First host reported and studied

Main source of human leptospirosis

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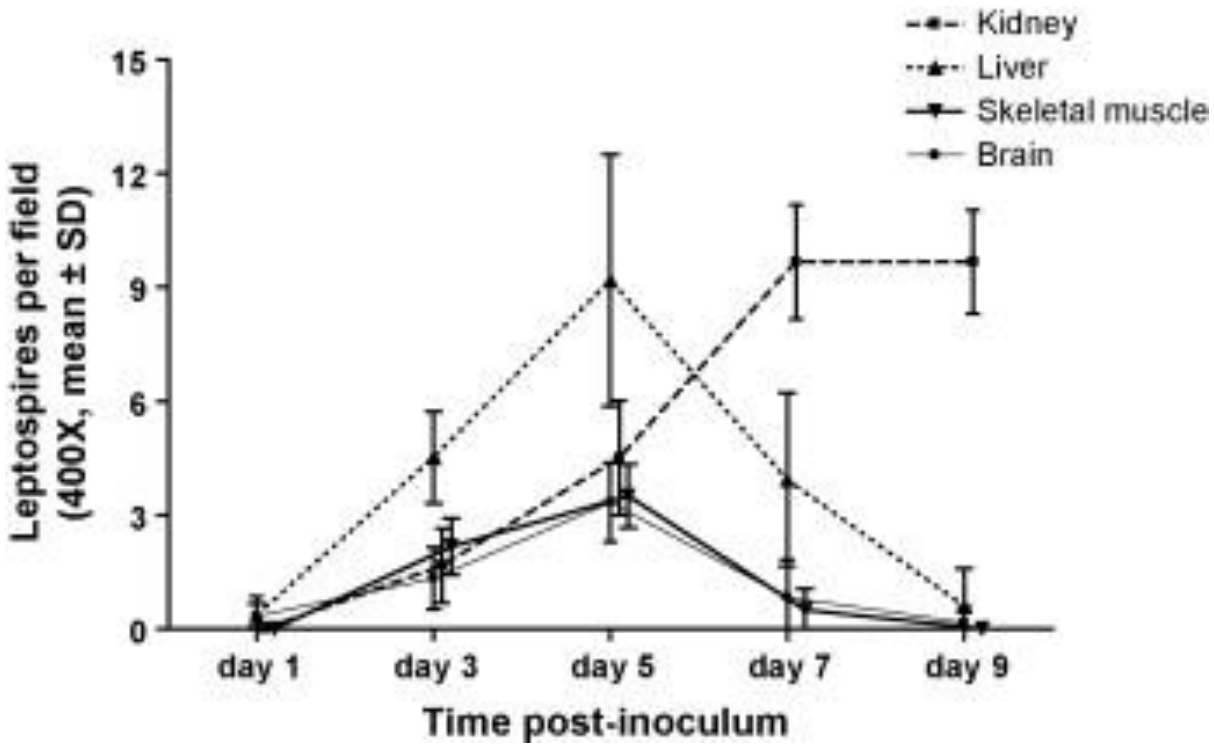
Infection dynamic and **kidney colonisation**



Athanazio et al. 2008

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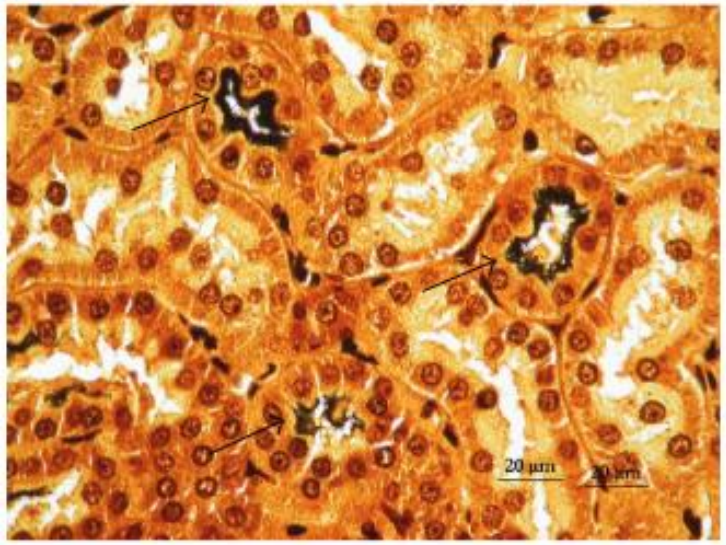

Leptospira in kidney tubules
Warthin-starry coloration

Zilber *et al.* 2016

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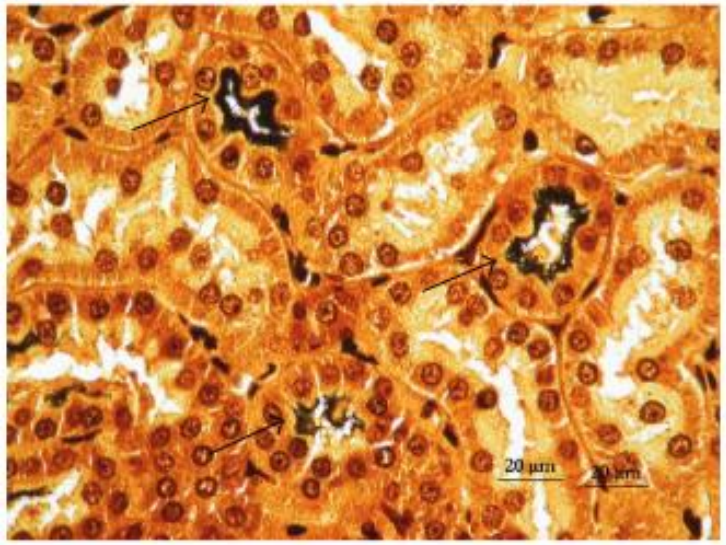
Urinary shedding 10^8 bacteria / mL



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Infection dynamic and **kidney colonisation**

Urinary shedding 10^8 bacteria / mL

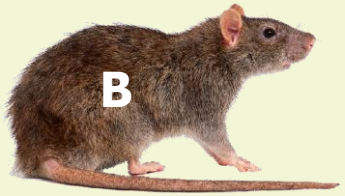
« Healthy » carriage period > 7 months

Selective carriage *L. interrogans* sg Icterohaemorrhagiae

→ Maintenance hosts
of *L. interrogans* sg Icterohaemorrhagiae

L. sg Icterohaemorrhagiae

> 7 months
Kidney & urine +

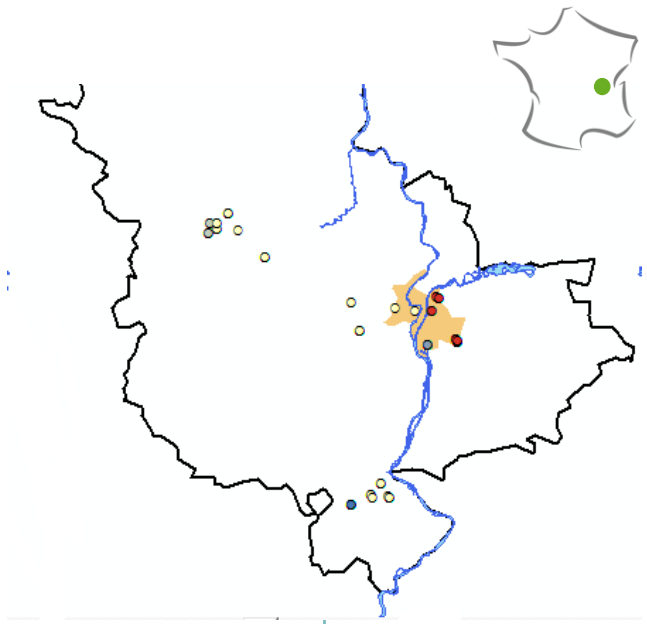


L. sg Grippotyphosa

Few weeks
Kidney & urine +

Thiermann 1981

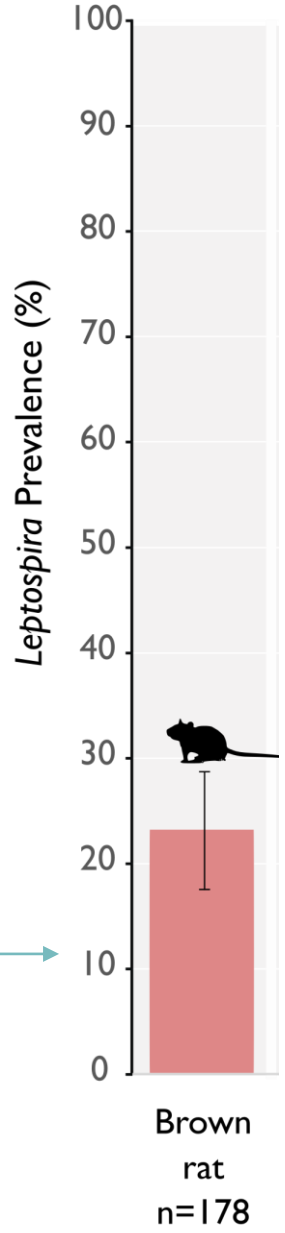
Leptospira maintenance hosts



Kidney / Urine

PCR + 16s typing

VNTR / MST



L. interrogans genogroupe *Icterohaemorrhagiae*

Ayral *et al.* 2014, 2015

Renal carriage > 20%

Selective carriage

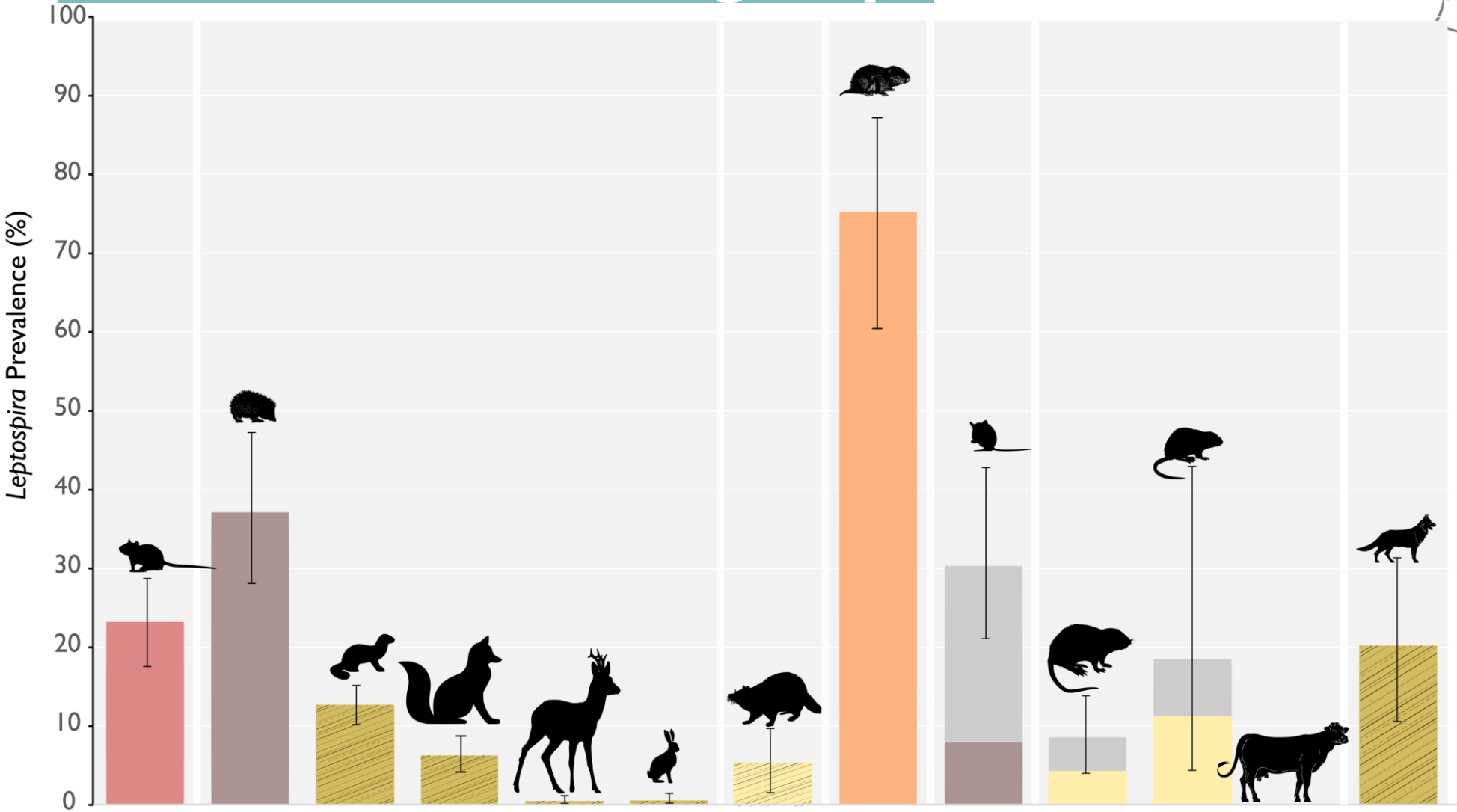
Independant populations

Urinary shedding

Absence of lesions

VetAgro Sup

Overview in wildlife groups



Epidemiological roles among animals

Renal carriage > 20%	✓	✓	✗	✗	✗	✗	✗	✓	✓	✗	✗	✓
Selective carriage	✓	✓	✗	✗	✗	✗	✗	✓	✓	✓	✗	✗
Independant populations	✓	✓					✓	✓	✓	✓	✓	✗
Urinary shedding	✓	✓					✓	✓	✓	✓	✗	✗
Absence of lesions	✓	✓					✓	✓	✓	✓	✓	✓

Ayral *et al.* 2014, 2015, 2016; Harran *et al.* 2023, 2024

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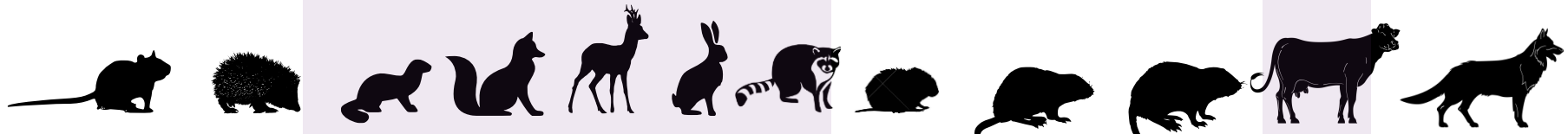
Potential maintenance hosts

Ayral *et al.* 2014, 2015, 2016; Harran *et al.* 2023, 2024

Epidemiological roles among animals



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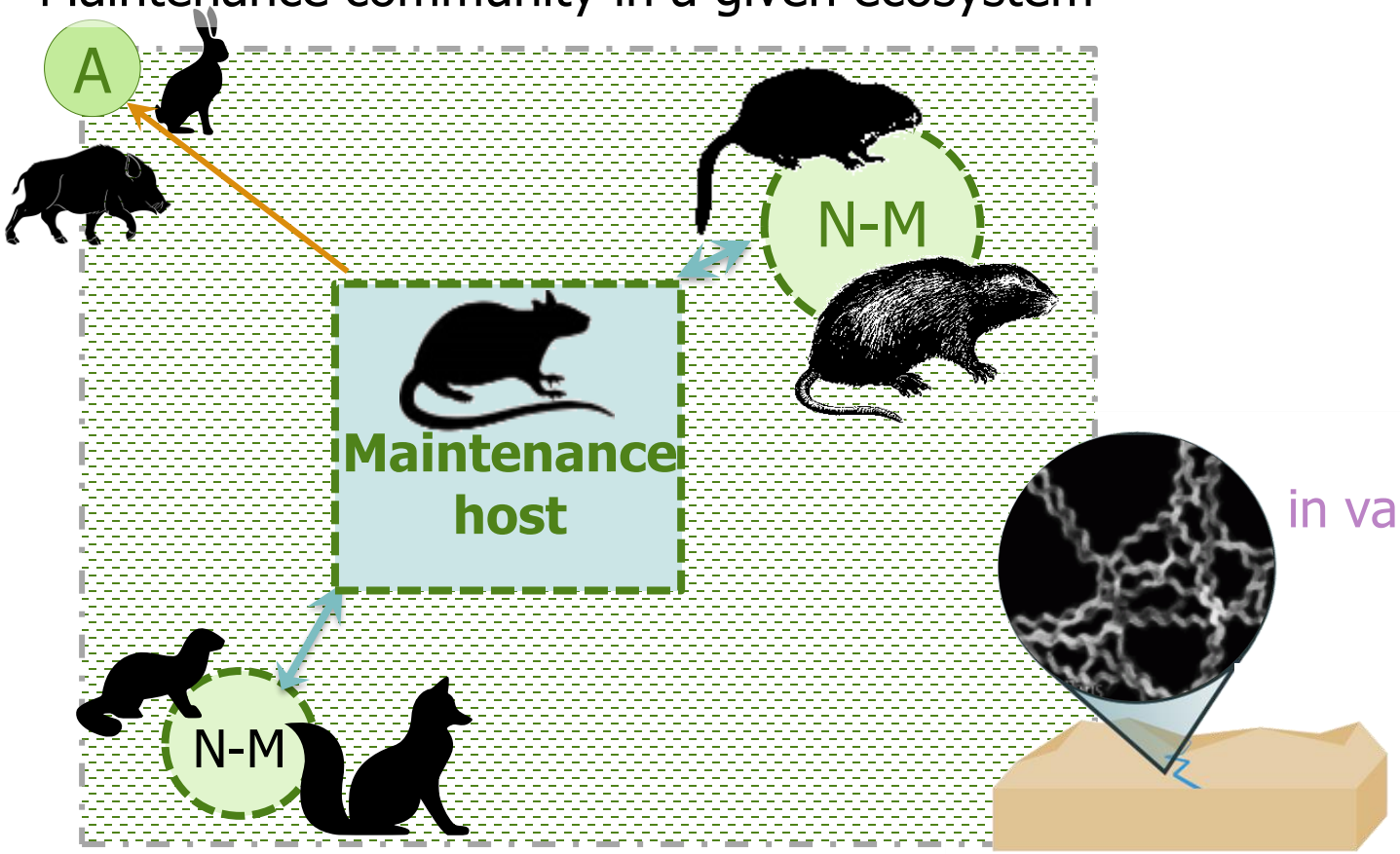
Independant populations	✓	✓					✓	✓	✓	✓	✓	✗
Urinary shedding	✓	✓					✓	✓	✓	✓	✗	✗
Absence of lesions	✓	✓					✓	✓	✓	✓	✓	✓

Potential non maintenance hosts

Ayral *et al.* 2014, 2015, 2016; Harran *et al.* 2023, 2024

Leptospira maintenance Community

L. interrogans sg Icterohaemorrhagiae
Maintenance community in a given ecosystem



Lead to diseases
in various mammal species

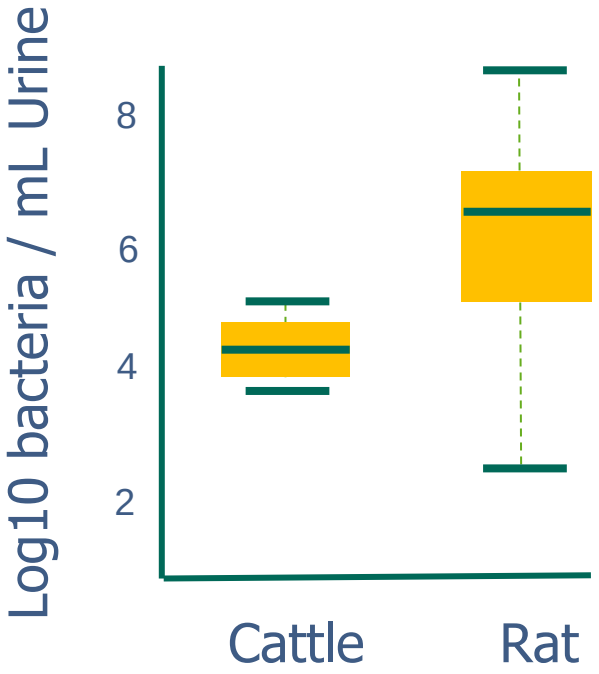
slido

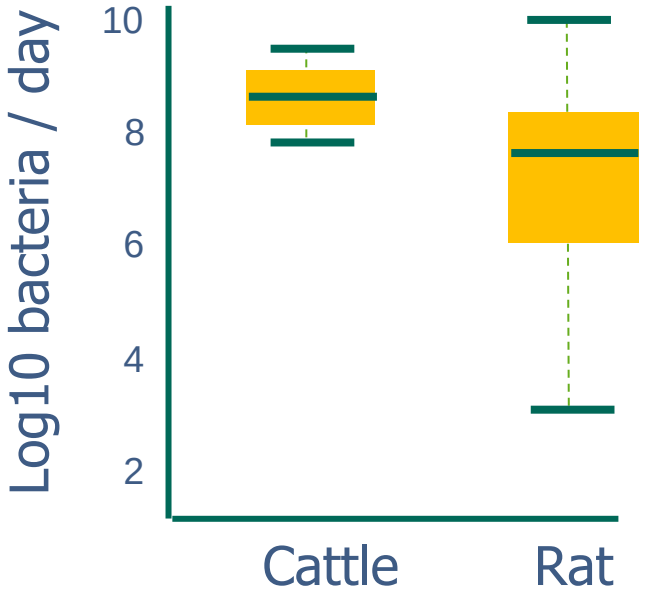
Please download and install the Slido app on all computers you use

To your opinion, rank the animal species depending on their contribution to soil contamination.

ⓘ Start presenting to display the poll results on this slide.

Leptospira loads in urines





Leptospira loads and urine volumes should be considered

Barragan *et al. BMC Res Notes (2017)*

Conclusion part 1

- *Leptospira* maintenance community takes into account the community of hosts rather than a single animal population

- Characterisation of the maintenance community should include
  - Epidemiological role
  - Load of *Leptospira* shedding
  - Population abundance
  - Interactions
  - Environmental parameters

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Leptospirosis status in animals ?

World Organisation for Animal Health
Founded as OIE

- Notification not required
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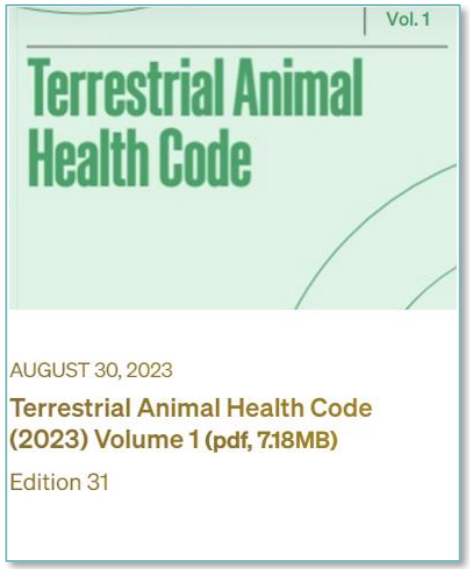
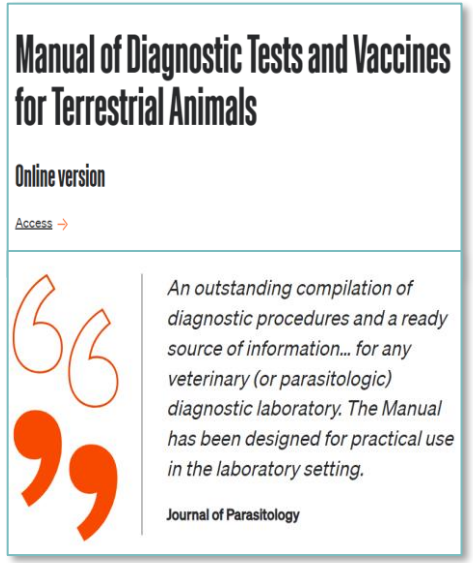
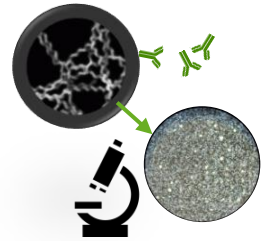




Diagnostic



Ref - Micro agglutination test

ELISA
Bacteriological culture
PCR

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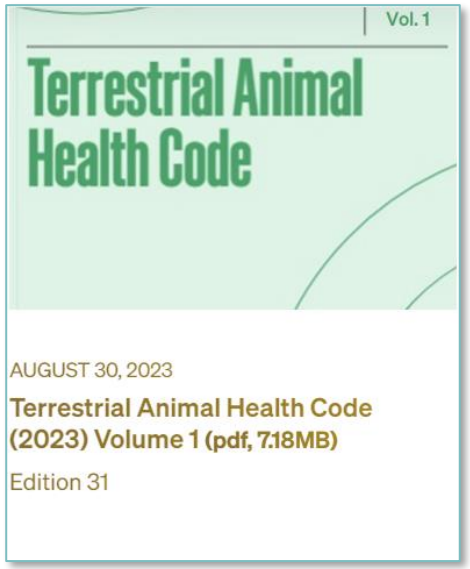

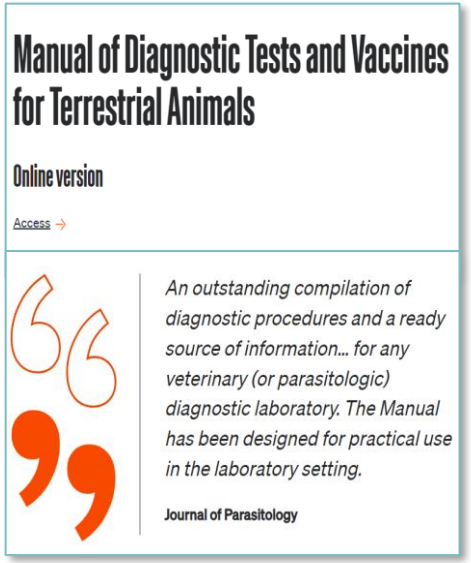

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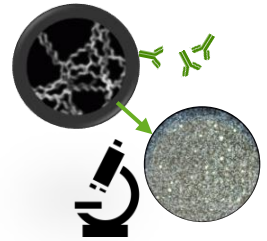

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Not categorised

COMMISSION IMPLEMENTING REGULATION (EU) 2018/1882

of 3 December 2018

on the application of certain disease prevention and control rules to categories of listed diseases and establishing a list of species and groups of species posing a considerable risk for the spread of those listed diseases

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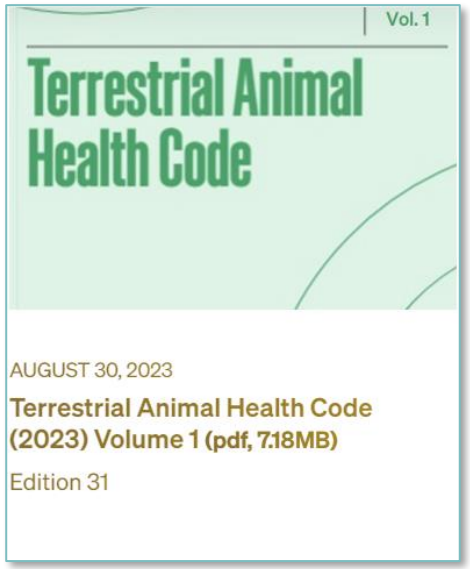

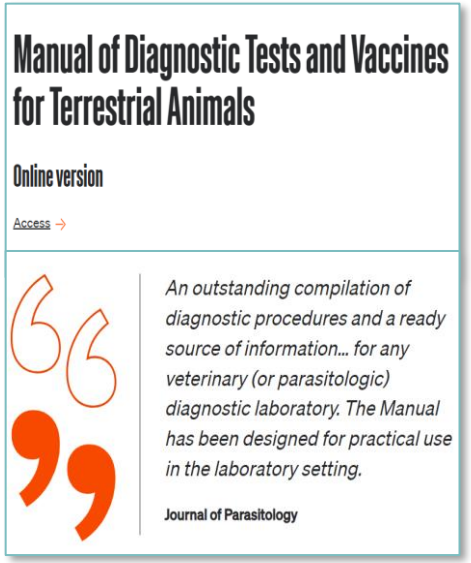

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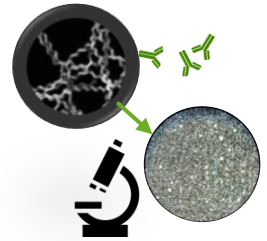

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Can be regulated at the country level

Diversity of animal leptospirosis

- Wide range of clinical manifestations depending on the animal species / individual
- Acute or chronic infections

e.g., Rattus norvegicus

Apparently healthy
Chronical infections (*L.* sg Icterohaemorrhagiae)
Acute infections for other sg.

e.g., Dogs

Severe diseases
Acute infections

VetAgro Sup

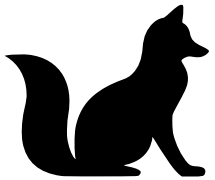
Wildlife leptospirosis

Some wildlife species are suceptible to *Leptospira* infections

European beavers (Marreros *et al., 2017*)

Guinea pig (Inada *et al.,* 1916)

Golden hamsters (Morton, 1942)



Red fox (SAGIR, 2024)

→ Some available data via surveillance systems of wildlife diseases

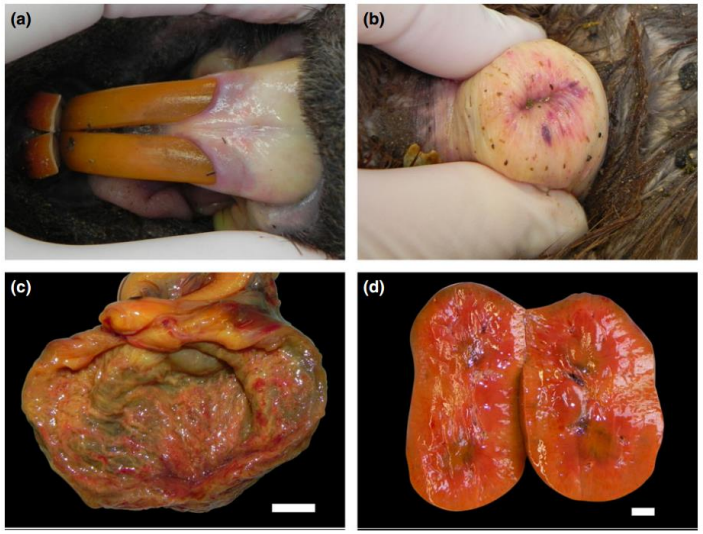
→ Research projects

VetAgro Sup

Wildlife leptospirosis

Natural disease in beavers

Castor fiber (n=13, 2010-14) :



- Icteric gingival mucosa (a), haemorrhage in cloacal (b), bladder (c) and lung (e),
- Icteric kidney and loss of demarcation between cortex and meddula (d)

Marreros *et al.*, 2017

Wildlife leptospirosis

Natural disease in beavers

Laboratory results for Eurasian beavers from Switzerland diagnosed with leptospirosis from 2010 through 2014

	PCR						MAT[b]								
	Kidney			Lung			Australis			Icterohaemorrhagiae			Autumnalis		Sejroe
ID[a]	Result	Ct	Profile	Result	Ct	Profile	BRAT	MUN	AUS	19	COP	VER	BIM	AKI	SAX
1	Pos	24.9	MW	Pos	27.3	MW	400	–	–	–	–	–	–	–	400
3	Pos	32.7	R1	Neg			–	–	–	–	200	–	–	–	–
4	Neg			Pos	30.8	Aare	100	–	–	800	400	–	400	–	–
5	Pos	27.6	Mi	Pos	29.7	Mi	NA	NA	NA	NA	NA	NA	NA	NA	NA
6	Neg			Neg			–	–	–	200	400	200	–	–	–
7	Pos	26.9	Aare[c]	Neg			100	800	–	3,200	3,200	–	1,600	800	–
8	Neg			Pos	31.1	R1	–	–	200	–	–	–	–	–	–
10	Neg			Neg			200	–	–	800	800	3,200	–	–	–
11	Pos	20.4	MW	Pos	24.7	MW	200	–	–	–	–	–	–	–	–
12	Pos	26.7	R1	Pos	27.1	R1	–	–	–	–	–	–	–	–	–
13	Pos	23.8	Mi	Pos	33.2	Mi	100	–	–	–	–	–	–	–	–

Marreros *et al.*, 2017

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3	Pos	32.7	R1	Neg			–	–	–	–	200	–	–	–	–
4	Neg			Pos	30.8	Aare	100	–	–	800	400	–	400	–	–
5	Pos	27.6	Mi	Pos	29.7	Mi	NA	NA	NA	NA	NA	NA	NA	NA	NA
6	Neg			Neg			–	–	–	200	400	200	–	–	–
7	Pos	26.9	Aare[c]	Neg			100	800	–	3,200	3,200	–	1,600	800	–
8	Neg			Pos	31.1	R1	–	–	200	–	–	–	–	–	–
10	Neg			Neg			200	–	–	800	800	3,200	–	–	–
11	Pos	20.4	MW	Pos	24.7	MW	200	–	–	–	–	–	–	–	–
12	Pos	26.7	R1	Pos	27.1	R1	–	–	–	–	–	–	–	–	–
13	Pos	23.8	Mi	Pos	33.2	Mi	100	–	–	–	–	–	–	–	–

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3	Pos	32.7	R1	Neg			–	–	–	–	200	–	–	–	–
4	Neg			Pos	30.8	Aare	100	–	–	800	400	–	400	–	–
5	Pos	27.6	Mi	Pos	29.7	Mi	NA	NA	NA	NA	NA	NA	NA	NA	NA
6	Neg			Neg			–	–	–	200	400	200	–	–	–
7	Pos	26.9	Aare[c]	Neg			100	800	–	3,200	3,200	–	1,600	800	–
8	Neg			Pos	31.1	R1	–	–	200	–	–	–	–	–	–
10	Neg			Neg			200	–	–	800	800	3,200	–	–	–
11	Pos	20.4	MW	Pos	24.7	MW	200	–	–	–	–	–	–	–	–
12	Pos	26.7	R1	Pos	27.1	R1	–	–	–	–	–	–	–	–	–
13	Pos	23.8	Mi	Pos	33.2	Mi	100	–	–	–	–	–	–	–	–

Marreros *et al.*, 2017

Wildlife leptospirosis

Natural disease in beavers

Laboratory results for Eurasian beavers from Switzerland diagnosed with leptospirosis from 2010 through 2014

	PCR						MAT[b]								
	Kidney			Lung			Australis			Icterohaemorrhagiae			Autumnalis		Sejroe
ID[a]	Result	Ct	Profile	Result	Ct	Profile	BRAT	MUN	AUS	19	COP	VER	BIM	AKI	SAX
1	Pos	24.9	MW	Pos	27.3	MW	400	–	–	–	–	–	–	–	400
3	Pos	32.7	R1	Neg			–	–	–	–	200	–	–	–	–
4	Neg			Pos	30.8	Aare	100	–	–	800	400	–	400	–	–
5	Pos	27.6	Mi	Pos	29.7	Mi	NA	NA	NA	NA	NA	NA	NA	NA	NA
6	Neg			Neg			–	–	–	200	400	200	–	–	–
7	Pos	26.9	Aare[c]	Neg			100	800	–	3,200	3,200	–	1,600	800	–
8	Neg			Pos	31.1	R1	–	–	200	–	–	–	–	–	–
10	Neg			Neg			200	–	–	800	800	3,200	–	–	–
11	Pos	20.4	MW	Pos	24.7	MW	200	–	–	–	–	–	–	–	–
12	Pos	26.7	R1	Pos	27.1	R1	–	–	–	–	–	–	–	–	–
13	Pos	23.8	Mi	Pos	33.2	Mi	100	–	–	–	–	–	–	–	–

Marreros *et al.*, 2017

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3	Pos	32.7	R1	Neg			–	–	–	–	200	–	–	–	–
4	Neg			Pos	30.8	Aare	100	–	–	800	400	–	400	–	–
5	Pos	27.6	Mi	Pos	29.7	Mi	NA	NA	NA	NA	NA	NA	NA	NA	NA
6	Neg			Neg			–	–	–	200	400	200	–	–	–
7	Pos	26.9	Aare[c]	Neg			100	800	–	3,200	3,200	–	1,600	800	–
8	Neg			Pos	31.1	R1	–	–	200	–	–	–	–	–	–
10	Neg			Neg			200	–	–	800	800	3,200	–	–	–
11	Pos	20.4	MW	Pos	24.7	MW	200	–	–	–	–	–	–	–	–
12	Pos	26.7	R1	Pos	27.1	R1	–	–	–	–	–	–	–	–	–
13	Pos	23.8	Mi	Pos	33.2	Mi	100	–	–	–	–	–	–	–	–

Marreros *et al.*, 2017

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5	Pos	27.6	Mi	Pos							NA	NA	NA	NA	NA
6	Neg									200	400	200	–	–	–
7	Pos	26.9	Aare[c]						–	3,200	3,200	–	1,600	800	–
8	Neg							–	200	–	–	–	–	–	–
10	Neg						200	–	–	800	800	3,200	–	–	–
11	Pos	20.4	MW		24.7	MW	200	–	–	–	–	–	–	–	–
12	Pos	26.7	R1	Pos	27.1	R1	–	–	–	–	–	–	–	–	–
13	Pos	23.8	Mi	Pos	33.2	Mi	100	–	–	–	–	–	–	–	–

Multiple tests required to increase the sensitivity of detection

Marreros *et al.*, 2017

VetAgro Sup

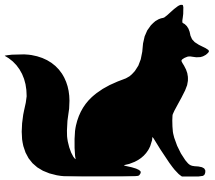
Wildlife leptospirosis

Some wildlife species are sensible to *Leptospira* infections

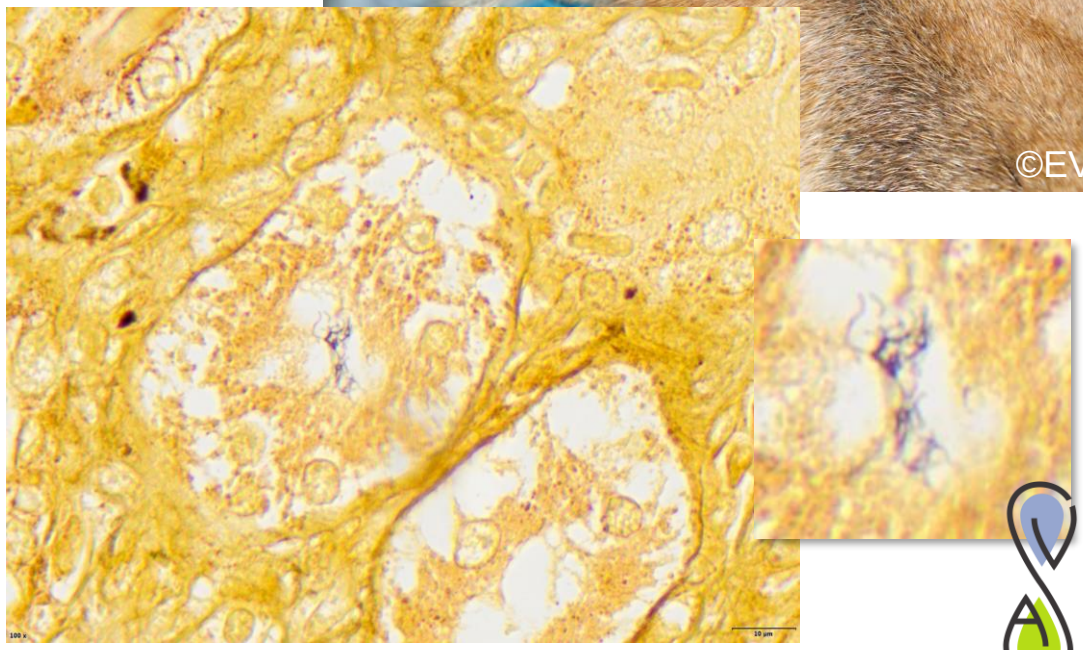
European beavers (Marreros *et al., 2017*)

Guinea pig (Inada *et al.,* 1916)

Golden hamsters (Morton, 1942)

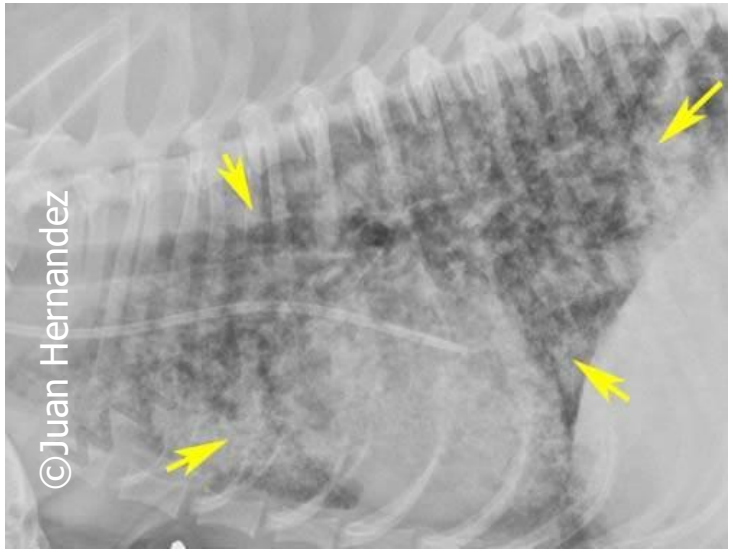


Red fox (SAGIR, 2024)



Kidney, Warthin-Starry, x1000 © EVAAS

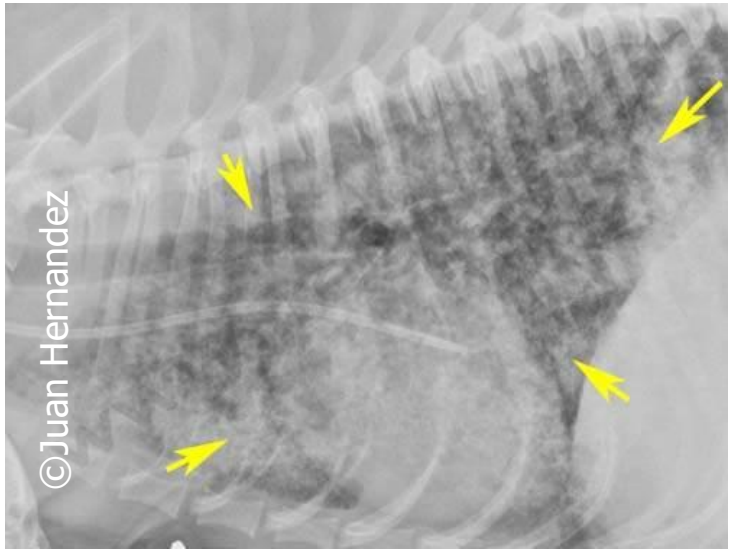
Domestic animal leptospirosis



Mayor *et al.* 2014

- Haemorrhage and icteric syndrome
- Incidence
  - Switzerland : 6 cases.100 000 dogs.year^{-1}
  - France : 150 cases.100 000 dogs.year^{-1} (unpublished data vet clinics)
- > 80% vaccinated (potential false positive)
- MAT kinetics recommended to show a 4-fold increased titers
- Many un reported cases

Domestic animal leptospirosis



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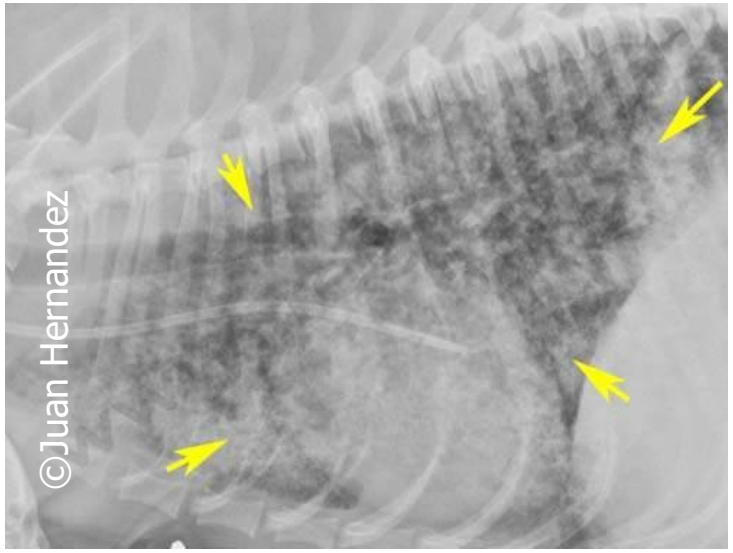
- > 80% vaccinated (potential false positive)
- MAT kinetics recommended to show a 4-fold increased titers
- Many un reported cases
- Healthy carriage in pack hounds
  - 11 of 32 dogs were PCR+ in urine

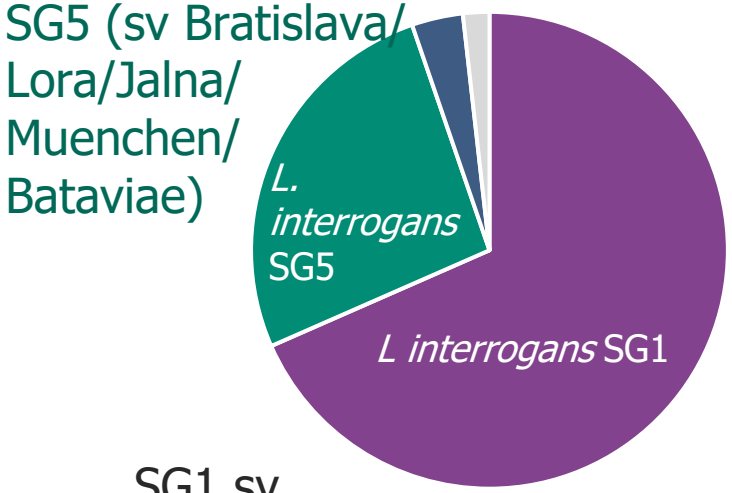
Domestic animal leptospirosis



Garcia Lopez *et al.* 2023

- Specie groups / Serogroups

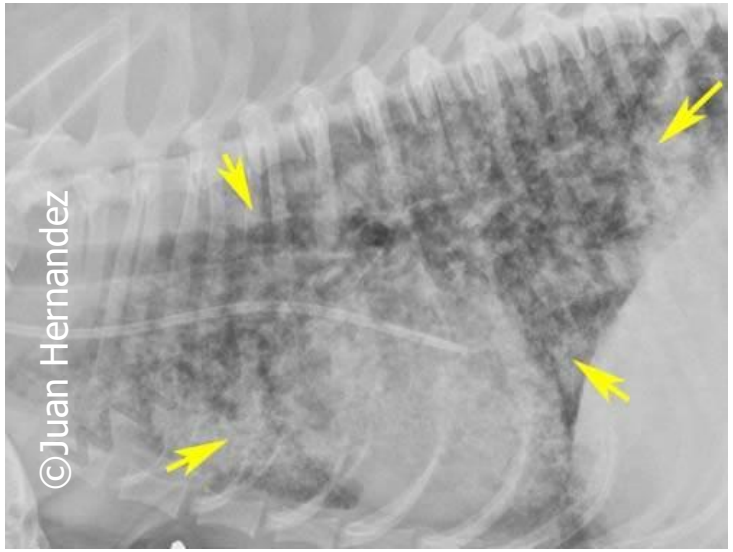
Lab data 2019 -21
Lfb1 gene typing
n=60



SG1 sv Icterohaemorrhagiae

VetAgro Sup

Domestic animal leptospirosis



Garcia Lopez *et al.* 2023

Specie groups / Serogroups

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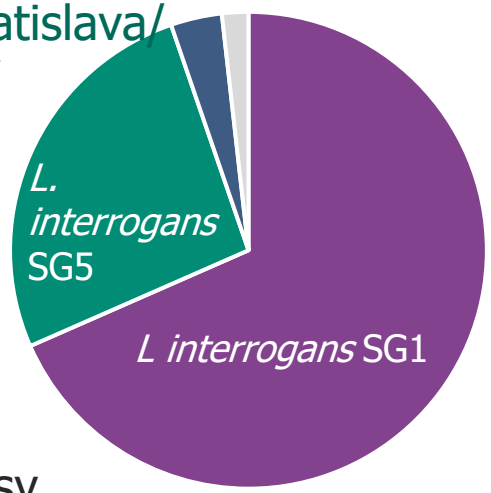
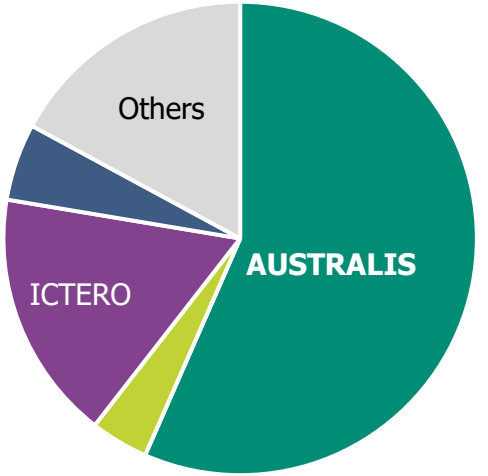
Lfb1 gene typing
n=60

SG5 (sv Bratislava/ Lora/Jalna/ Muenchen/ Bataviae)



SG1 sv Icterohaemorrhagiae

Lab data 2022
Micro aggl test
n=68



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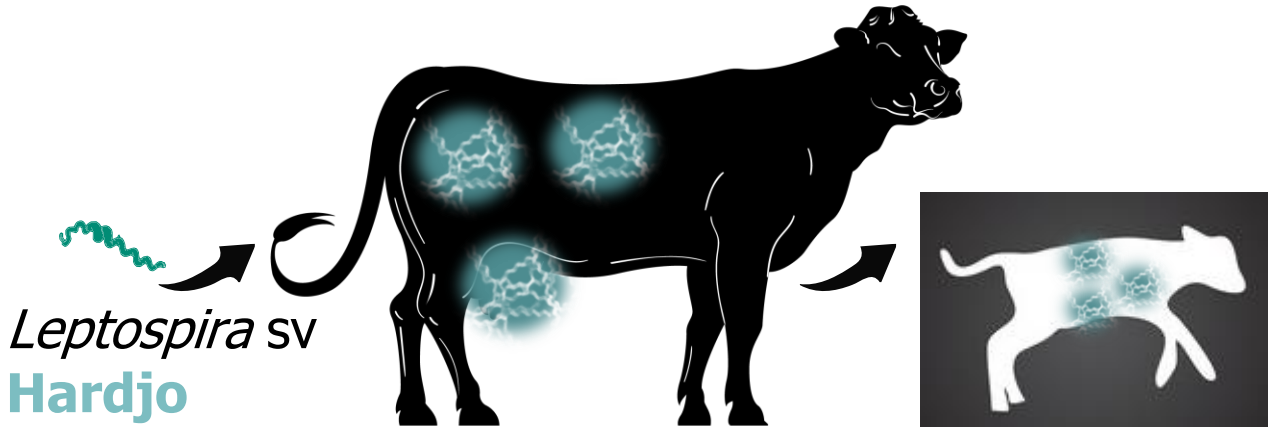
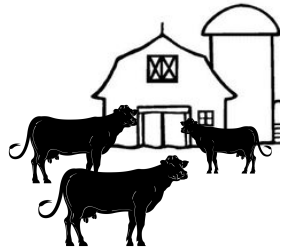
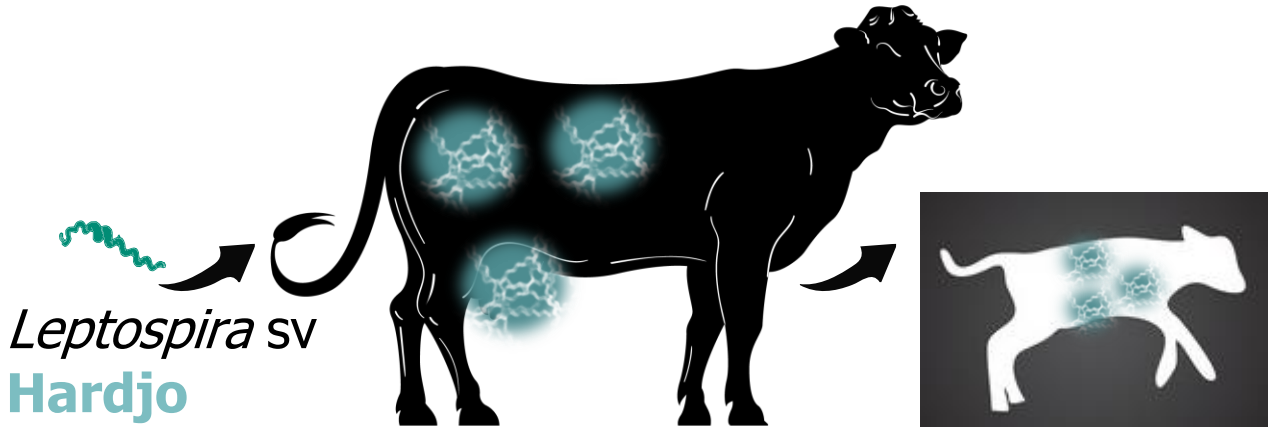
Livestock leptospirosis



Hoares *et al.* 1972; Thiermann 1982

Livestock leptospirosis





- Milk production loss > 50% cattle

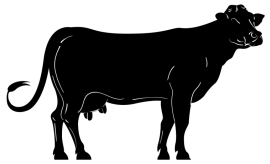
- > 10% abortions

- Cows without any consequences

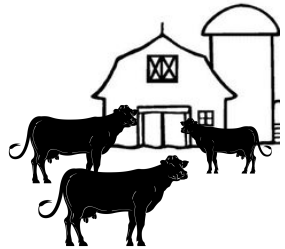
Hoares *et al.* 1972; Thiermann 1982

VetAgro Sup

Livestock leptospirosis

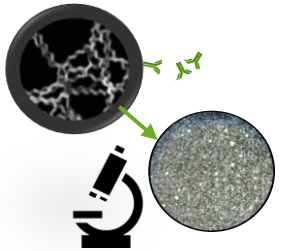


Blood d4-5 → Urine // >500



Diagnostic limitation in individual

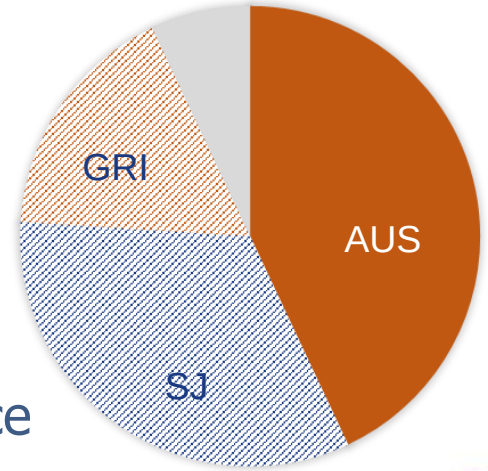
→ Herd diagnosis recommended by the WOAH Manual



PCR low sensitivity even in urine
MAT - Titer threshold ≥ 1:100
Se ≤ 50%
Sp < 90%

MAT - Titer threshold ≥ 1:100
≥ 10% of the herd

Lab data
N=394 herds,
2008-12, France



WOAH Manual 2021; Ayral et al. 2014

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Other domestic animals

- Performance decrease
- Abortion
- Uveitis potentially progressing in blindness
- Frequent inapparent infection
- MAT+ horses on aqueous of the eye without clinical manifestations (23%, n=48)*

*Agnès Benamou-Smith 2013 unpublished data

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11.7%, $_{95\%}$CI [9.3%-14.6%]

3.7 %, $_{95\%}$CI [1.7%-8.1%]

12.8 %, $_{95\%}$CI [3.2%-39.9%]

- Low evidence of disease related to *Leptospira* infection

→ Epidemiological contribution appeared limited, to be confirmed

Ricardo *et al.* 2023

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I need to find data on Leptospira circulating among dog leptospirosis in the country, I should look for them using

ⓘ Start presenting to display the poll results on this slide.

Limitation of *Leptospira* screening in animals

Wildlife

- Endangered species, trapping bias,
- A single test is poorly sensitive
- Scarce data available (syndromic surveillance, research projects)

Domestic animals

- More structured source of data (Lab data)
- Use of a single serological test is unproper for diagnostic
  - Limit of vaccinated animals
  - Limit to detect infection in chronically infected animals

Outline

This session consists of the following elements

1. Introduction to *Leptospira* Maintenance Community

2. Diversity of animal leptospirosis / infections and data available

3. Case study integrating the analysis of the maintenance community in a natural ecosystem

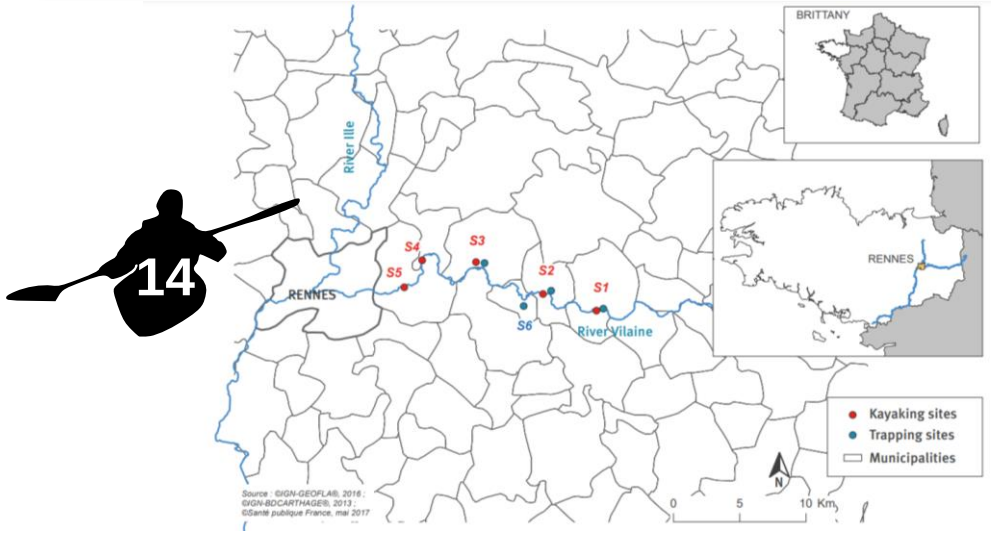
Brittany context

2016

SURVEILLANCE AND OUTBREAK REPORT

An outbreak of leptospirosis among kayakers in Brittany, North-West France, 2016

Yvonnick Guillois[1], Pascale Bourhy[2], Florence Ayral[3], Mathilde Pivette[1], Anouk Decors[4], José Héctor Aranda Grau[5], Benoît Champenois[5], Célia Malhère[6], Benoît Combes[7], Céline Richomme[8], Marine Le Guyader[3], Lisa Antoinette King[1], Alexandra Septfons[9,10]



Leptospira ***kirschneri*** (1) sg **Grippotyphosa** (5)

Brittany context

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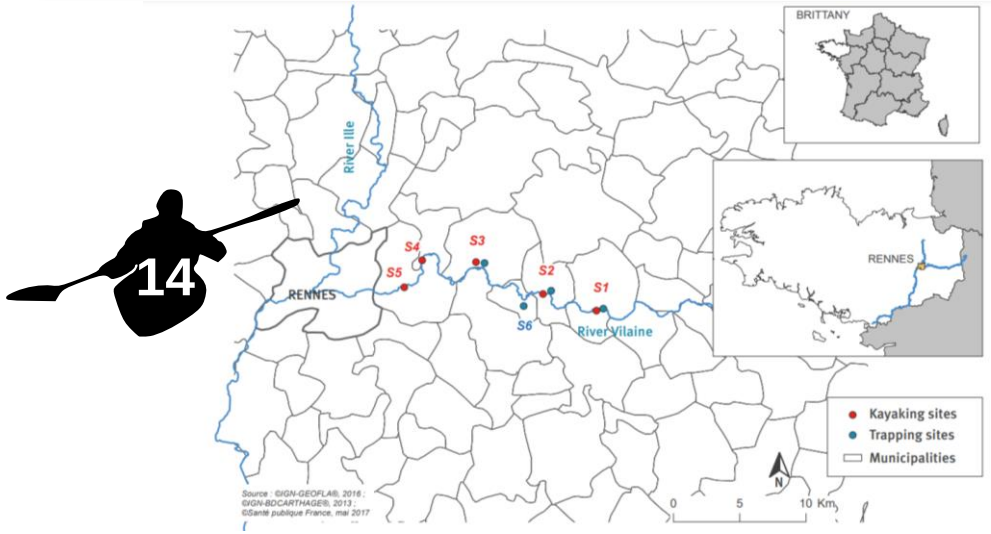

14

Leptospira ***kirschneri*** (1) sg **Grippotyphosa** (5)

Carriers of **various** *Leptospira* species

NO *L. kirschneri*

NO *L.* sg Grippotyphosa

Brittany context

2018

Preliminary fieldwork

Brittany context

2018

Preliminary fieldwork

Mustélidés	*Martes foina*
Bovidés	*Bos taurus taurus*
Bovidés	*Ovis aries*
Vespertilionidés	*Barbastella barbastellus*
Vespertilionidés	*Myotis alcathoe*
Vespertilionidés	*Myotis nattereri*
Vespertilionidés	*Pipistrellus pipistrellus*
Vespertilionidés	*Pipistrellus kuhlii*
Muridés	*Apodemus sylvaticus*
Muridés	*Micromys minutus*
Mustélidés	*Martes martes*
Muridés	*Rattus norvegicus*
Cricetidés	*Ondatra zibethicus*
Erinacéidés	*Erinaceus europaeus*
Gliridés	*Muscardinus avellanarius*
Hominidés	*Homo sapiens*
Sciuridés	*Sciurus vulgaris*
Talpidés	*Talpa europaea*

Léporidés	*Oryctolagus cuniculus*
Suidés	*Sus scrofa*
Cervidés	*Capreolus capreolus*
Léporidés	*Lepus europaeus*
Félidés	*Felis silvestris catus*
Canidés	*vulpes vulpes*
Mustélidés	*Mustela nivalis*
Soricidés	*Crocidura russula*
Soricidés	*Neomys fodiens*
Soricidés	*Sorex coronatus*
Canidés	*Canis lupus familiaris*
Myocastoridés	*Myocastor coypus*
Mustélidés	*Meles meles*
Cricetidés	*Arvicola sapidus*
Cricetidés	*Microtus arvalis*
Cricetidés	*Myodes glareolus*
Cricetidés	*Microtus subterraneus*

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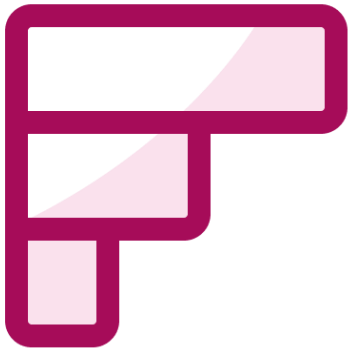


Which populations would you like to test in priority ?

ⓘ Start presenting to display the poll results on this slide.

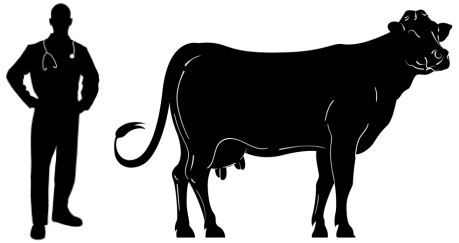
Brittany context

2018

Preliminary fieldwork

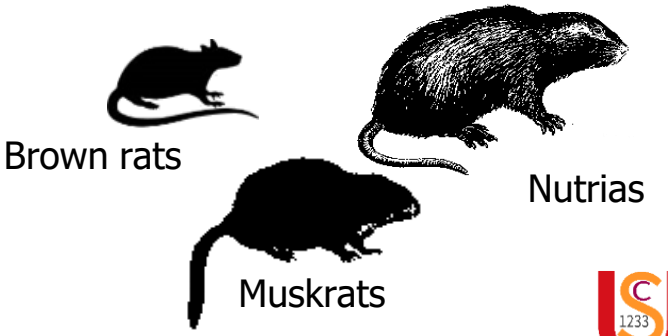
2019

Network involved



GDS Bretagne

& private vets



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Which samples / tests would you like to perform in cattle ?

ⓘ Start presenting to display the poll results on this slide.

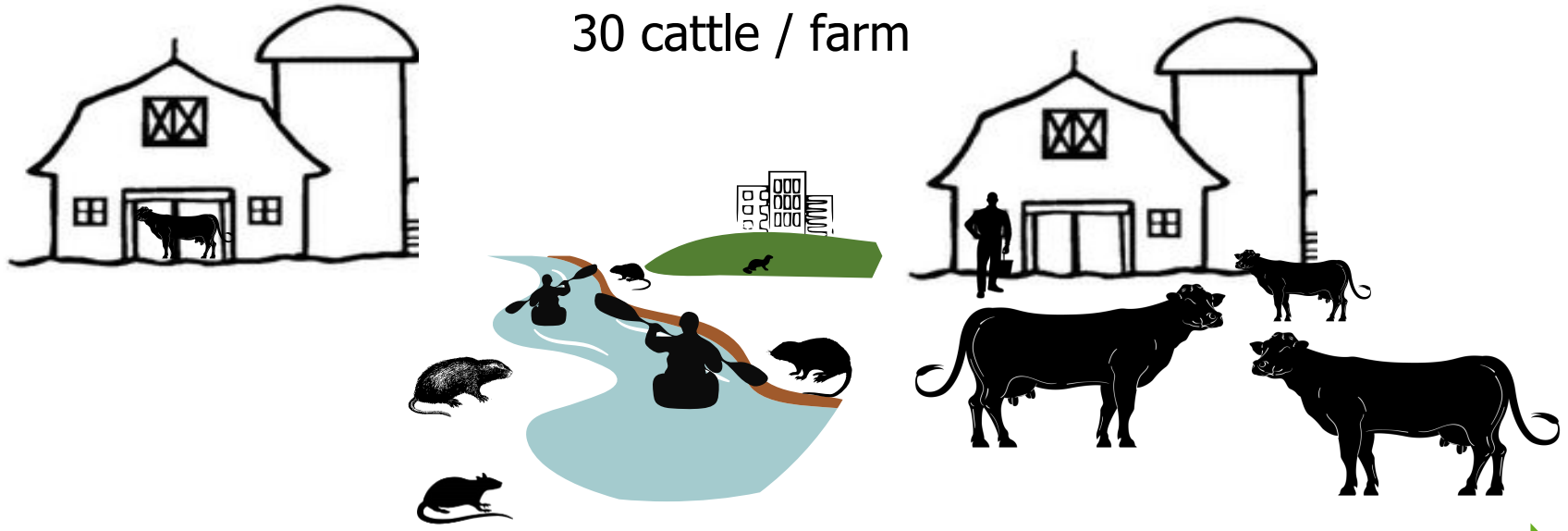
Investigations

March – April ... **November**

Before grazing

After grazing

8 farms
30 cattle / farm



March ... **November**

qPCR
Leptospira pathogène

Waggoner et al. 2014

cPCR *lfb1*

Merien et al. 2005

Sanger Typing

Micro agglutination test

Results 1/3

March – April — **November**

Before grazing — ***After grazing***

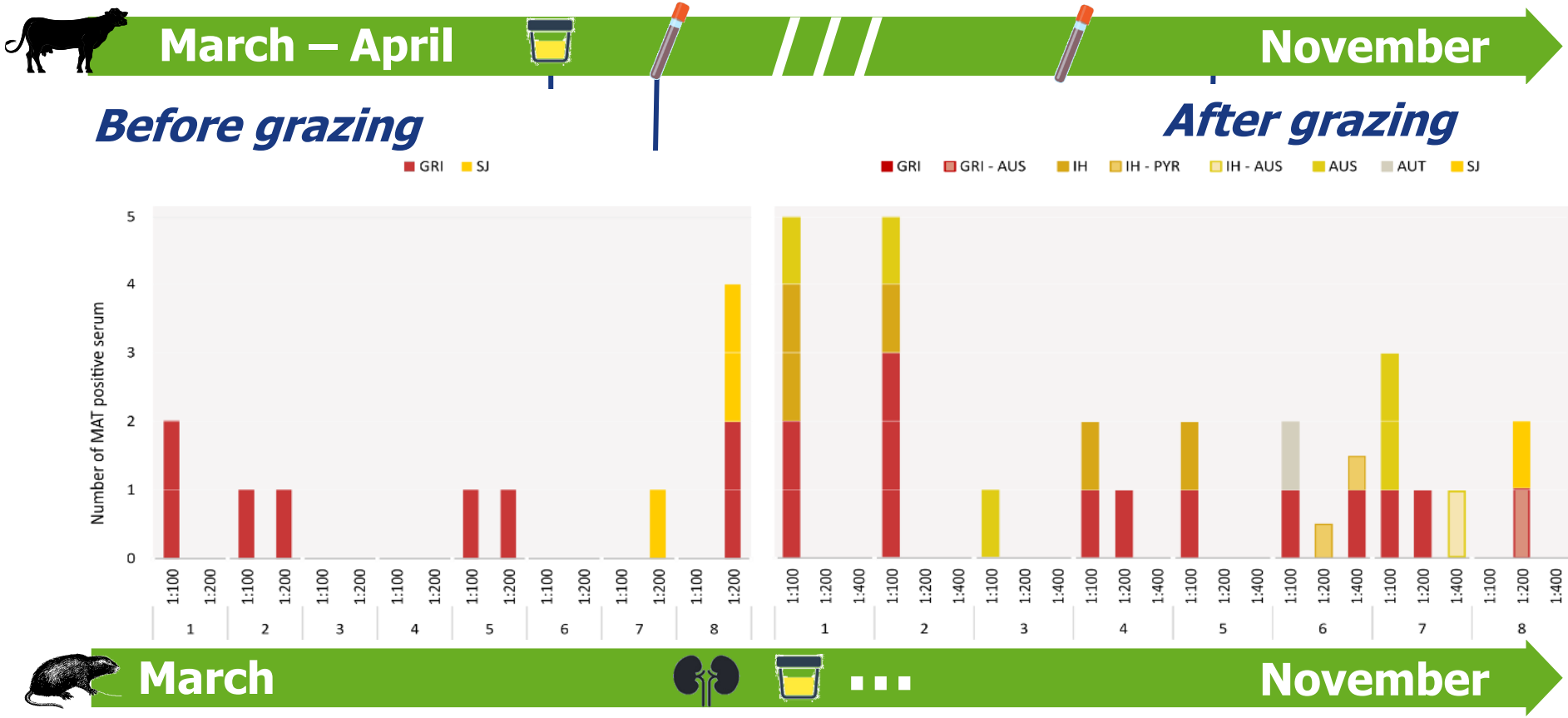
145 urine samples from 6 farms
All culture negative
All PCR negative

212 serum from 8 farms
5% seropositive cattle
5 seropositive farms

227 serum from 8 farms
12% seropositive cattle
8 seropositive farms

March — **November**

Results 2/3


March – April
November
Before grazing
After grazing
GRI
SJ
GRI
GRI - AUS
IH
IH - PYR
IH - AUS
AUS
AUT
SJ
Number of MAT positive serum
0
1
2
3
4
5
1:100
1:200
1:400
1
2
3
4
5
6
7
8
March
November

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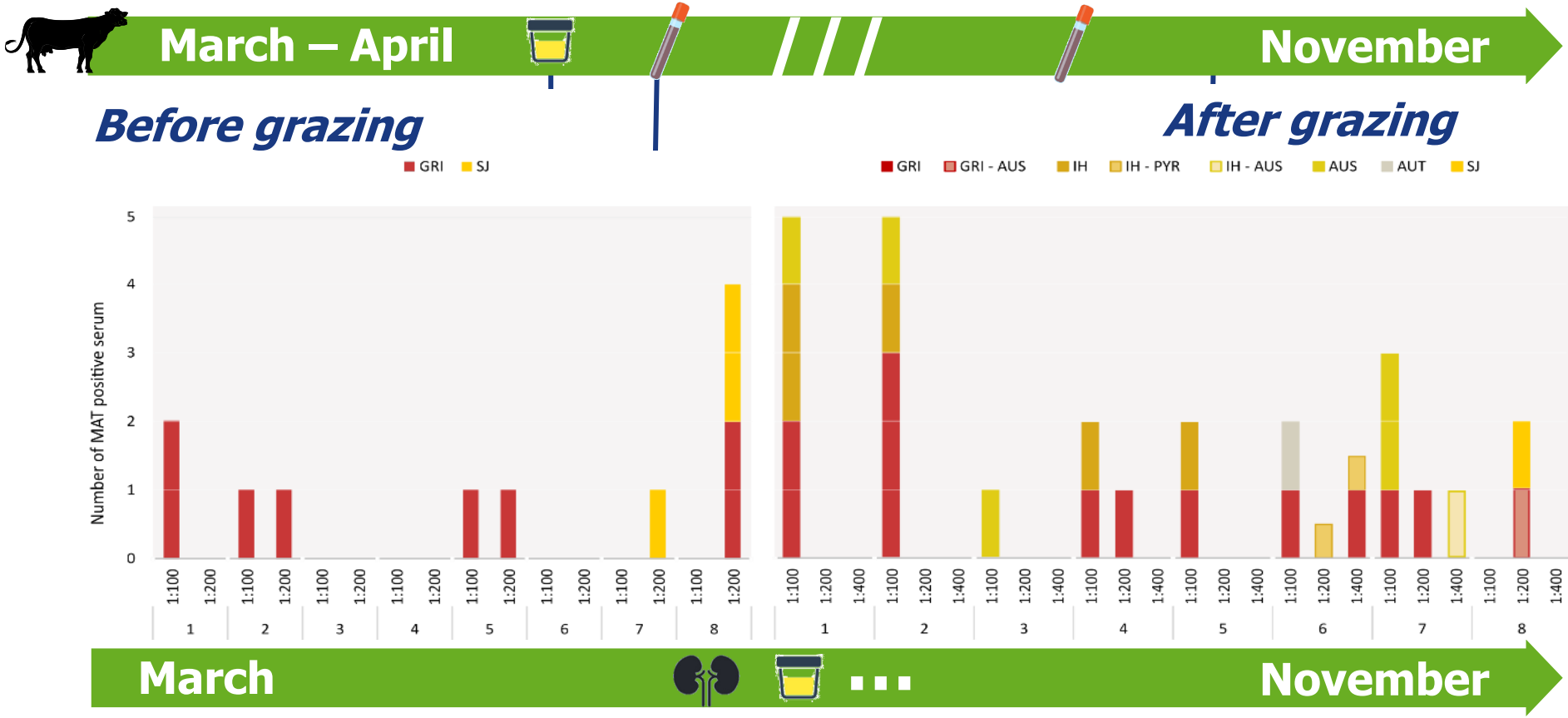
How certain are we that cattle are guilty ?

ⓘ Start presenting to display the poll results on this slide.

Results 3/3



L. interrogans = 1/2

	n =143	PCR+ = 12	*L. interrogans* = 3
	n =17	PCR+ = 3	*L. interrogans* = 2
	n =10	PCR+ = 2	*L. interrogans* = 2

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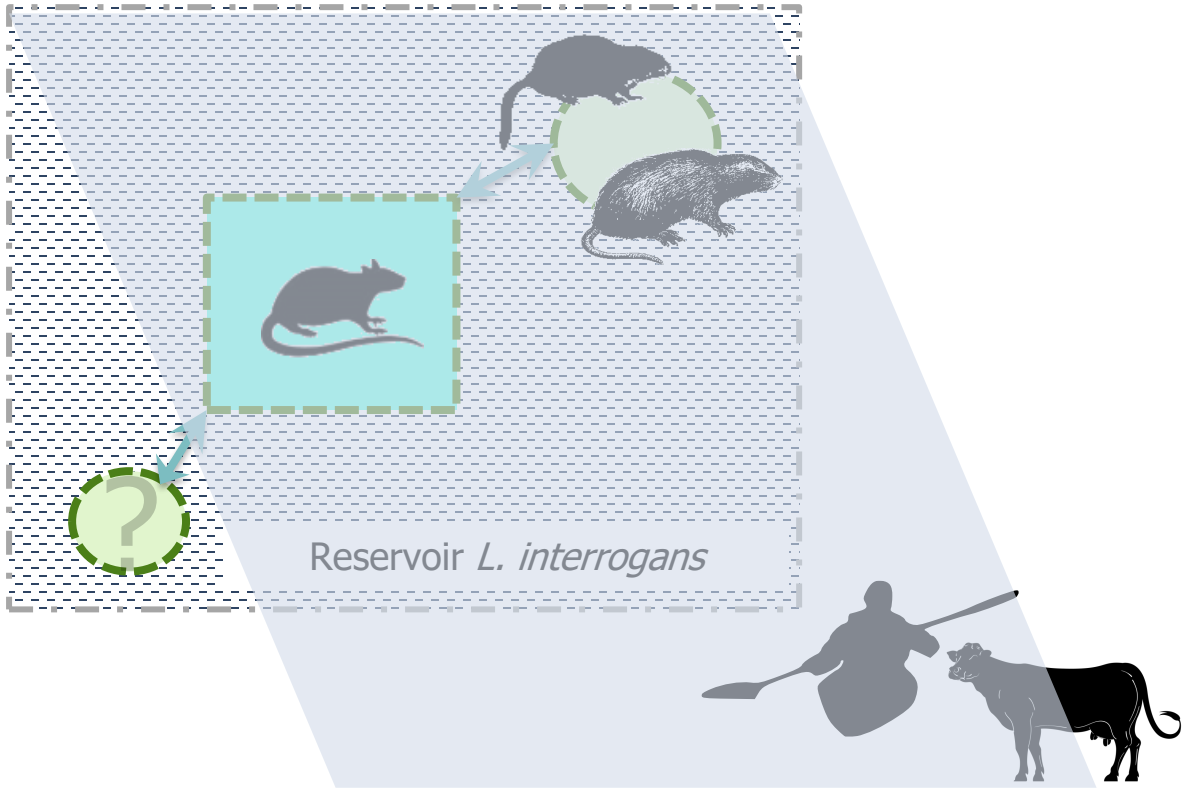
Are rodents responsible for human cases ?

ⓘ Start presenting to display the poll results on this slide.

Conclusions of the investigations

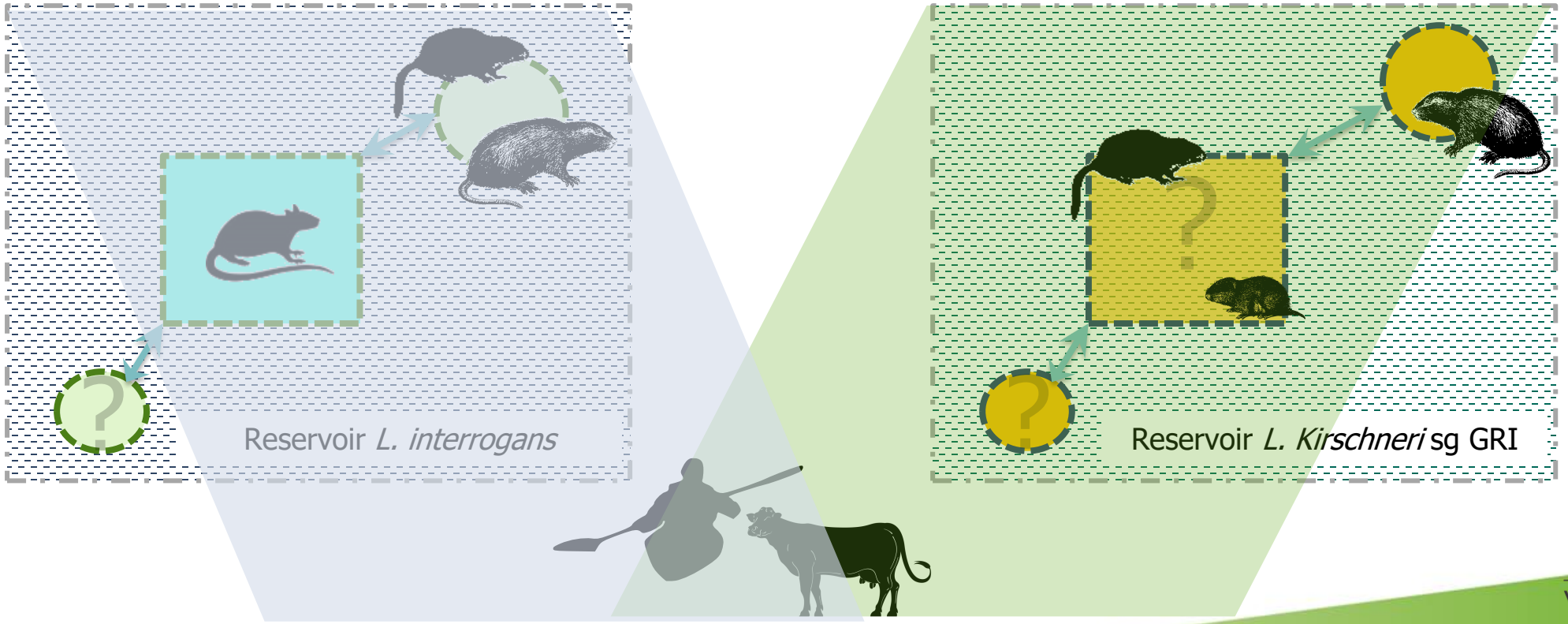
- Unknown *L. interrogans* genotype
- Rodents may have been the reservoirs for humans infected with *L. interrogans*
- Potentially not the only one to contribute to the water contamination



Conclusions of the investigations

- Unknown *L. interrogans* genotype
- Rodents may have been the reservoirs for humans infected with *L. interrogans*
- Potentially not the only one to contribute to the water contamination

- 2016 – 2019, causative bacteria were *L. kirschneri* sg Grippotyphosa (7), *L. interrogans* (1) or unknown (3)
- Cattle was significantly exposed to *Leptospira* sg Grippotyphosa during grazing period
- Cattle was not a *Leptospira* spreader



Take home messages

- Tracking *Leptospira* sources is challenging even with a One Health approach
- Inventory animal populations, check for available data, complete with additional screening and appropriate testing, test for genotype profiles.
- Contribution of the 3 sectors has made it possible to obtain a more complex but also more realistic picture of *Leptospira* epidemiology in a natural ecosystem

Next step : One health workforce was created and maintains its effort to build a local network able to investigate future leptospirosis occurrences according to an eco epidemiological survey

Further reading

Roberts, M.G. and Heesterbeek, J.A.P. (2020) Characterizing reservoirs of infection and the maintenance of pathogens in ecosystems, *Journal of the Royal Society Interface*, 17(162), p. 20190540. https://doi.org/10.1098/rsif.2019.0540.

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Other questions

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