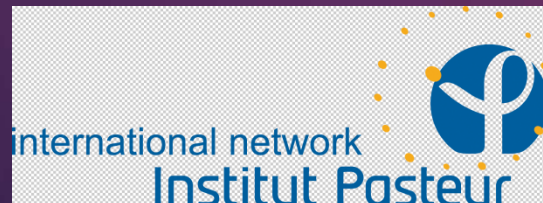


# Multicenter hospital-based case-control study to identify determinants of leptospirosis in the Yangon region (ECOMORE 2)

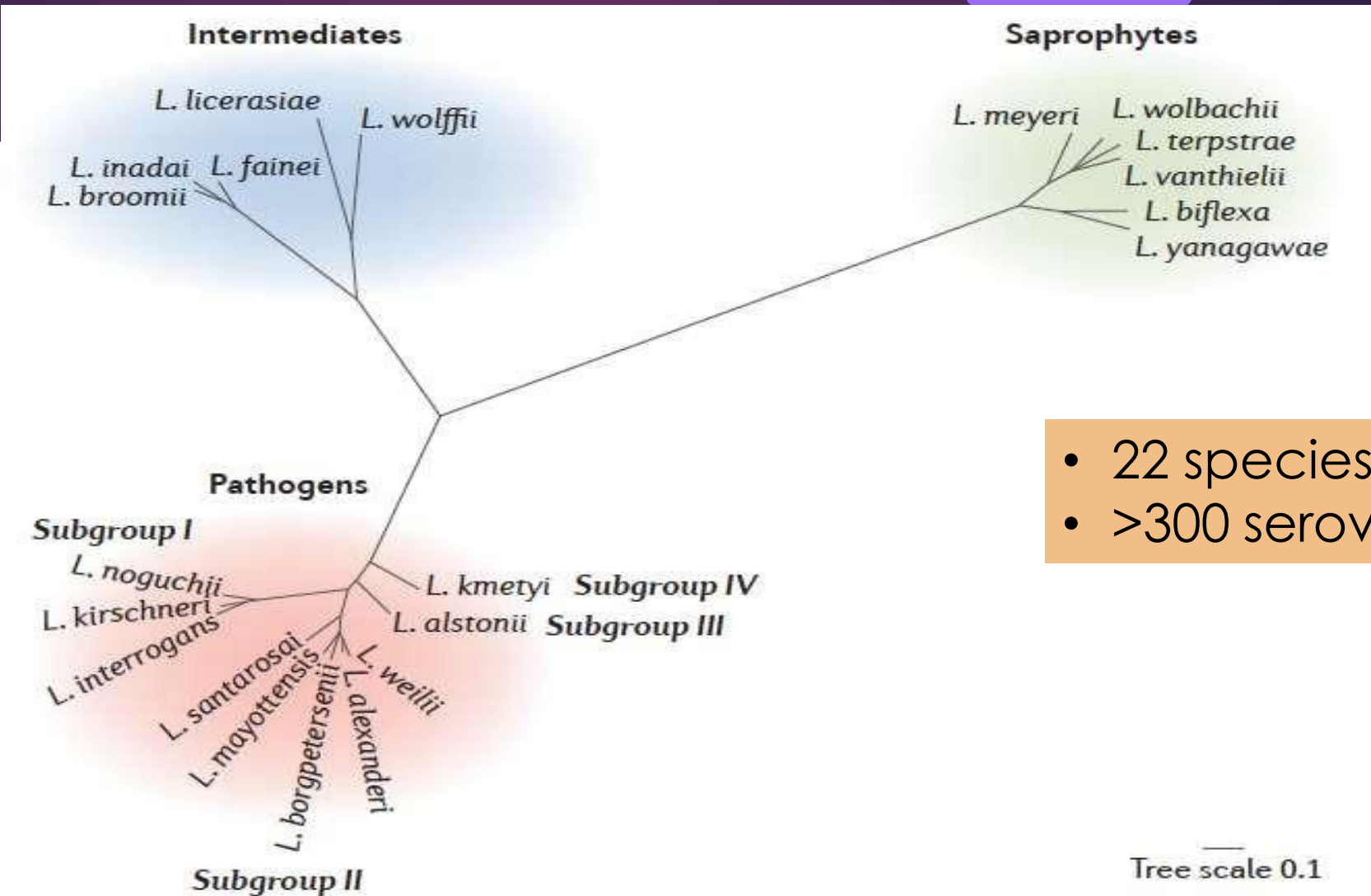


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**CONSULTANT MICROBIOLOGIST**  
**NHL**

# Overall summary of the research

- ▶ **Leptospirosis** - widespread zoonosis disease
- ▶ **Causal organism-** A spirochete bacteria belong to the genus *Leptospira*

# The *Leptospira* genus: a highly heterogeneous group of bacteria



- 22 species
- >300 serovars

Maximum-likelihood phylogenetic tree based on the concatenation of 491 core genes

# Overall summary of the research

- ▶ **MOT: directly from animal to human or indirectly from water contaminated with animal urine.**
- ▶ **Epidemic of infectious disease which can occur after natural disasters pose challenges in terms of diagnosis in emergency situations.**
- ▶ **Leptospirosis outbreaks can be associated with extreme weather events such as heavy rain fall and floods.**
- ▶ **Little is known about leptospirosis magnitude in Myanmar where floods are a priori increasingly frequent.**

# Overall summary of the research

- ▶ One health approach is considered and included in this study.
- ▶ Leptospirosis in Myanmar is suspected to be endemic but remains underdiagnosed.
- ▶ No national surveillance of leptospirosis is performed.
- ▶ NHL only received an average 200 samples per year during the past 6 years.
- ▶ Among 4-22% of these samples were positive for either IgM ELISA or IgG/IgM rapid test (SD).
- ▶ Compared to Sri Lanka, 5000 cases are reported annually.

# Overall summary of the research

## ► Investigators

**PI : Prof: Dr. Htay Htay Tin, Deputy Director General (Labs)**

**Co PI : Dr. Khin Nyein Zan ,Consultant Microbiologist,NHL**

# Overall summary of the research

## ▶ Associated Organizations

1. Institut Pasteur(New Caledonia)
2. Institut Pasteur Du Canbodge (Cambodia)
3. National Institute of Hygiene and Epidemiology (Vietnam)
4. National Health Laboratory (Myanmar)

## ▶ Funded by AFD (French Development Agency)

# Primary Objective

- ▶ **Identify determinants for leptospirosis from laboratory-confirmed human cases in Yangon region, Myanmar.**



# Secondary Objectives

- ▶ To determine an epidemic threshold (alert threshold) for leptospirosis at hospital level.
- ▶ To perform a spatial analysis of the confirmed human cases to investigate which aspects of the landscape and land use patterns are important in the transmission of leptospirosis.
- ▶ To set up the capacity of the NHL to diagnose Leptospirosis (Bacteriology Unit) and help to identify the circulating strains of pathogenic *Leptospira* in the area.
- ▶ To raise awareness and hasten clinical management of leptospirosis cases at hospital level.

# Methodology

## ▶ Period of study

1. 19 months including 2 months pilot period.(August 2018 to Jan 2020)

## ▶ Study population

1. Clinically suspected
2. Admitted to OPD of nine public hospital in Yangon region
3. Living in Yangon region for at least one month
4. Under 5 years old will not be included.

<b>Hospital</b>	<b>Area</b>	<b>No of beds at IPD</b>
<b>Yangon General Hospital</b>	<b>Urban</b>	<b>2000</b>
<b>New Yangon General Hospital</b>	<b>Urban</b>	<b>200</b>
<b>East Yangon Hospital</b>	<b>Urban</b>	<b>200</b>
<b>West Yangon General Hospital</b>	<b>Urban</b>	<b>200</b>
<b>Yankin Children Hospital</b>	<b>Urban</b>	<b>550</b>
<b>North Okkalapa Teaching and General Hospital</b>	<b>Peri-urban</b>	<b>800</b>
<b>Thingangyun Sanpya General Hospital</b>	<b>Peri-urban</b>	<b>500</b>
<b>Insein General Hospital</b>	<b>Peri-urban</b>	<b>500</b>
<b>Thanlyin Hospital</b>	<b>Peri-urban</b>	<b>200</b>

# Methodology

- ▶ **Sample size**
  - ▶ Case to control ratio 1:2
  - ▶ 280 laboratory-confirmed cases are required.
  - ▶ 560 control cases.

# Methodology

## ▶ Inclusion Criteria

1. Patients admitted to Outpatient Departments in the nine selected public hospitals,
2. Aged five years old or more,
3. Living in Yangon region for one month at least before recruitment,
4. Presenting a clinical **score of 12 or above** for part A (Modified Faine's Criteria ) at the screening interview
5. The patient or the accompanying person gives a written informed consent.

## ▶ Exclusion Criteria

1. When the patient is critically ill and the accompanying persons are unable to provide answer for screening interview at OPD.

# WHO guidelines, Modified Faine's Criteria - part A - (with amendment) 2012 used for screening patients

<b>Part A: Clinical data</b>	<b>Score</b>
<b>Headache of sudden onset</b>	<b>2</b>
<b>Fever or history of fever over the past 48 hours</b>	<b>2</b>
<b>    If fever, body temperature is 39°C or over</b>	<b>2</b>
<b>Conjunctival suffusion (bilateral)</b>	<b>4</b>
<b>Meningism</b>	<b>4</b>
<b>Myalgia (especially calf muscles)</b>	<b>4</b>
<b>Jaundice</b>	<b>1</b>
<b>Albuminuria or nitrogen retention - To be done only for patient scoring 10 or 11 for all the other criteria</b>	<b>2</b>
<b>Haemoptysis / dyspnoea</b>	<b>2</b>

# Methodology

- ▶ **A confirmed case**

- ▶ **A suspected case with DNA from pathogenic *Leptospira* species detected by q-PCR into the acute-phase sample**

**Or**

- ▶ **A suspected case showing a seroconversion between the two consecutive anti-leptospiral IgM ELISA reaction on acute- and convalescent-phase samples**

**Or**

- ▶ **A probable case showing an increase in titer between the two consecutive anti-leptospiral IgM ELISA reaction on acute- and convalescent-phase samples**

# Methodology

- ▶ **A negative case**
  - ▶ **A suspected case showing a negative PCR and**
  - ▶ **A double negative result at the two consecutive anti-leptospiral IgM ELISA reaction on acute- and convalescent-phase samples.**



# Methodology

- ▶ **A control case**

- ▶ **A suspected, non probable and non confirmed case, matched to a confirmed case on the following variables:**

- 1. the age range: plus or minus five years,**
- 2. the OPD of recruitment and,**
- 3. the week of consultation.**

# Methodology

- ▶ **Analysis algorithm**

# Clinical suspicion of Leptospirosis

Faine's modified Score (part A)  $\geq 12$  at OPD

Written informed consent

**Suspected Case**

1<sup>st</sup> sample collection at OPD

d0: 1 plain tube (4ml)

2<sup>nd</sup> sample collection at the patient household

d10-14: 1 plain tube (4ml)

## ① Rt-PCR

PCR positive

**Confirmed case**

PCR negative

DNA Positive extracts

Genotyping

Identification of serogroup (IPNC external support)

Right after

## ② Anti-leptospiral IgM ELISA

1<sup>st</sup> IgM ELISA positive

**Probable case**

1<sup>st</sup> IgM ELISA negative

2<sup>nd</sup> IgM ELISA positive

Titer increase

**Confirmed case**

2<sup>nd</sup> IgM ELISA positive

Titer  $\leq$

**Probable case**

2<sup>nd</sup> IgM ELISA positive

**Confirmed case**

2<sup>nd</sup> IgM ELISA negative

**Negative case**

MAT on ELISA positive sera

Identification of serogroup (IPNC external support)

external support)



# Methodology

## ▶ **Statistical methods**

1. Epi-Data for data entry
2. STATA or R software for statistical analysis.

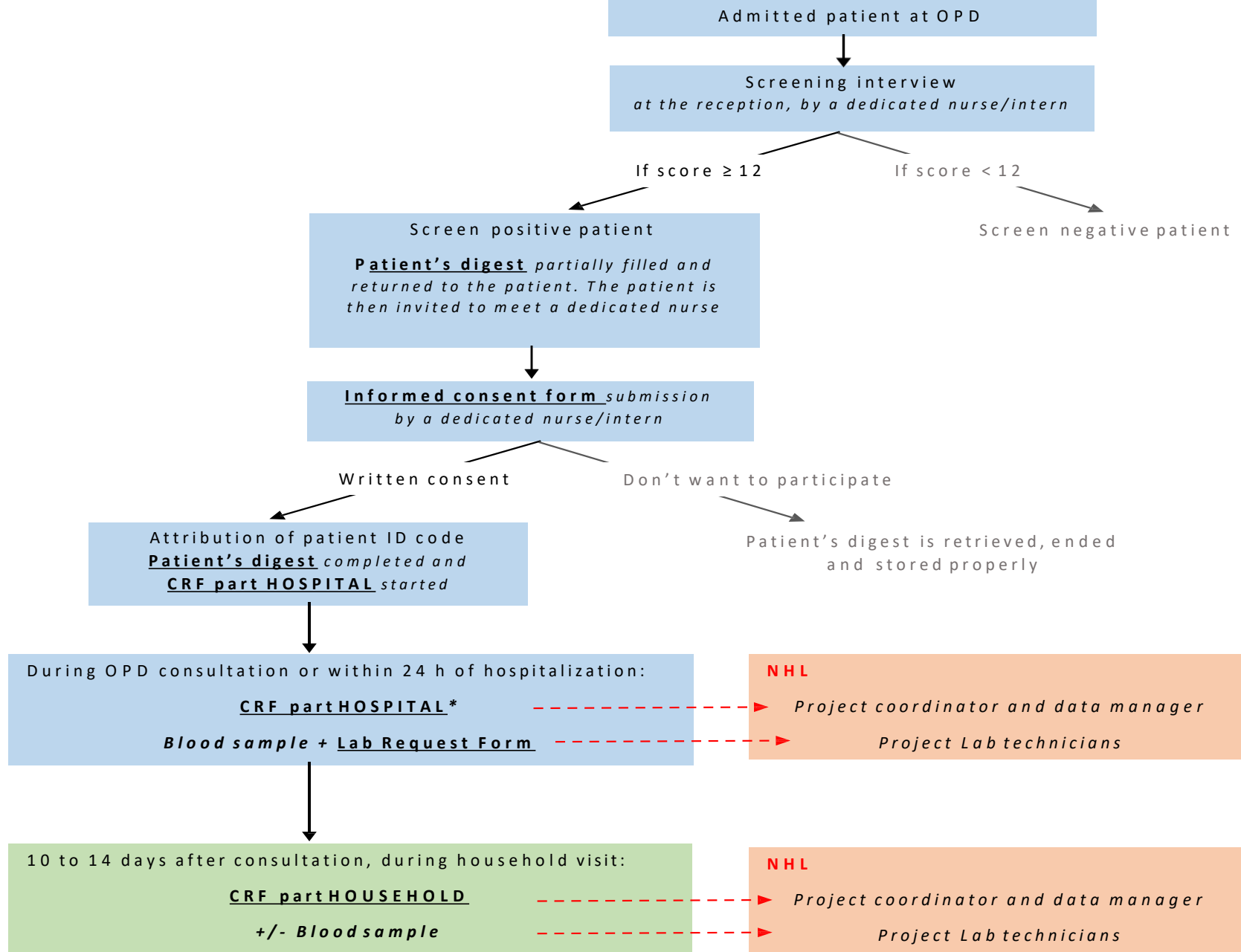
# Methodology

## ▶ Ethical approval

1. National legislation of Myanmar
2. International regulations
3. French regulations

# Methodology

- ▶ Procedure (data and sample work flow)



Legend:

\* Associated with the corresponding *informed consent form* and *patient's digest*

Hospital level

NHL level

Household level

# Data collection instruments

- ▶ Patient's Digest
- ▶ Consent Form
- ▶ Case Report Form Part 1 (Hospital)
- ▶ Case Report Form Part 2 (Household)
- ▶ 1<sup>st</sup> time blood taking
- ▶ 2<sup>nd</sup> time blood taking



# Data collection instruments

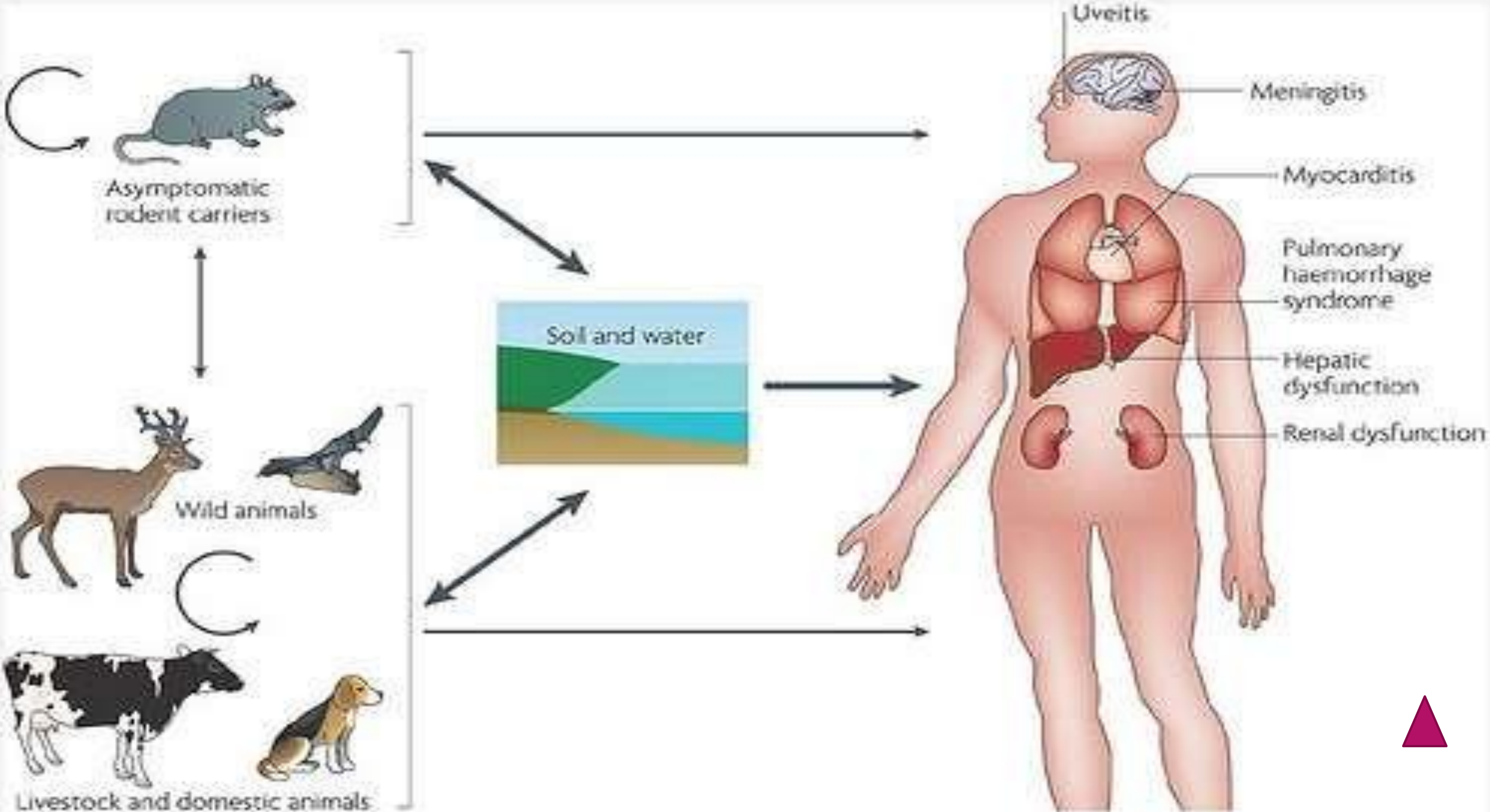
- ▶ OPD staff will be in charge of the first interview
- ▶ Coordinators will be in charge of the second interview at the patient's household.
- ▶ All interviewers will be trained prior to the pilot period.
- ▶ Geospatial and meteorological data will be collected by project data managers

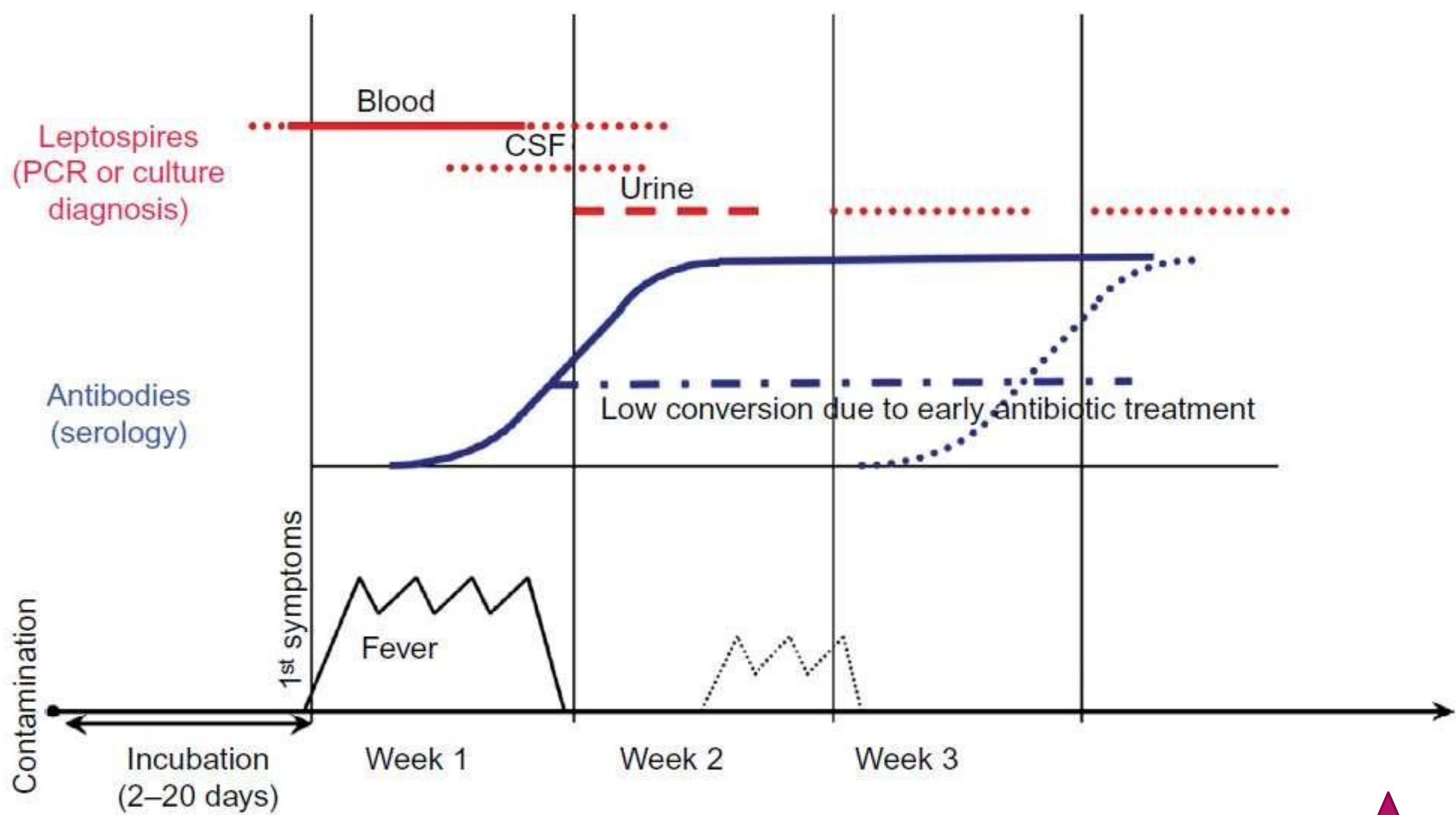
# Results and expected outcomes

- ▶ Results will be published in 2020.
- ▶ Aims at raising awareness on leptospirosis: increase suspicion, early treatment and lab testing, identify the circulating pathogenic strains and so on.
- ▶ And also aims to initiate relevant and sustainable surveillance system in the near future.

# Feedback to the hospital

- ▶ 1<sup>st</sup> time lab: results
- ▶ 2<sup>nd</sup> time lab: results





**Figure 3** Basic principles underlying the biological diagnosis of leptospirosis.

**Notes:** Adapted from Turner. Leptospirosis I. *Trans R Soc Trop Med Hyg.* 1967;61(6):842–855,<sup>124</sup> by permission of Oxford University Press.

**Abbreviations:** PCR, polymerase chain reaction; CSF, cerebrospinal fluid.

The background of the slide is a dark purple gradient. It features several large, semi-transparent purple circles of varying sizes. A vertical pink rectangle is positioned in the top right corner. The text "Thank you." is centered in a white, sans-serif font.

**Thank you.**

**Question and Answer.**