Leptospirosis associated AKI: Clinical Challenges and Public Health Perspectives

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- I have no conflicts of interest which relate to my presentation

TABLE 1 Specific causes of acute kidney injury in the tropics

Tropical infection	Toxins	Environment

Bacterial infection
• Leptospirosis
• Rickettsial disease
• Enteric fever: salmonellosis, shigellosis
• Melioidosis
	Animal toxins
	• Snake envenomation
	• Arthropods
	  ○ Bee, wasp, hornet sting
	  ○ Caterpillars
	  ○ Spider bite
	  ○ Scorpion sting
	• Jellyfish sting
		Heat stroke

Viral infection • Dengue virus • Hantavirus • Chikungunya virus	Plant toxins • Djenkol beans • Starfruit • Mushroom • Marking nut	Chemical • Paraquat • Ethylene glycol • Ethylene dibromide • Copper sulfate • Chromic acid • Formic acid
Parasitic infection • Malaria • Filariasis • Leishmaniasis	Herbs • Impila food plants • Carp gallbladder or bile	Miscellaneous • Natural disasters • Obstetric complications

Specific Etiologies of CA-AKI

NEPHROLOGY

REVIEW ARTICLE

NEPHROLOGY WILEY

Acute kidney injury in the tropics

Prit Kusirisin[1,2,3,4] | Geraldo Bezerra da Silva Junior[5,6] | Visith Sitprija[1,7] | Nattachai Srisawat[1,2,3,8]

Kusirisin et al, Nephrology. 2022;1–16.

Ryokichi Inada (1874–1950)

THE ETIOLOGY, MODE OF INFECTION, AND SPECIFIC THERAPY OF WEIL'S DISEASE (SPIROCHÆTOSIS ICTEROHÆMORRHAGICA).

By RYOKICHI INADA, M.D., YUTAKA IDO, M.D., ROKURO HOKI, M.D., RENJIRO KANEKO, M.D., and HIROSHI ITO, M.D.

(*From the First Medical Clinic of the Imperial University in Kyushu, Fukuoka.*)

Plates 56 to 62.

(Received for publication, December 1, 1915.)

INTRODUCTION.

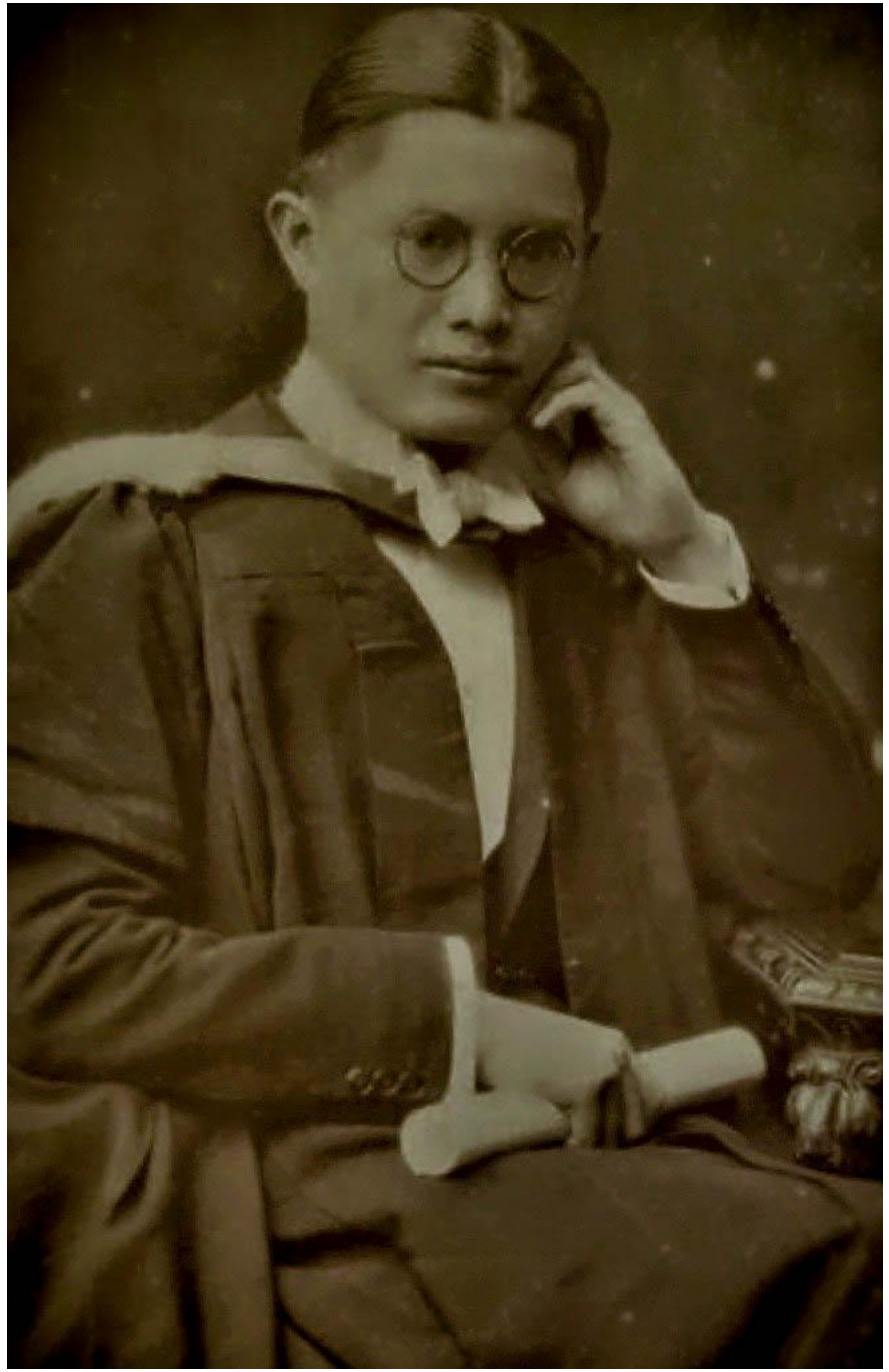
In this communication we have summarized and in some details extended the publications on this subject which have appeared in the Japanese literature.[1] In the course of our investigations of that endemic disease of portions of Japan, which agrees clinically with Weil's disease, so called, we discovered a spirochætal microorganism which is now believed to be the cause of the disease. In the experiments

The first isolation of Leptospira in 1916. In Japan, where Weil's disease was common in coal miners, injected guinea-pigs intraperitoneally with the blood of Weil's disease patients and succeeded in reproducing typical, acute leptospirosis in the animals

observed in Chiba, in the eastern part of Japan, near Tokyo, where the patients numbered 178. Thus this disease appears to be prevalent in various parts of Japan, although to a small extent.

We have been interested in Weil's disease in Kyushu for many years, and at the end of November, 1914, we detected a spirochæta in the liver of a guinea pig injected with the blood of a patient suffering from Weil's disease. We came to the conclusion, in January, 1915, that this spirochæta is the pathogenic cause of Weil's disease, and we named it *Spirochæta icterohæmorrhagiæ*. At Chiba, a distance of more than 700 miles from Kyushu, we detected in the blood of five out of

[1] A full bibliography is appended.



Jai Yunibandhu

First report of Weil's disease in Thailand. (1942)
J Med Assoc Thai 1943; 26: 83-139

Professor Emeritus Visith Sitprija

Renal Involvement in Human Leptospirosis

VISITH SITPRIJA,* M.D., PH.D.

Brit. med. J. 1968, **2**, 656–658

Renal involvement is common in leptospirosis. Azotaemia and proteinuria with abnormal urinary sediment are frequently noted. While definite pathological changes of acute tubular necrosis and interstitial nephritis have been described (Gsell, 1952, Areán, 1962), it has been stated that temporary azotaemia and oliguria may occur in the absence of significant renal damage (Edwards, 1959). Clinical improvement after intravenous fluid administration, along with the increase in urinary output, suggests that azotaemia is secondary to deficiency in volume. In one report the decreased renal function was mentioned (Cora, 1956). The glomerular filtration rate was markedly reduced, and the excretion of para-aminohippurate (P.A.H.) was almost negligible. Because of the discrepancy in the clinical data this investigation was undertaken to clarify the clinical patterns of renal function disturbances encountered in leptospirosis.

Materials and Methods

A study was made of 10 patients aged from 24 to 63 years, with leptospirosis proved by haemoculture or serology, whose blood urea nitrogen was over 40 mg./100 ml. Eight were males and two were females. In all cases the causative micro-organisms were *Leptospira bataviae*. They were admitted to hospital on the fifth to the seventh day of illness. Immediately after admission the blood volume was measured by the summation method with both ^{131}I-labelled albumin and ^{51}Cr-tagged red blood cells (Moore *et al.*, 1963). Endogenous creatinine and P.A.H. clearances were ascertained by the standard technique (Smith, 1956) before antibiotic therapy. Blood chemistry, including blood urea nitrogen (B.U.N.), serum creatinine, electrolytes, and osmolality, was determined every other day until the return to normal. Urinalysis was performed at two-day intervals until no abnormal finding was noted. Twenty-four-hour urine was collected on alternate days for determination of urea nitrogen, creatinine, sodium, and osmolality.

* Senior Lecturer in Medicine, Chulalongkorn Hospital Medical School, Bangkok, Thailand.

Results

Clinical Observations.—Body temperature ranged from 37.3 to 39.2° C., and usually subsided three to four days after penicillin administration. All patients had stable vital signs. Jaundice was present in five patients whose total bilirubin varied from 5 to 24 mg./100 ml. The liver-function test showed only a minimal degree of parenchymal hepatic damage. The patients are classified into two groups according to the serum creatinine. Group 1 comprises five patients with levels above 2 mg./100 ml.; the other five (group 2) had levels below 2 mg./100 ml. The pertinent clinical data are shown in Table I.

Blood Chemistry.—Serum sodium and potassium were within normal limits. Six patients had a CO_2 content below 20 mEq/l., probably indicating metabolic acidosis. Five of these patients were in group 1. The average B.U.N. and creatinine in group 1 were 105.2 and 4.9 mg./100 ml. respectively, in contrast with the values of 54.2 and 1.6 mg. in group 2 (Table I). The association between jaundice and impaired renal function was striking in group 1, and this might reflect the more severe form of infection. The elevated B.U.N. and creatinine returned to normal within 7 to 10 days in group 1 and within 24 to 48 hours in group 2.

Urinary Output and Sediment.—The urine volume on the first hospital day ranged from 180 to 890 ml./24 hours, with an average of 485 ml., in group 1. There was only a slight increase in urine flow after fluid load during the clearance study. In group 2 the urinary output varied from 235 to 700 ml./24 hours, with a mean of 463 ml. (Table I). After

Professor Chih-Wei Yang

Leptospiral Outer Membrane Protein Induces Extracellular Matrix Accumulation through a TGF-β1/Smad-Dependent Pathway

Ya-Chung Tian,* Yung-Chang Chen,* Cheng-Chieh Hung,* Chiz-Tzung Chang,* Mai-Szu Wu,* Aled O. Phillips,† Chih-Wei Yang*

*Kidney Institute, Department of Nephrology, Chang Gung Memorial Hospital, Taipei, and Chang Gung University, Tao Yuan, Taiwan; and †Institute of Nephrology, Cardiff University, Wales, United Kingdom

Leptospirosis is an underestimated cause of renal failure in Taiwan and elsewhere. The consequence of leptospira-induced acute tubulointerstitial nephritis is tubulointerstitial fibrosis if left untreated. The aim of the study was to examine the effect of an outer membrane protein (OMP) of *Leptospira santarosai* serovar Shermani on extracellular matrix (ECM) accumulation in proximal tubular cells, HK-2 cells. The addition of *Leptospira santarosai* serovar Shermani OMP for 72 h led to an increase of type I and type IV collagens, measured by real-time PCR and Western blot analysis in a dose-response manner. After addition of *Leptospira santarosai* serovar Shermani OMP, active TGF-β1 secretion was increased by nearly two-fold. The addition of anti–TGF-β1–neutralizing antibodies attenuated the *Leptospira santarosai* serovar Shermani OMP–induced type I and type IV collagen production, implicating TGF-β1 in this process. Overexpression of the dominant negative Smad3 prevented the *Leptospira santarosai* serovar Shermani OMP–induced increase of type I or type IV collagen production. In conclusion, this study clearly demonstrated the stimulatory effect of *Leptospira santarosai* serovar Shermani OMP on ECM production by enhancing ECM synthesis, which was mediated by a TGF-β1/Smad-dependent pathway.

J Am Soc Nephrol 17: 2792–2798, 2006. doi: 10.1681/ASN.2006020159

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Review Article

Leptospirosis kidney disease: Evolution from acute to chronic kidney disea

Li-Fang Chou [a,d], Huang-Yu Yang
Ya-Chung Tian [a,b,c], Shen-Hsing H

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Biochemistry, Chang Gung University, Taoyuan, Tai

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Cellular senescence links severe *Leptospira* infection to chronic kidney disease progression

Shen-Hsing Hsu [a,b,c,*], Yi-Chun Liu [a,c], Li-Fang Chou [a,c], Chien Li [a], Ming-Yang Chang [a,c], Ya-Chung Tian [a,c], Huang-Yu Yang [a,c], Chih-Wei Yang [a,c,d,*]

[a] Kidney Research Center, Chang Gung Memorial Hospital, Taoyuan, Taiwan
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[c] Department of Nephrology, Chang Gung Memorial Hospital, Linkou, Taoyuan, Taiwan
[d] College of Medicine, Chang Gung University, Taoyuan, Taiwan

Global incidence of leptospirosis --> 5 cases per 100,000 population

Table 2 Selected regions, districts, and provinces with a high human leptospirosis incidence[a]

Region/district/province	Country	Annual incidence per million population
Andaman Islands	India	500
Loei	Thailand	467.8
Guadeloupe	France	311.9
Roi Et	Thailand	299.3
North Queensland	Australia	288
Khon Kaen	Thailand	286.4
Kalasin	Thailand	286
Lampang	Thailand	269.3
Pollonaruwa	Sri Lanka	247.2
Surin	Thailand	240
Matale	Sri Lanka	236
Kegalle	Sri Lanka	228.2
Matara	Sri Lanka	215
Kalutara	Sri Lanka	200
Brunca	Costa Rica	171
French Polynesia	France	105.8
Azores	Portugal	83
New Caledonia	France	59.3

[a] Data as indicated in the text. Data for Andaman Islands are from an International Leptospirosis Society Survey, available at: http://www.leptonet.net/html/ils_worldwide_survey.asp.

Thailand, the prevalence of leptospirosis was estimated at 5-10 cases per 100,000 population --> 24.7-46.7 per 100,000 population (high endemic area)

Tropic of Cancer

Tropics

Equator

Mortality rate at 0.8-1 % --> 15-30% (high endemic area)
30% of leptospirosis admission cases are severe and contain mortality upto 40%

Tropic of Capricorn

Hinjoy S. Epidemiology of Leptospirosis from Thai National Disease Surveillance System, 2003–2012. OSIR 2014; 7(36): 1–5.
WHO. Report of the second meeting of the leptospirosis burden epidemiology reference group. Geneva: World Health Organization; 2011
Anual epidemiology surveillance report 2013: Leptospirosis [Internet]. Department of Disease Control, Thailand. 2013-2015

World Leptospirosis Incidence

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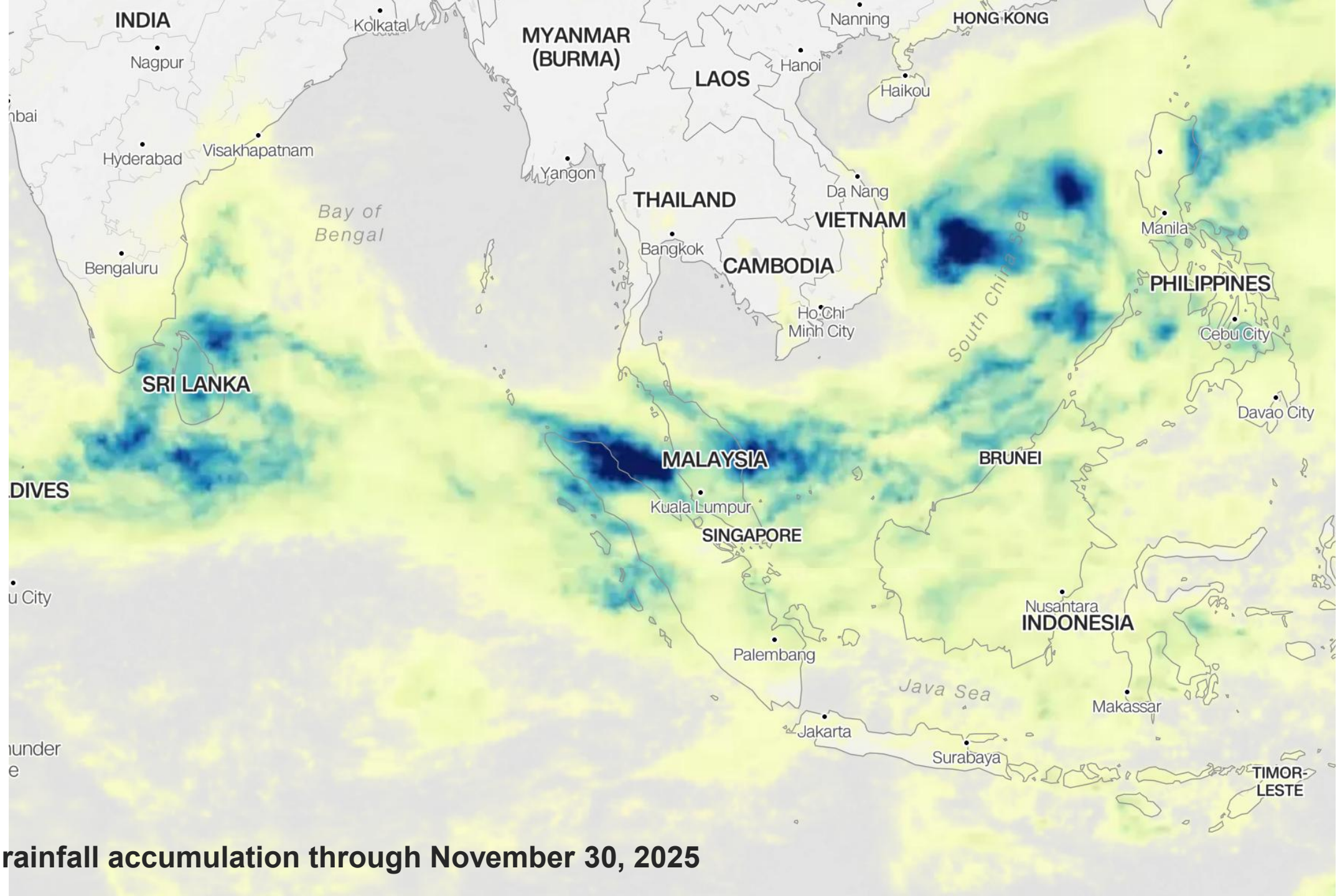
Lampang	Thailand	269.3
Pollonaruwa	Sri Lanka	247.2
Surin	Thailand	240
Matale	Sri Lanka	236
Kegalle	Sri Lanka	228.2
Matara	Sri Lanka	215
Kalutara	Sri Lanka	200
Brunca	Costa Rica	171
French Polynesia	France	105.8
Azores	Portugal	83
New Caledonia	France	59.3

[a] Data as indicated in the text. Data for Andaman Islands are from an International Leptospirosis Society Survey, available at: http://www.leptonet.net/html/ils_worldwide_survey.asp.

First 10 regions of world leptospirosis incidence
Rural part of Thailand, Srilanka, India, French polynesia

Pappas et al, Int J Infect Dis 2008; 12: 351



7-day rainfall accumulation through November 30, 2025

Hat Yai, a major transport and trade hub in Thailand's Songkhla province, saw floodwaters as high as eight feet surge through its streets.

A drone view shows cars parked in a flooded area in Hat Yai district, in Songkhla province, Thailand, November 25. *REUTERS/Tannarin Suchipong*

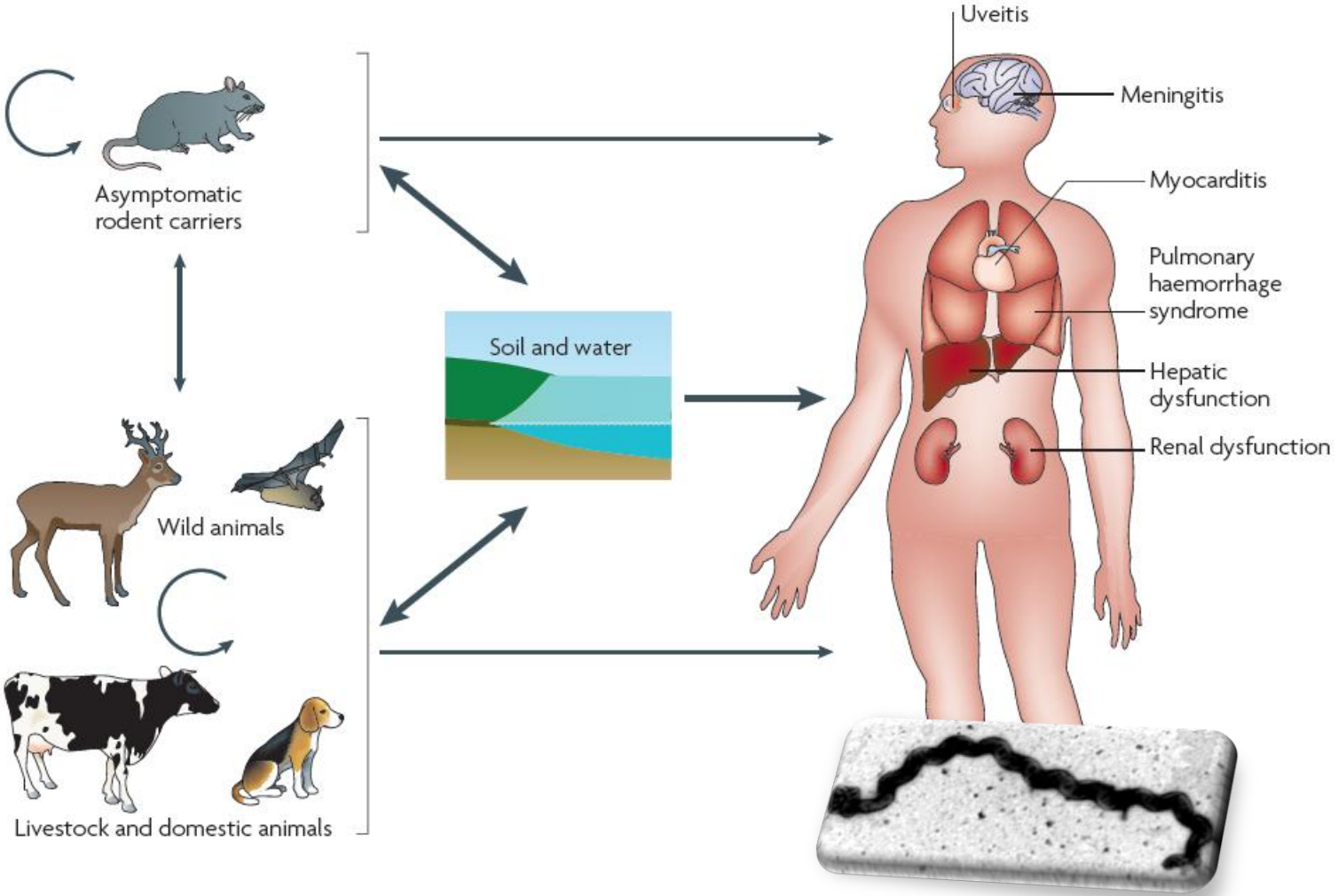

LEO
แอร์ AI
30%
สงขลา
SONGKHLA


แอร์ รถยนต์


RESCUE

Pathogenesis

- Poorly understood
- Incubation period 7-14 days, disseminate to different organs
- Gram negative bacteria, with helical shape



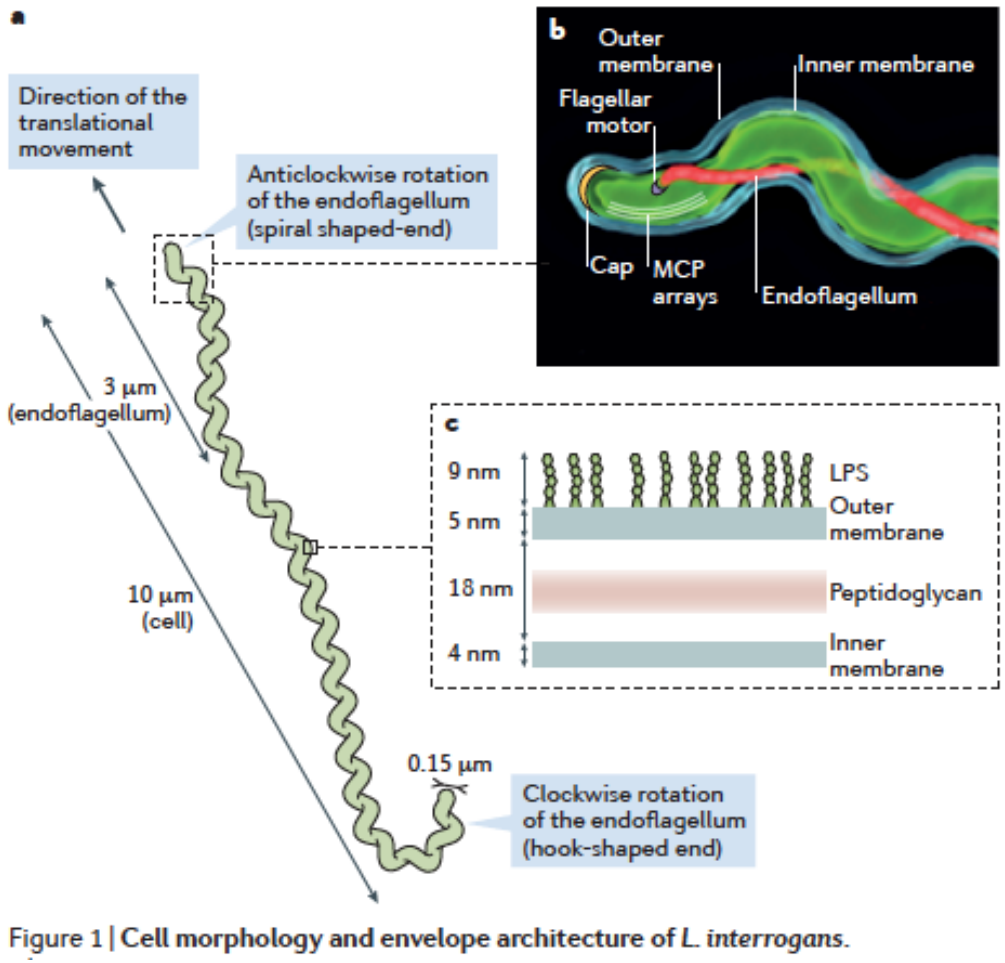


Figure 1 | **Cell morphology and envelope architecture of *L. interrogans*.**

Clinical manifestation of Leptospirosis

Mild influenza-like illness

85-90%

Weil syndrome

5-10%

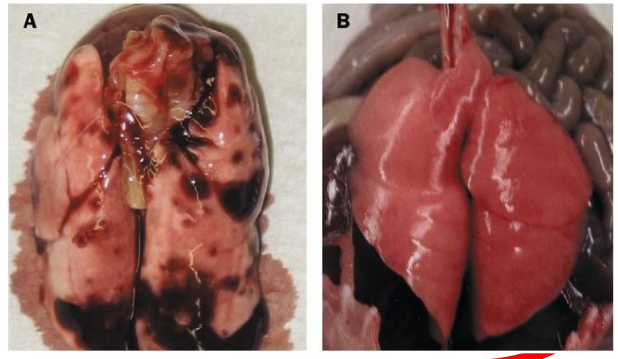
No good biomarkers to predict severe leptospirosis

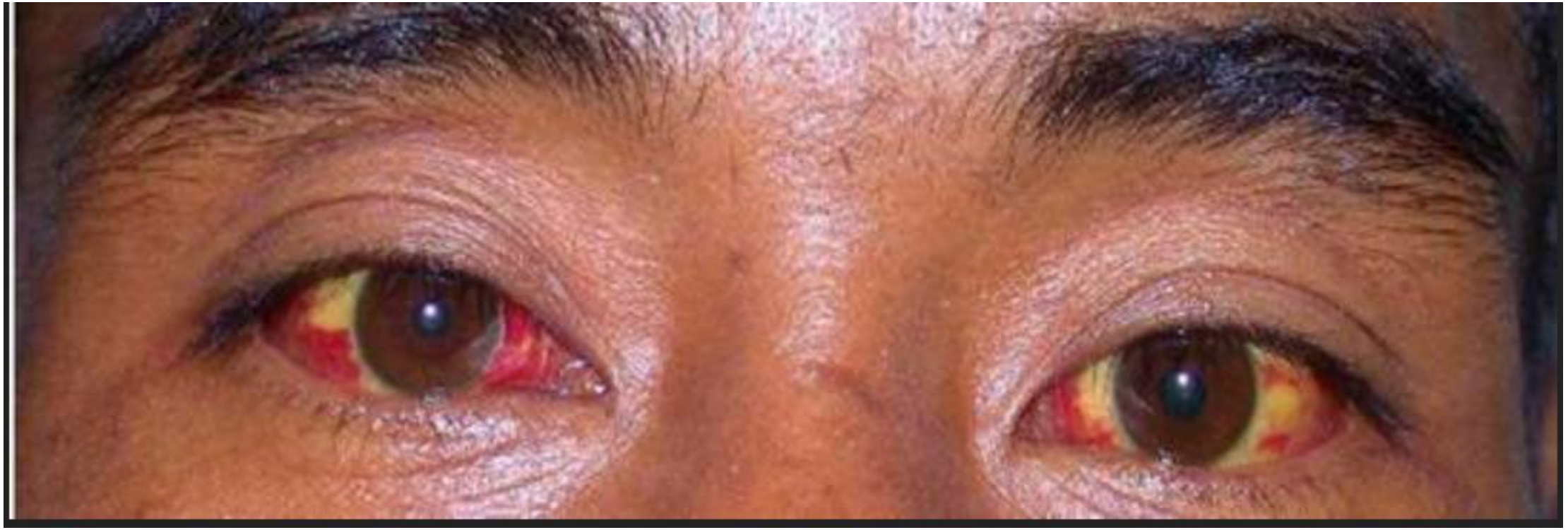
Meningoencepahalitis

Acute Kidney Injury

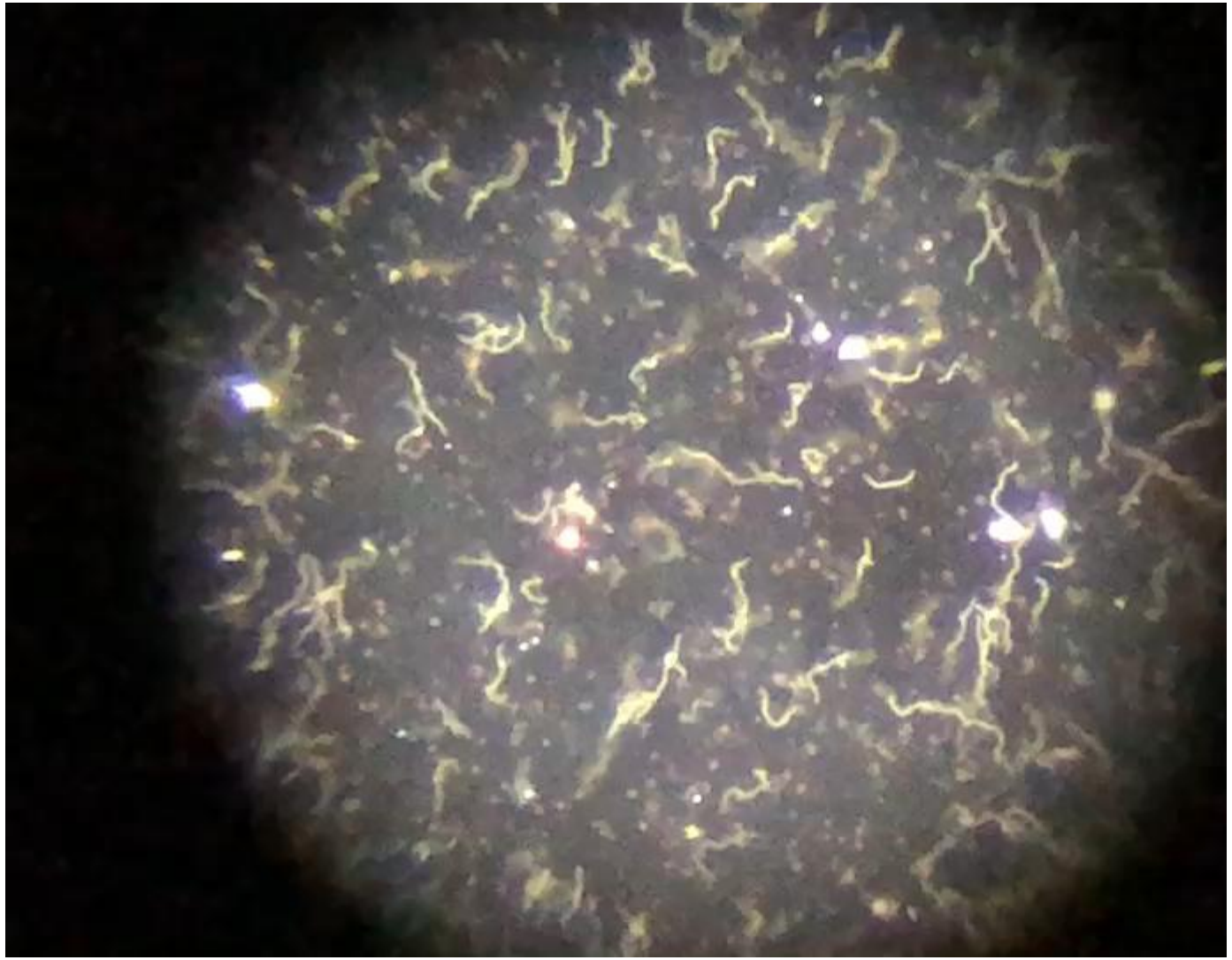
Acute Liver Failure

Pulmonary hemorrhage





Conjunctival suffusion/hemorrhage



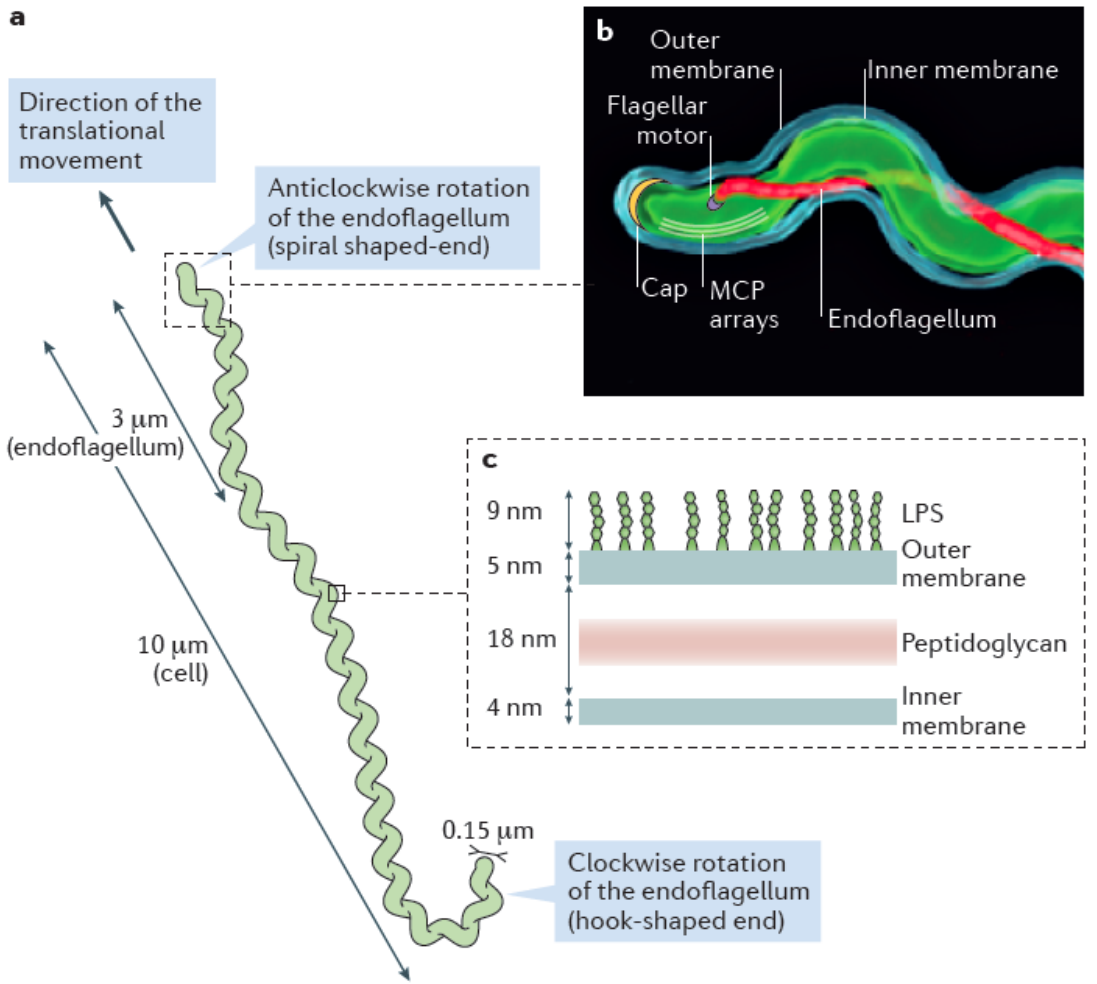
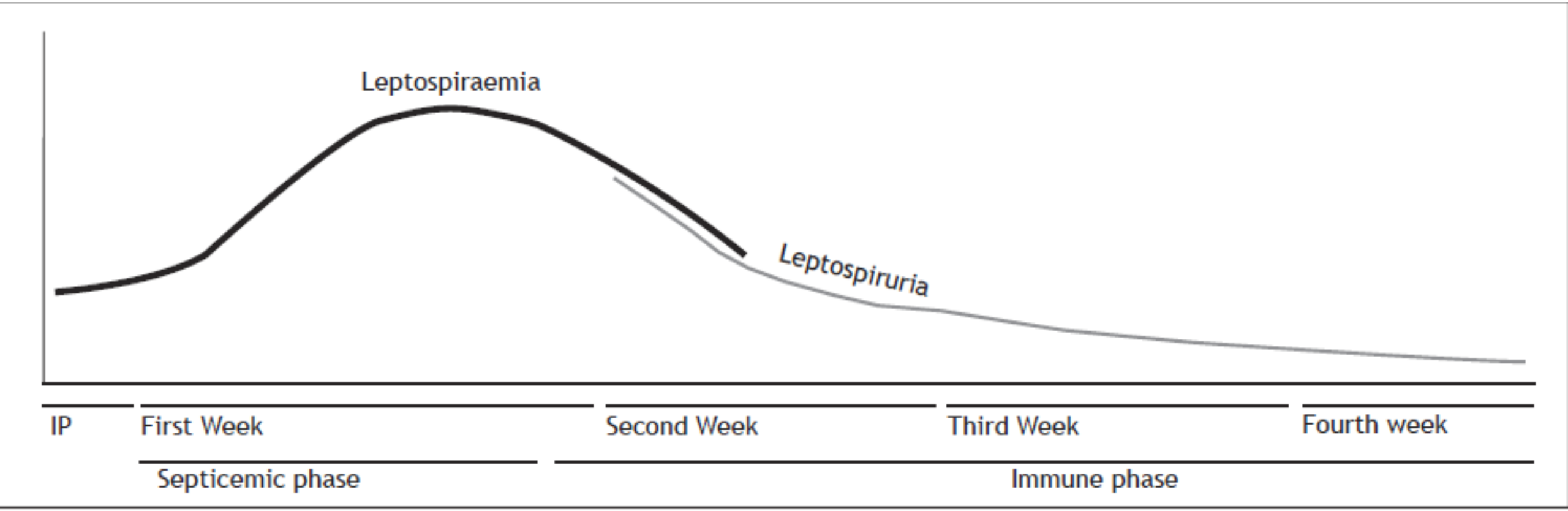


Figure 1 | **Cell morphology and envelope architecture of *L. interrogans*.**

Different stage of leptospirosis



Detection with culture, PCR, Leptospirosis Antigen (not available)

Detection with Antibody (IgM, IgG)

Rapid test

Kusirisin et al, Nephrology. 2022;1–16.

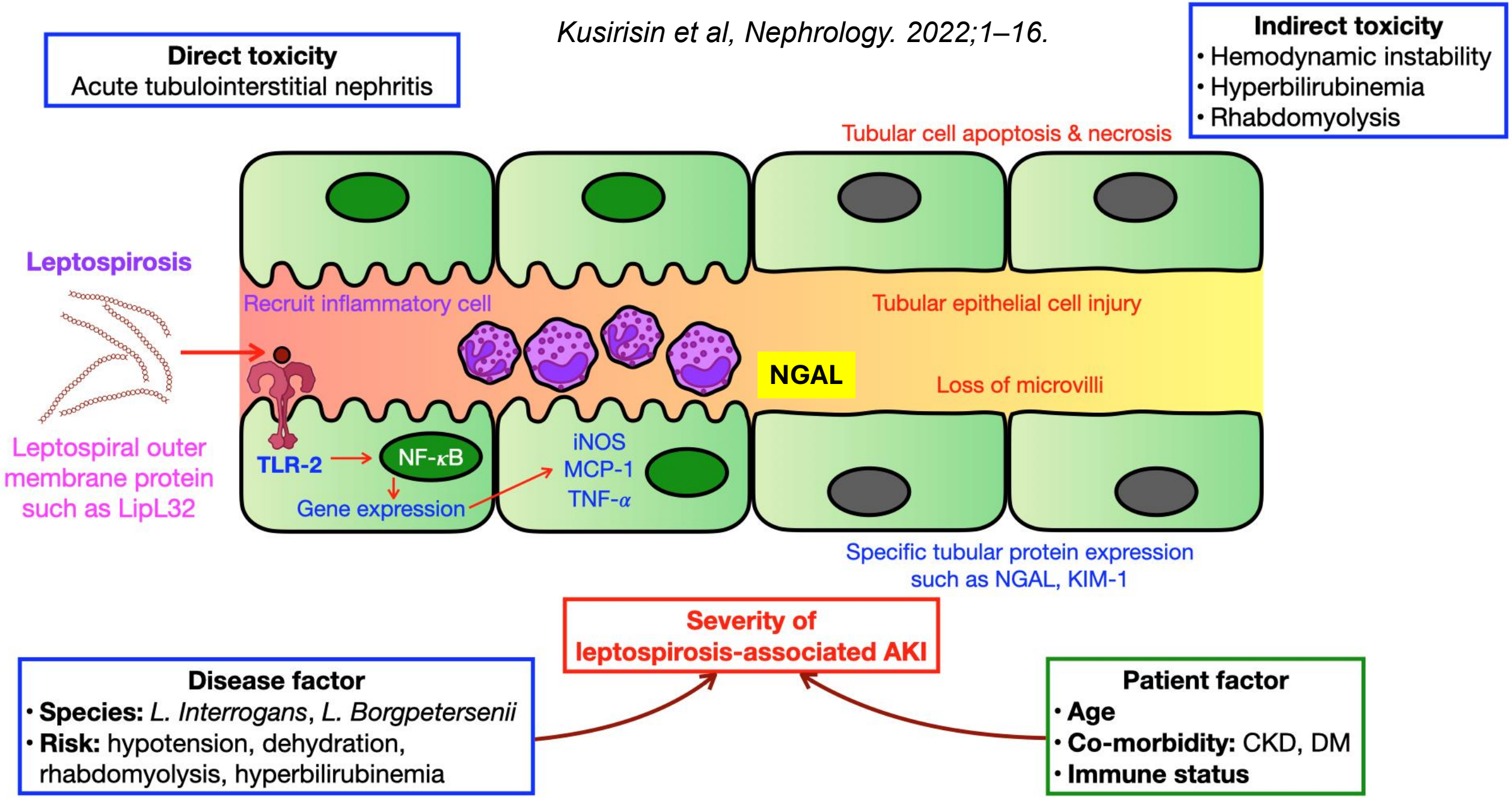
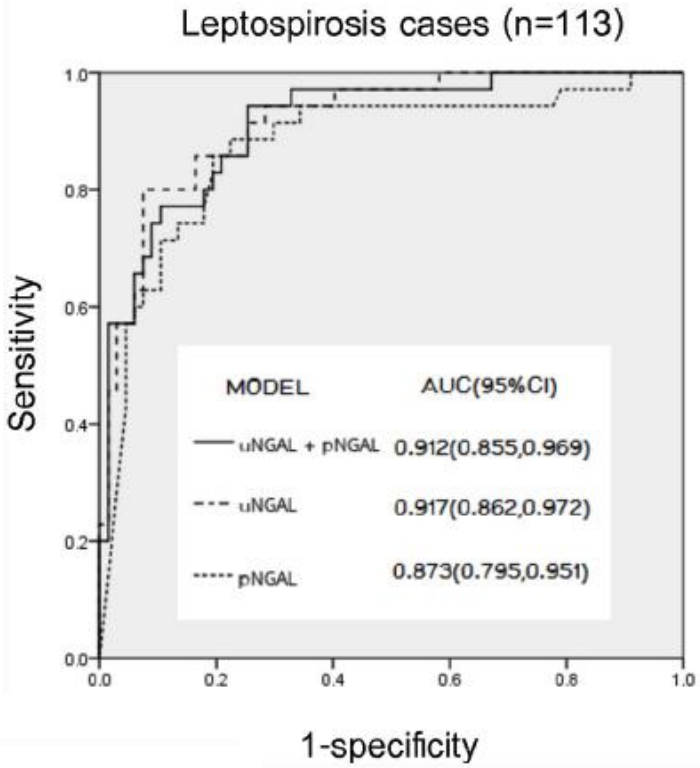


Fig. 1 Pathogenesis of leptospirosis-associated AKI

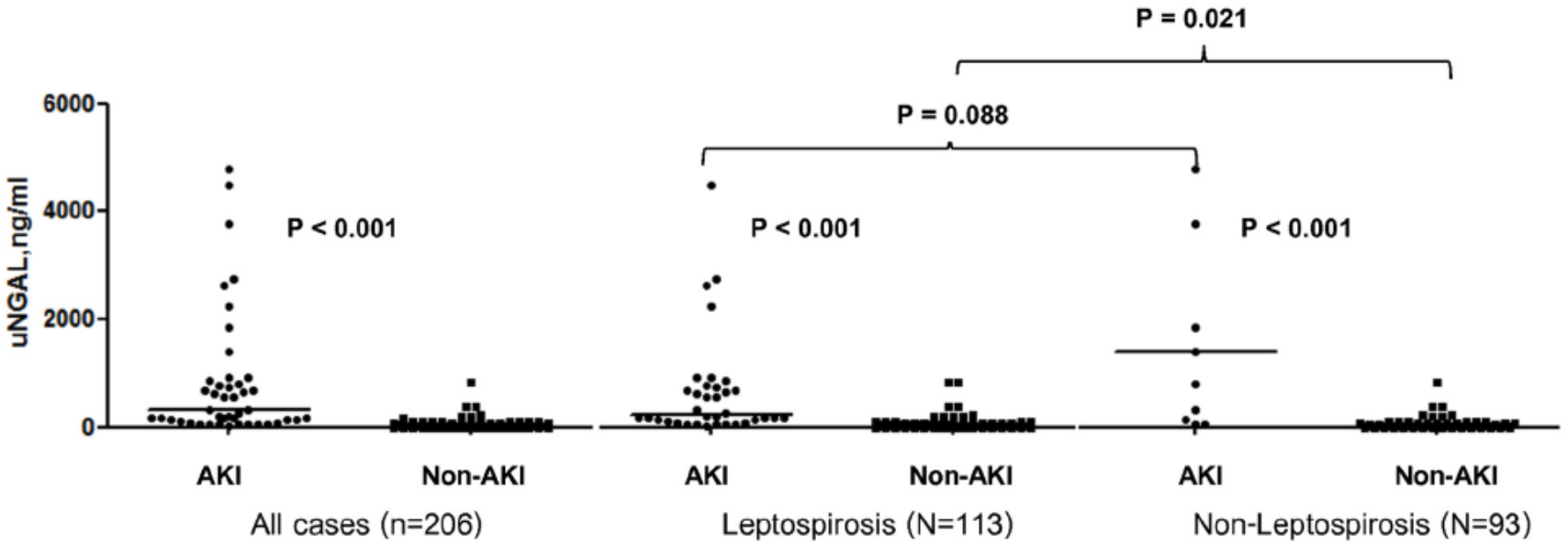
RESEARCH ARTICLE

Neutrophil Gelatinase Associated Lipocalin (NGAL) in Leptospirosis Acute Kidney Injury: A Multicenter Study in Thailand

Nattachai Srisawat[1,2]*, Kearkiat Praditpornsilpa[1], Kanitha Patarakul[3], Malee Techapornrung[4], Tinnapop Daraswang[5], Theerapon Sukmark[6], Kamol Khositrangsikun[7], Apinya Fakthongyoo[8], Petchdee Oranrigsupak[9], Laksamon Praderm[10], Ummarit Suwattanasilpa[11], Sadudee Peerapornratana[1], Passisd Loahaveeravat[1], Nattachai Suwachittanont[1], Thaksa-on Wirotwan[1], Chayanat Phonork[1], Sarinya Kumpunya[1], Khajohn Tiranathanagul[1], Chintana Chirathaworn[3], Somchai Eiam-ong[1], Kriang Tungsanga[1], Visith Sitprija[1,12], John A. Kellum[2], Natavudh Townamchai[1], Thai Lepto-AKI study group¶



N = 200 leptospirosis suspicious cases



Biomarkers and Leptospirosis AKI

PLOS ONE

PLoS ONE 10(12):e0143367.

TABLE 2 Comparison clinical features of common tropical infections causing AKI

Disease	Leptospirosis	Scrub typhus	Dengue	Malaria
Incidence of AKI	10%–87%	10%–60%	0.2%–35.7%	1%–60%
Endemic area	Caribbean islands, LA, SA, SEA, Oceania	SA, SEA, LA	LA, Caribbean islands, SA, SEA	Sub-Saharan Africa, SEA, SA, LA
Genus/species cause AKI	Spirochetes *Leptospira*: *L. interrogans*, *L. borgpetersenii*	*Orientia tsutsugamushi*	Dengue virus type 1–4	Parasite *Plasmodium*: *P. falciparum*, *P. vivax*, *P. knowlesi*
Reservoirs/ vectors	Rodents, cattle, horses, pigs, dogs	*Leptotrombidium deliense* (chigger) mite larva	*Aedes* mosquitoes: *A. aegypti*, *A. albopictus*	*Anopheles* mosquitoes
Pathogenesis of AKI	ATIN, hemodynamic alteration	ATN, hemodynamic alteration	Hemodynamic alteration, hypercytokinemia	Hemodynamic alteration, cytoadherence of RBCs, hypercytokinemia
Characteristics of AKI	ATN, AIN, vasculitis, hypokalemia	ATN, AIN, GN, TMA	ATN, proteinuria, GN, atypical HUS	ATN, TMA, GN, hyponatremia, hypo/hyperkalemia
Treatment	Penicillin G, ceftriaxone, cefotaxime	Doxycycline	Supportive care	Artesunate, quinine

Abbreviations: AIN, acute interstitial nephritis; AKI, acute kidney injury; ATIN, acute tubulointerstitial nephritis; ATN, acute tubular necrosis; GN, glomerulonephritis; HUS, hemolytic uremic syndrome; LA, Latin America; SA, South Asia; SEA, Southeast Asia; TMA, thrombotic microangiopathy.

Kusirisin et al, Nephrology. 2022;1–16.

Clinical Challenges: Lack of .....

Zero Death for Leptospirosis

Early awareness

- Self/public awareness

- Health care providers

GPs

Internists

The Department of Disease Control, MOPH has warned members of the public who are living in places with high amounts of rain to be wary about Leptospirosis

Why we need to increase lepto awareness ?

- **Lack of clinical experience:** Village health volunteers (VHV), general practitioners, internists
- Many similar infectious diseases with **similar presentation** such as dengue, melioidosis, influenza, malaria, scrub typhus, etc
- Early refer to higher level care for **confirm diagnosis** and treatment
- **Mitigate organ injury** especially AKI, severe liver dysnfunction and pulmonary hemorrhage

Thai Leptospirosis Networking: 12 years cohort

2012 — 2014 — 2015 — 2017 — 2018 — 2019 — Present

1st cohort: Inpatients

- Periods: June 2012 to April 2014.
- 9 centers around Thailand
- N = 221 suspected leptospirosis cases

2nd cohort: Inpatients (Relationship between Leptospires species and severity of disease: **RLSS**)

- Periods: November 2015 to October 2017
- 15 centers at Sisaket province
- N = 330 suspected leptospirosis cases

3rd cohort: Outpatients (Leptospirosis at outpatient departments: **OPD**)

- Periods: December 2017 to November 2018
- 4 centers at Sisaket province
- N= 260 suspected leptospirosis cases

4th cohort: Inpatients (Care bundle)

- Periods: October 2019 to Present
- 6 centers at Sisaket province and 6 centers at Nakhon Si Thammarat
- Ongoing

1000 cases

Early awareness of leptospirosis suspicious cases

- This study developed and internally validated the OPD Lepto Score, a practical clinical risk score for the diagnosis of leptospirosis in suspected patients with acute undifferentiated fever who presented to the outpatient clinics in high endemic areas.

PLOS | NEGLECTED TROPICAL DISEASES 2020

RESEARCH ARTICLE

Development and Validation of a simple score for diagnosis of Leptospirosis at outpatient departments

Parameter	Score
1. Wet ground at workplace	2
2. Contact animal water reservoir	1
3. Urine protein positive	1
4. Urine blood positive	1.5
5. Neutrophil count ≥80%	1.5

OPD score ≥3.5

↓

Presumptive diagnosis of leptospirosis

↓

AuROC: 0.72
Sensitivity: 72.4%
Specificity: 61.7%
PPV: 46.2%
NPV: 83.1%

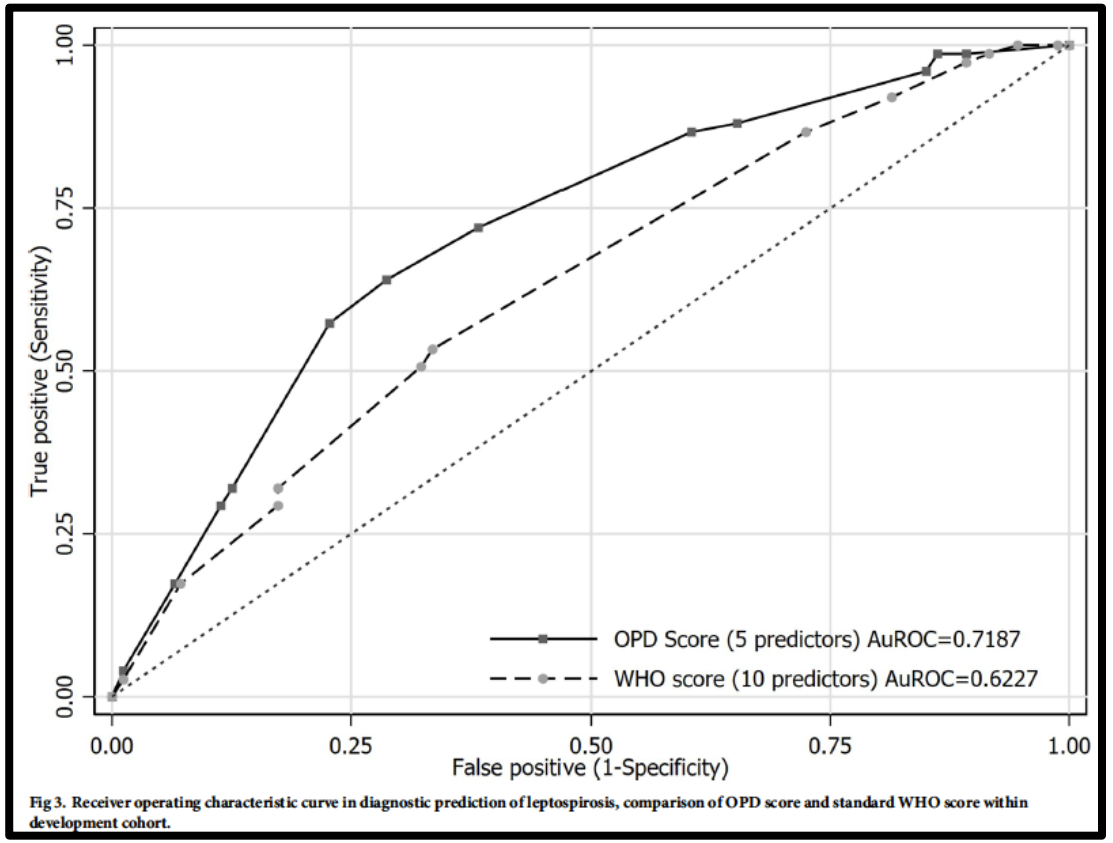
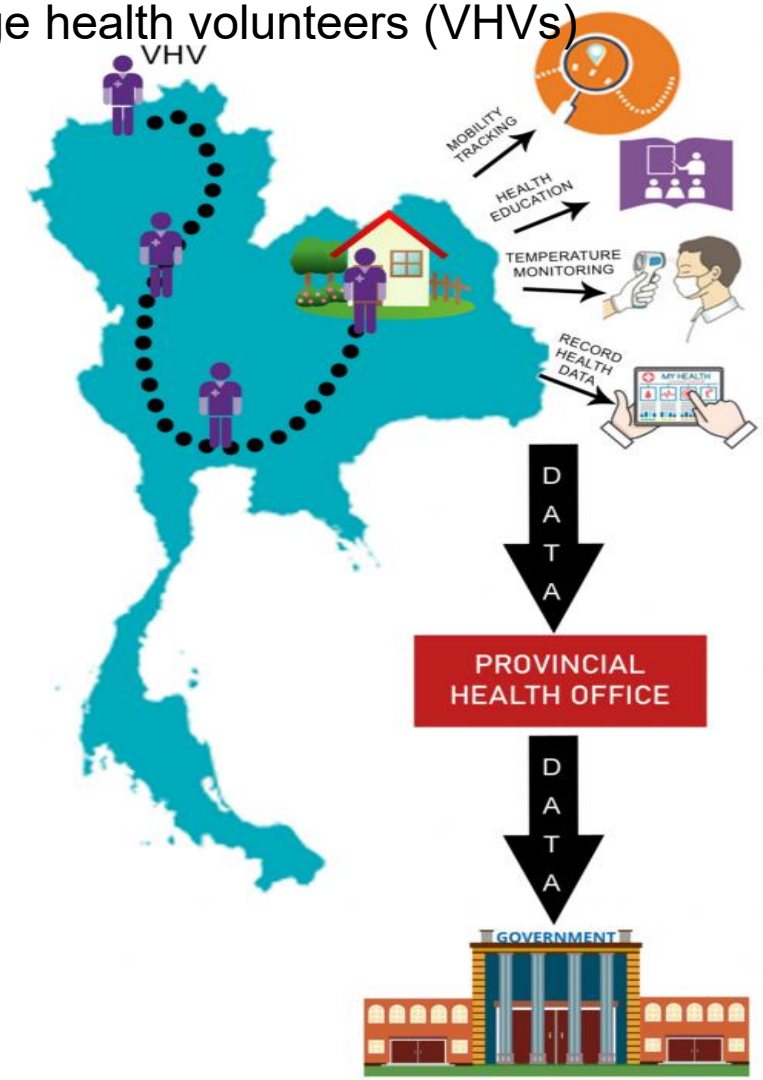


Fig 3. Receiver operating characteristic curve in diagnostic prediction of leptospirosis, comparison of OPD score and standard WHO score within development cohort.

>With 5 predictors, the score was more practical for outpatient setting than the conventional WHO score with 10 predictors.

Implementation to Leptospirosis Guideline by DDC, MOPH, Thailand 2022

Village health volunteers (VHVs)



VHV's role during COVID-19 in Thailand

การใช้ THAI-LEPTO Score

THAI-LEPTO Score เป็นระบบการให้คะแนนผู้ป่วย โดยใช้อาการทางคลินิก ประวัติเสี่ยงต่อการติดเชื้อ ร่วมกับการส่งตรวจทางห้องปฏิบัติการพื้นฐาน (Clinical prediction score) ช่วยในการวินิจฉัยเบื้องต้น (presumptive diagnosis) ในผู้ป่วยที่สงสัยโรคเลปโตสไปโรสิส เพื่อที่จะได้เริ่มการรักษาผู้ป่วยก่อนที่ผลการตรวจยืนยันจะรายงานผล (confirmatory test)

THAI-LEPTO Score[a]

ปัจจัยทำนาย	คะแนน
1. Clinical hypotension: ความดันโลหิตต่ำที่จำเป็นต้องให้สารน้ำอย่างรวดเร็ว (volume resuscitation) หรือ vasopressors (ก่อนนำส่งโรงพยาบาลหรือได้รับการรักษาแล้ว)	3
2. Clinical Jaundice: ผู้ป่วยมีภาวะตาเหลืองและ/หรือตัวเหลือง	2
3. Muscle pain: ปวดกล้ามเนื้อรุนแรง หรือกดเจ็บตามกล้ามเนื้อ โดยเฉพาะกล้ามเนื้อน่อง	2
4. Acute kidney injury: creatinine ≥ 0.3 mg/dL หรือ 1.5 เท่าจากของเดิม (ถ้าไม่มีข้อมูลเดิม และผู้ป่วยไม่มีโรคไตเรื้อรังมาก่อน ให้ประมาณว่า eGFR ปกติที่ 75 mL/min/1.73m^2)	1.5
5. Hemoglobin < 12 g/dL	3
6. Serum sodium < 135 mEq/L ร่วมกับ serum potassium < 3.5 mEq/L	3
7. ผู้ป่วยมี PMN ≥ 80 % ร่วมกับ White Blood Count < 10,000 cell/mcL	1

* จำเป็นต้องแยกโรค hepatobiliary tract infection, bacterial sepsis, malaria ออกก่อนเสมอ

ผลรวมคะแนน ≥ 4 วินิจฉัยเบื้องต้น เป็นโรคเลปโตสไปโรสิส ด้วยโอกาสความน่าจะเป็น (PPV)[b] = 0.74 (sensitivity 0.74, specificity 0.74)

[a] วินิจฉัยได้ดีเฉพาะโรคเลปโตสไปโรสิสชนิดรุนแรงที่ต้องนอนโรงพยาบาล โดยแยกโรคได้ดีสุดในช่วงเวลา 3-4 วัน หลังจากเริ่มมีไข้

[b] ในสภาวะ pretest probability = 0.5

หากมีข้อสงสัยกรุณาติดต่อ: กองโรคติดต่อทั่วไป กรมควบคุมโรค โทร. 02-590-3177-8

Leptospirosis Guideline

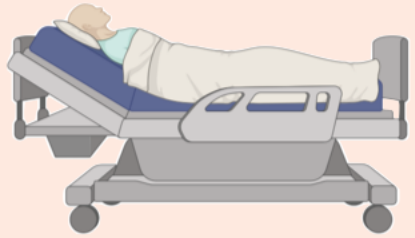
Community hospitals

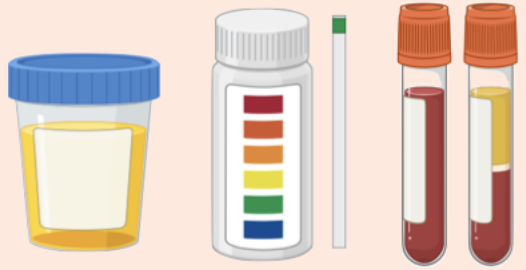
Clinical risk scores

- Mehran score
- Renal angina index
- Leptospirosis: OPD score, THAI-LEPTO score

- AKI biomakers: NGAL, KIM-1

Who will perform Thai lepto score ?
- VHVs





General practitioners / Internists

Provincial hospitals / Regional hospitals

Telemedicine

- AKI care bundle
- Referral for kidney replacement therapy

Nephrologists

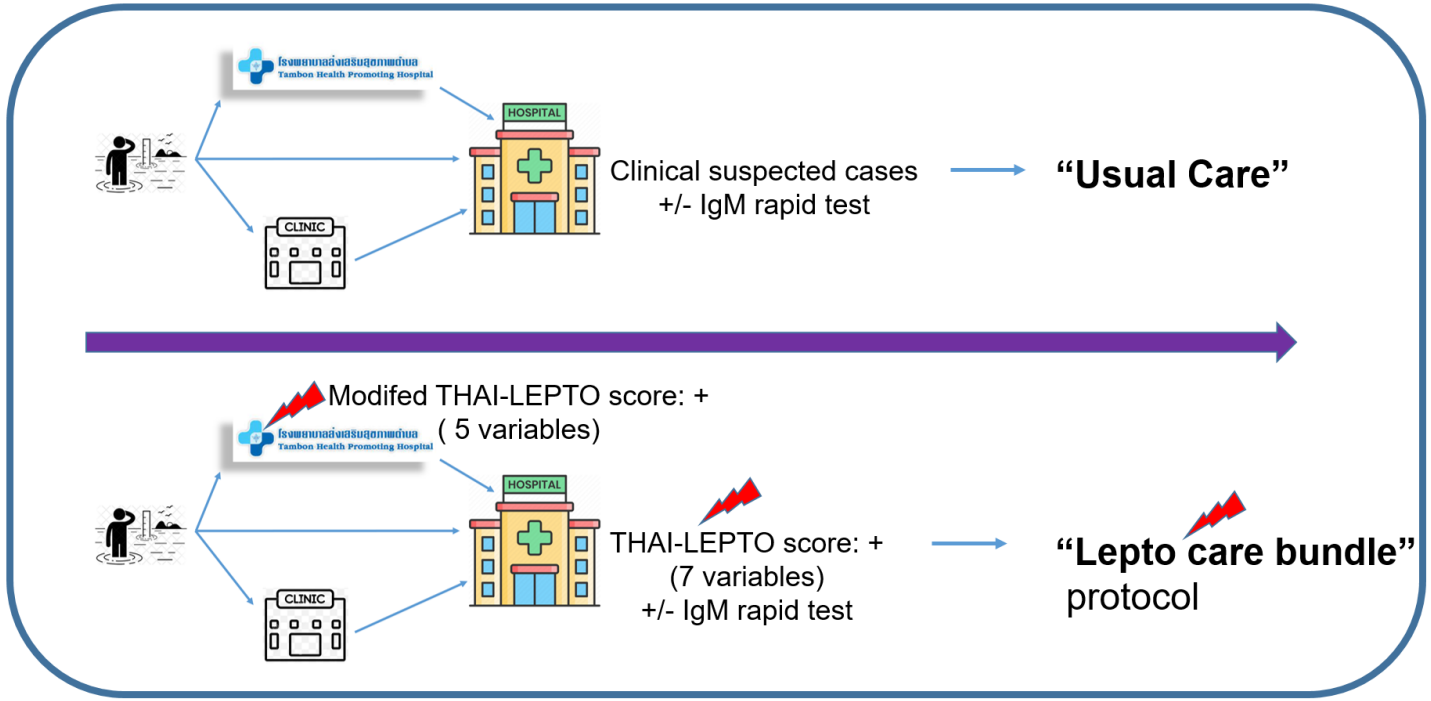
Early Referral/Treatment/ Organ Support

LEPTOSPIROSIS CARE BUNDLE VS USUAL CARE

FOR DECREASING SEVERITY OF LEPTOSPIROSIS:

A MULTICENTER RANDOMIZED CONTROLLED TRIAL, AN INTERIM ANALYSIS

Theerapon Sukmark M.D.[1], Janejira Dinhuzen M.Sc.[2,3], Sasipha Tachaboon M.Sc.[2,3], Atchara Aksornrat M.D.[4], Jane Pitanupong M.D.[5], Nattachai Srisawat M.D.[2,3,6,7]



Reduction of AKI stage 3

Oral presentation in 6th APAC AKI CRRT on Oct 3, 2025

Clinical Challenges: Lack of ……..

Zero Death for Leptospirosis

Early awareness

- Self awareness
- Health care provider

GPs

Internists

Early detection/diagnosis

- Barriers to detection/diagnose

early leptospirosis

- Current available tests
- Future

Confirmation test

Current rapid test for Leptospirosis diagnosis showed low sensitivity

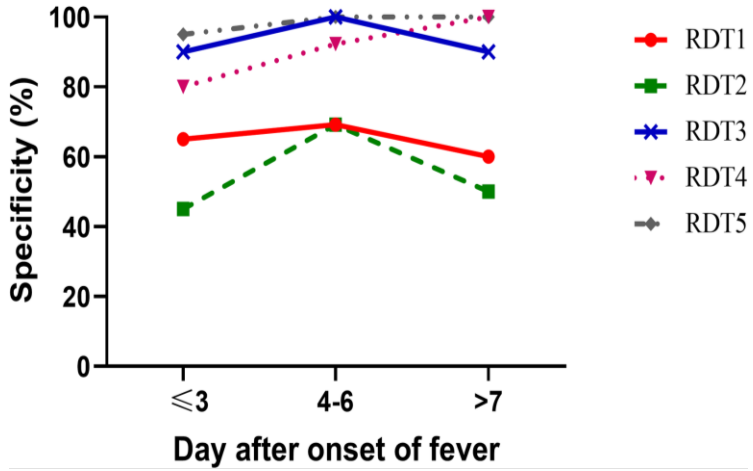
PLOS NEGLECTED TROPICAL DISEASES **2021**

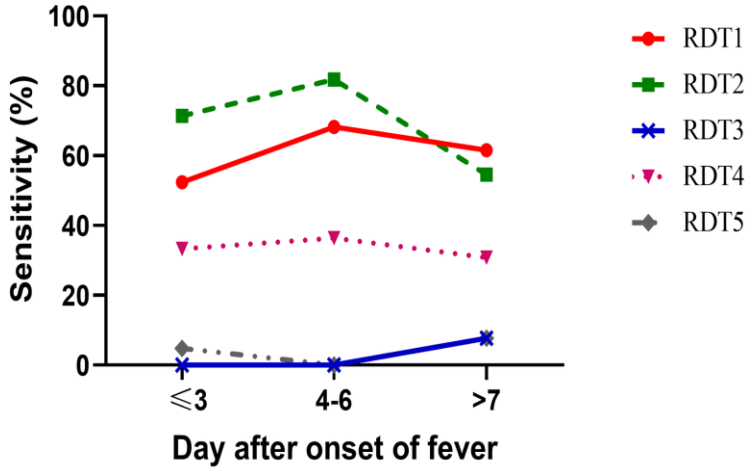
RESEARCH ARTICLE

A prospective study to evaluate the accuracy of rapid diagnostic tests for diagnosis of human leptospirosis: Result from THAI-LEPTO AKI study

- We evaluated the diagnostic performance of five commercially available RDTs in Thai population

Test kit	Sensitivity %	Specificity %	PPV %	NPV %
RTD1	60.70	65.10	69.40	56.00
RTD2	75.00	53.50	67.70	62.20
RTD3	1.80	93.00	25.00	42.10
RTD4	33.90	88.40	79.20	50.70
RTD5	3.60	97.70	66.70	43.80





- RDTs showed low sensitivity and might not be an appropriate test for acute leptospirosis screening in the Thai population.

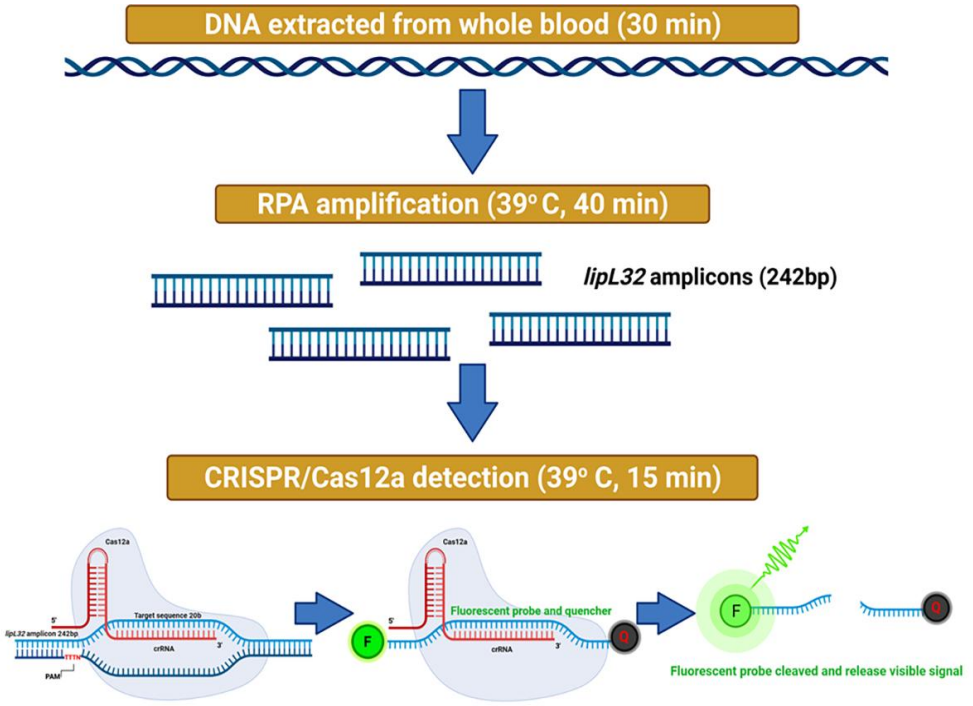
Early Diagnosis of Leptospirosis

PLOS NEGLECTED TROPICAL DISEASES 2021

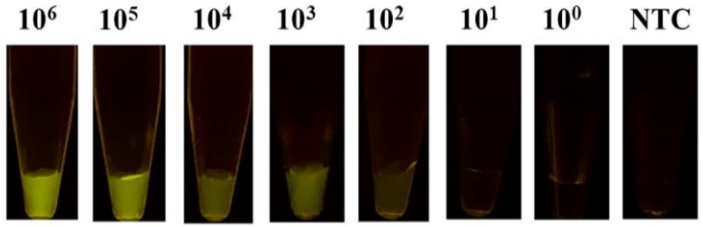
RESEARCH ARTICLE

Rapid and sensitive point-of-care detection of *Leptospira* by RPA-CRISPR/Cas12a targeting *lipL32*

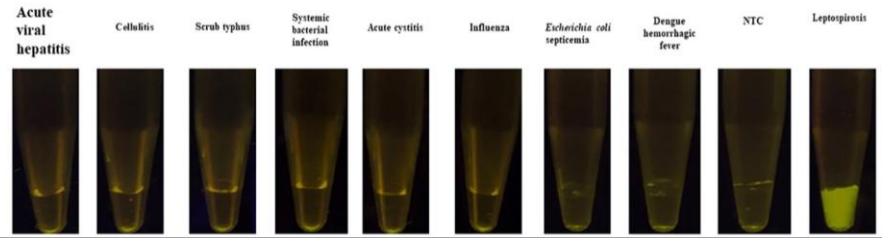
(a)

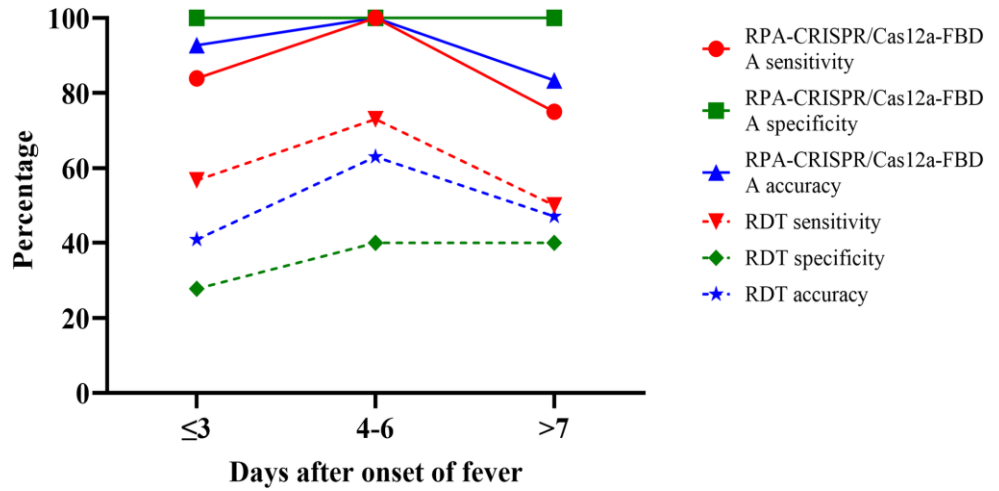


(b)



(c)





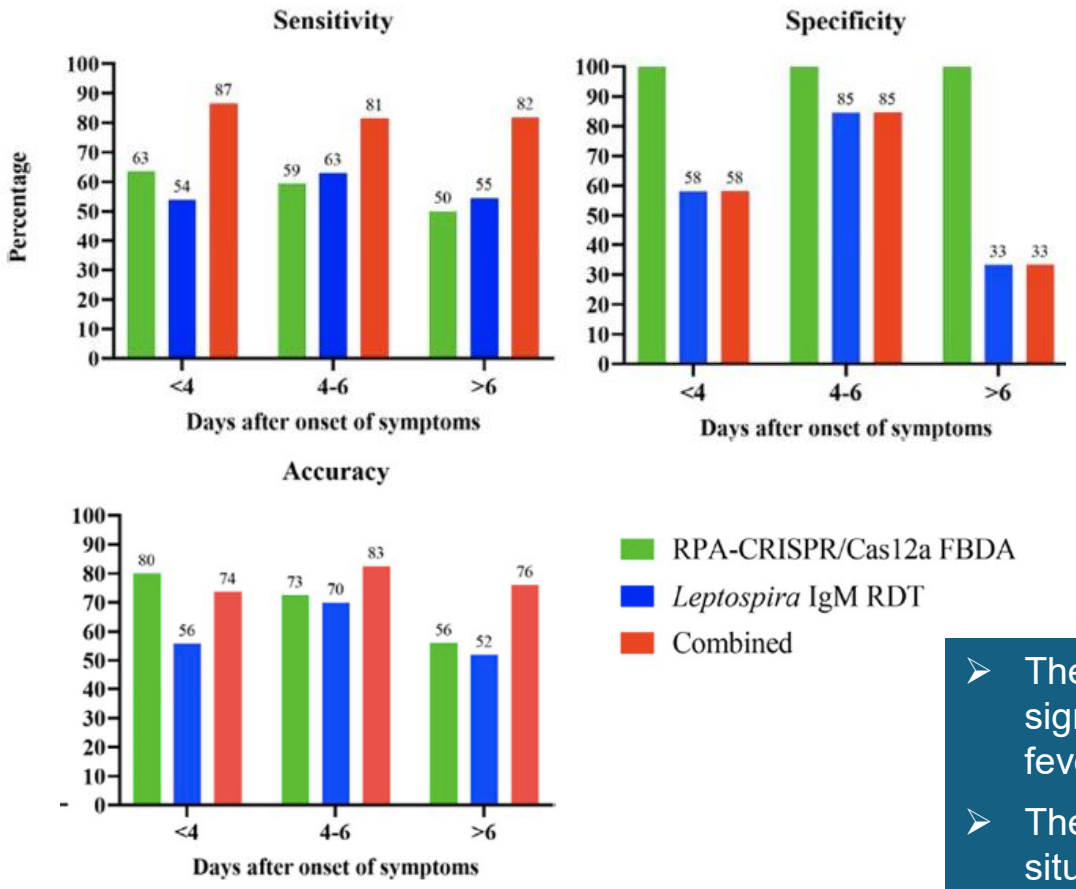
- The RPA-CRISPR/Cas12 targeting the *lipL32* gene demonstrated acceptable sensitivity and excellent specificity for detection of leptospires.
- This assay might be an appropriate test for acute leptospirosis screening in limited-resource settings.

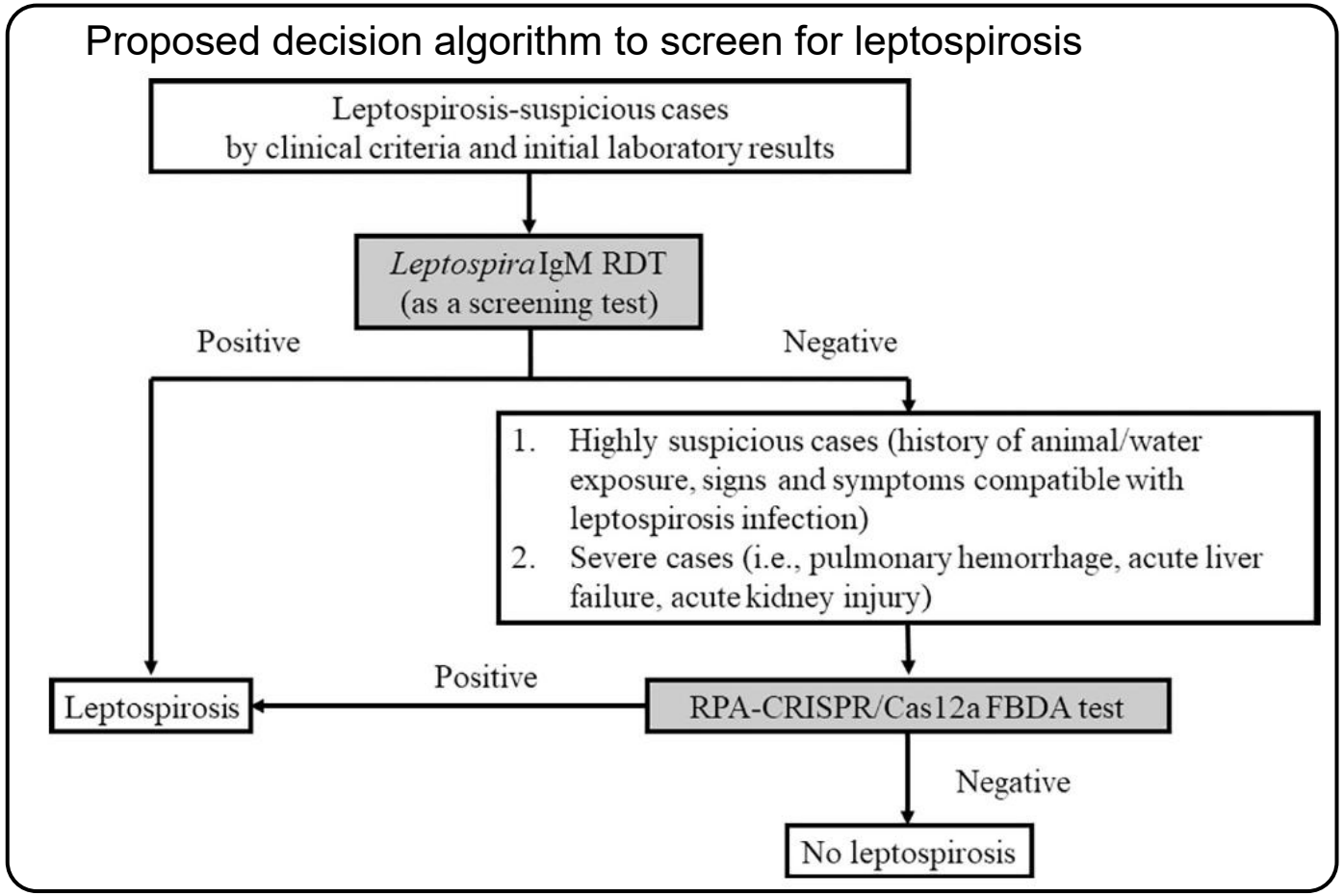
Early Diagnosis of Leptospirosis

PLOS NEGLECTED TROPICAL DISEASES 2023

RESEARCH ARTICLE

The combination of RPA-CRISPR/Cas12a and *Leptospira* IgM RDT enhances the early detection of leptospirosis





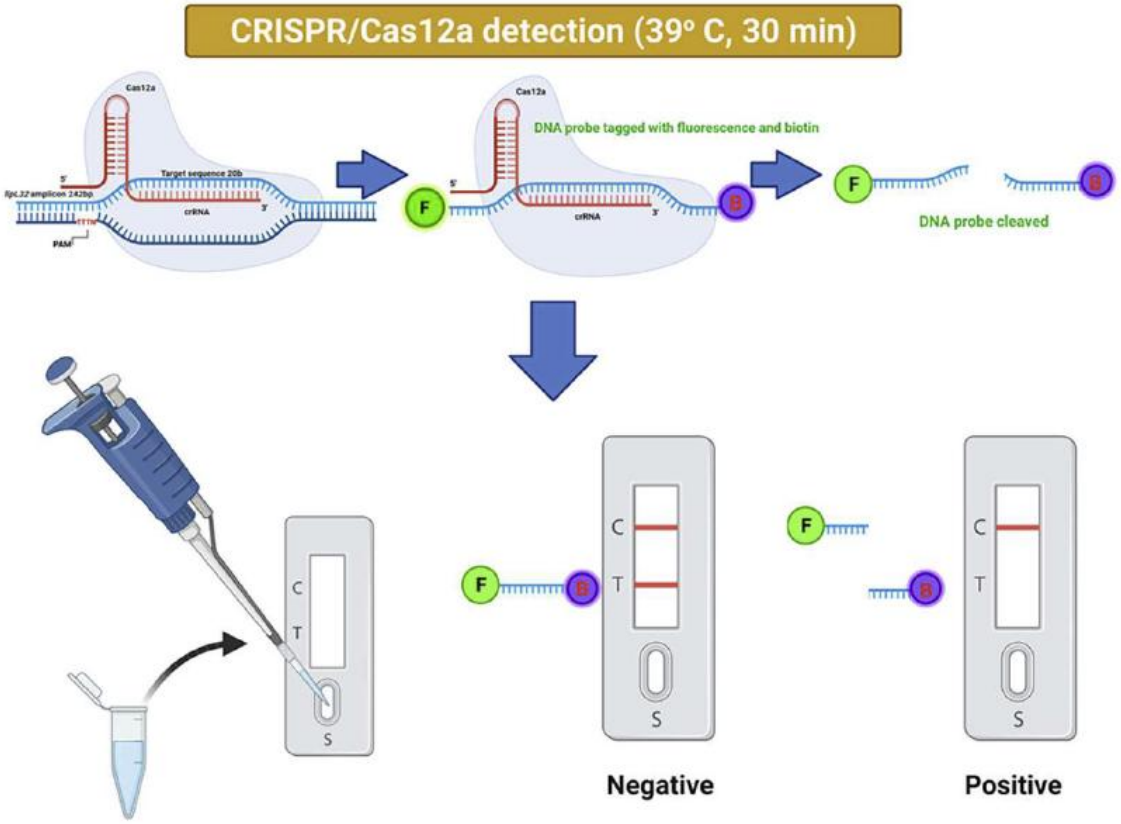
- The combination of Leptospira IgM RDT and RPA-CRISPR/Cas12 FBDA exhibited significant sensitivity for the detection of leptospires at various days after the onset of fever, thereby reducing the likelihood of misdiagnosis.
- The combination of these assays may be suitable for early leptospirosis screening in situations with limited resources

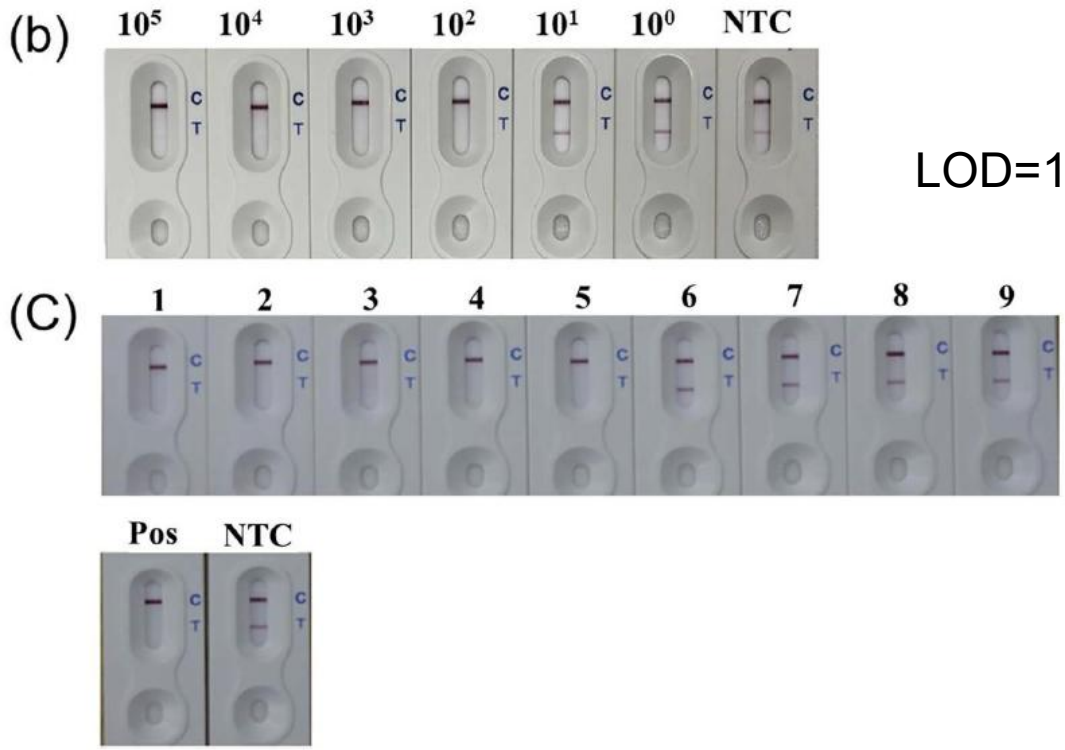
Early Diagnosis of Leptospirosis

PLOS NEGLECTED TROPICAL DISEASES 2021

RESEARCH ARTICLE

Rapid and sensitive point-of-care detection of *Leptospira* by RPA-CRISPR/Cas12a targeting *lipL32*





LOD=100 cells/mL

Fig 3. The RPA-CRISPR/Cas12a-LFDA. (A) The RPA-CRISPR/Cas12a-LFDA's workflow (Created with BioRender.com), (B) LOD, and (C) clinical sample validation [1–5 and 6–9 are known positive and negative samples, respectively, while NTC and Pos are the no-template negative and positive control, respectively].

- We also developed a lateral flow detection assay (LFDA) combined with RPA-CRISPR/Cas12a to make the test more accessible and easier to interpret.
- This assay may be an appropriate test for acute leptospirosis screening in limited-resource settings.

Clinical Challenges: Lack of ……..

Zero Death for Leptospirosis

Early awareness

- Self awareness
- Health care provider

GPs
Internists

Early detection/diagnosis

- Barriers to detection/diagnose

early leptospirosis

- Current available tests
- Future

Confirmation test

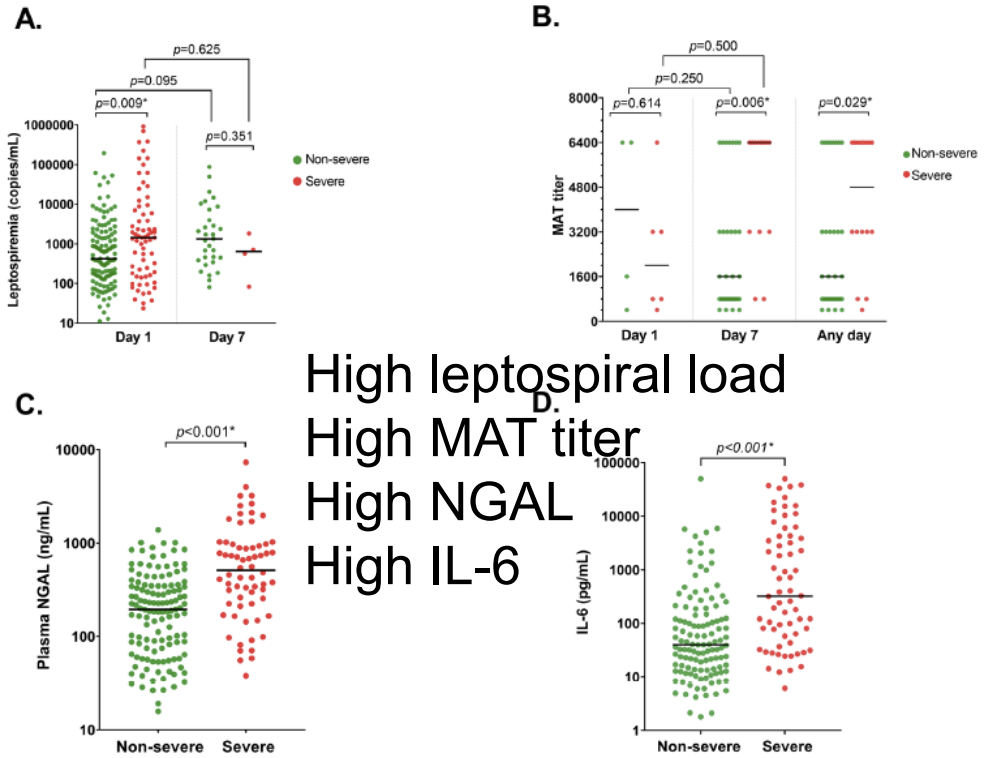
Early prediction severity

- Barriers to predict severe leptospirosis
- Utility of biomarkers for severity
  - Early Referral/Treatment: Lepto care bundle
  - Early Organ Support: CRRT Ventilatory support, ECMO

Biomarkers to predict severe leptospirosis

scientific reports 2021

The role of leptospiremia and specific immune response in severe leptospirosis



High leptospiral load
High MAT titer
High NGAL
High IL-6

Table 2. Area under the receiver operating curve for the association between baseline biomarkers and severe leptospirosis.

Parameters	AUC ROC	SE	p value	95% CI	Cut-off	Sensitivity	Specificity
Leptospiremia	0.61	0.04	0.010*	0.52–0.70	953	0.59	0.67
MAT titer	0.40	0.20	0.594	0.00–0.80	600	0.83	0.25
NGAL	0.75	0.04	<0.001	0.67–0.82	360	0.62	0.78
IL-6	0.75	0.04	<0.001	0.67–0.82	121	0.64	0.74

Table 3. Regression analysis of factors associated with severe leptospirosis.

Parameters	Odds ratio (95% CI) unadjusted	p-value	Odds ratio (95% CI) Adjusted[a]	p-value
Gender	1.02 (0.48–2.16)	0.967	1.00 (0.99–1.02)	0.807
Age	1.00 (0.99–1.02)	0.731	0.96 (0.44–2.11)	0.925
Days of fever until enrollment	1.05 (0.92–1.21)	0.456	1.05 (0.92–1.21)	0.465
Leptospiremia (log_{10} copies/ml)	1.66 (1.21–2.27)	0.002*	1.70 (1.23–2.34)	0.001*
MAT titer (log scale)	0.49 (0.03–8.11)	0.617	0.35 (0.01–8.79)	0.523
Plasma NGAL (log_{10} ng/ml)	8.51 (3.88–18.67)	<0.001*	9.46 (4.20–21.33)	<0.001*
IL-6 (log_{10} pg/ml)	2.61 (1.84–3.70)	<0.001*	2.82 (1.96–4.07)	<0.001*

- High leptospiremia, pNGAL, and IL-6 level at baseline were associated with severe leptospirosis.

Figure 3. Level of all biomarkers in severe and non-severe leptospirosis

Discovery and validation of novel biomarkers for severe leptospirosis

PLOS NEGLECTED TROPICAL DISEASES 2020

RESEARCH ARTICLE

Circulating microtranscriptome profiles reveal distinct expression of microRNAs in severe leptospirosis

Umaporn Limothai[1,2,3], Janejira Dinhuzen[2,3], Titipon Payongsri[4], Sasipha Tachaboon[2,3], Pisit Tangkijvanich[1], Natthaya Chuaypen[1]*, Nattachai Srisawat[2,3,5,6,7,8]*

DOI: 10.1371/journal.pntd.0008809

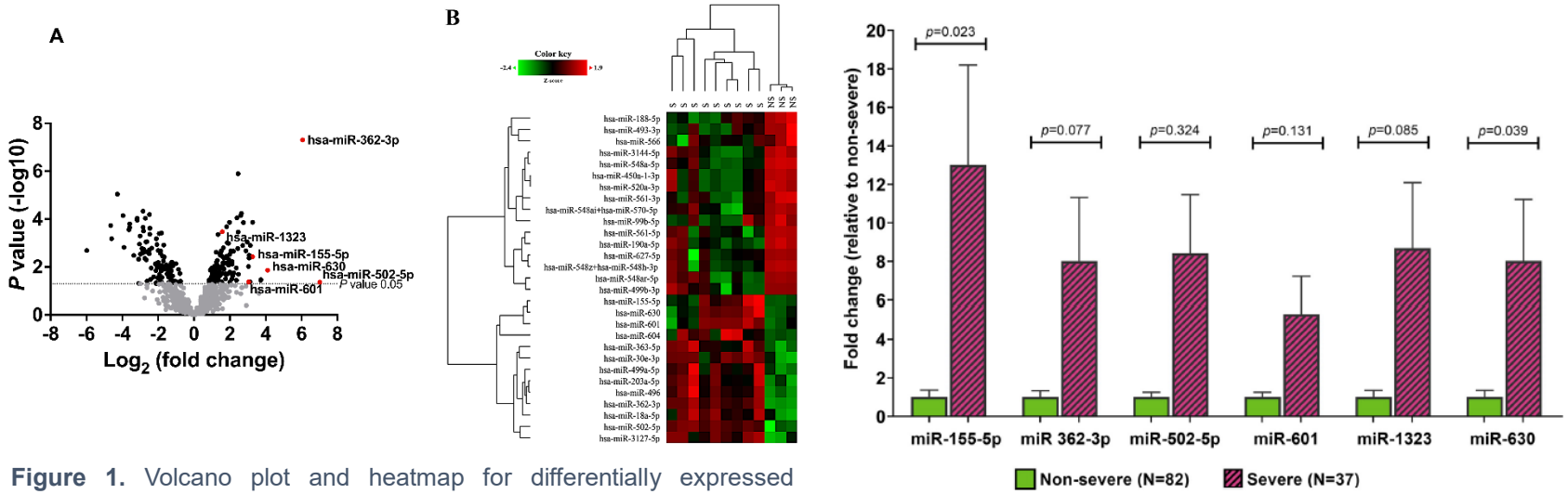


Figure 1. Volcano plot and heatmap for differentially expressed miRNAs between severe and non-severe leptospirosis groups.

Fig 2. Relative expression of circulating microRNAs in patients with leptospirosis.

PLOS ONE 2021

RESEARCH ARTICLE

Identification and validation of circulating miRNAs as potential new biomarkers for severe liver disease in patients with leptospirosis

Natthaya Chuaypen[1], Umaporn Limothai[2], Pattapon Kunadirek[1], Pornchai Kaewsapsak[3], Patipark Kueanjinda[4], Nattachai Srisawat[2], Pisit Tangkijvanich[1]*

DOI: 10.1371/journal.pone.0257805

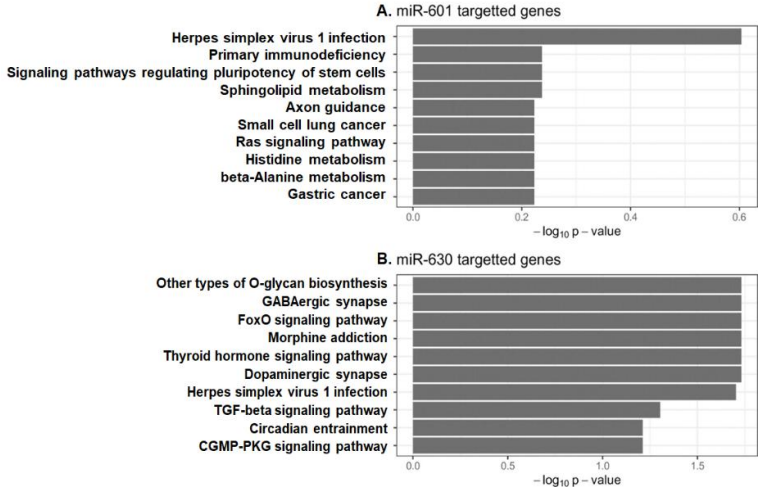


Figure 3. KEGG pathways mapped based on miR-601 (A) and miR-630 (B) candidate target genes.

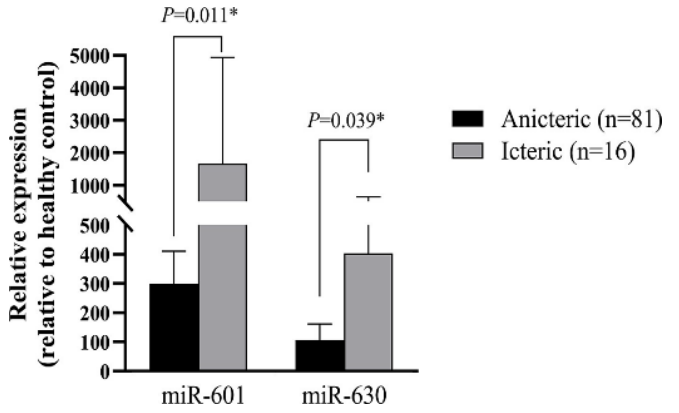


Figure 4. Relative expression of serum miR-601 and miR-630

Journal of Infection 90 (2025) 106400

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Infectious Disease Practice

MicroRNA biomarkers and host response pathways in severe pulmonary hemorrhagic syndrome due to leptospirosis: A multi-omics study

Phu Nguyen Trong Tran [a,b,c], Umaporn Limothai [b,d], Janejira Dinhuzen [b,d], Sasipha Tachaboon [b,d], Theerapon Sukmark [e], Chayomon Dokpong [f], Sittiruk Roytrakul [g], David A. Haake [h,i], Nattachai Srisawat [a,b,d,j,k,l,*]

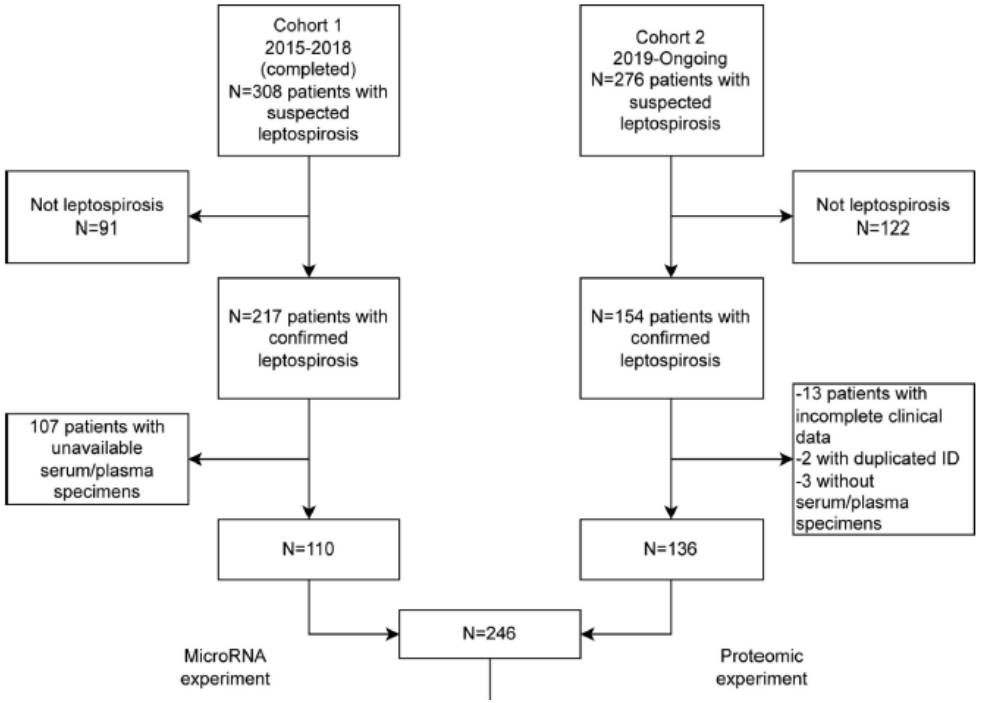


Table 1
Baseline characteristics of the patients included in this study.

	Discovery set (N=12)			Valid		
	Non-SPHS (n = 7)	SPHS (n = 5)	Overall (n = 12)	Non-		
Age (years), Median [Q1,Q3]	54.0 [44.5,58.5]	30.0 [28.0,66.0]	51.5 [36.8,61.0]	47.0		
Male sex, n(%)	6 (85.7)	5 (100)	11 (91.7)	116		
BMI (Kg/m^2, Mean (SD)	24.6 (5.31)	24.2 (4.03)	24.5 (4.73)	22.5		
Diabetes, n(%)	1 (14.3)	0 (0)	1 (8.3)	4 (2.9		
Hypertension, n(%)	1 (14.3)	0 (0)	1 (8.3)	11 (7		
Alcoholism, n(%)	7 (100)	5 (100)	12 (100)	5 (3.6)	2 (7.1)	7 (4.2)
Smoking, n(%)	3 (42.9)	2 (40.0)	5 (41.7)	71 (50.7)	13 (46.4)	84 (50.0)
Days of illness (days) Median [Q1,Q3]	3 [1,3]	3 [0,3]	3 [1,3]	3 [1,75,4]	3 [2,75,4]	3 [2,4]
Clinical manifestation at specimen collection						
Temperature (^{0}C) Mean (SD)	38.7 (1.38)	37.6 (1.66)	38.2 (1.54)	38.4 (1.21)	37.8 (0.987)	38.3 (1.19)
Systolic blood pressure (mmHg)						
Mean (SD)	122 (15.5)	86.6 (22.5)	107 (25.3)	115 (23.1)	90.6 (16.5)	111 (23.9)
Diastolic blood pressure (mmHg)						
Mean (SD)	68.9 (13.6)	50.6 (17.8)	61.3 (17.5)	66.4 (11.5)	57.0 (15.9)	64.8 (12.8)
Hemoptysis, n(%)	0 (0)	2 (40.0)	2 (16.7)	0 (0)	11 (38.3)	11 (6.5)
Jaundice, n(%)	0 (0)	1 (20.0)	1 (8.3)	12 (8.6)	6 (21.4)	18 (10.7)
Hemoglobin (g/dL) Median [Q1,Q3]	12.7 [10.8,12.9]	8.60 [8.40,12.5]	11.7 [8.55,12.7]	12.2 [11.1,13.3]	11.2 [9.13,12.5]	12.1 [10.8,13.2]
Hematocrit (%) Median [Q1,Q3]	38.0 [34.0,39.3]	26.3 [24.9,38.0]	36.0 [26.1,39.2]	38.0 [34.0,40.8]	32.6 [26.3,36.1]	37.0 [33.2,40.0]
Leukocytes (1000/uL) Median [Q1,Q3]	13.2 [10.8,15.3]	8.7 [8.6,12.2]	12.3 [8.7,15.1	10 [7.5,12.6]	9.9 [6.4,12.9]	10 [7.1,12.6]
% Neutrophils Median [Q1,Q3]	80.0 [75.0,85.5]	84.0 [82.0,91.0]	82.5 [79.3,88.7]	83.0 [73.0,87.9]	86.0 [82.5,90.9]	84.0 [74.9,88.0]
% Lymphocytes Median [Q1,Q3]	11.0 [7.00,18.4]	7.10 [6.00,9.00]	9.50 [5.50,12.0]	9.95 [6.80,17.0]	7.05 [4.00,9.25]	9.00 [6.00,15.0]
Platelets (1000/uL) Median [Q1,Q3]	188 [117,244]	54 [19,69]	85 [50.8,188]	139 [82.3,199]	37.5 [22.8,60]	109 [53.5,190]
Blood urea nitrogen (mg/dL) Median [Q1,Q3]	16.5 [13.9,44.0]	26.0 [24.0,36.3]	24.0 [14.6,44.7]	16.9 [13.0,26.0]	36.3 [25.0,52.4]	19.7 [13.9,31.3]
Serum creatinin (mg/dL) Median [Q1, Q3]	1.05 [0.915,3.55]	2.00 [1.22,3.04]	1.61 [1.03,3.33]	1.20 [0.930,1.60]	2.23 [1.63,4.28]	1.30 [0.960,1.96]
Serum total bilirubin (mg/dL) Median [Q1,Q3]	0.800 [0.700,1.19]	2.40 [1.60,3.01]	1.19 [0.700,2.55]	1.10 [0.700,2.10]	3.11 [1.28,7.68]	1.20 [0.700,2.40]
Serum SGOT (UI/L) Median [Q1,Q3]	39.0 [31.5,57.5]	98.0 [50.0,101]	44.5 [37.8,98.8]	50.0 [32.0,87.5]	94.0 [54.0,141]	53.5 [34.0,104]
Serum SGPT (UI/L) Median [Q1,Q3]	36.0 [30.5,56.5]	32.0 [32.0,78.0]	34.0 [31.3,75.8]	40.5 [25.8,90.0]	44.0 [32.0,65.0]	43.0 [27.0,81.0]
Serum albumin (g/dL) Median [Q1,Q3]	3.25 [2.95,3.55]	2.50 [2.20,3.20]	3.10 [2.65,3.50]	3.50 [3.11,3.88]	2.77 [2.30,3.13]	3.40 [2.99,3.80]
Serum sodium (meq/L) Mean (SD)	137 (3.51)	138 (3.27)	137 (3.27)	135 (4.59)	134 (4.90)	134 (4.64)
Serum potassium (meq/L) Median [Q1,Q3]	3.67 [3.50,3.95]	3.60 [3.60,4.30]	3.64 [3.55,4.23]	3.60 [3.30,3.92]	3.60 [3.35,3.98]	3.60 [3.30,3.93]
Serum chloride (meq/L) Mean (SD)	99.9 (4.34)	104 (10.9)	102 (7.61)	97.9 (8.10)	99.1 (6.51)	98.1 (7.84)
Serum bicarbonate (meq/L)						
Mean (SD)	24.9 (3.11)	19.3 (7.02)	22.6 (5.60)	24.6 (7.80)	19.5 (5.26)	23.7 (7.66)
SOFA score Median [Q1,Q3]	0 [0,5]	10 [8,14]	6 [0,8.5]	2 [1,4]	12.5 [10.8,14.3]	3 [1,6]
Number of organ involvement						
Median [Q1,Q3]	0 [0,1.5]	4 [2,4]	2 [0,3.25]	1 [0,1]	4 [3,5]	1 [0,2]
Leptospiral diagnostic features						
Positive MAT, n (%)	1 (14.3)	1 (20.0)	2 (16.7)	47 (33.6)	10 (35.7)	57 (33.9)
Leptospiremia[a], n (%)	7 (100)	5 (100)	12 (100)	117 (83.6)	27 (96.4)	144 (85.7)
Patient outcomes						
ICU admission, n (%)	1 (14.3)	4 (80.0)	5 (41.2)	7 (5.0)	24 (85.7)	31 (18.5)
Hospital mortality, n (%)	0 (0)	1 (20.0)	1 (8.3)	3 (2.1)	8 (28.6)	11 (6.5)
90-day mortality, n (%)	0 (0)	1 (20.0)	1 (8.3)	4 (2.9)	9 (32.1)	13 (7.7)

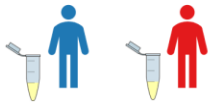
[a] Leptospiremia was defined as either positive blood qPCR for pathogenic Leptospira spp. or a positive blood culture.

MicroRNA Biomarkers and Host Response Pathways in Severe Pulmonary Hemorrhagic Syndrome due to Leptospirosis: A Multi-Omics Study

MiRNA as biomarker of leptospiros SPHS

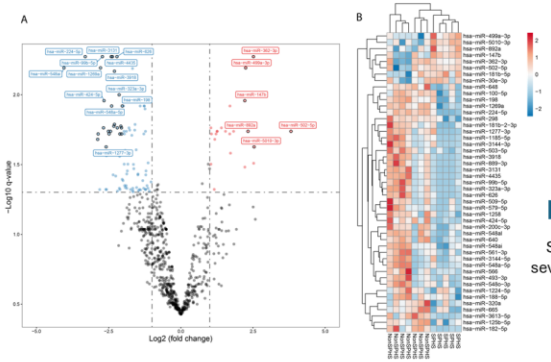
nanoString

Profiling of 798 miRNAs



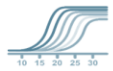
NonSPHS N=7 | NonSPHS N=5

Serum at enrolment

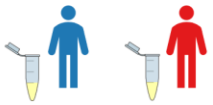


MiRNA biomarker discovery

Select top seven miRNAs



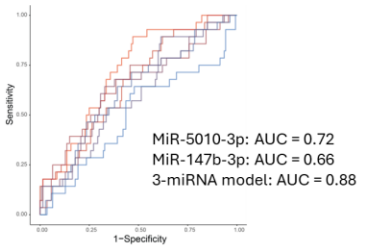
RT-qPCR



NonSPHS N=140 | NonSPHS N=28

Serum at enrolment

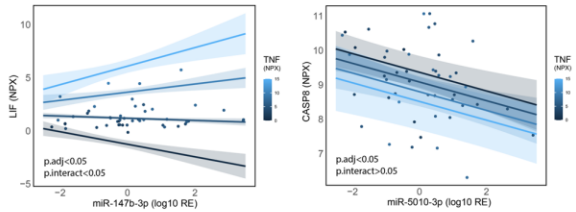
168 patients

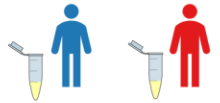


MiR-5010-3p and **miR-147b-3p** are potential biomarkers of SPHS

MiRNA biomarker validation

MiRNA biomarkers & host response pathways





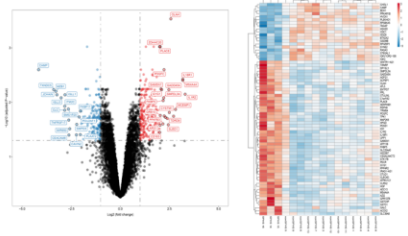
NonSPHS N=32 | NonSPHS N=15

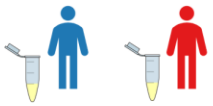
MiRNA biomarkers **correlate** with TNF signaling pathway proteins and their principal components

Host response pathway in leptospirosis SPHS

GEO Gene Expression Omnibus

Whole blood transcriptomics

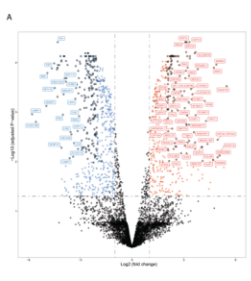


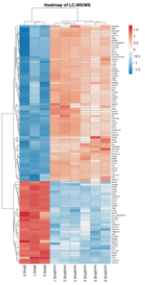


NonSPHS N=57 | NonSPHS N=19

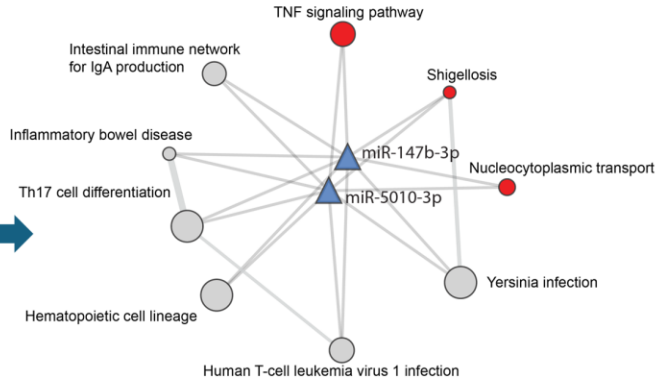
Plasma at enrolment (pooled)

LC-MS/MS



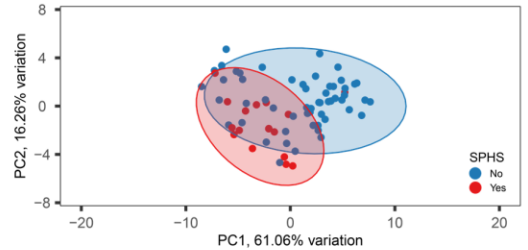


Transcriptomic and proteomic data generation



TNF signaling pathway is among the most significant pathways from combined evidence

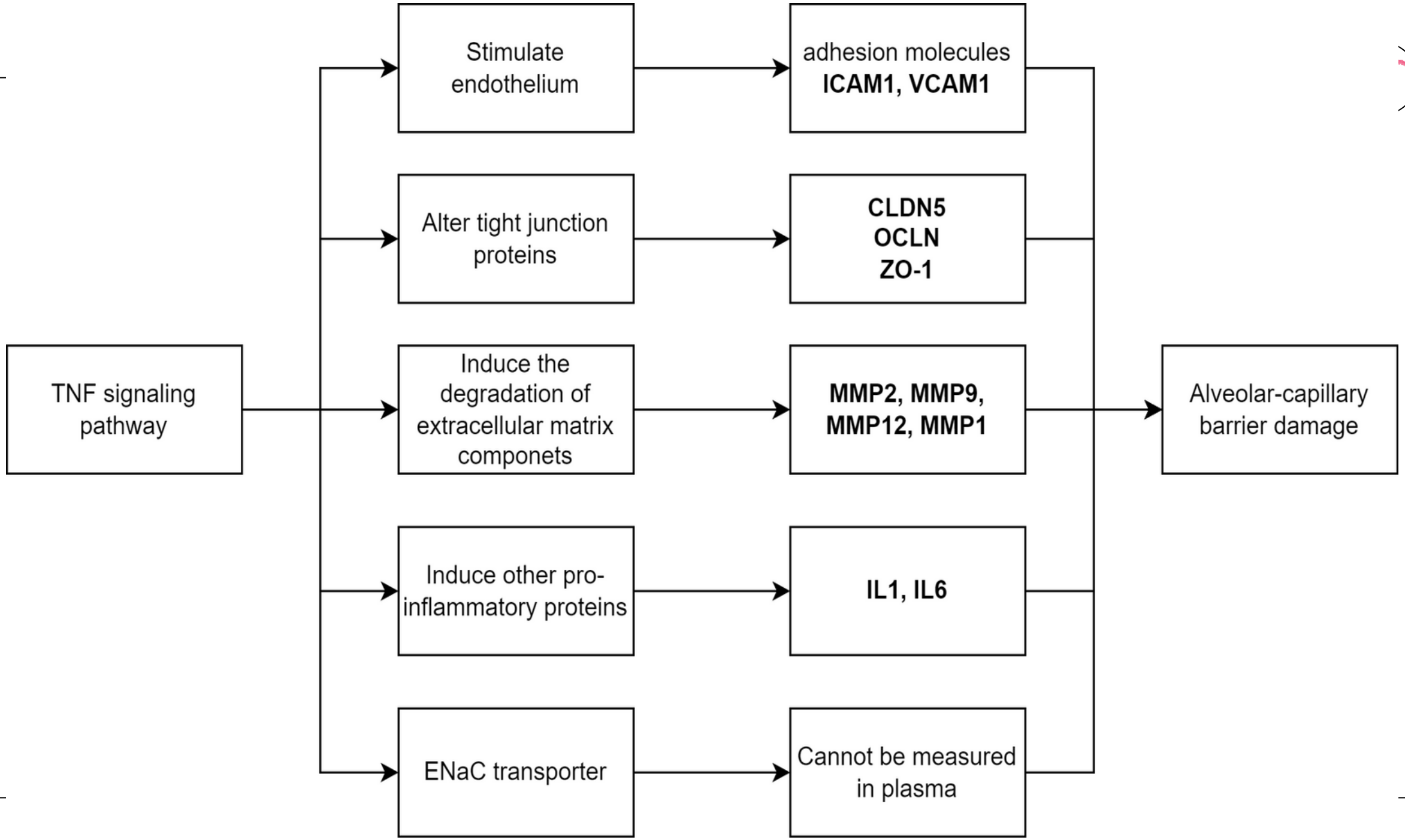
Multi-omics pathway analysis



NonSPHS N=55 | NonSPHS N=17

Olink target innflammaiton

Validation of TNF signaling pathway proteins


TNF signaling pathway
Stimulate endothelium
adhesion molecules
ICAM1, VCAM1
Alter tight junction proteins
CLDN5
OCLN
ZO-1
Induce the degradation of extracellular matrix componets
MMP2, MMP9, MMP12, MMP1
Induce other pro-inflammatory proteins
IL1, IL6
ENaC transporter
Cannot be measured in plasma
Alveolar-capillary barrier damage

Clinical Challenges: the 4th challenge

Zero Death for Leptospirosis

Early awareness

- Self awareness
- Health care provider

GPs
Internists

Early detection/diagnosis

- Barriers to detection/diagnose

early leptospirosis

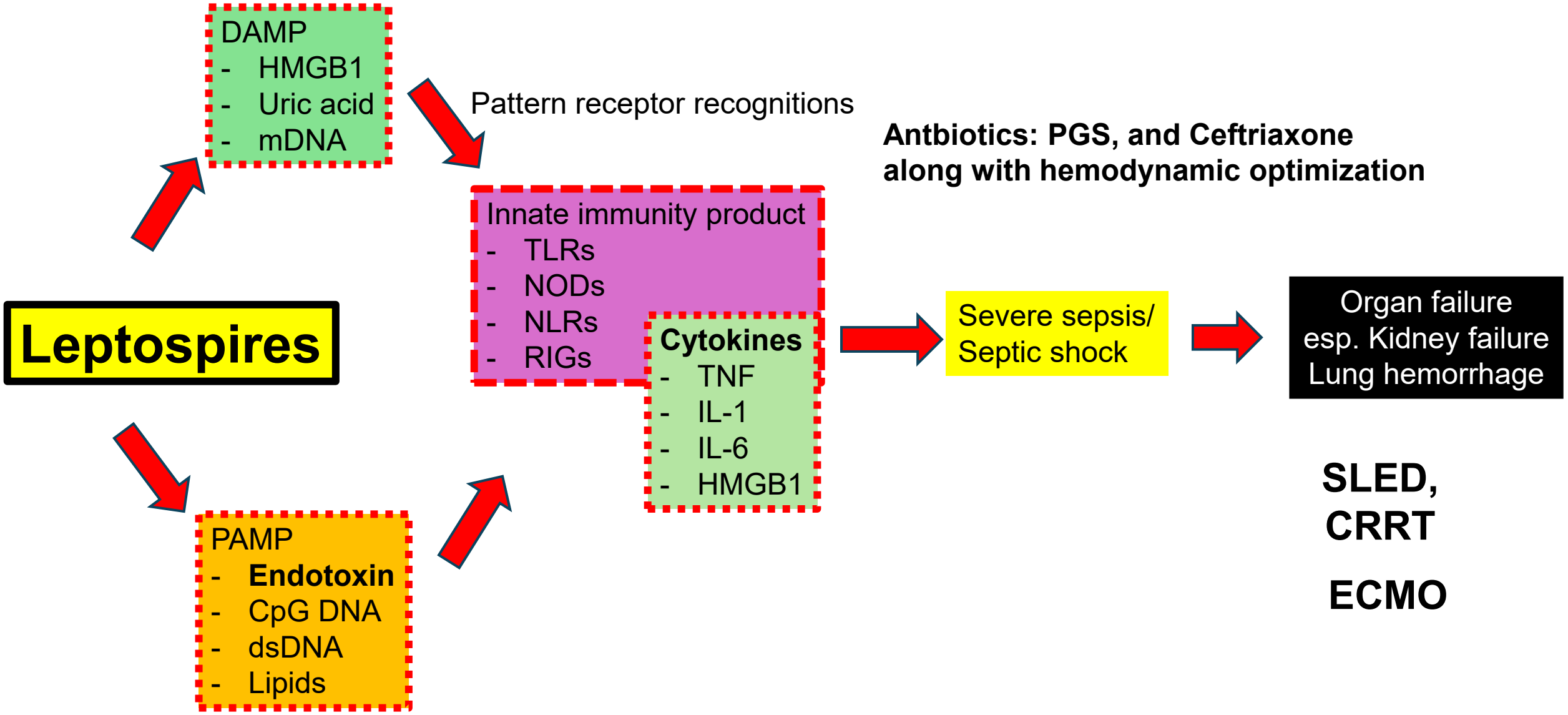
- Current available tests
- Future

Confirmation test

Early prediction severity

- Barriers to predict severe leptospirosis
- Utility of biomarkers for severity
  - Early Referral/Treatment: Lepto care bundle
  - Early Organ Support: CRRT Ventilatory support, ECMO

Treatment of Leptospirosis



Door-to-Dialysis Time and Daily Hemodialysis in Patients with Leptospirosis: Impact on Mortality

BUN/Creatinine = 200/6 mg/dL !!!

Lúcia Andrade,*† Sérgio Cleto,* and Antonio C. Seguro*†

*Intensive Care Unit, Emílio Ribas Institute of Infectology, and †Laboratory of Basic Scie
University of São Paulo School of Medicine, São Paulo, Brazil

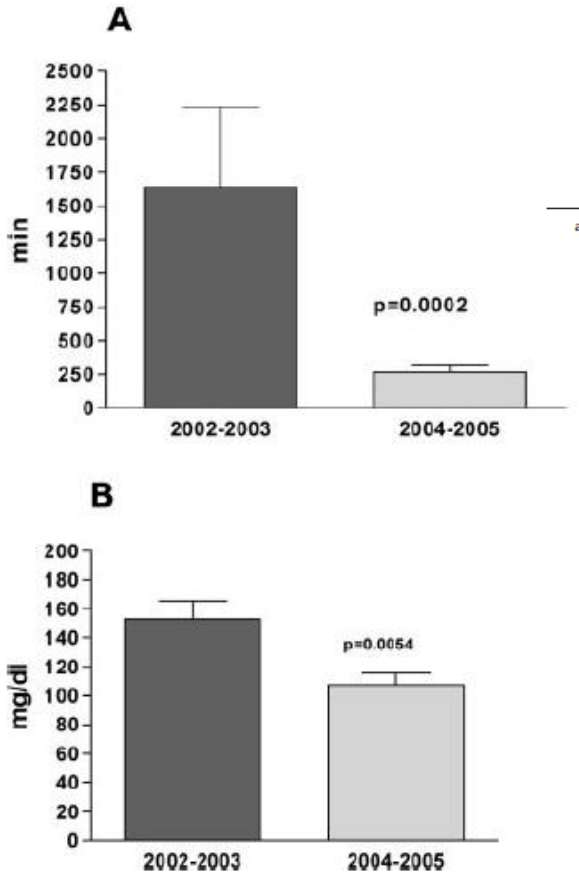


Figure 1. (A) Door-to-dialysis time (from intensive care unit admission to the initiation of dialysis); (B) mean serum urea during the dialysis treatment period.

Table 1. Clinical characteristics of patients at admission[a]

Variable	2002 to 2003 (n = 15)	2004 to 2005 (n = 18)	P
Age (yr)	44 ± 4.6	42 ± 3.7	NS
APACHE II score	26 ± 1.2	24.5 ± 1.4	NS
Urinary volume (ml/d)	1135 ± 539	1963 ± 458	NS
Urea (mg/dl)	232 ± 19.5	207 ± 18.4	NS
Creatinine (mg/dl)	6.2 ± 0.6	6.6 ± 0.6	NS
Sodium (mEq/L)	136 ± 1.7	139 ± 1.4	NS
Potassium (mEq/L)	4.2 ± 0.2	4.2 ± 0.2	NS
pH	7.28 ± 0.03	7.26 ± 0.03	NS
Bicarbonate (mEq/L)	18 ± 1	17 ± 1	NS
CPK (IU/L)	1410 ± 244	2069 ± 409	NS
Br (mg/dl)	15.4 ± 2.4	15.3 ± 2.7	NS

[a]Data are means ± SEM; Mann-Whitney test. Br, direct bilirubin; CPK, creatine phosphokinase.

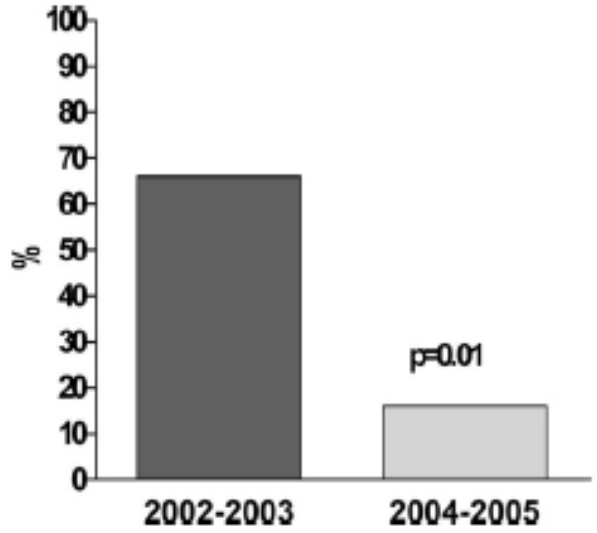


Figure 2. Mortality according to treatment group.

Clin J Am Soc Nephrol 2007; 2: 739–744

Lower Dosage Acute Peritoneal Dialysis versus Acute Intermittent Hemodialysis in Acute Kidney Injury: A Randomized Controlled Trial

CJASN
Clinical Journal of the American Society of Nephrology

Methods and Cohort

- **Multicenter randomized controlled trial**
- **Thailand**
- **AKI Patients**
  N = 157
- **May 2018 to January 2021**

Intervention

	Outcomes		
	28-day mortality	**28-day dialysis-free survival**	**7-days fluid balance (mL)**
Acute lower dosage PD 18-24 liters per day N = 80	**50%**	**41.8%**	**3018**
	Risk difference 0.60 (-15.0,16.3)	Risk difference 4.6 (-11.1,20.3)	Not significantly different
Intermittent HD Three times a Week N = 77	**49.4%**	**37.1%**	**3200**

Conclusions: In this study, there was no significant difference in 28-day mortality between acute PD and intermittent HD.

Watanyu Parapiboon, Sajja Tatiyanupanwong, Kamol Khositrangsikun, et al. **Lower Dosage Acute Peritoneal Dialysis versus Acute Intermittent Hemodialysis in Acute Kidney Injury: A Randomized Controlled Trial.** *CJASN.*
DOI: 10.2215/CJN.0000000000000482
Visual Abstract by Denisse Arellano, MD

Re-Examining Acute Peritoneal Dialysis

Back to the Future!

Pei Shan Lee,[1] Brett Cullis,[2] and Christopher T. Chan[1]

CJASN 19: 941–943, 2024. doi: https://doi.org/10.2215/CJN.0000000000000513

Peritoneal dialysis (PD) has been a longstanding option for treating AKI since its introduction in 1946. Despite demonstrating comparable outcomes with daily intermittent hemodialysis (HID) and continuous kidney replacement therapy (CKRT), PD remains underutilized. Its advantages, including cost-effectiveness, cardiovascular stability, and potential for earlier kidney recovery, are often overshadowed by misconceptions and doubts among clinicians.[1] As evidence has accumulated of equivalent outcomes and guidelines evolve, it is imperative to reconsider PD as a viable modality in routine AKI management even in those within the critical care setting.[2]

The bias against PD may stem from our conventional approach to assessing kidney replacement therapy efficiency. Currently, we rely on urea removal quantification by Kt/V urea, which may not adequately capture the clearance of larger solutes some of which may be responsible for associated morbidity. While CKRT dosing guidelines are well defined, optimal dosing for PD and hemodialysis in AKI remains ambiguous because of limited trials and methodological variations. This prompts a re-evaluation of whether urea clearance should continue to serve as the primary marker for dosing adequacy in the context of AKI. In addition, the AKI syndrome is heterogeneous with presentation from single to multiple-organ dysfunction along with variable degrees of acuity throughout the disease process, and one-size-fits-all dosing may be inappropriate.

Parapiboon *et al.*[3] aimed to address concerns of PD utilization in the acute setting and the determination of an ideal dose. Questions that, if answered, can potentially affect clinical practice and resource allocation globally. In this issue, the authors reported a multicenter randomized controlled trial involving 157 patients in four tertiary hospitals in Thailand comparing outcomes between low-dose PD and two to three times per week IHD in patients with incident AKI. The authors previously challenged the International Society for Peritoneal Dialysis's (ISPD) guideline target Kt/V by randomizing patients to the recommended or lower dose target Kt/V and showed there was no difference in outcomes.

This noninferiority study is a follow-up using the lower target compared with hemodialysis using a margin of 20%, and they examined 28-day mortality as the primary outcome and 28-day dialysis-free survival, kidney recovery, metabolic profile, and procedure-related complications as secondary outcomes. There was no significant difference in 28-day mortality between the groups in both intention-to-treat and per-protocol analyses. Secondary outcomes also showed no significant difference, although the PD group experienced higher incidences of catheter-related complications (10% developed peritonitis and 2.5% experienced leaks).

Although these results may indicate that PD holds promise as an option, several limitations must be acknowledged to contextualize its clinical implications. Particularly noteworthy is the variance in achieved clearance between the groups, which may introduce bias into the comparisons. The PD group's median achieved weekly Kt/V dose of 2.11 fell slightly below the ISPD[4] recommended threshold of 2.2. By contrast, the hemodialysis group's median dose of 2.87 was lower than the Kidney Disease: Improving Global Outcomes recommendation of 3.9.[5] It should be noted, however, that it was significantly higher than the largest randomized trial of high versus low-intensity IHD, which showed similar survival in the low intensity arm that achieved a weekly Kt/V of 2.1.[6] The inability of the hemodialysis group to achieve the prescribed targets are attributed to treatment disruptions, often stemming from hemodynamic instability. This raises the possibility that PD could present a viable alternative in such patients, especially when CKRT is unavailable. The use of low-flux dialyzers that were reused may

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[2]Department of Renal and Solid Organ Transplantation, Red Cross War Memorial Childrens Hospital, University of Cape Town, Cape Town, South Africa

Correspondence: Dr. Christopher T. Chan, email: christopher.chan@uhn.ca

Published Online Ahead of Print: July 16, 2024

See related article, "Lower Dosage Acute Peritoneal Dialysis versus Acute Intermittent Hemodialysis in Acute Kidney Injury: A Randomized Controlled Trial," on pages 970–977.

Best of ASN Journals (2024)

Updated: 9/9/2024
Contains: 12 items

The editors of *CJASN*, *JASN*, and *Kidney360* proudly present the high-impact articles published in 2024 featured during the *Best of ASN Journals* session at Kidney Week 2024. Join us on October 25 at 2:00PM in Ballroom 20B/C for a lively discussion.

Articles selected address:

- Key advances in kidney disease research including high impact research
- Therapeutic breakthroughs and advances for the treatment of kidney diseases
- Mechanistic studies that inform kidney disease treatment

Kidney Diseases covered:

- AKI and Intensive Care Unit Nephrology
- Glomerular Diseases
- Therapeutic Advances in CKD
- Care of Patients Undergoing Long-Term Dialysis

Established acute PD Program in Mittaphab Hospital, Vientiane, Laos PDR

Saiphet Syhalath, MD, former ISN Fellow

Pulmonary involvement (5%):

Bland hemorrhage but less inflammation

- Day 4-6 after symptom onset
- SOB, hemoptysis, acute respiratory failure and need MV (high mortality 51%)

Figure 3. The lung parenchyma shows a picture of diffuse alveolar damage, characterized by hyaline membranes (arrow) and alveolar edema (*), adjacent to areas of alveolar hemorrhage (top left). HE x100.

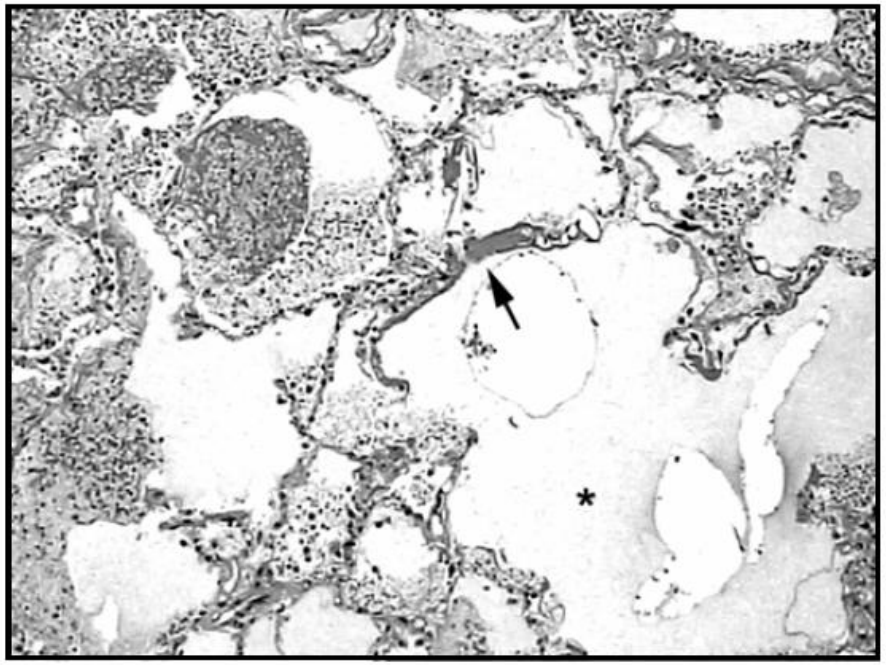
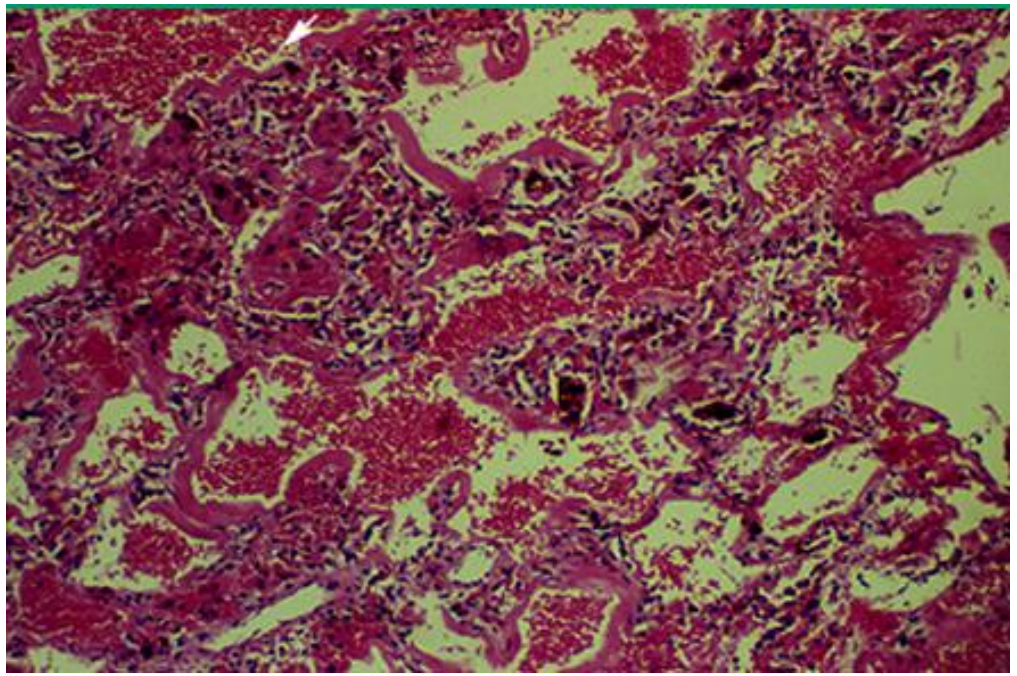


Figure 4. Hyaline membranes lining the alveolar septa in a patient with ARDS related to leptospirosis. HE x200.



BJID 2007;11:142-148

OPEN ACCESS

Case report

Leptospirosis manifested with severe pulmonary haemorrhagic syndrome successfully treated with venovenous extracorporeal membrane oxygenation

Jukkaphop Chaikajornwat ,[1,2] Pornpan Rattanajiajaroen,[2,3] Nattachai Srisawat,[2,4] Kamon Kawkitinarong[2,3]

A 39-year- old, Thai man, a street vendor who lives in Bangkok, presented to the emergency department with a 5-day fever and myalgia.

ECMO duration: 8 days
IJ-Femoral approach
Flow 2-5 L/min

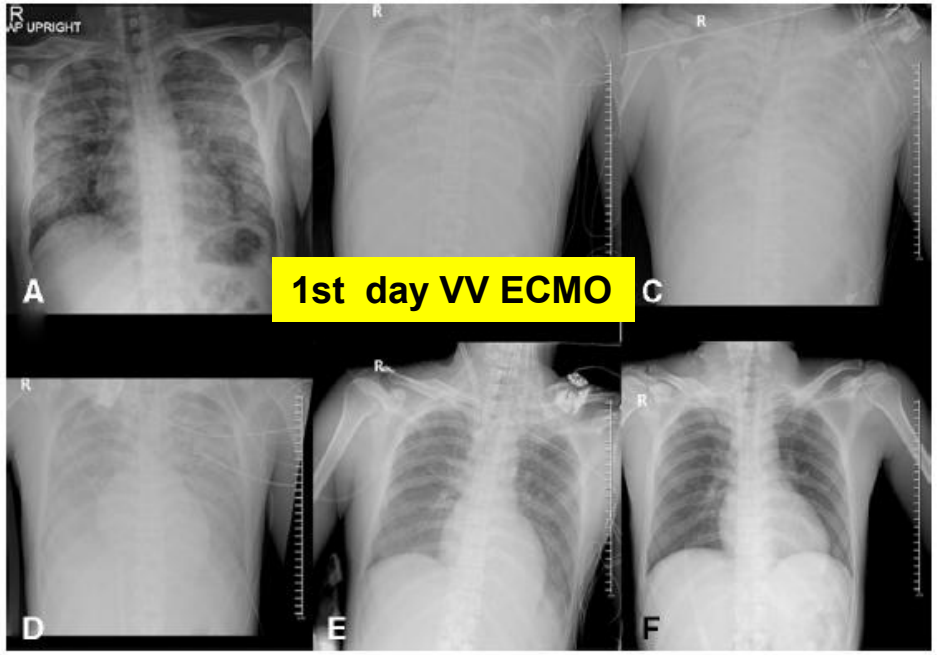


Figure 1 (A) Chest X-ray of the patient on day 1 before VV-ECMO. (B) Chest X-ray of the patient on day 1 after VV-ECMO. (C) Chest X-ray of the patient on day 2. (D) Chest X-ray of the patient on day 3. (E) Chest X-ray of the patient on day 5. (F) Chest X-ray of the patient on day 10. VV-ECMO, venovenous extracorporeal membrane oxygenation.

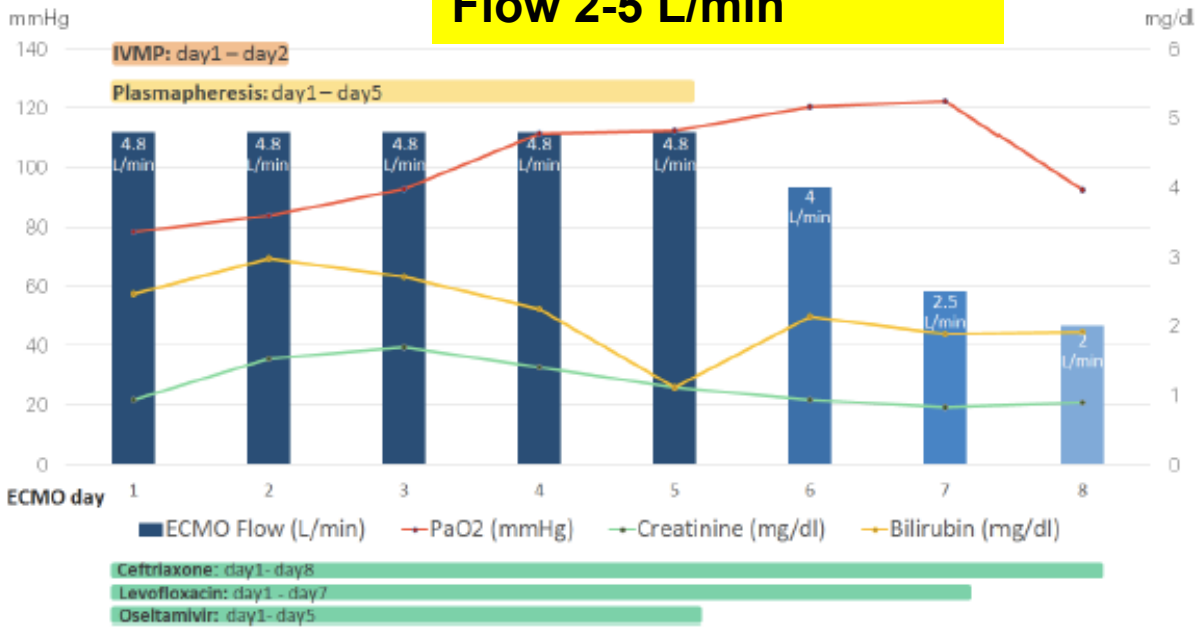


Figure 2 Clinical course of the patient. Bar chart demonstrates ECMO flow (L/min); red line shows PaO_2; green line shows creatinine, yellow line shows bilirubin. ECMO, extracorporeal membrane oxygenation; IVMP, Intravenous pulse methylprednisolone.

Table 1 Review of the case report: leptospirosis with pulmonary haemorrhage

	Arokianathan *et al*[30]	Assimakopoulos *et al*[31]				Kahn *et al*[32]	Liao *et al*[33]	Ludwig *et al*[34]	Cantwell *et al*[35]	Umei *et al*[36]	Jukkkaphop C *et al* (this case)
Age (year)	30	28	57	80	58	N/A	32	34	39	50	39
Gender	Male	Male	Male	Male	Male	Male	Male	Male	Male	Male	Male
Comorbidity	None	None	None	HT, AF, T2DM, HF	Ulcerative colitis, T2DM	N/A	None	None	Obesity	None	None
Presentation	4 days of myalgia, jaundice	2 days of fever, headache, dyspnoea and haemoptysis	10 days of fever, haemoptysis, jaundice, AKI	2 days of fever, myalgia, haemoptysis and AKI,	4 days of fever, myalgias, non-bloody diarrhoea and AKI	Flu-like symptom	2 days of fever, myalgia and jaundice	7 days of fatigue and vomiting, and presentation with dyspnoea, jaundice and AKI	Fever, myalgia, headache, progressive dyspnoea and AKI	2 days of fever, myalgia and jaundice	5 days of fever, myalgia; 6 hours of dyspnoea and haemoptysis
Haemoptysis	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
PaO_2/FiO_2 ratio	N/A	210	200	90	150	N/A	163	N/A	131	70	74.2
Treatment	MV MARS	MV	MV RRT	MV RRT	MV RRT	MV RRT	MV	MV Plasmapheresis RRT	MV	MV RRT	MV Plasmapheresis
ECMO Initiate day	VV-ECMO 183 hours	Not done	Not done	Not done	Not done	VA-ECMO 60 hours	VV-ECMO, 1 day and total of 6 days	VV-ECMO, 1 day	VV-ECMO, 2 days after admission, double membrane oxygenator, in parallel	VV-ECMO, 3 days after admission, (day 5 after symptom)	VV-ECMO, 12 hours and total of 8 days
Outcome	Improved	Improved	Improved	Improved	Dead (multiorgan failure)	Improved	Improved	Dead, 29 hours after initial presentation (multiorgan failure)	Improved	Improved	Improved

ECMO duration: 6-8 days

6/7 (85%) survive !!!

AF, atrial fibrillation; AKI, acute kidney injury; ECMO, extracorporeal membrane oxygenation; HF, heart failure; HT, hypertension; MARS, molecular adsorbent recirculating system; MV, mechanical ventilator;N/A, not available; RRT, renal replacement therapy; T2DM, type 2 diabetes mellitus; VA-ECMO, veno-arterial extracorporeal membrane oxygenation.

Challenging points:

- cannnot give heparin at the beginning of ECMO
- Long term respiratory function: good > bad
- Accessibility ???

Challenges: How to access CRRT/ECMO /HP in resource limited settings?

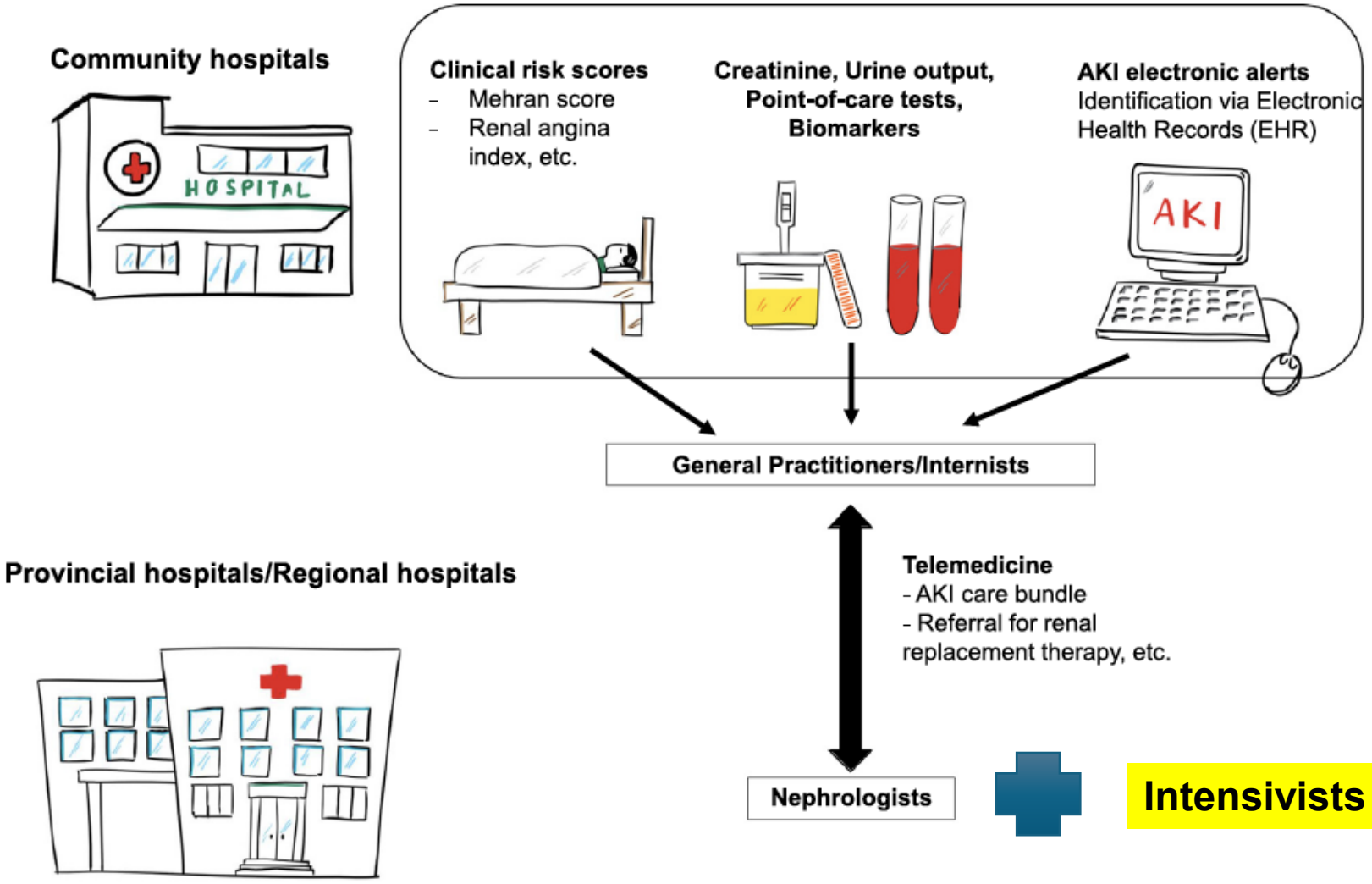
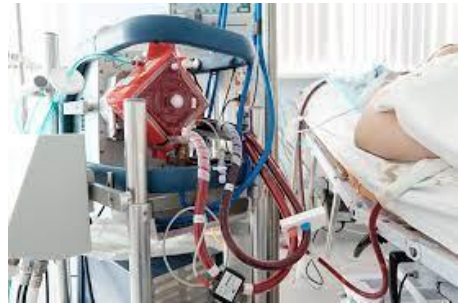
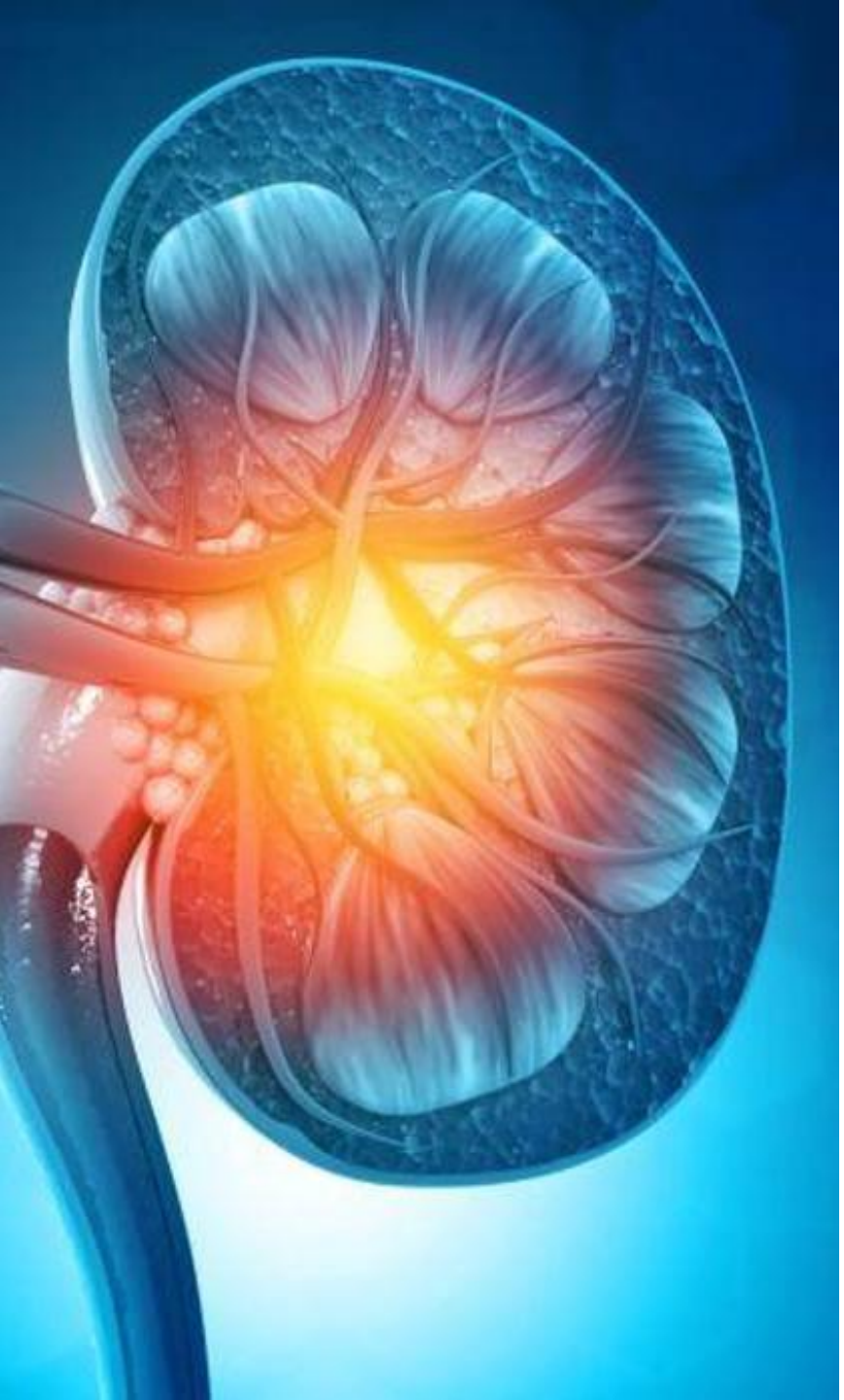


Figure 4. Schematic diagram for improvement in acute kidney injury (AKI) recognition in Asia (limited-resource settings). A combination of clinical risk scores, point-of-care tests and biomarkers, and AKI electronic alerts can increase the diagnostic yield of AKI for general practitioners/internists. General practitioners/internists can confer with nephrologists by telemedicine whether the patient should receive an AKI care bundle or be referred for renal replacement therapy.

ECMO



CRRT



Long term follow up care

What are the risk factors of leptospiral CKD and CKD progression?

- Acute Kidney Injury During Initial Infection?
- Persistent Leptospiral Infection?
- Proper antibiotic treatment/ Antibiotic Resistance?
- Host Genetic Factors?
- Environmental and Occupational Exposure?
- Underlying Health Conditions?
- Biomarkers?

Long-term kidney outcomes after leptospirosis: a prospective multicenter cohort study in Thailand

Background

Leptospirosis is one of the most important public-health zoonotic diseases in the tropics.
Long-term kidney outcomes in patients after leptospirosis infection are rarely investigated.

Methods

15 centers
Sisaket province, Thailand

217 confirmed leptospirosis cases
(**32.7%** severe cases)

Major-adverse kidney event
- Death
- RRT dependence
- New-onset CKD
  (eGFR < 60 or tubulopathy)

MAKE

Results

Admission period
Dec 1, 2015 to Nov 30, 2018

6.9%
In-hospital mortality

Follow-up period
Feb 1, 2020 to Oct 31, 2020

Median follow-up 4.18 years

Severe leptospirosis
(mSOFA score > 2)

MAKE
Adjusted HR
2.45; 95% CI 1.44–4.18

New-onset CKD
Adjusted OR
3.22; 95% CI 1.04–9.96

*adjusted by age, sex, and comorbidities

Mg PO_4 Increased renal magnesium and phosphate wasting

Conclusion

Severe leptospirosis is associated with long-term kidney sequelae. Long-term follow-up and specific interventions are still needed.

ERA ndt NEPHROLOGY DIALYSIS TRANSPLANTATION

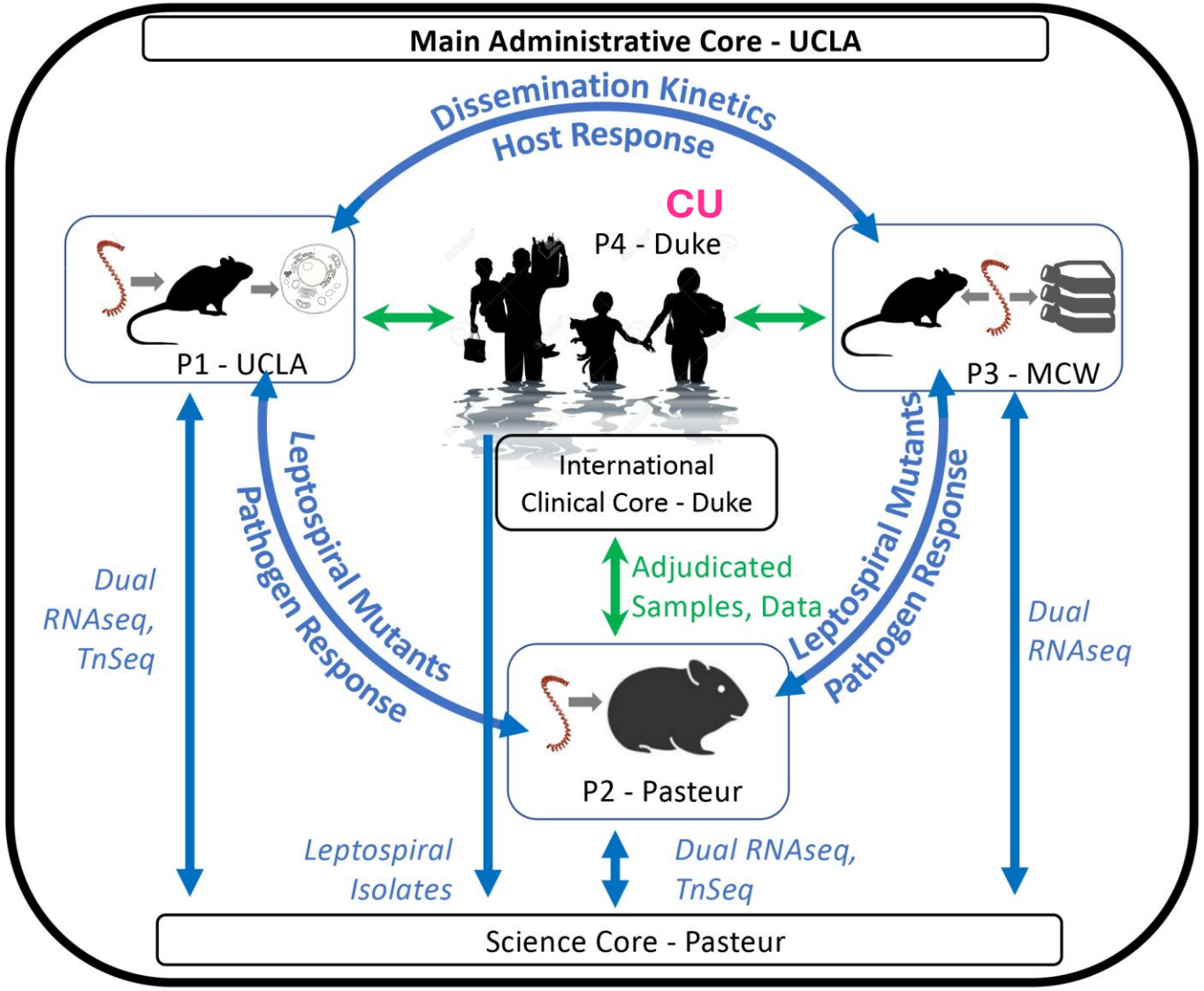
Long term follow up care

Phannajit, J., et al. NDT (2023)
@NDTSocial

Future direction

- Integrate knowledge from both the basic sciences and clinical sciences to understand the pathogenesis of leptospirosis induced long term kidney damage
- Study more on the impact of leptospirosis in chronic kidney disease in endemic area
- Identify risk profile for predict CKD and CKD progression in severe leptospirosis.
- Identify predictive biomarkers of leptospiral CKD and CKD progression
- Assess the intervention that can modify the long-term sequelae of severe leptospirosis.

Future direction



Specific Aims

Aim 1: Patient Cohorts

- Expand the biorepository by recruiting suspected leptospirosis patients at 15 hospitals (Sisaket) & 2 hospitals (Nakhon Si Thammarat), Thailand.
- Conduct longitudinal follow-ups on severe cases to analyze host response dynamics.

Aim 2: Biomarkers for POC Rapid Diagnosis

- Proteomics analysis of Day 1 plasma samples (leptospirosis, AFI, healthy controls).
- Validate leptospirosis-specific biomarkers in biorepository & prospective cohorts.
- Assess RPA-CRISPR/Cas12a-LFDA for rapid, sensitive, cost-effective diagnosis.

Aim 3: Biomarkers for Severe Outcome Prediction

- Identify novel plasma biomarkers linked to severe disease using proteomics & network analysis.
- Validate biomarkers for predicting severe leptospirosis cases.

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