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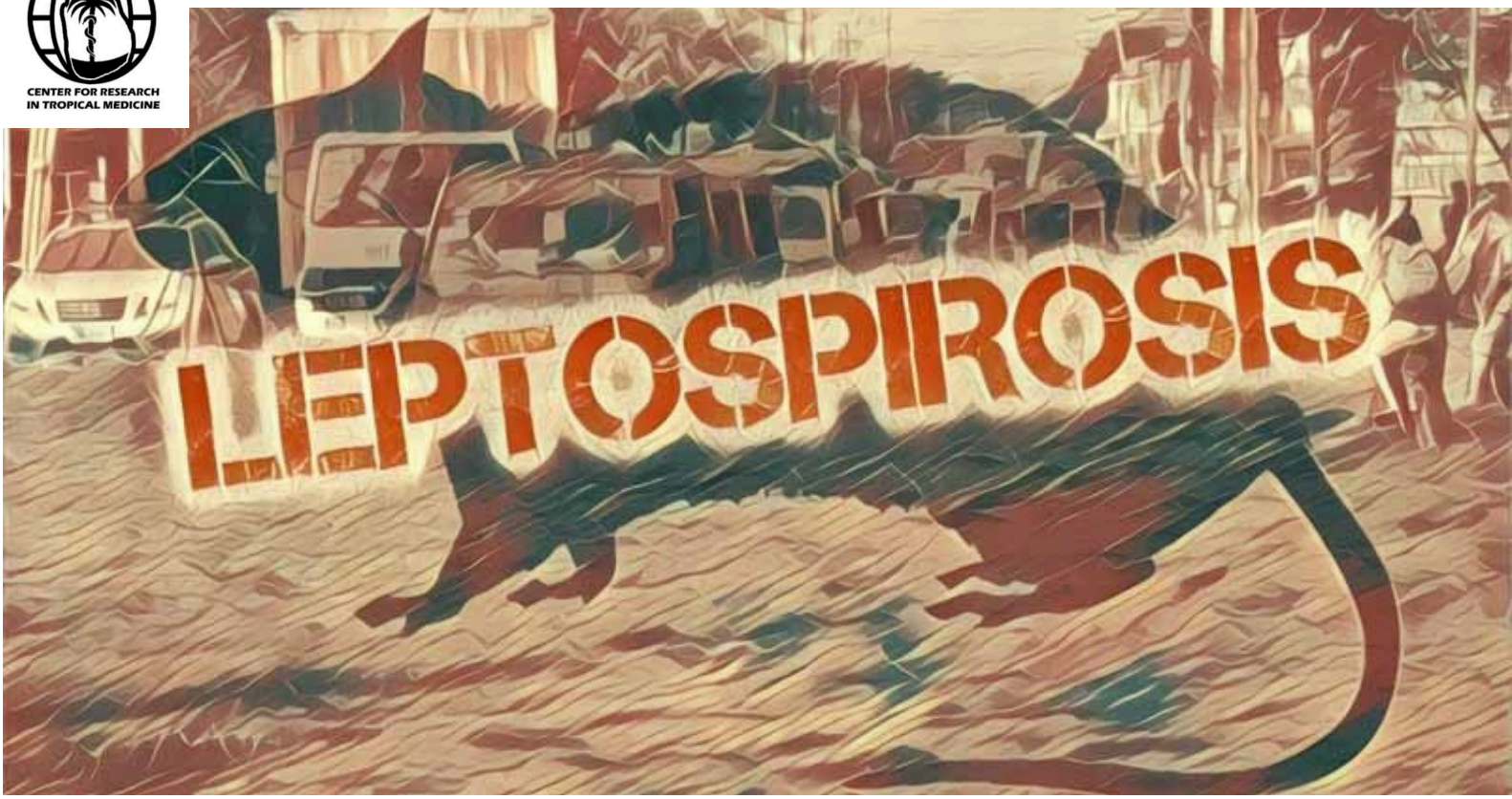
THE CRTM NEWSLETTER

CENTRE FOR RESEARCH IN TROPICAL MEDICINE
UNIVERSITY OF PERADENIYA



Committee

Inside..

DIRECTOR'S MESSAGE

PROF UDAYA RALAPANAWA

Professor of Medicine
Director, CRTM
Faculty of Medicine
University of Peradeniya
Sri Lanka

As we navigate another year of challenges and opportunities in tropical medicine, we are reminded of the profound responsibility we carry as custodians of knowledge in a field that continues to receive far less attention than it deserves. This responsibility is especially important as Sri Lanka continues to confront leptospirosis, a re-emerging and potentially fatal infectious disease that places a considerable burden on individuals, families and the healthcare system.

Leptospirosis remains a major public health concern across the island, affecting both rural and urban communities. Although traditionally associated with agricultural work and exposure to contaminated water or soil, the disease can affect individuals from a wide range of occupational and social backgrounds. Delayed recognition and treatment may lead to severe complications involving the kidneys, liver, lungs, heart and nervous system, with potentially devastating consequences.

This continued burden reminds us why tropical medicine deserves greater attention at both national and international levels. Sri Lanka is uniquely positioned at the crossroads of many tropical diseases that have shaped the health, livelihoods and history of our people. These infections have evolved alongside agriculture, environmental change, urbanisation and population movement, continuously testing the resilience of our communities and healthcare services.

This newsletter has been developed with a clear mission: to strengthen awareness and understanding of leptospirosis among medical professionals and the general public. Recognising risk factors and early clinical features, initiating timely investigations and treatment, understanding severe manifestations and promoting effective preventive measures can make a profound difference in reducing morbidity and mortality.

Since our founding in 1985 and formal recognition in 1994, we have remained committed to advancing the understanding of tropical diseases. Our predecessors, Professor S. N. Arsecularatne and Professor Nimal Senanayake, laid strong foundations through remarkable collaborations, dedicated scholarship and groundbreaking research

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This newsletter represents another important step forward a platform to share knowledge, highlight clinical and scientific developments and strengthen collaboration. I invite healthcare professionals, researchers, students and members of the public to engage actively with its content and contribute to reducing the burden of leptospirosis in Sri Lanka.

Leptospirosis Symposium 2026

Advancing Knowledge from Global Perspectives to Clinical Practice

The Centre for Research in Tropical Medicine (CRTM), Faculty of Medicine, University of Peradeniya, successfully hosted the Leptospirosis Symposium 2026 on 26 February 2026 at the Department of Forensic Medicine.

Held under the theme “Leptospirosis: From Global Perspectives to One Health and Severe Disease Management,” the symposium provided a comprehensive platform for discussing the evolving landscape of leptospirosis. The programme explored a broad range of topics, from the global burden and microbiological foundations of the disease to One Health approaches, preventive strategies, and the management of severe leptospirosis.

The academic programme featured a distinguished panel of experts who delivered informative and clinically relevant presentations. Professor Udaya Ralapanawa discussed the historical and global perspectives of leptospirosis and its impact on human health. Professor Nilanthi Dissanayake explored the causative organism, the importance of the One Health approach, and available prevention strategies. Emeritus Professor S. A. M. Kularatne delivered a focused session on the recognition and management of severe leptospirosis.

The symposium attracted a diverse group of participants, including medical officers, postgraduate trainees, and specialists representing medicine, paediatrics, emergency medicine, anaesthesia and critical care, microbiology, and allied health sciences.
The interactive sessions encouraged meaningful discussion and knowledge exchange among participants, strengthening their understanding of the diagnosis, prevention, and clinical management of leptospirosis. The programme was particularly relevant to the Sri Lankan healthcare setting, where leptospirosis continues to pose a significant public health and clinical challenge.

Through this symposium, the CRTM reaffirmed its commitment to promoting multidisciplinary collaboration, evidence-based clinical practice, and research aimed at improving the prevention and management of tropical diseases.

Leptospirosis Symposium 2026

Advancing Knowledge from Global Perspectives to Clinical Practice

Leptospirosis: Historical and global perspectives and impact on human health

Prof Udaya Ralapanawa
Professor of Medicine
Director - CRTM
Faculty of Medicine
University of Peradeniya

Introduction

Leptospirosis may not dominate global health headlines, but the numbers tell a sobering story. The World Health Organization estimates approximately 1.03 million cases and nearly 58,900 deaths occur annually worldwide [1,13]. Despite this burden, the disease remains chronically under-recognized frequently misdiagnosed as dengue fever or influenza and is classified as a neglected tropical disease [1]. In an era of climate change and rapid urbanization, understanding leptospirosis is no longer optional for clinicians working in tropical and subtropical regions.

A Disease Through the Ages: Historical Milestones

The clinical story of leptospirosis begins in 1886, when German physician Adolf Weil first described a severe multisystem illness characterized by jaundice, renal failure, hemorrhage, and high fever. This grave presentation was subsequently termed Weil's disease [1]. The causative organism remained unknown until 1907–1915, when Japanese scientist Ryukichi Inada and colleagues isolated and named it Leptospira interrogans describing its thin, spiral morphology and distinctive "question mark" appearance under microscopy [2].

By the early twentieth century, leptospirosis was increasingly recognized as an occupational hazard. Sewer workers, rice field farmers, miners, and slaughterhouse workers bore a disproportionate burden, giving rise to colloquial names such as "mud fever," "cane cutter's disease," and "swineherd's disease." European outbreaks were frequently tied to rat infestation in urban environments [1].

The World Wars provided unwitting epidemiological insight: large outbreaks among soldiers in muddy trenches, tropical battlefields, and flooded environments solidified understanding of environmental transmission via contaminated water [4]. By mid-century, research confirmed that rats serve as primary reservoirs, with cattle, pigs, dogs, and wild animals also capable of harboring the organism. Infection spreads via urine-contaminated water, firmly establishing leptospirosis as a zoonotic disease [3].

Leptospirosis perspectives...

Modern diagnostic advances including the Microscopic Agglutination Test (MAT), serological serovar classification, and PCR-based methods have sharpened understanding of pathogenesis. Today, leptospirosis is firmly recognized as a major public health problem in tropical countries, strongly associated with flooding and climate change, and endemic across much of South Asia including Sri Lanka [1].

Global Burden: Inequitable, Underestimated, and Expanding

Leptospirosis is endemic in over 160 countries, with the highest incidence in South and Southeast Asia, Oceania, and Latin America [2]. Incidence rates in tropical hotspots can reach 10–100 cases per 100,000 population, compared to fewer than 1 per 100,000 in developed nations a disparity rooted in structural differences in climate, agriculture, sanitation, and rodent control [2].

The Disability-Adjusted Life Year (DALY) burden is substantial and widely considered an underestimate, given that surveillance remains highly heterogeneous across countries and the disease is frequently misclassified in febrile illness registries [1,13]. Several factors drive emergence and re-emergence: climate variability with heavy rainfall and flooding; rapid urbanization with inadequate water and sanitation infrastructure; poverty and occupational exposure; population displacement following disasters; ecosystem changes that alter rodent populations; and breakdown of surveillance in conflict-affected settings [3].

In developed nations, the low incidence reflects cold winters limiting bacterial survival, mechanized farming practices, use of personal protective equipment, closed sewage systems, and structured rodent control programmes. The most common exposure in such settings is recreational water sports a stark contrast to the farming and flood-related exposures dominant in tropical regions [6].

Leptospirosis in Sri Lanka: A National Hotspot

Sri Lanka offers a particularly instructive case study. The island's tropical climate, extensive paddy cultivation, and high rodent density have likely sustained leptospirosis transmission for over a century, though formal recognition began only in the mid-twentieth century, primarily among paddy farmers, irrigation workers, and estate labourers [7].

The 2008 outbreak represented a watershed moment one of Sri Lanka's largest on record, with approximately 7,000 reported cases, high mortality, and clear links to flooding and agricultural exposure. This crisis catalyzed meaningful public health responses: strengthened national surveillance systems, the introduction of doxycycline prophylaxis policies for high-risk groups, and expanded laboratory diagnostic capacity [1,4].

Today, leptospirosis remains endemic in the Western, Sabaragamuwa, and Central Provinces, and Sri Lanka is now recognized internationally as a global hotspot for the disease [4]. Seasonal peaks align with monsoon seasons and post-flood periods. Urban transmission via inadequate drainage adds a further dimension to an already complex epidemiological picture [1].

Leptospirosis perspectives...

Transmission: How Humans Become Accidental Hosts

Leptospira interrogans resides in the renal tubules of infected mammals and is shed continuously or intermittently in urine throughout the animal's life often without causing illness in the reservoir host. Approximately 160 mammalian species have been identified as natural carriers [9]. The organism can survive for days to months in urine-contaminated soil and freshwater, creating an environmental reservoir that persists long after animal contact [11].

Humans are accidental hosts. Infection typically occurs through cuts or abraded skin, mucous membranes, or conjunctivae following contact with contaminated water, soil, or animal urine. Ingestion of contaminated food or water is another recognized route, as is direct contact with reproductive fluids from infected animals. Animal bites represent a rare transmission pathway. Human-to-human transmission is exceptionally uncommon but has been documented via sexual intercourse and breastfeeding [12].

Occupational risk groups include farmers (rice, sugarcane, vegetable, and livestock), sewerage and abattoir workers, veterinarians, laboratory staff, miners, soldiers, and inland fishermen. Recreational exposures swimming, sailing, gardening, and marathon running also carry risk, particularly in endemic regions [1].

Clinical Presentation: Recognizing a Chameleon Disease

The clinical spectrum of leptospirosis is broad, ranging from entirely asymptomatic infection (approximately 90% of cases) to fatal multisystem disease [12].
Anicteric Leptospirosis is the most common symptomatic form, classically described as a biphasic illness, though most patients experience only the acute phase. The acute phase typically begins 5–14 days after exposure (incubation range: 2–30 days) and lasts approximately two to nine days. It presents as a non-specific febrile illness with abrupt onset of fever, rigors, severe myalgia (particularly in the calves and lower back), and headache occurring in 75–100% of patients. Approximately half experience nausea, vomiting, and diarrhea; non-productive cough occurs in 25–35% [13].
A distinguishing clinical feature is conjunctival suffusion (hyperemia without discharge), present in over half of patients a sign that is widely under-recognized in practice [1]. Subconjunctival hemorrhage, muscle tenderness, splenomegaly, lymphadenopathy, and skin rash may also be observed.
A minority of patients enter the "immune phase," characterized by return of fever, headache, and myalgia, complicated by aseptic meningitis (occurring in approximately half of those affected) and uveitis. Leptospires are absent from the blood during this phase, but may be detectable in urine; IgM antibodies appear and MAT becomes positive [5].
Icteric Leptospirosis (Weil's Disease) occurs in 5–10% of patients and carries a mortality rate of 5–15%. It is a rapidly progressive multisystem illness featuring fever, jaundice, and renal failure. Pulmonary hemorrhage is the most feared complication, reported as fatal in 50–70% of affected patients [14].

Leptospirosis perspectives...

Laboratory findings commonly include neutrophilia, thrombocytopenia, elevated C-reactive protein (CRP), raised creatinine, elevated aminotransferases, and elevated creatine kinase (reflecting rhabdomyolysis in approximately half of patients). Urinalysis frequently reveals proteinuria, pyuria, and granular casts [10].
Red flags warranting urgent escalation include oliguria, hypotension, hemoptysis, altered sensorium, and rapid platelet decline [9].

Diagnosis and Clinical Decision-Making

The diagnostic window varies by phase of illness. Blood culture and PCR are positive in Week 1 (leptospiraemia); urine culture and PCR become positive from Week 2 onward. MAT and ELISA become positive from Week 2, persisting for months to years [7].
Critically, clinicians are advised not to wait for serological confirmation before initiating treatment. In any patient presenting with acute febrile illness and a relevant exposure history (flood water, paddy field work, rodent contact, sewer cleaning), clinical suspicion alone warrants immediate antibiotic therapy [1].
Key diagnostic differentiators from dengue include the presence of leukocytosis rather than leucopenia, significantly elevated CRP, conjunctival suffusion, and marked calf tenderness a combination highly suggestive of leptospirosis [2].

Treatment: Early Intervention Is Paramount

Treatment should be initiated promptly upon clinical suspicion, as early antibiotics reduce disease severity and duration [8].
For mild disease, doxycycline (100 mg orally, twice daily for 7 days) is the drug of choice, where not contraindicated. Alternatives include azithromycin (500 mg once daily for 3 days), ampicillin (500–750 mg every 6 hours for 7 days), or amoxicillin (500 mg every 6 hours for 7 days).
For severe disease, intravenous penicillin (1.5 million units every 6 hours) is the first-line agent, with ceftriaxone (1 g IV every 24 hours) as an effective alternative [1].
Daily reassessment of renal function within 24 hours of admission is strongly recommended [1].

Health Systems and Societal Impact

Beyond individual patient outcomes, leptospirosis imposes considerable systemic costs. Diagnostic uncertainty delays recognition; limited access to reliable testing compounds this challenge. During outbreaks, district laboratories and intensive care units face significant strain [14]. Underreporting driven by misclassification in febrile illness surveillance means that burden estimates consistently underrepresent true disease impact [13].
Economically, the disease disproportionately affects working-age adults in agriculture-dependent regions. Hospitalization, ICU costs, and productivity losses are substantial. Recurrent outbreaks disrupt local economies, and the DALY burden reflects the combined toll of both premature mortality and lasting morbidity [1].

Leptospirosis perspectives...

Looking Ahead: Climate, Urbanization, and Research Gaps

The future trajectory of leptospirosis is inseparable from climate change. Increasing frequency of extreme rainfall events and flooding both well-established amplifiers of transmission suggest outbreak frequency will rise [1,3,7]. Urban growth, particularly in settings with inadequate water and sanitation infrastructure, threatens to expand the at-risk population in previously lower-burden settings [6].
Priority areas for action include standardized global surveillance systems, improved point-of-care diagnostics accessible in resource-limited settings, and robust research into long-term outcomes following severe leptospirosis an area that remains poorly characterized in the literature [1].

Conclusion: Think Leptospirosis

Leptospirosis is a treatable disease with an eminently recognizable clinical profile provided clinicians think to consider it. In the context of a monsoon-season febrile illness, calf tenderness and conjunctival redness constitute a compelling diagnostic clue. Laboratory findings of thrombocytopenia, leukocytosis, and elevated CRP should heighten suspicion. Most importantly: do not wait for laboratory confirmation. Early antibiotics save kidneys, lungs, and lives.
As climate pressures intensify and urbanization continues, leptospirosis demands proportionate clinical vigilance, public health investment, and research attention.

Leptospirosis perspectives...

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Epidemiology of Leptospirosis: Global and Sri Lankan Burden, Risk Factors, and Prevention Strategies

Prof Samidi Navaratna
MBBS, DCH, MSc, MD
Professor in Community Medicine
Department of Community Medicine
Faculty of Medicine
University of Peradeniya

Leptospirosis is an important zoonotic bacterial disease caused by pathogenic species of Leptospira, transmitted to humans mainly through contact with water or soil contaminated by the urine of infected animals, especially rodents[1]. It is often under-recognised because its early symptoms resemble many other acute febrile illnesses, yet it can progress to severe disease with jaundice, renal failure, pulmonary haemorrhage, and death[1]. Although once considered mainly an occupational infection, leptospirosis is now recognised as a neglected tropical disease with a substantial global burden, particularly in tropical and flood-prone settings[1].

Introduction

Leptospira organisms persist in animal reservoirs through chronic renal carriage and are shed into the environment through urine, where they can survive in water and moist soil[1]. Humans are accidental hosts and acquire infection through breaks in the skin, abrasions, or mucous membranes after exposure to contaminated environments[1]. Most infections are mild and self-limited, but a minority develop severe manifestations such as Weil's disease or pulmonary haemorrhagic syndrome, which may be fatal if diagnosis and treatment are delayed[1]. The disease is also difficult to detect early because the symptoms overlap with dengue, influenza, typhoid, and other common tropical infections, and many endemic settings still lack rapid laboratory confirmation[1,2].

Global burden

The global burden of leptospirosis is much higher than previously appreciated. A WHO-supported systematic review estimated approximately 1.03 million cases and 58,900 deaths each year worldwide[3]. A companion analysis estimated about 2.90 million disability-adjusted life years (DALYs) lost annually, showing that leptospirosis is among the more burdensome bacterial zoonoses globally[4]. The burden is concentrated in tropical regions, particularly South and South-East Asia, the Western Pacific, Africa, and Latin America, and it disproportionately affects working-age men because of occupational and environmental exposure[4].

Epidemiology of Leptospirosis...

Regional studies reinforce this picture. In Africa, leptospirosis has been described as a neglected zoonosis requiring a One Health approach involving human, animal, and environmental health sectors[5]. In Latin America, outbreaks are often linked to heavy rainfall and flooding, while in Malaysia surveillance data show increased risk among agricultural workers, town-service workers, and animal handlers[6,7]. Even in Europe, recent flood-related clusters in Greece and wartime-related increases in Ukraine show that environmental disruption can trigger outbreaks outside traditionally endemic tropical regions[8,9].

Sri Lankan burden

Sri Lanka is one of the countries most affected by leptospirosis and has reported high incidence for many years[10]. The disease became notifiable in 2008 after a major outbreak, reflecting its growing public-health importance[10]. A systematic review estimated that between 2008 and 2015 the annual caseload was about 10,423, with approximately 730 deaths per year and a pooled case fatality ratio of 7.0%[10]. Hospital-based estimates suggested a national burden of roughly 300 cases per 100,000 population after adjusting for under-ascertainment[10].

Surveillance data indicate that the burden remains substantial and episodic. Large outbreaks have occurred after periods of heavy rainfall and floo ling, including the major outbreak reported in 2024[11]. Districts such as Kegalle, Kandy, Gampaha, Ratnapura, and Kalutara repeatedly report higher numbers of cases, suggesting strong geographic clustering[11,12]. Under-reporting remains an important issue because many cases are never confirmed by laboratory testing or captured through routine notification systems[10,13].

Risk factors

Environmental and climatic factors are key drivers of leptospirosis transmission. Rainfall and flooding are consistently associated with outbreaks because they increase human exposure to contaminated water and help spread organisms from soil and animal urine into the environment[14]. Temperature, humidity, and other weather variables also influence the survival of Leptospira in water and soil[12]. In Sri Lanka, local studies from Kandy and other districts have shown clear associations between monthly leptospirosis incidence and rainfall patterns, including broader climate variations[12,14,15].

Occupational exposure remains one of the most important risk factors. Agricultural work, especially rice farming, exposes workers to flooded fields and contaminated mud, and similar risks affect plantation workers, sanitation workers, sewer workers, animal handlers, and disaster-response personnel[15,16]. Behavioural and demographic factors also matter: men and working-age adults are affected more often, largely because they are more likely to engage in high-risk outdoor work[4,17]. In addition, disaster-related conditions such as floods, landslides, and infrastructure disruption can sharply increase exposure, and urban transmission is increasingly recognised where rodent infestation and poor sanitation persist[8,9,18].

Epidemiology of Leptospirosis...

Prevention strategies

Prevention is best understood through a One Health framework that combines human, animal, and environmental interventions[19]. At the community level, rodent control, improved sanitation, drainage, safe water management, and environmental cleanup can reduce exposure to contaminated water and soil[19]. Personal protection is also important, especially for high-risk groups, and includes wearing boots and gloves, covering wounds, washing after exposure, and avoiding contact with floodwater when possible[2,16].

Public-health surveillance and diagnostics are central to prevention. Earlier diagnosis improves clinical outcomes and helps distinguish leptospirosis from other febrile illnesses, while better surveillance gives a more accurate picture of national burden[1,20]. Doxycycline prophylaxis may be used for limited high-risk situations such as flood response or military deployment, though it is not suitable for routine mass use[2]. Vaccination of animals can also reduce environmental shedding, although a broadly protective human vaccine is still unavailable[1].

Sri Lanka has also moved toward climate-informed control strategies, including early warning systems and improved intersectoral coordination[11,19]. These measures are especially important because outbreaks tend to follow monsoon rains and extreme weather events, allowing preventive action before case numbers rise[11,12].

The pictorial abstract below illustrates the life cycle of Leptospira and provides a concise visual summary of the key concepts discussed in this article (Figure 1).

Conclusion

Leptospirosis remains a major but underappreciated public-health problem globally and in Sri Lanka[3,10]. Its burden is driven by climate, occupation, animal reservoirs, and environmental exposure, and control will require stronger surveillance, better diagnostics, personal protection, rodent control, and integrated One Health strategies tailored to local risk patterns[1,19].

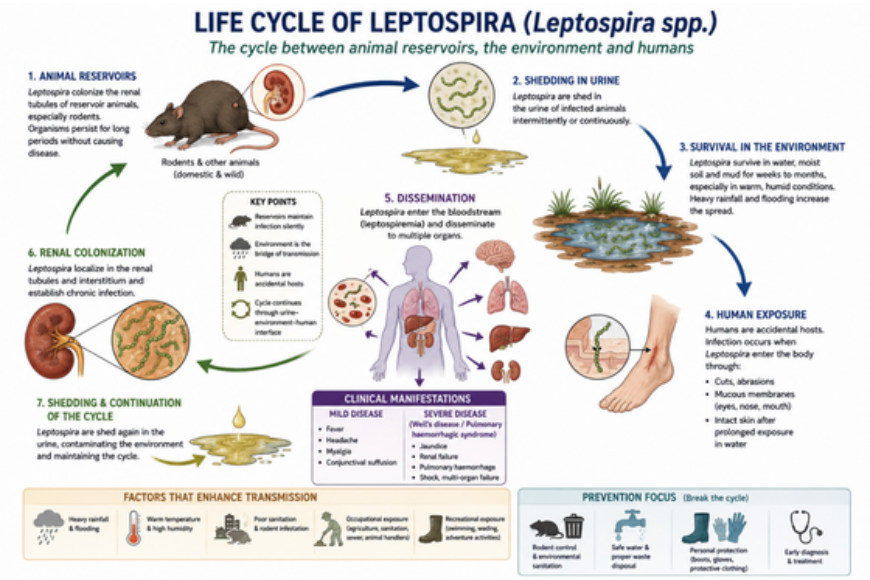

Figure 1. Pictorial abstract illustrating the life cycle of Leptospira and summarizing the key epidemiological findings and prevention strategies discussed in this article

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The Microbe, One Health, and Prevention

Prof. Nilanthi Dissanayake
Professor in Microbiology
Department of Microbiology
Faculty of Medicine
University of Peradeniya

Consultant Microbiologist
Teaching Hospital, Peradeniya

Mr. Nipun Rathnayake (BSc. MPhil)

For nearly 40 years after the early 1970s, leptospirosis was not treated as a major medical issue in Sri Lanka [1, 2]. Many people saw it simply as an occasional, expected risk of rural farming life [1, 5]. However, that complacency shattered in 2008 when a massive nationwide outbreak struck Sri Lanka, overwhelming hospitals and leaving hundreds dead [1, 3].

Today, leptospirosis is officially recognized as one of Sri Lanka's most urgent public health threats [2, 3]. Yet, despite thousands of patients being hospitalized every year, scientists have long struggled to identify the exact leptospira strains causing the illness or which animals were spreading them [1, 3]. Though diagnostics are available only in limited facilities in the country, most diagnoses relied on clinical diagnosis based on history, general symptoms or basic blood tests that could not confirm leptospirosis nor identify the specific types of leptospira involved [1, 2].

Research studies focused on genetic, environmental, and veterinary aspects of leptospirosis is being carried out at different parts of the country providing new insights to this diease. By using advanced DNA testing methods such as Sanger sequencing and, Multilocus Sequence Typing (MLST) researchers are uncovering a complex transmission web involving many different animals [1, 4]. These discoveries challenge old assumptions about how the disease spreads through farming waterways and why certain bacterial strains are causing severe, unusual complications in patients [1, 4].

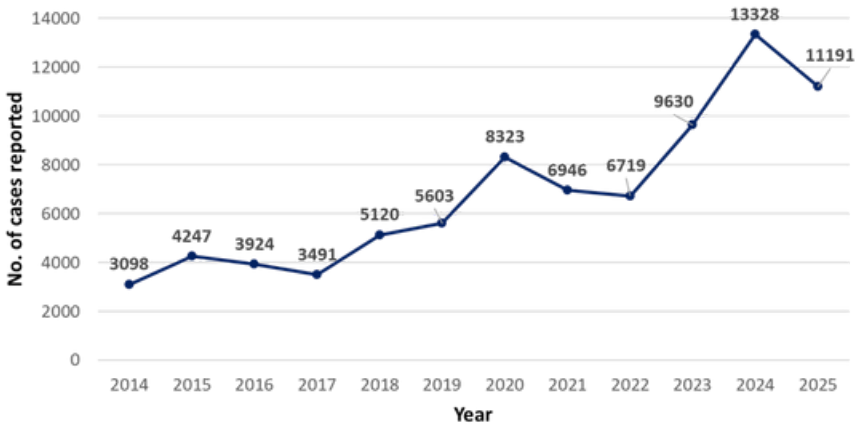

Figure 01: Suspected cases of leptospirosis reported in Sri Lanka over the last 10 years.

The Microbe, One Health, and Prevention

The Pathogen and the Clinical Surge: More Than a Simple Fever

Leptospirosis is a disease caused by spiral-shaped bacteria called Leptospira [5, 6]. These tiny, highly active bacteria have hooked ends and tail-like flagella that help them burrow through tissue barriers and enter the bloodstream [7, 8]. Scientists classify the genus into four evolutionary groups: P1 (severe disease-causing pathogens), P2 (intermediate, milder pathogens), S1, and S2 (harmless environmental bacteria) [6, 9].

Globally, leptospirosis causes about 1 million infections and 58,900 deaths every year, with death rates climbing between 5% and 15% in severe cases [5, 10]. Sri Lanka is a major tropical hotspot for the disease [11, 12]. Studies show that an average of 52.1 out of every 100,000 people are hospitalized with leptospirosis annually, and the national death rate is around 7.0% [1, 11]. While infections occur across the entire island, the highest numbers are concentrated in the rain-heavy wet zone (including Colombo, Gampaha, Kalutara, Galle, Matara, Kandy, Matale, Nuwara Eliya, Ratnapura, and Kegalle districts), where flooded paddy fields create ideal conditions for leptospira to survive and spread [12, 13].

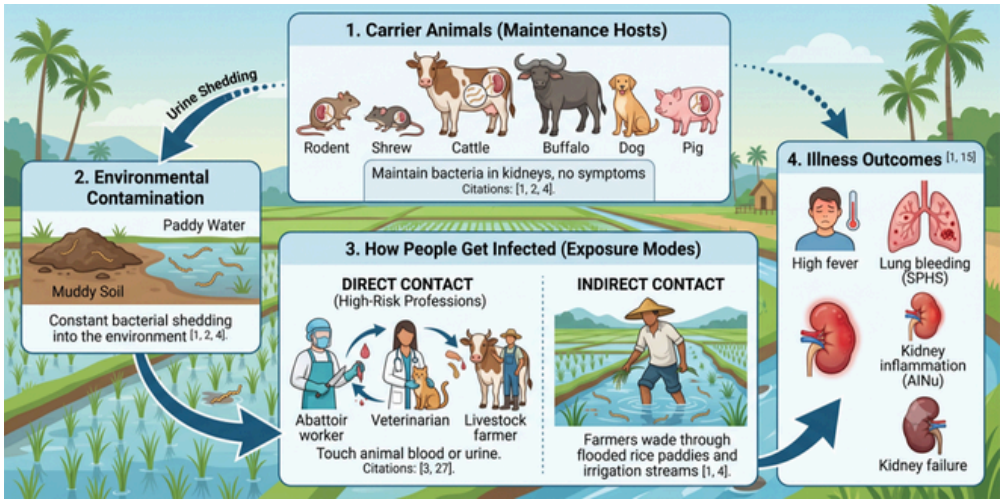

Figure 02: Leptospira transmission web in Sri Lanka

In the past, human leptospirosis in Sri Lanka mostly knew as a cause of fever or classical Weil's syndrome, which presents withjaundice, kidney failure, and bleeding [1, 14]. Today, however, medical community reporting more complications:

- ·**Severe Pulmonary Haemorrhagic Syndrome (SPHS) (1)**
- ·**Pancreatitis & Myocarditis (1)**
- ·**Acute Interstitial Nephritis** (AINu) and possible CKDu: Recent studies by Premarathne et al. show that leptospirosis can cause sudden kidney inflammation (AINu). This may contribute to or worsen Chronic Kidney Disease of uncertain etiology (CKDu), a widespread kidney disease in Sri Lanka's dry zones [15].

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Diagnosis: Timing the Test to the Infection Phase

Diagnosing leptospirosis quickly is challenging e [16, 17]. After a person is exposed, symptoms appear within 2 to 20 days. During the first week of fever (the acute phase), leptospira multiply actively in the patient [16, 18]. By the second week (the immune phase), the body's immune system clears the microbe from blood, but the organism move to the kidneys and are excreted in urine [16, 18].

Because the body takes at least 3 to 10 days to produce antibodies against leptospira upon exposure, diagnostic tests must be selected based on how many days the patient has had a fever [19, 20]:

- **Early Phase (Days 1–7)**: Standard antibody blood tests are not very helpful. To detect the disease during this early phase, bacterial DNA detection using Blood/Plasma PCR or LAMP tests are recommended., Culture of leptospira in special culturemedia at 28–30 °C after bed side inoculation of blood of the patient under strict aseptic precautions is also possible. This culture method is cumbersome, and frequently provides negative results if patient has taken antibiotics before collecting the culture. Also, culture media can get contaminated if strict aseptic methods were not followed making this a less useful diagnostic test. [16, 21].
- **Late Phase (Days 7–14+)**: Once the leptospira leave the bloodstream, diagnostic tests based on the detection of antibody —such as IgM ELISA, rapid test strips to detect IgM, and the Microscopic Agglutination Test (MAT)—are useful [16, 22]. MAT is a widely available test and it detects total antibodies (IgG + IgM) for leptospira. Therefore, either a seroconversion or a four-old rise in antibody needs to be demonstrated in acute and convalescent sera to confirm the diagnosis, which is not practical for patient diagnostics. A single MAT antibody titer has to be carefully interpreted as a universal cut-off titer is not available.

Unlocking the Genome: A Diverse Bacterial Landscape

For decades, researchers knew very little about which specific Leptospira strains were circulating in Sri Lanka. Early DNA studies mistakenly suggested that only one strain dominated each region [1].

A major study by Karunanayake et al. (2020) used Multilocus Sequence Typing (MLST) a method that examines seven essential genes (glmU, pntA, sucA, tpiA, pfkB, mreA, and caiB)—to study samples from human patients and rodents [1]. They discovered 15 distinct Sequence Types (STs) belonging to five major serogroups (Autumnalis, Grippotyphosa, Hebdomadis, Javanica, and Pyrogenes), including six completely new genetic types [1]:

- ***Leptospira interrogans* Serogroup Pyrogenes (ST75 & ST308):** ST75 was identified as a widespread strain in Sri Lanka in this study[1]. Genetic analysis showed that a new strain, ST308, evolved directly from ST75 [1]. Both ST75 and ST308 were isolated from patients with severe leptospirosis, linking this bacterial family to hospitalized patients during the outbreaks [1].
- ***Leptospira borgpetersenii* Serogroup Javanica (ST143 & ST144):** ST144 was found at the same time in both a human patient and a black rat (Rattus rattus) in Uva Province, proving evidence for possible direct transmission between rats and humans [1].

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Outbreak-Associated Strains: Three newly discovered strains, ST308, ST313, and ST314 were found exclusively in severe cases of leptospirosis during a major outbreak in Elpitiya, Southern Province [1].

Table 01: Leptospira spp., serogroups, and sequence types found in Sri Lanka

Species	Serogroup	Major Sequence Types (STs)	Known Host Animals in Sri Lanka
L. interrogans	*Pyrogenes*	ST75, ST308 (New), ST30, ST74	Humans, Buffaloes, Black rats [1, 26]
L. interrogans	*Autumnalis*	ST34, ST44, ST314 (New), ST317 (New)	Humans, Bandicoot rats [1]
L. interrogans	*Hebdomadis*	ST80	Humans [1]
L. borgpetersenii	*Javanica*	ST143, ST144	Humans, Black rats, Field mice, Shrews [1, 26]
L. kirschneri	*Grippotyphosa*	ST318 (New), ST389 (New)	Humans, Cattle, Field mice, Long-tailed mice [1, 26]
L. licerasiae	Unidentified	P2 Intermediate Group	Humans, Dogs, Pigs, Field mice [3, 26]

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Reservoirs: Rats to Farm Animals

While black rats have long been blamed as the main carriers of leptospirosis, recent animal studies show that many different species help spread the disease across Sri Lanka [1, 2]:

1. Rodents and Shrews: The Household Risk
A study by Sluydts et al. (2022) around rural rice storage sheds found that 12% of small mammals carried pathogenic leptospira [2]. Black rats carried the widest variety of l strains, while Asian house shrews (Suncus murinus) had the highest infection rate (31.8%) [2]. Furthermore, a 2026 study by Rathnayake et al. discovered that long-tailed mice (Vandeleuria sp.) and little Indian field mice (Mus booduga) also carry novel and intermediate strains of the leptospira [26].

2. Cattle and Buffaloes: The Agricultural Spreaders
In farming areas, cattle and buffaloes release much larger amounts of urine than rats, heavily contaminating muddy paddies before planting season [27, 28]. Studies show that between 12% and 20% of smallholder dairy cattle in Sri Lanka carry leptospira, especially the Sejroe and Hebdomadis serogroups [28, 29].

3. Companion Dogs: The Pet Hazard
A study by Athapattu et al. found that nearly 16% of healthy pet dogs studied in Kandy District carry Leptospira in their kidneys [30]. Surprisingly, dogs that had received standard leptospirosis vaccines shed the leptospira at the same rate as unvaccinated dogs [30]. DNA testing confirmed that these dogs shed strains identical to those infecting local human patients [30].

4. Pigs: The Overlooked Abattoir Threat
Research by Rathnayake et al. examined pigs slaughtered for food in Colombo and Kegalle [3]. They found that 13.8% of healthy-looking pigs carried Leptospira spp. [3]. Testing confirmed the presence of both severe P1 pathogens (L. interrogans) and milder P2 intermediate strains (L. licerasiae) [3]. Repeated sampling on a Colombo farm showed that pigs transmit these infections to one another, keeping human-disease strains circulating on farms [3].

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Conclusion: A Call for a "One Health" Strategy

Controlling leptospirosis in Sri Lanka requires more than simply killing rats or giving prophylactic antibiotics to farmers [1, 2]. Genetic studies prove that human outbreaks are driven by a diverse bacterial population shared across livestock, pets, and wildlife [1, 2, 3, 30].
To protect public health, Sri Lanka needs a One Health approach that connects human, animal, and environmental management [3]:

1. Human Health Sector: Expand early-stage diagnostic tests (Molecular based diagnostic tests, rapid IgM detection tests) and improve reporting to track true case numbers [16, 21]. Also, should look into better practical strategies of preventing humans getting exposed to animal urine and risky environments that have got contaminated with such animal urine.
2. Animal Health Sector: Regularly test farm animals and slaughterhouses for leptospira carriage. Update veterinary vaccines for dogs and livestock to protect against local Sri Lankan strains (such as Sejroe and Autumnalis) instead of relying only on standard imported vaccines [3, 28, 30].
3. Environmental Sector: Improve farm sanitation and wastewater drainage around dairy and pig farms to prevent animal urine from washing into irrigation streams. This should be combined with better flood management in high-risk wet zone districts[3, 4, 13].

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Management of Severe Leptospirosis

Prof S.A.M Kularatne
Emeritus Professor of Medicine
Faculty of Medicine
University of Peradeniya
Sri Lanka

Introduction

Infection with pathogenic spirochetes may remain asymptomatic or present as a mild, self-limiting anicteric febrile illness. However, some patients experience a rapid clinical deterioration (1). The severe form of the disease is characterized by deep icterus, profound bleeding, and multi-organ dysfunction syndrome (MODS), which carries an exceptionally high mortality rate if the interventions are delayed (2,3).

This progression into the severe form is driven by a complex, two-armed pathological response that coordinates direct structural damage exaggerated by dysregulated host immune response. First is the direct tissue invasion where, following entry through the breaches in skin or mucous membranes, Leptospira rapidly disseminate through the bloodstream to actively penetrate all endothelial cells and host connective tissues using their specialized corkscrew motility. This severely disrupts cell-to-cell adhesion in the liver and directly damages the host cell membranes of the proximal convoluted tubes (PCT) in the kidneys (4). The second mechanism is the cytokine storm, occurring in parallel with tissue invasion and propagating the immune phase of the illness. This is driven by hypercytokinemia, which triggers catastrophic, massive overproduction of both pro-inflammatory cytokines (TNF & IL-6) as well as anti-inflammatory cytokines (IL-10) (5). The ensuing systemic cascade induces a severe, widespread vasculitis, endothelial leakage, and immunoparesis, resulting in a massive migration of fluids from intravascular spaces into the interstitial compartment, leading to severe tissue hypoxemia and multi-organ failure.

Clinical Progression & Complications

Severe icteric leptospirosis, historically described as Weil's disease in 1886 by Adolf Weil (2,6), classically presents as an acute medical emergency, typically progressing sequentially from a 3-7 day septicemic phase into a profound immune phase, presenting clinically as a combination of severe jaundice, spontaneous systemic hemorrhages, progressive acute renal failure, and acute myocarditis (1). The clinical management of severe disease requires early anticipation of specific organ failures, which mandates Intensive Care Unit (ICU) admission.

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The disease is notorious for its renal and metabolic complications, among which, the acute kidney injury (AKI) is the commonest and the most severe complication affecting upto 86.7% of complicated cases (7). This can manifest suddenly as anuria or severe oliguria. The most debilitative complication in these patients is the sudden development of silent, severe hyperkalemia. If left unmanaged, coupled with the rising serum creatinine and metabolic acidosis, this severe hyperkalemia carries an immediate risk of lethal cardiac decompensation (3,8). Primary causes of rapid mortality in the severe disease is caused by Severe Pulmonary Hemorrhage Syndrome (SPHS) and Acute Respiratory Distress Syndrome (ARDS), carrying a specific case fatality rate of 41.5% (7). Patients typically develop SPHS rapidly within the first week of illness, peaking on days 4 and 5, presenting as progressive shortness of breath, mild to severe hemoptysis, and catastrophic arterial hypoxemia (1,7). Chest radiography characteristically demonstrates progressive, widespread, bilateral patchy radio-opaque shadows signifying extensive alveolar flooding.

Severe disease frequently manifests as refractory hypotension and profound septic shock requiring intensive inotropic support. Direct myocardial involvement leads to severe acute myocarditis, often characterized on electrocardiography (ECG) by widespread T-wave inversions, elevated troponin level and on echocardiography by severe left ventricular hypokinesia with reduction of ejection fraction down to 30% (3). However, trivial myocarditis produces only mild hypoxemia, tachypnoea and mild hypotension, which may progress to a severe form if not detected and intervened promptly. This is often accompanied by a severe thrombocytopenia and advanced Disseminated Intravascular Coagulation (DIC) amplifying the patient's internal bleeding tendencies (2).

Rapid Diagnosis and Monitoring

In resource-limited settings and highly endemic settings, clinical diagnosis and through observation for impending severe complications must take precedence over laboratory confirmation (9). Because leptospirosis shares a common and non-specific symptomatology with many acute febrile illnesses, establishing an exact cause of illness at presentation is difficult (10). Therefore, clinicians must be highly vigilant and maintain a high degree of suspicion to initiate close monitoring for multi-organ progression before the serological data is available. This is further complicated by hyper-endemic regions by the potential co-infections such as dengue fever, which can completely mask the classical diagnostic features and cause a highly atypical clinical picture (11).

Prompt identification of the severe disease relies on tracking routine hematological, biochemical and blood gas parameters (12). Key laboratory indicators of severe sepsis or immune-mediated complications include leukopenia or normal white cell counts with marked neutrophilic shift with significant thrombocytopenia (2,12). Extreme elevations of C-reactive protein (CRP) exceeding 300 mg/L serve as a vital marker of severe systemic inflammation and immune activation.

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In addition to this, serial arterial blood gas (ABG) monitoring helps reveal severe presentations with uncompensated metabolic acidosis with profound hypoxemia, which drives severe hyperventilation and compensatory respiratory alkalosis. Rapidly rising serum creatinine and increasing total bilirubin further prove the evolving kidney injury and hepatorenal dysfunction (1,3,10).

Definitive mapping of the pathogen requires a combination of culture, serology and molecular diagnosis (9). Microscopic Agglutination Test (MAT) is the recognized core serological standard, which checks for seroconversion or a four-fold increase in anti-leptospiral antibody titers using reference panels. In acute settings however, a single reciprocal MAT titer of 400 is taken as lab confirmed positive (13,14). ELISA (IgM) or, Enzyme Linked Immunosorbent Assay detecting anti-leptospiral IgM antibodies is a highly accessible as well as widely utilized tool for confirming probable or definitive cases during the immune phase of the illness (12) and Polymerase Chain Reaction (PCR) methods like Quantitative PCT (qPCR) or nested PCR targeting pathogenic genes can be used in the early phase of the illness, specifically during the first 7 to 10 days where the spirochetes are actively circulating but antibodies have not been formed (10).

Advanced Management and Therapeutic Modalities.

The immediate management of leptospirosis focuses on rapid resuscitation, using intravenous saline for fluid replacement and inotropes to counter severe septic shock. Targeted antimicrobial therapy must be initiated immediately upon clinical suspicion without waiting for laboratory confirmation. Intravenous Penicillin G (2 million units QDS) or third-generation cephalosporin such as IV Ceftriaxone (1g TDS) remain the primary mainstay of therapy (3). In the situation of penicillin allergy, doxycycline is recommended. Administration of these antibiotics should not be withheld or delayed for laboratory confirmation.

Recognizing the powerful and devastating mortality due to the cytokine storm, the clinical treatment focus now includes systemic immunomodulation. Current practice dictates early administration of high-dose bolus IV methylprednisolone (MP) (e.g., 500mg to 1g daily pulses for three consecutive days) (1–3). To reduce the morbidity in severe cases, this therapy should be initiated before the development of irreversible multiple organ failure (2). This is more relevant to mitigating myocarditis by reducing myocardial inflammation. However, exclusion of other causes of severe sepsis is needed before embarking on MP therapy.

Then, patients progress to MODS or SPHS, standard therapies often fall short, necessitating more aggressive salvage interventions like plasmapheresis, renal replacement therapy, administration of blood products, as well as the use of ECMO methods. Plasmapheresis has emerged recently as a vital life-saving modality for clearing the circulating cytokines, immune complexes and endotoxins in patients with severe multi-organ failure and septic shock (1,3,15). If initiated within 48 hours of detecting pulmonary hemorrhage, survival rates become noticeably higher (upto 74.5%) (7). For patients with AKI, early initiation of peritoneal dialysis is vital in stabilizing the metabolic derangements and assist in fluid management (8).

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Given the severe thrombocytopenia and consumptive coagulopathy inherent to the disease, prophylactic platelet transfusions are routinely utilized to mitigate devastating bleeding risks and have been shown to reduce death rates. Fresh frozen plasma (FFP) and cryoprecipitate are also heavily relied upon, particularly as replacement fluids during TPE. Extracorporeal Membrane Oxygenation (ECMO) and Extracorporeal Life Support (ECLS) are increasingly recognised as promising salvage strategies for severe ARDS and refractory pulmonary haemorrhage (15). Severe leptospirosis still causes deaths despite using above therapeutic modalities. Myocarditis with circulatory failure resulting lactic acidosis, intracranial bleeding and extended multiple organ system involvements observed to be some causes of death.

Conclusion.

For the management of severe leptospirosis, the National Guidelines on Management of Leptospirosis, research evidence and expert advice are necessary, along with early detection and transfer of patients to treatment centres where advanced therapeutics are available. Patients must be closely monitored with assessment of vital parameters. The public should be educated to avoid non-steroidal anti-inflammatory drugs (NSAIDs) and excess dosing of paracetamol to reduce fever and pain, and seek medical advice without delay.

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Severe Leptospirosis : A Case Report

Prof. Manoji Pathirage
Professor in Medicine
Department of Medicine
Faculty of Medicine
University of Peradeniya

Introduction

Leptospirosis is the most widespread zoonotic disease worldwide and remains a significant public health concern, particularly in tropical and subtropical regions. It is estimated to cause approximately 1.03 million human cases and 58,900 deaths annually[1], with the highest disease burden occurring in areas where occupational exposure to animals and contaminated environments, as well as recreational water activities, are common. Although leptospirosis is most prevalent in tropical regions, it also occurs in temperate climates. The highest incidence has been reported in South and Southeast Asia, Oceania, the Caribbean, parts of sub-Saharan Africa, and Latin America.

Leptospirosis is caused by pathogenic Leptospira species and exhibits a broad spectrum of clinical manifestations, ranging from a self-limiting febrile illness to severe multisystem disease with hepatic, renal, cardiovascular, and pulmonary involvement. Among its severe complications, pulmonary haemorrhage is particularly devastating and is associated with a high mortality rate. Despite advances in supportive care, the optimal management of severe pulmonary leptospirosis remains challenging. Therapeutic plasma exchange (TPE) has been used as an adjunctive treatment in selected cases of severe leptospirosis, particularly those complicated by pulmonary haemorrhage; however, the evidence supporting its efficacy remains limited and its role in clinical practice is yet to be clearly established.

Case Presentation

A previously healthy Sri Lankan male in his late teens presented to the Emergency Treatment Unit (ETU) of Teaching Hospital Peradeniya with a three-day history of high intermittent fever associated with severe myalgia, arthralgia, and progressive shortness of breath. One week prior to symptom onset, he had participated in white-water rafting in Kitulgala.

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On admission, he was febrile, dehydrated, icteric and had conjunctival suffusion. He had tachycardia, and was in respiratory distress with a respiratory rate of 36/min and Oxygen saturation of 84% on air.
Bilateral coarse inspiratory crepitations were heard throughout both lung fields. Urine output was initially preserved, and the remainder of the systemic examination was unremarkable.

Laboratory investigations demonstrated neutrophilic leucocytosis, thrombocytopenia, markedly elevated C-reactive protein, hypokalaemia, acute kidney injury, and biochemical evidence of haemolysis with progressive anaemia. Blood cultures were sterile. Chest radiography demonstrated bilateral patchy alveolar infiltrates consistent with diffuse pulmonary haemorrhage.

Based on the epidemiological exposure, clinical presentation, and laboratory findings, a diagnosis of severe leptospirosis complicated by pulmonary haemorrhage, acute kidney injury, and haemolytic anaemia was made. Subsequent serological testing confirmed leptospiral infection.

The patient was transferred to the intensive care unit for multidisciplinary management. He received intravenous ceftriaxone and oral doxycycline as definitive antimicrobial therapy together with high-dose intravenous methylprednisolone pulses. Owing to rapidly progressive pulmonary involvement and worsening renal dysfunction, therapeutic plasma exchange was commenced in conjunction with intermittent haemodialysis.

Following two sessions of plasma exchange and haemodialysis, the patient's respiratory status improved significantly. His oxygen requirement decreased, inflammatory markers declined, and renal function stabilised. He was transferred to the medical ward on the fourth day of admission, where two additional haemodialysis sessions and plasma exchange cycles were completed.

On the fifth day of illness, the patient's jaundice became more pronounced, accompanied by worsening indirect hyperbilirubinaemia and a progressive decline in haemoglobin levels. Peripheral blood film examination demonstrated features of haemolysis, which was further supported by an elevated reticulocyte count and markedly increased lactate dehydrogenase (LDH) levels. A positive direct antiglobulin test (DAT) confirmed immune-mediated haemolysis. The patient was managed conservatively with continued intravenous ceftriaxone, corticosteroid therapy, folic acid supplementation, meticulous fluid management, and close clinical and biochemical monitoring. This approach resulted in gradual clinical and laboratory improvement, with recovery of renal function without the need for long-term renal replacement therapy.

By the thirteenth day of illness, the patient was afebrile with complete resolution of respiratory symptoms, improving renal function, recovery of haematological parameters, and resolving liver dysfunction. He was discharged home in good clinical condition with arrangements for outpatient follow-up.

Discussion

Severe leptospirosis is characterised by widespread endothelial injury and systemic vasculitis resulting from both direct bacterial toxicity and an exaggerated host immune response. Pulmonary haemorrhage represents one of the most devastating manifestations, with mortality rates ranging from 30% to over 70%, particularly among patients requiring mechanical ventilation or renal replacement therapy[2,3].

The patient's recent freshwater exposure during white-water rafting in Kitulgala provided an important epidemiological clue. Recreational exposure to contaminated freshwater has become an increasingly recognised risk factor for leptospirosis in endemic countries, including Sri Lanka.

The coexistence of pulmonary haemorrhage, acute kidney injury, and haemolytic anaemia reflected severe multisystem disease. Although haemolytic anaemia is an uncommon manifestation of leptospirosis, immune-mediated haemolysis and microangiopathic processes have been described in severe infections.

The benefit of therapeutic plasma exchange in severe leptospirosis remains incompletely established. The proposed mechanisms include removal of circulating endotoxins, inflammatory cytokines, immune complexes, and other pathogenic plasma factors responsible for endothelial injury and capillary leak. Plasma exchange may also replenish deficient plasma proteins and coagulation factors while reducing ongoing immune-mediated tissue injury[4].

Several observational studies from Sri Lanka have suggested improved survival among patients with pulmonary haemorrhage treated with plasma exchange in addition to corticosteroids and conventional supportive care[5]. Although randomised controlled trials are lacking, national and regional treatment protocols have incorporated plasma exchange as a rescue therapy for selected patients with life-threatening pulmonary involvement. Our patient's rapid clinical improvement following two sessions of plasma exchange supports its potential role as an adjunctive therapy in carefully selected patients.

The favourable outcome was likely multifactorial, reflecting prompt recognition of severe leptospirosis, early administration of appropriate antibiotics, aggressive organ support including haemodialysis, corticosteroid therapy, and timely initiation of therapeutic plasma exchange. Whether plasma exchange independently altered the disease course cannot be conclusively established from a single case; however, the temporal association between initiation of therapy and rapid clinical recovery is noteworthy.

Conclusion

This case illustrates the successful management of severe leptospirosis complicated by diffuse pulmonary haemorrhage, acute kidney injury, and haemolytic anaemia using a combination of antimicrobial therapy, corticosteroids, haemodialysis, and therapeutic plasma exchange. In endemic settings, leptospirosis should be considered in patients presenting with acute febrile illness following freshwater exposure. Although high-quality evidence remains limited, therapeutic plasma exchange may represent a valuable adjunctive treatment in selected patients with severe pulmonary involvement and multiorgan dysfunction. Further prospective studies are required to better define its role in the management of severe leptospirosis.

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Critical Care Leptospirosis Challenge

A Self-Assessment Quiz in Six Domains
12 Questions · Evidence-Based · CME Self-Assessment

Dr Senani Samarasinghe
Consultant Anaesthetist / Senior Lecturer II
Special Interest training in Transplant Anaesthesia and Intensive care
Department of Anaesthesiology and Critical care
Faculty of Medicine
Teaching Hospital
Peradeniya

CONTENTS

Instructions: For each question, identify the single best answer before checking the key. Explanations and full citations follow every question. Recommended for ICU trainees, internal medicine residents, and tropical medicine fellows.

SECTION 01
EXTRACORPOREAL THERAPY

Therapeutic Plasma Exchange in Severe Leptospirosis

References: Trivedi et al., Indian J Crit Care Med 2022 · Ahmad & Tan, Trop Med Infect Dis 2023 · Fernando et al., Trop Biomed 2018

QUESTION 1 of 2

A 34-year-old farmer presents with Weil's disease, progressive jaundice, AKI, thrombocytopenia, and ARDS. Despite 48 h of IV penicillin and ventilatory support, he remains oliguric with rising bilirubin. Which mechanism best justifies initiating therapeutic plasma exchange (TPE) in this context?

A	**Direct bactericidal effect supplementing antibiotic therapy**
B	**Removal of circulating leptospiral toxins, cytokines, and immune complexes with replacement of consumed coagulation factors and albumin**
C	**Correction of hyponatraemia by plasmapheresis-driven sodium equilibration**
D	**Prevention of Jarisch–Herxheimer reaction upon antibiotic initiation**

✓ CORRECT ANSWER: B

EXPLANATION

TPE in severe leptospirosis works by removing high-molecular-weight mediators — circulating leptospiral outer membrane proteins, lipopolysaccharide fragments, pro-inflammatory cytokines (IL-6, TNF-α), and immune complexes — while simultaneously replenishing fibrinogen, clotting factors, and albumin depleted by the Weil's disease process. It does not have a direct bactericidal role.

Trivedi SV et al. "Therapeutic plasma exchange in severe leptospirosis." Indian J Crit Care Med. 2022;26(1):42–49. |Ahmad A & Tan LH. Trop Med Infect Dis. 2023;8(3):155.

QUESTION 2 of 2

According to the 2023 South Asian literature on TPE in leptospirosis, which clinical-laboratory threshold constellation is most evidence-supported as an initiation criterion for TPE?

A	**Bilirubin >10 mg/dL with platelet count <150 × 10^9/L**
B	**Bilirubin >20 mg/dL + creatinine >4 mg/dL + platelet <50 × 10^9/L failing conventional therapy for ≥48 h**
C	**Positive MAT titre ≥1:400 alone**
D	**Urine output <0.5 mL/kg/h for 6 h regardless of bilirubin**

✓ CORRECT ANSWER: B

EXPLANATION

South Asian series and the Rajasekaran criteria suggest TPE should be considered in severe Weil's disease when bilirubin exceeds 20 mg/dL, serum creatinine exceeds 4 mg/dL, AND platelets fall below 50 × 10^9/L despite ≥48 h of appropriate antimicrobial and supportive care. Serology alone or oliguria alone is insufficient justification.

Rajasekaran S et al. J Assoc Physicians India. 2020;68:50–55. | Chrispal A et al. Ann Trop Med Parasitol. 2010;104(2):151–161.

SECTION 02
NEPHROLOGY IN CRITICAL CARE

Renal Replacement Therapy & Dialysis in Leptospiral AKI

References: Daher EF et al., Nephrol Dial Transplant 2012 · KDIGO AKI 2012 · WHO Leptospirosis Guidelines 2003

QUESTION 1 of 2

The predominant renal lesion responsible for AKI in leptospirosis is best described as:

A	**Membranoproliferative glomerulonephritis mediated by immune complex deposition**
B	**Acute tubulointerstitial nephritis with tubular necrosis, predominantly in the distal tubule and collecting duct, with relative sparing of the glomerulus**
C	**Renal cortical necrosis from thrombotic microangiopathy**
D	**Rhabdomyolysis-induced proximal tubular cast nephropathy**

✓ CORRECT ANSWER: B

EXPLANATION

Leptospiral AKI is characterised by acute tubulointerstitial nephritis (ATIN) — leptospires invade and damage tubular epithelium, particularly in the distal nephron, causing tubular cell necrosis, interstitial oedema and mononuclear infiltration. Glomeruli are relatively spared. This explains the classic non-oliguric AKI with hypokalaemia and salt wasting seen early in leptospirosis.

Daher EF et al. Nephrol Dial Transplant. 2012;27(8):3100–3106. | Sitprija V. Nephrol Dial Transplant. 2005;20(suppl 1):i6–i8.

QUESTION 2 of 2

A patient with leptospiral AKI requires dialysis. Which KDIGO AKI 2012 criterion, when present, constitutes an emergency (absolute) indication for immediate renal replacement therapy initiation?

A	**Serum creatinine >4 mg/dL for 24 h**
B	**Urine output <0.3 mL/kg/h for 24 h (oliguria) without other absolute indications**
C	**Life-threatening hyperkalaemia (K^+ >6.5 mEq/L) refractory to medical management, or fluid overload causing respiratory failure**
D	**Metabolic acidosis with pH 7.28 responding to bicarbonate infusion**

✓ CORRECT ANSWER: C

EXPLANATION

KDIGO 2012 identifies life-threatening metabolic emergencies as absolute RRT triggers: refractory hyperkalaemia (≥6.5 mEq/L or with ECG changes), volume overload causing pulmonary oedema unresponsive to diuretics, refractory metabolic acidosis (pH <7.1), and uraemic complications (pericarditis, encephalopathy). Creatinine level or urine output alone are relative, not absolute, indications.

KDIGO AKI Work Group. Kidney Int Suppl. 2012;2(1):1–138. | Daher EF et al. Clin Nephrol. 2014;82(3):206–212.

SECTION 03
CONTINUOUS RENAL REPLACEMENT THERAPY

CRRT Strategy in Severe Leptospirosis

References: Uchino S et al., JAMA 2005 · KDIGO AKI 2012 · Bellomo R et al., NEJM 2009 (RENAL) · Randhawa et al., Indian J Nephrol 2023

QUESTION 1 of 2

In a haemodynamically unstable patient with leptospiral multiorgan failure (MAP 58 mmHg on noradrenaline 0.3 mcg/kg/min), which RRT modality is preferred over intermittent haemodialysis?

A	**Standard intermittent haemodialysis (IHD) 4 h sessions**
B	**Continuous veno-venous haemofiltration (CVVH) or CVVHDF — better haemodynamic tolerance due to slow solute and fluid removal rates**
C	**Peritoneal dialysis through a Tenckhoff catheter**
D	**High-volume intermittent haemofiltration (HVIH) 6 h daily**

✓ CORRECT ANSWER: B

EXPLANATION
CRRT (CVVH/CVVHDF) is preferred in haemodynamically unstable patients because it provides gradual, continuous fluid and solute removal, minimising intradialytic hypotension. Multiple studies including the BEST Kidney and RENAL trials confirm better MAP stability with CRRT vs IHD in shocked ICU patients. KDIGO 2012 recommends CRRT for haemodynamically unstable AKI (Grade 2B).
KDIGO AKI. Kidney Int Suppl. 2012;2:1–138. |Uchino S et al. JAMA. 2005;294(7):813–818. |Bellomo R et al. N Engl J Med. 2009;361:1627–1638 (RENAL trial).

QUESTION 2 of 2

The KDIGO 2012-recommended effluent dose for CRRT in AKI (including leptospiral AKI) is:

A	**20 mL/kg/h — low-dose, adequate for stable patients**
B	**25–30 mL/kg/h delivered dose — balances clearance with complications; higher doses (≥35 mL/kg/h) showed no survival benefit in ATN and RENAL trials**
C	**45–50 mL/kg/h — high-volume haemofiltration recommended universally**
D	**≥70 mL/kg/h in sepsis-associated AKI to maximise cytokine removal**

✓ CORRECT ANSWER: B

EXPLANATION

KDIGO 2012 recommends a delivered CRRT effluent dose of 20–25 mL/kg/h, with prescription set at 25–30 mL/kg/h to account for circuit downtime. Both the VA/NIH ATN trial and the RENAL trial demonstrated that higher doses (35–45 mL/kg/h) conferred no additional 28-day or 90-day survival benefit. Prescribe 25–30 mL/kg/h as standard.

KDIGO AKI 2012.| Palevsky PM et al. N Engl J Med. 2008;359:7–20 (ATN trial). | Bellomo R et al. N Engl J Med. 2009;361:1627–1638 (RENAL).

SECTION 04
CRITICAL CARE MANAGEMENT

Multiorgan Failure in Severe Leptospirosis

References: Rajapakse S., Trop Med Int Health 2022 · Chrispal A et al., Ann Trop Med 2010 · ARDSNet 2000 · Guérin C et al. (PROSEVA), NEJM 2013

QUESTION 1 of 2

In Weil's disease, the classic triad of organ involvement that defines severe leptospirosis is:

A	**Jaundice, AKI, and myocarditis**
B	**Jaundice, AKI, and bleeding (classically pulmonary haemorrhage or thrombocytopenic bleeding)**
C	**Meningitis, AKI, and uveitis**
D	**Hepatic failure, pneumonia, and rhabdomyolysis**

✓ CORRECT ANSWER: B

EXPLANATION
Adolf Weil's original 1886 description and subsequent refinements define Weil's disease as jaundice + AKI + haemorrhage (most characteristically pulmonary — Severe Pulmonary Haemorrhage Syndrome, SPHS). Mortality in Weil's disease with all three features exceeds 40–50% in reported series. Myocarditis can co-occur but is not part of the defining triad.
Levett PN. Clin Microbiol Rev. 2001;14(2):296–326. | Rajapakse S. Trop Med Int Health. 2022;27(3):224–239

QUESTION 2 of 2

Leptospiral myocarditis can cause haemodynamic instability in the ICU. Which ECG/cardiac finding is most characteristic?

A	**ST-elevation MI pattern (STEMI) requiring urgent coronary angiography**
B	**Atrial fibrillation with rapid ventricular response**
C	**Conduction defects (first-degree to complete heart block), ST-T changes, ventricular tachyarrhythmias — without obstructive coronary disease; troponin elevation with preserved or reduced LVEF on echo**
D	**Right bundle branch block exclusively**

✓ CORRECT ANSWER: C

EXPLANATION

Leptospiral myocarditis causes a spectrum of ECG abnormalities: conduction defects (PR prolongation to complete heart block), non-specific ST-T changes, and ventricular arrhythmias. Troponin is elevated. Echocardiography shows focal or global hypokinesia without coronary artery disease. Up to 10–15% of severe leptospirosis patients develop significant myocardial involvement. Vasopressor and antiarrhythmic support may be required.

Pesaro AEP et al. Int J Cardiol. 2009;136(3):379–381. | Rajapakse S. Trop Med Int Health. 2022;27:224–239.

SECTION 05
RESPIRATORY CRITICAL CARE

Pulmonary Haemorrhage Syndrome (SPHS) in Leptospirosis

References: Zaki & Shieh, Emerg Infect Dis 1996 · Amilasan et al., Emerg Infect Dis 2012 · Marotto et al., Am J Respir Crit Care Med 1999 · Shenoy N et al., IJCCM 2022

QUESTION 1 of 2

The primary pathological mechanism of pulmonary haemorrhage in severe leptospirosis (SPHS) is:

A	**Thrombocytopenia-induced spontaneous alveolar bleeding**
B	**Leptospiral endothelial injury → immune-mediated alveolar capillaritis and increased vascular permeability (NOT primarily thrombocytopenic bleeding) — haemorrhage often occurs with platelet counts >50 × 10^9/L**
C	**Pulmonary arteriovenous malformations triggered by hepatic failure**
D	**Aspiration of haematemesis from gastric variceal bleeding**

✓ CORRECT ANSWER: B

EXPLANATION
Key clinical pearl: SPHS in leptospirosis is predominantly caused by direct leptospiral toxin-mediated endothelial injury of alveolar capillaries, triggering immune-mediated capillaritis and massive vascular permeability — NOT simply coagulopathy or thrombocytopenia. Haemorrhage can occur even with near-normal platelet counts. This is why platelet transfusion alone is insufficient as management. *Zaki SR & Shieh WJ. Emerg Infect Dis. 1996;2(2):146–148. | Amilasan AT et al. Emerg Infect Dis. 2012;18(1):58–64. | Marotto PCF et al. Am J Respir Crit Care Med. 1999;160(5):1568–1572.*

QUESTION 2 of 2

A patient with confirmed leptospirosis develops massive haemoptysis, SpO_2 78% on 15L NRB mask, and bilateral whiteout on CXR. Immediate next step in management is:

A	**Urgent platelet transfusion to >100 × 10^9/L then reassess**
B	**Urgent endotracheal intubation with lung-protective ventilation; PEEP 8–12 cmH_2O; concurrent IV methylprednisolone 1g; correct coagulopathy; ensure IV antibiotics continue**
C	**High-flow nasal cannula oxygen at 60 L/min; avoid intubation to preserve cough reflex**
D	**Right bundle branch block exclusively**

✓ CORRECT ANSWER: B

EXPLANATION

Massive SPHS with bilateral involvement and refractory hypoxaemia is an immediate intubation indication. Lung-protective MV with PEEP (acting as pneumatic tamponade to alveolar haemorrhage) is life-saving. IV methylprednisolone (1 mg/kg or pulse 1g) is widely used in South Asian and Brazilian centres for its theoretical immunosuppressive effect on capillaritis — though RCT evidence is limited. Coagulopathy correction and continued antibiotics are concurrent priorities. HFNO is insufficient for this degree of haemorrhage/hypoxia.

Shenoy N et al. Indian J Crit Care Med. 2022;26(3):320–328. | Marotto PCF et al. Am J Respir Crit Care Med. 1999;160:1568–1572. | Rodrigues C et al. J Infect. 2020;81(3):400–407.

SECTION 06
HAEMATOLOGY IN CRITICAL CARE

Coagulation Disturbances in Leptospirosis: Diagnosis & Management

References: Wagenaar et al., J Infect Dis 2009 · ISTH DIC Scoring 2001 · Levi M & van der Poll T, NEJM 2017 · Shetty et al., IJCCM 2022

QUESTION 1 of 2

In severe leptospirosis, which coagulation disturbance pattern is MOST commonly reported on laboratory evaluation?

A	**Isolated thrombocytopenia with normal coagulation times and fibrinogen**
B	**Disseminated intravascular coagulation (DIC) — thrombocytopenia + prolonged PT/aPTT + raised D-dimer + low fibrinogen, mediated by endothelial activation and systemic pro-coagulant state**
C	**Vitamin K deficiency coagulopathy from hepatic failure exclusively**
D	**Haemophilia-like factor VIII deficiency**

✓ CORRECT ANSWER: B

EXPLANATION
Severe leptospirosis frequently triggers overt DIC (ISTH score ≥5): thrombocytopenia (<100 × 10^9/L in ~50%, <50 × 10^9/L in ~25%), prolonged PT/aPTT, markedly elevated D-dimer/FDPs, hypofibrinogenaemia, and microangiopathic haemolysis. This coagulopathy has both consumptive (DIC) and hepatic (reduced synthetic function) contributions. Wagenaar et al. demonstrated near-universal coagulation abnormalities in Weil's disease.
Wagenaar JFP et al. J Infect Dis. 2009;199(9):1261–1268. | Taylor FB et al. Thromb Haemost. 2001;86(5):1327–1330 (ISTH criteria).

QUESTION 2 of 2

The ISTH overt DIC score in a leptospirosis patient shows: platelets 42 × 10^9/L (score 2), PT ratio 1.8 (score 2), fibrinogen 0.8 g/L (score 1), D-dimer markedly elevated (score 3). Total = 8. Appropriate management includes:

A	**Low-dose therapeutic anticoagulation with LMWH to interrupt the coagulation cascade as primary treatment**
B	**Treat the underlying cause (IV penicillin G or ceftriaxone), transfuse FFP (10–15 mL/kg) for PT/aPTT correction, cryoprecipitate for fibrinogen <1.5 g/L in bleeding patient, platelet transfusion if <50 × 10^9/L with active bleeding; no routine anticoagulation in DIC with bleeding phenotype**
C	**Recombinant activated factor VII (rFVIIa) as first-line haemostatic agent**
D	**Tranexamic acid 1g IV bolus as first-line fibrinolysis inhibitor regardless of DIC type**

✓ CORRECT ANSWER: B

EXPLANATION

DIC management hierarchy: (1) treat the trigger — effective antibiotics are the most important intervention; (2) replace depleted haemostatic factors (FFP for PT/aPTT, cryoprecipitate for fibrinogen <1.5 g/L in active bleeding, platelets if <50 × 10^9/L with haemorrhage); (3) anticoagulation (heparin) is reserved for thrombotic-predominant DIC (purpura fulminans, acral ischaemia) — contraindicated in the haemorrhagic phenotype common in leptospirosis.

Levi M & van der Poll T. N Engl J Med. 2017;376:1253–1262. | ISTH SSC. J Thromb Haemost. 2009;7(1):203–205. | Shetty S et al. Indian J Crit Care Med. 2022;26(10):1100–1107.

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Contact Us
+94 81 239 6000
+94 81 239 6360
+94 81 238 9106
crtmoffice@med.pdn.ac.lk
crtmoffice@gmail.com

Editor
Prof. Samidi Navaratna
MBBS, DCH, MSc, MD
Professor in Community Medicine
Department of Community Medicine
Faculty of Medicine
University of Peradeniya

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Research Assistant
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