



सत्यमेव जयते

Ministry of Health & Family Welfare
Government of India

A Comprehensive Learning Guide

Leptospirosis



**NATIONAL CENTRE FOR DISEASE CONTROL
DIRECTORATE GENERAL OF HEALTH SERVICES**
Ministry of Health & Family Welfare, Government of India



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National Centre for Disease Control
Directorate General of Health Services
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स्वास्थ्य सेवा महानिदेशक

DIRECTOR GENERAL OF HEALTH SERVICES



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स्वास्थ्य एवं परिवार कल्याण मंत्रालय
स्वास्थ्य सेवा महानिदेशालय

Government of India
Ministry of Health & Family Welfare
Directorate General of Health Services



Message

Zoonotic diseases pose a significant and ongoing threat to biodiversity, human and public health and economic stability. Given India's diverse ecosystem, high population density and increasing human-animal action, the country remains particularly susceptible to zoonotic outbreaks. Past occurrences of plague, Nipah virus, avian influenza, leptospirosis, and Kyasanur Forest Disease emphasizes a critical need for robust surveillance, early detection, and a coordinated, intersectoral response.

Recognizing the importance of addressing zoonotic diseases as a public health priority, the Centre for One Health, under the National Centre for Disease Control (NCDC), is committed for strengthening surveillance, prevention, and response mechanisms through an integrated One Health approach. As part of this effort, the Centre for One Health has developed comprehensive learning guides on Priority Zoonotic Diseases. These modules provide scientifically validated, evidence-based guidance on the epidemiology, diagnosis, treatment, and prevention of key zoonotic diseases.

Strengthening disease surveillance, ensuring early diagnosis, and implementing timely interventions through a coordinated and multi-sectoral approach are critical to mitigating the risks associated with zoonotic diseases.

I am pleased to release these learning guides as a significant step in our ongoing efforts to combat zoonotic diseases. I urge all healthcare professionals, veterinary experts, and community leaders to actively utilize these resources to enhance their clinical index of suspicion for zoonosis and eventually contribute towards strengthening our health care system for responding timely and more efficiently to future outbreaks.

(Atul Goel)



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MESSAGE

It is my pleasure to know that the Centre for One Health at NCDC has prepared **Comprehensive Learning Guides** on 10 priority zoonotic diseases, which is now being shared with all concerned.

These resources become relevant in considering; India has encountered multiple zoonotic disease outbreaks in recent years, highlighting their persistent and evolving threat to public health. The re-emergence of **Nipah virus** in Kerala, **Kyasanur Forest Disease (KFD)** in Karnataka, and **avian influenza** across several states underscores the complex interconnections between human, animal, and environmental health. The rising cases of **leptospirosis** and **scrub typhus**, driven by climatic changes and ecological disruptions, further illustrate the unpredictable nature of zoonotic spillovers. With the additional challenges posed by **emerging coronaviruses** and **antimicrobial resistance (AMR)**, there is an urgent need for a **cohesive, evidence-based approach** to mitigate these risks effectively.

In recognition of this pressing need, the **National Centre for Disease Control (NCDC)** has intensified its efforts to fortify **zoonotic disease surveillance, outbreak preparedness, and intersectoral coordination**. As part of this initiative, the **Centre for One Health, NCDC**, has meticulously curated **Comprehensive Learning Guides** on priority zoonotic diseases. These guides, underpinned by the latest scientific insights and global best practices, serve as indispensable resources for **healthcare professionals, veterinarians, and epidemiologists**, equipping them with the knowledge to anticipate, detect, and mitigate zoonotic threats with precision.

To effectively curtail the impact of zoonotic diseases, a **harmonized One Health approach** is paramount—one that transcends disciplinary boundaries and fosters synergies across the human, animal, and environmental health sectors. I urge all stakeholders to **leverage these scholarly resources, enhance disease intelligence networks, and champion research-driven interventions**. By embracing a proactive and interdisciplinary ethos, we can **bolster pandemic preparedness, fortify national health security, and avert future spillover events**.

I sincerely **appreciate** my colleagues at the Centre for One Health, NCDC for their dedication to strengthening zoonotic disease control. Their efforts in enhancing surveillance, preparedness, and public health response are crucial in preventing and managing emerging health threats.

I am glad to see their commitment translating into evidence-based interventions and capacity-building initiatives that enhance zoonotic disease surveillance, outbreak preparedness, and overall health system resilience.

Through continuous innovation, collaboration, and unwavering dedication, we can fortify our health systems and safeguard our nation against zoonotic threats.

Wishing you all happy learning and skill enhancement wherever possible.

रंजन दास 19/3/25
Prof. (Dr.) Ranjan Das



Antibiotic resistance Containment Stewardship: Our Role, Our Responsibility
Judicious Use of Antibiotic: Key to Contain Antibiotic Resistance





भारत सरकार

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Message

Zoonotic diseases of public health importance continue to pose significant challenges to public health. These diseases, often driven by intricate human-animal-environment interactions, present substantial health risks, particularly to vulnerable populations, and demand a coordinated and robust response from the health sector.

In recognition of the pivotal role healthcare providers play in addressing these challenges, the **Centre for One Health** has developed a **Comprehensive Learning Guide for Priority Zoonotic Diseases**. This guide is designed to build capacity across the health sector, equipping professionals with the essential knowledge and skills needed to identify, manage, and prevent these diseases effectively. By enhancing surveillance systems, fostering rapid and accurate diagnostics, and implementing targeted prevention and control measures, healthcare providers can play a transformative role in mitigating the impact of zoonotic diseases.

The guide emphasizes the importance of building a resilient health workforce capable of responding to outbreaks, engaging communities, and collaborating across disciplines. Through these efforts, we aim to reduce the burden of zoonotic diseases, improve health outcomes, and contribute to the creation of a safer and healthier future.

I encourage all healthcare professionals to utilize this guide as a resource for improving their understanding and response to zoonotic diseases. Together, let us strengthen our health systems and work towards a future free from the threats posed by zoonotic diseases.

Dr. Simmi Tiwari
Joint Director and Head
Centre for One Health



Antibiotic Resistance Containment Stewardship: Our Role, Our Responsibility
Judicious Use of Antibiotic: Key to Contain Antibiotic Resistance



Acknowledgement

The **Comprehensive Learning Guide** for Leptospirosis has been developed to address the significant public health challenges posed by zoonotic diseases, which have serious health, economic, and social implications, particularly for vulnerable populations. The priority zoonotic diseases necessitate robust surveillance, timely diagnosis, and effective prevention and control measures. This guide aims to strengthen the capacity of healthcare professionals by equipping them with the requisite knowledge and skills to mitigate these public health threats and improve health outcomes.

We acknowledge with deep appreciation the valuable contributions of the **subject matter experts** from leading medical institutions and research organizations, whose guidance and technical expertise has been critical in shaping this **Comprehensive Learning Guide**.

The Centre for One Health, NCDC, expresses its sincere gratitude to Ms. Punya Salila Srivastava, Secretary, Ministry of Health and Family Welfare, Government of India; Ms. L.S. Changsan, Additional Secretary, Ministry of Health and Family Welfare, Government of India; Prof. (Dr.) Atul Goel, Director General of Health Services (DGHS), Government of India; Ms. Latha Ganapathy, Joint Secretary, Department of Health & Family Welfare, Government of India for their leadership, guidance, and support.

Lastly, we acknowledge the USAID-funded RISE project team, implemented by Jhpiego, for their technical support in drafting and finalizing this guide. Their collaboration has been pivotal in ensuring the quality and relevance of this resource.

Dr. Simmi Tiwari
Joint Director and Head,
Centre for One Health
National Centre for Disease Control
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Preface

Leptospirosis is an infectious disease caused by pathogenic organisms belonging to the genus *Leptospira*, that are transmitted directly or indirectly from animals to humans. This training module aims to equip learners with the knowledge and tools necessary to educate and train individuals involved in various aspects of Leptospirosis management. It provides a comprehensive overview of the disease, covering its epidemiology, clinical presentation, laboratory diagnosis, treatment availability, and preventive measures. The module is structured in a user-friendly manner, allowing learners to effectively communicate complex scientific concepts to their audience. It contains detailed explanations to enhance understanding and engagement. The content is supported by the latest scientific research and public health guidelines, ensuring the information presented is accurate and up to date.

It is our sincere hope that this module will serve as a valuable resource for learners and educators, enabling them to grasp essential knowledge and skills. By equipping professionals and individuals at risk with the necessary information, we can enhance our collective ability to detect, prevent, and respond to Leptospirosis outbreaks, thereby safeguarding public health.

We would like to express our gratitude to all the experts, researchers, and contributors who have provided their invaluable insights and expertise in developing this scientific module. Their dedication and commitment to public health have been instrumental in creating a comprehensive resource that will contribute to the effective management of Leptospirosis.

We hope you find this module informative, engaging, and ultimately, empowering. Together, let us work towards building a safer and healthier future by combating Leptospirosis through knowledge and preparedness.

Abbreviations

AKI	Acute Kidney Injury
ALT	Alanine Transaminase
ARDS	Acute Respiratory Distress Syndrome
AST	Aspartate Transaminase
BCC	Behaviour Change Communication
CBC	Complete Blood Count
CDC	Centre for Disease Control
CFR	Case Fatality Rate
CHC	Community Health Centre
CPK	Creatine Phosphokinase
CSF	Cerebrospinal Fluid
CT	Computed Tomography
DALY	Disability Adjusted Life Years
DC	Differential Count
DH	District Hospital
DIC	Disseminated Intravascular Coagulation
ECG	Electrocardiogram
ELISA	Enzyme Linked Immunosorbent Assay
GBD	Global Burden of Disease
Hb	Hemoglobin
ICU	Intensive Care Unit
IDSP	Integrated Disease Surveillance Programme
IHIP	Integrated Health Information Platform
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IV	Intravenous
LFT	Liver Function Test
MAT	Microscopic Agglutination Test
MO	Medical Officer
NCDC	National Centre for Disease Control
NDMA	National Disaster Management Authority
NTDs	Neglected Tropical Diseases
PCR	Polymerase Chain Reaction
PHC	Primary Health Centre
RCCE	Risk Communication and Community Engagement
RDT	Rapid Diagnostic Test
RFT	Renal Function Test
RRT	Rapid Response Team
SDH	Sub-District Hospital
SPHS	Severe Pulmonary Hemorrhage Syndrome
TC	Total Count
UV	Ultraviolet
WHO	World Health Organization

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Introduction to Learning Guide for Leptospirosis

Historically, zoonotic diseases have had a significant impact on human evolution, particularly on cultures and societies that domesticated and raised animals for food and clothing. Zoonoses pose a frequent and feared risk to humanity, transcending natural boundaries and occurring worldwide. Their profound effect on the global economy and health is well recognized, ranging from the international movement of animals and the importation of diseases to bans on animal product imports and restrictions on other international trade practices. Thus, zoonoses are no longer confined to national borders, and global surveillance is necessary for effective control.

Controlling zoonoses remains a priority for international agencies, addressing the specific health and economic challenges of each region. They equally impact animal, human, and environmental sectors, causing substantial damage to the nation's economy. To protect all the sectors, it is essential to rapidly identify, diagnose, and manage these diseases. The One Health approach plays a crucial role in this endeavor, as we have learned valuable lessons from the COVID-19 pandemic regarding the need for strong surveillance and diagnostic preparedness to handle future pandemic situations.

To provide comprehensive training, the Center for One Health, NCDC has developed learning guide. This guide serve as both trainers' guides and self-directed learning resources. The guide or training courses focuses on zoonoses and zoonotic diseases of public health importance in India (ZPHI) and emphasizes the One Health approach to respond to zoonotic diseases. By the end of the training, participants should have a solid understanding of the core principles of Leptospirosis, its outbreak potential, health emergencies, risk communication, diagnostic procedures, laboratory safety, surveillance, data reporting, and their applications.

The guide is based on national and international guidelines and serve as a comprehensive training resource for individuals involved in zoonotic disease diagnosis and surveillance activities. The curriculum is designed to enable facilitators and learners to undergo step-by-step learning within a specified time frame, ensuring a thorough understanding of each module.

The guide caters to various audiences, including medical professionals including doctors, veterinarians, paramedical staff and laboratory personnel who are expected to acquire knowledge and competencies beyond their regular field of work.

The guide consists of a Facilitators' Guide (FG) which provides instructional processes and supports educators in facilitating and assessing learning. Each module follows a standardized structure, including a session outline, detailed session plans, slide decks, and a wide range of references and resources for further reading. These resources offer comprehensive information on the respective topics.

The learning guide aims to provide a comprehensive education for medical professionals including doctors, veterinarians, paramedical staff and laboratory personnel. It helps them understand, identify, and differentiate between zoonotic diseases and equips them with the necessary knowledge and orientation for diagnostics procedures and surveillance systems.

COURSE DESCRIPTION

Course Design

This comprehensive Leptospirosis guide is tailored for medical professionals including doctors, paramedical staff, and laboratory personnel. The course is designed to enhance their understanding and expertise in dealing with Leptospirosis cases, spanning various aspects of prevention, diagnosis, and treatment. The training approach emphasizes practical application, aiming to equip participants with hands-on skills and competencies that can be directly applied in their professional roles.

Evaluation Approach

The evaluation approach for the Leptospirosis preparedness and response guide includes a comprehensive pre and post-training quiz questionnaire designed to assess participant's knowledge and learning progression. The questionnaire utilizes multiple-choice questions (MCQs) to gauge participant's understanding of Leptospirosis disease before and after the training. This approach allows a clear measurement of knowledge enhancement and provides valuable insights into the effectiveness of the training program.

- ***Pre-Training Quiz:***

Before the training begins, participants will undergo a pre-training questionnaire. This questionnaire serves as a baseline assessment of participant's existing knowledge and awareness of Leptospirosis. The pre-training quiz will consist of MCQs that cover various aspects of Leptospirosis, including its etiology, modes of transmission, clinical manifestations, preventive measures, and response strategies. The purpose of the pre-training quiz is to establish a starting point and identify areas where participants may require more focused training.

- ***Post-Training Quiz:***

Upon completion of the Leptospirosis preparedness and response guide, participants will be given a post-training quiz questionnaire. This questionnaire will contain a similar set of MCQs as the pre-training quiz, covering the same topics related to Leptospirosis. The aim of the post-training quiz is to evaluate participant's knowledge advancement and to measure the effectiveness of the training in enhancing their understanding of Leptospirosis.

COURSE SYLLABUS

Course Goals

- Foster an in-depth comprehension of Leptospirosis and its diverse forms.
- Equip participants with skills for Leptospirosis diagnosis, management, and prevention.
- Emphasize the importance of the One Health approach in addressing zoonotic diseases.
- Develop proficiency in risk associated with the disease, laboratory safety, and surveillance strategies.

Participant's Learning Objectives

By the course's conclusion, participants will be able to:

- Identify various Leptospirosis forms and their clinical characteristics.
- Apply diagnostic and treatment protocols for Leptospirosis management.
- Implement preventive strategies and outbreak management strategies.

Participant Selection Criteria

Participants for the Leptospirosis response and preparedness training should be professionals from various fields involved in emergency response and public health:

- Emergency Responders: Including public health experts, medical personnel, and first responders.
- Laboratory and Biosafety Staff: Those experienced in handling biohazards.
- Government and Decision-Makers: Officials with authority in emergency coordination.
- Community Leaders and Experts: Community influencers, researchers, and mental health specialists.

Using the Resource Guide

All training activities in this course will be conducted in an interactive, participatory manner using the guide appropriately as suggested in the course outline in the facilitator's guide. To accomplish this, the trainer will have to change roles throughout the course. For example, the trainer is a facilitator when conducting small group discussions and finally, when objectively assessing performance, the trainer serves as an evaluator.

Composition of participants

The training is intended for 15-20 participants hailing from various state and healthcare fraternities. There can be a single facilitator as an expert of the disease.

COURSE SCHEDULE

Morning Session

Introduce and welcome participants

- Discuss participant expectations and prior knowledge.
- Outline the objectives of the course and learning outcomes.

Review the course schedule and its components

- Provide an overview of the training guide materials.
- Conduct a pre-course knowledge assessment to gauge participants' baseline understanding.
- Distribute course materials, including handouts and resources.

Interactive presentations

- Take Sessions 1-4 and discuss in detail about basics of Leptospirosis, its epidemiology, and its significant features in humans and animals.
- Interactive discussion and Q&A session after the lecture

Afternoon Session

Interactive presentations

- Take Sessions 5-10 and discuss in detail about frequently asked questions, diagnosis of Leptospirosis, its treatment, prevention & control, outbreak management and surveillance.

Debriefing and group discussions on simulation outcomes

- Interactive discussion and Q&A session after the lecture

Review, Assessment, and Closing

- Comprehensive review of key concepts covered during the training.
- Interactive quiz to reinforce learning.
- Final assessment to measure participants' understanding of course material.
- Reflection session: Participants share insights and takeaways from the course.
- Closing remarks, thanking participants for their engagement.

COURSE OUTLINE

The course outline presented here follows a model structure for the training curriculum. It delineates the enabling objectives necessary to achieve the participant learning goals outlined in the course syllabus. The outline offers recommendations for suitable learning activities and essential resources and materials for each enabling objective. Depending on specific participant requirements, the trainer has the option to introduce supplementary practice activities, devise case studies, roleplay scenarios, or tailor learning situations accordingly.

The course outline comprises four columns:

- **Duration:** This column specifies the estimated time allocated for each learning activity. This allocation ensures an equitable distribution of time across the diverse training components.
- **Learning Objectives:** This column lays out the enabling objectives and their alignment with corresponding learning activities. The objectives are sequenced to provide guidance on the training structure. The interplay of objectives and activities ranging from icebreakers and interactive group tasks to practical exercises and breaks constitutes the overall training progression.
- **Pre-requisite Knowledge/Skill:** This column addresses the foundational knowledge or skills that participants should possess prior to the session. It underscores the importance of existing competencies for effective engagement in the training.
- **Competencies to be Achieved:** The fourth column enumerates the competencies participants are expected to acquire by the conclusion of the session. It underscores the practical outcomes that participants will attain through engagement in the training.

AGENDA

S. No	Topic	Duration
1.	Welcome & Introduction of the training agenda and setting ground rules	15 min
2.	Ice Breaker: Talk about yourself - Contribution to the management & control of zoonoses - Expectations from the training	30 min
3.	Training objectives	15 min
4.	Pre-Test Quiz	20 min
5.	Session 1: Introduction to Leptospirosis	15 min
6.	Session 2: Epidemiology	15 min
7.	Session 3: Leptospirosis in Human	15 min
8.	Session 4: Leptospirosis in Animals	30 min
9.	Session 5: Diagnosis	20 min
10.	Session 6: Prevention & Treatment	45 min
11.	Session 7: Surveillance	30 min
12.	Post - Test Quiz	20 min
13.	Q/A session, review and discussion	15 min
14.	Closing remarks	05 min

Session-1

Introduction to Leptospirosis

Course No. 001	Session 1: Introduction to Leptospirosis
Duration	15 minutes
Learning Objective	• Describe the disease overview, including its global significance and impact. • Explain the causative agent <i>Leptospira</i>, highlighting its unique structural features and genetic diversity. • Outline the disease transmission process, focusing on environmental contamination and contact with infected animals.
Pre-requisite knowledge/skill	• Basic understanding of bacterial morphology and classification. • Awareness of zoonotic diseases and their public health relevance. • Familiarity with modes of disease transmission and environmental health concepts.
Competencies to be achieved	• Learners will acquire comprehensive knowledge of leptospirosis, covering its history, epidemiology, and public health significance. • Gain insights into the morphological and genetic classification of <i>Leptospira</i> and its role in diagnosis and epidemiology. • Learn the key transmission pathways and preventive measures to reduce the risk of infection.

INTRODUCTION TO LEPTOSPIROSIS

Definition and Importance

Leptospirosis is a widespread and potentially fatal zoonosis that is endemic in many tropical regions. Outbreaks of leptospirosis tend to occur after heavy rainfall or flooding in endemic areas, especially areas with poor housing and sanitation conditions. It is caused by bacteria from the *Leptospira* genus, which have shown increasing genetic diversity over time. So far, 38 species of pathogenic *Leptospira* have been identified, with new ones being discovered regularly. The disease impacts are significant, with an estimated 1 million human cases each year and around 60,000 deaths. It is estimated that 2.90 million disability-adjusted life years (DALYs) are lost annually due to leptospirosis.

Historical Background

Leptospirosis has a rich history, marked by significant scientific discoveries over the previous century. Adolf Weil first described the severe form of the disease in 1886, leading to the term “Weil’s disease” being used to denote those cases manifesting with jaundice, splenomegaly, and renal failure. In 1907, Stimson demonstrated the bacterium responsible for leptospirosis by silver staining the presence of clumps of spirochetes in the kidney tubules of a patient who reportedly died of yellow fever. The spirochetes with the hooked ends were named *Spirochaeta interrogans* by Stimson owing to their resemblance to a question mark. The German researchers Hubener and Uhlenhuth successfully transmitted the disease to guinea pigs in 1915, confirming the pathogenic nature of the leptospiral bacterium. Ido, a Japanese scientist first demonstrated the transmission of leptospirosis from rats to humans in 1917. This finding was later corroborated by European and American researchers.

Dr. Noguchi in 1918 coined the genus name “*Leptospira*”, meaning “thin spirals,” in order to differentiate these bacteria from other spirochetes. Over the years, leptospirosis was found to be occupationally linked, especially to cane farmers, leading to the disease being dubbed “cane-cutter’s disease”. It was also recognized as an occupational hazard of rice harvesting in ancient China. Advances in microscopy in the 1960s and 1970s revealed more details about the structure of the bacteria. Further, with the development of molecular techniques like PCR, rapid diagnosis has been made possible in the recent decades.

Microbiology of *Leptospira*

Leptospira are spiral-shaped, highly motile aerobic spirochetes with 18 or more coils per cell. It can be distinguished morphologically from other spirochetes by its unique “question mark” hook at the end of the bacterium. The cell is encased in a three to five-layer outer membrane or envelope. Beneath this outer membrane are the flexible, helical peptidoglycan layer and the

cytoplasmic membrane these encompass the cytoplasmic contents of the cell. The structures surrounded by the outer membrane are collectively called the protoplasmic cylinder. An unusual feature of the spirochetes is the location of the flagella, which lie between the outer membrane and the peptidoglycan layer. They are referred to as periplasmic flagella. The periplasmic flagella are attached to the protoplasmic cylinder sub-terminally at each end and extend toward the center of the cell. The number of periplasmic flagella per cell varies among the spirochetes. The motility of bacteria with external flagella is impeded in viscous environments, but that of spirochetes is enhanced.

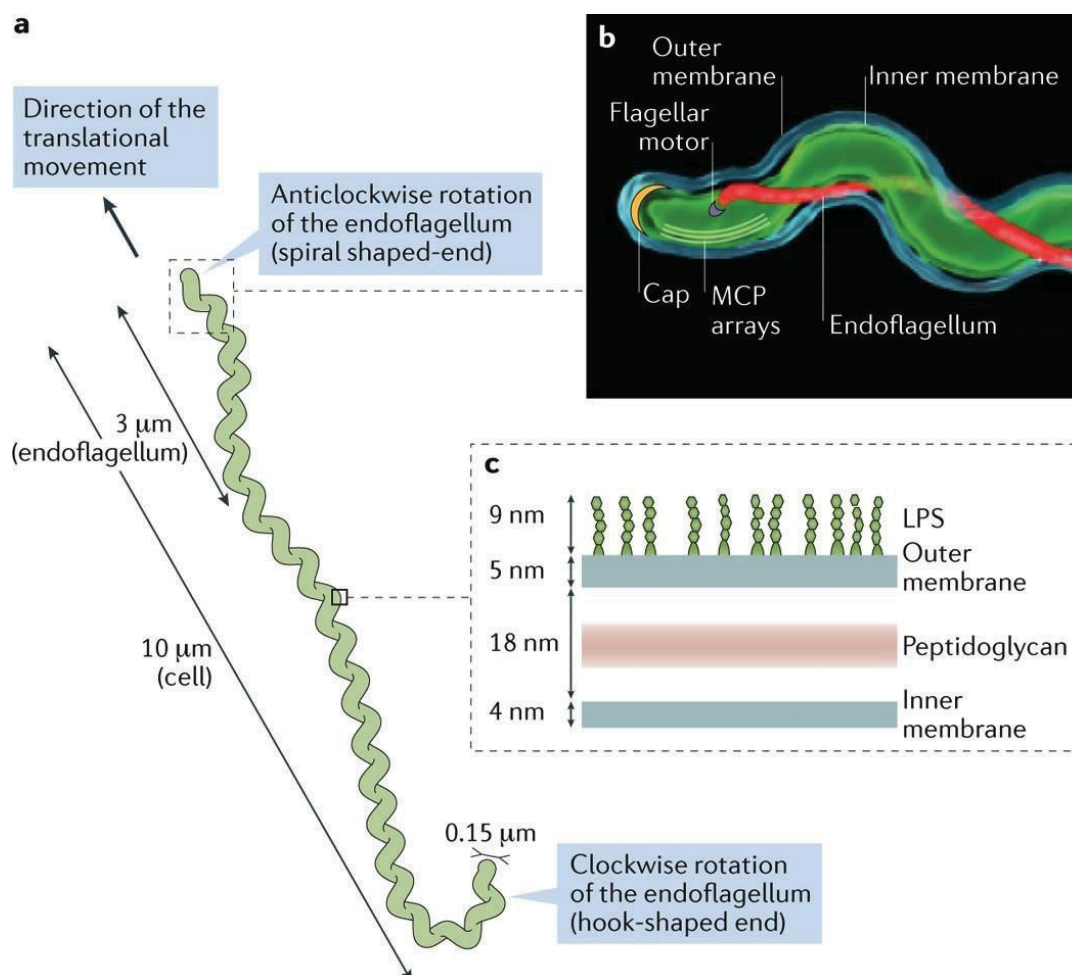


Fig 1: Cell morphology and envelope architecture of *L. interrogans*.

The slender (0.1 μm by 8 to 20 μm) leptospire is a tightly coiled, flexible cell. In liquid media, one or both ends are usually hooked. Leptospire is too slender to be visualized with the bright-field microscope but is clearly seen by dark-field or phase microscopy. They do not stain well with aniline dyes. The leptospire has two periplasmic flagella, one originating at each end of the cell. The free ends of the periplasmic flagella extend toward the center of the cell, but do not overlap as they do in other spirochetes.

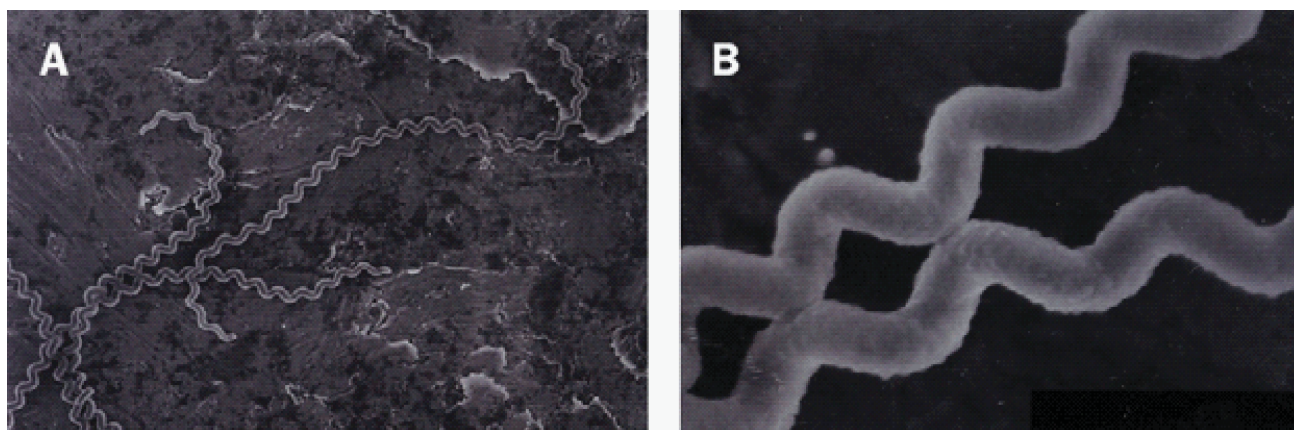


Fig 2: High-resolution scanning electron micrograph of *Leptospira interrogans* serovar *copenhageni* (Ajay R et al, 2003). (A) Note characteristic hooked ends. (B) At high magnification the surface of the spirochete seems ruffled and beaded.

Classification and Taxonomy

The genus *Leptospira* consists of a highly diverse group of bacteria that can be broadly divided into two main categories: pathogenic and saprophytic species, based on their ability to cause disease and their environmental behaviour. Over time, the classification of *Leptospira* has evolved from being based primarily on serological characteristics to incorporating advanced genetic techniques, significantly expanding our understanding of this genus.

Serological Classification

The traditional method of classifying *Leptospira* is based on serological differences, specifically the antigenic variations in the lipopolysaccharides (LPS) found on the bacterial surface. These differences are detected using serological tests such as the microscopic agglutination test (MAT), where antibodies in a patient's serum bind to specific antigens on the bacteria's surface.

In this system, the basic unit of classification is the serovar, which refers to strains of *Leptospira* that are antigenically distinct from one another. More than 300 serovars have been identified, with over 200 of these considered pathogenic. These serovars are grouped into serogroups, which are clusters of antigenically related serovars. For example, serovars such as *L. icterohaemorrhagiae* (linked to rats) and *L. canicola* (linked to dogs) are part of specific serogroups. While these serogroups are useful for epidemiological studies, they do not hold formal taxonomic standing.

This serological classification system remains valuable for clinical and diagnostic purposes, as identifying the serovar helps determine the source of infection and informs appropriate control measures. However, this method has limitations when it comes to understanding the genetic diversity of *Leptospira*, which has prompted a shift toward more precise molecular methods.

Genetic Classification

The advent of genomic sequencing has revolutionized the classification of *Leptospira*. While the initial taxonomy was based on phenotypic traits like antigenic properties and pathogenicity,

genetic studies have revealed greater complexity within the genus. For instance, the DNA-DNA hybridization technique has shown that many strains previously considered the same species based on serology are, in fact, genetically distinct.

This genomic approach has led to the identification of several new species. In addition to the traditionally recognized *Leptospira interrogans* (pathogenic) and *Leptospira biflexa* (saprophytic), more species like *L. borgpetersenii*, *L. inadai*, and *L. meyeri* have been described. Importantly, some species contain both pathogenic and nonpathogenic serovars, which illustrates the need for genetic classification to complement serological methods.

Currently, over 68 species of *Leptospira* have been recognized, which are divided into four major subclades based on their pathogenicity:

- Pathogenic subclade 1 (P1) includes species that cause disease in humans and animals.
- Pathogenic subclade 2 (P2) contains species that are intermediate in pathogenicity.
- Saprophytic subclade 1 (S1) and Saprophytic subclade 2 (S2) contain species that are primarily environmental and nonpathogenic.

The development of whole genome sequencing (WGS) and 16S rRNA analysis has allowed for deeper insights into *Leptospira* phylogeny, showing that even strains with similar serological properties can have distinct genetic lineages. As the number of sequenced genomes grows, this classification system is expected to continue evolving, providing more accurate tools for identifying and controlling leptospirosis.

Both the serological and genetic classification systems are used today primarily by researchers, though they serve different purposes. Serotyping remains important for epidemiology and understanding host-pathogen interactions, especially for identifying host-specific serovars like *L. hardjo* (found in cattle) or *L. pomona* (found in pigs). On the other hand, genetic classification offers insights into the evolutionary relationships between species and provides a more precise framework for taxonomy.

Modes of Transmission

Spread of disease occurs primarily through the direct or indirect contact of nasal, oral, or eye mucosal membranes or abraded or traumatized skin with urine or carcasses of infected animals. Damaged skin increases the probability of leptospiral infection, and this has been demonstrated with animal models using hamsters. This shows that skin integrity is a crucial immune barrier for protection against leptospires.

Urine: Indirect exposure to leptospirosis happens by water, soil, or foods contaminated by urine from infected animals is the most common route. In the mammalian reservoir host, pathogenic leptospires live in the proximal renal tubules where they are hidden in an immune privileged compartment of the body. After a short period of circulating high levels of the spirochete in their blood, animals shed the spirochete in their urine, contaminating the environment.

Human-to-human transmission is rare which is mainly documented through sexual intercourse and breastfeeding. Transmission has also occurred through animal bites, although it is very rare.

POINTS TO REMEMBER

- Leptospirosis is a widespread zoonosis, endemic in tropical regions, with outbreaks often following heavy rainfall or flooding.
- It leads to significant public health impacts, contributing to an estimated 1 million cases and 60,000 deaths annually. The loss of disability adjusted life years (DALYs) due to the disease reaches 2.90 million per year.
- *Leptospira* bacteria are spiral shaped spirochetes with unique periplasmic flagella that enhance their motility, even in viscous environments.
- The genus *Leptospira* is classified serologically into over 300 serovars, and genetically into 68 species, using advanced techniques like DNA-DNA hybridization and whole genome sequencing.
- Transmission primarily occurs through contact with water or soil contaminated by the urine of infected animals.

Introduction

Definition and Importance

- Leptospirosis is a widespread, potentially fatal zoonotic disease
- Endemic in many tropical regions
- Outbreaks often occur after heavy rainfall or flooding
- Common in areas with poor housing and sanitation

Cause

- Bacteria from the *Leptospira* genus
- Exhibits increasing genetic diversity
- 38 pathogenic *Leptospira* species identified, with new ones regularly discovered

Global Impact

- Approximately 1 million human cases annually
- Around 60,000 deaths per year
- Estimated 2.90 million Disability Adjusted Life Years (DALYs) lost annually



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Historical Overview of Leptospirosis

- 1886** - Adolf Weil described the severe form of the disease, known as Weil's disease, marked by jaundice, splenomegaly, and renal failure.
- 1907** - Stimson identified the bacterium responsible by observing spirochetes in kidney tubules using silver staining, naming them *Spirochaeta interrogans* due to their hooked, question mark like appearance.
- 1915** - German researchers Hubener and Uhlenhuth successfully transmitted the disease to guinea pigs, confirming its pathogenic nature.
- 1917** - Ido, a Japanese scientist, demonstrated transmission of leptospirosis from rats to humans, a finding later corroborated by European and American researchers.
- 1918** - Dr. Noguchi coined the genus name "*Leptospira*" (meaning "thin spirals") to distinguish it from other spirochetes.
- Occupational Links** - Historically linked to high-risk occupations
 - Cane farmers in sugarcane fields, leading to the nickname "cane-cutter's disease."
 - Recognized as a risk for rice harvesters in ancient China.
- 1960s-1970s** - Advances in microscopy revealed more structural details of the bacteria.
- Recent Decades** - Development of molecular techniques (e.g., PCR) has enabled rapid diagnosis of leptospirosis.

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LEPTOSPIROSIS

Microbiology of *Leptospira*

Leptospira Characteristics

- Shape:** Spiral-shaped, highly motile, aerobic spirochetes
- Coils:** 18+ coils per cell
- Unique Feature:** "Question mark" hook at one end

Cell Structure

- Outer Membrane:** Three- to five-layer envelope encasing the cell
- Internal Layers:**
 - Flexible, helical peptidoglycan layer
 - Cytoplasmic membrane

- Protoplasmic Cylinder:** All structures inside the outer membrane

Flagella and Motility

- Flagella Type:** Periplasmic flagella (located between outer membrane and peptidoglycan layer)
- Attachment:** Attached sub-terminally at each end, extending toward the center
- Motility in Viscous Environments:** Enhanced compared to bacteria with external flagella

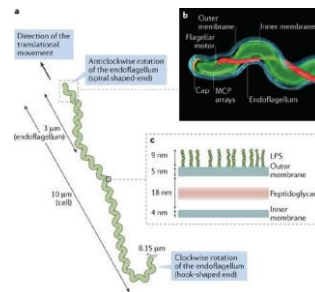


Fig 1: Cell morphology and envelope architecture of *L. interrogans*.

Picardau, M. Virulence of the zoonotic agent of leptospirosis, *sifl terra incognita?*. *Nat Rev Microbiol* 15, 297–307 (2017). <https://doi.org/10.1038/nrmicro.2017.5>

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LEPTOSPIROSIS

Classification and Taxonomy

Classification	Description
Main Categories	Pathogenic and saprophytic species based on disease causing ability and environmental behavior.
Serological Classification	- Based on antigenic differences in bacterial LPS. - Uses tests like MAT to detect antibody antigen reactions. - More than 300 serovars, over 200 pathogenic.
Genetic Classification	- DNA-DNA hybridization and genomic sequencing reveal complex diversity. - Identification of new species, e.g., <i>L. borgpetersenii</i>, <i>L. inadai</i>, <i>L. meyeri</i>.
Subclades (by Pathogenicity)	Pathogenic (P1) - Human/animal disease-causing. Intermediate (P2) - Variable pathogenicity. Saprophytic (S1, S2) - Environmental, nonpathogenic.
Importance	Serology: Useful for identifying host specific serovars in epidemiology. Genetics: Provides evolutionary insights and precise taxonomy.

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LEPTOSPIROSIS

Modes of Transmission

Classification	Description
Direct Contact	Transmission through direct contact of nasal, oral, or eye mucosal membranes or broken skin with urine or carcasses of infected animals. Damaged skin increases infection risk, as demonstrated in animal models.
Indirect Contact (Environmental)	Indirect exposure via contaminated water, soil, or food. Pathogenic leptospires live in the renal tubules of reservoir hosts and are shed in urine, contaminating the environment.
Human-to-Human	Very rare; documented in sexual intercourse and breastfeeding.
Animal Bites	Rare instances of transmission via animal bites.

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LEPTOSPIROSIS

Notes

Session-2

Epidemiology of Leptospirosis

Course No. 002	Session 2: Epidemiology of Leptospirosis
Duration	20 minutes
Learning Objective	• Explain the global burden and incidence of leptospirosis, including key regions affected and the economic impact. • Describe the epidemiological scenario in India, highlighting outbreaks, endemic regions, and factors contributing to disease spread. • Discuss the role of animal reservoirs, including the relationship between reservoir hosts and the environmental contamination of leptospires. • Analyze ecological factors and the impact of climate change, urbanization, and occupational and recreational exposures on disease transmission.
Pre-requisite knowledge/skill	• Understanding of basic epidemiological terms and concepts (incidence, prevalence, endemicity). • Awareness of zoonotic reservoirs and environmental health interactions. • Familiarity with the impact of climate, urbanization, and human activities on infectious disease transmission.
Competencies to be achieved	• Explain the global burden and incidence of leptospirosis, including key regions affected and the economic impact. • Describe the epidemiological scenario in India, highlighting outbreaks, endemic regions, and factors contributing to disease spread. • Discuss the role of animal reservoirs, including the relationship between reservoir hosts and the environmental contamination of leptospires. • Analyze ecological factors and the impact of climate change, urbanization, and occupational and recreational exposures on disease transmission.

EPIDEMIOLOGY OF LEPTOSPIROSIS

Global Burden and Incidence

Leptospirosis is considered to be the most widespread zoonotic disease globally, yet it remains significantly underreported. Accurate global incidence figures are lacking, as leptospirosis was not included as a distinct entity in the Global Burden of Disease (GBD) study. This left a gap in understanding its comparative burden alongside other neglected tropical diseases (NTDs). However, a 2015 study by Costa et al. estimated the global incidence at 1.03 million cases and 58,900 deaths annually. These figures may be underestimating the actual burden due to limited awareness about the disease, non-specific clinical manifestations, inadequate availability of diagnostic facilities, and poorly reliable surveillance systems. Current diagnostic tools miss up to 40% of cases. A study by Torgerson et al. estimated that leptospirosis results in approximately 2.90 million disability adjusted life years (DALYs) lost annually.

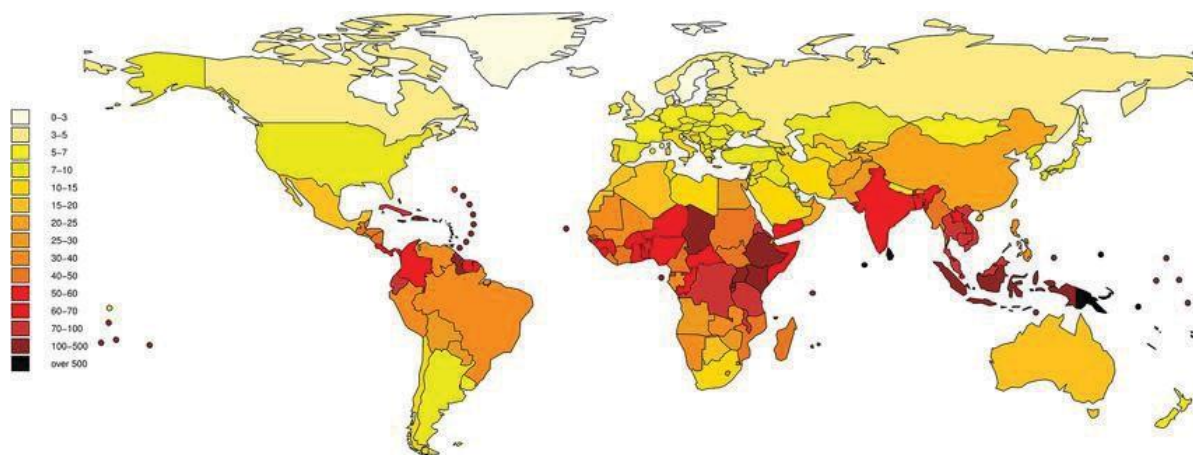


Fig 3: Burden of leptospirosis in terms of DALYs/100,000 per year.

A systematic survey found that the highest morbidity and mortality from leptospirosis occur in regions such as South and Southeast Asia, Oceania, the Caribbean, Andean, Central, and Tropical Latin America, and Eastern Sub-Saharan Africa. Sri Lanka has the highest global incidence, with over 700 deaths annually more than double that of dengue fever and an estimated hospital admission rate of 52.1 patients per 100,000 population. While leptospirosis has a global distribution, its incidence is particularly high in tropical climates, affecting regions like sub-Saharan Africa, Latin America, the Caribbean, and parts of Asia.

In 2019, the global average annual cost of leptospirosis, primarily due to lost productivity, was estimated at \$29.3 billion, with a potential upper limit of \$52.3 billion. The countries incurring the highest costs were China (\$4.8 billion), India (\$4.6 billion), Indonesia (\$2.8 billion), Sri Lanka (\$2.1 billion), and the United States (\$1.3 billion). Most of the highest-cost countries were located in the Asia-Pacific region. Additionally, lower middle-income countries faced a combined annual cost of \$13.8 billion.

Indian Scenario

India is considered a hotspot for leptospirosis, a disease that leads to significant morbidity and mortality, though it is often underestimated and underdiagnosed. Despite being known for decades, public concern over the disease has not developed fully because awareness remains low.

In the late 1980s, mysterious outbreaks of a febrile illness began in India, marked by severe haemoptysis (coughing up blood) and high case fatality rates. This illness was named Andaman Haemorrhagic Fever (AHF), but the cause remained unknown for five years. In 1995, a study during an outbreak in North Andaman revealed that the cause of AHF was leptospirosis, making it the first documented case of severe pulmonary haemorrhage from leptospirosis in India. Since then, numerous outbreaks and isolated cases have been reported across the country in places like Surat, Cochin, Odisha, Mumbai, and Chennai, all caused by *Leptospira* bacteria.

From 1988 to 2005, surveillance in the Andaman and Nicobar Islands identified 1,126 cases of leptospirosis. Gujarat saw 3,121 cases with 383 deaths between 1997 and 2005, while Chennai reported 5,452 cases from 2004 to 2006. Maharashtra recorded 4,484 cases with 394 deaths from 1998 to 2005. Other states, such as Punjab, Haryana, Himachal Pradesh, and Karnataka, have also reported cases, particularly following floods or cyclones in urban areas. The disease is most prevalent in central, southern, western, and eastern India, where factors like animal rearing, unplanned urbanization, rural lifestyles, and heavy monsoons contribute to its spread. Cases peak between July and October each year.

Over the last 30 years, leptospirosis outbreaks in India have been on the rise, driven by poor sanitation, a lack of diagnostic facilities, and public unawareness. To combat this, the Government of India launched the Programme for Prevention and Control of Leptospirosis during the 12th Five-year Plan. The main objective of this program was to reduce morbidity and mortality due to Leptospirosis. The infection rate is highest in southern India, followed by the western, central, eastern, and northern regions. Leptospirosis is endemic in five states—Gujarat, Maharashtra, Kerala, Tamil Nadu, and Karnataka as well as the Andaman and Nicobar Islands.

Animal Reservoirs

Leptospirosis has an unusually broad range of natural hosts, encompassing both rodents and non-rodent animals. Key reservoir hosts include rodents, foxes, wild cats, and rabbits. The relationship between leptospires and their hosts is intricate, as leptospires are not highly specific to any one species. However, certain hosts do have a preference, with rodents being particularly significant. These animals are often infected for life and carry specific serovars endemic to their region. Rodents, especially, have a high capacity to shed large amounts of leptospires in their urine, which is a primary source of environmental contamination and a major factor in human and animal infections. As a result, the serovars present in rodents reflect the epidemiology of leptospirosis in any given area. Rodents are considered the largest reservoir group responsible for the spread of leptospires to humans and other animals.

In addition to rodents, various wild and domestic animals also serve as reservoirs. The bacteria persist in the renal tubules of these animals and are expelled through their urine. Humans, typically considered deadend hosts, become infected when exposed to the urine of infected rodents or animals, either directly or through environmental contact. The bacteria enter the body through the skin or mucous membranes, such as the eyes or mouth, often during activities related to domestic chores, work, or recreation.

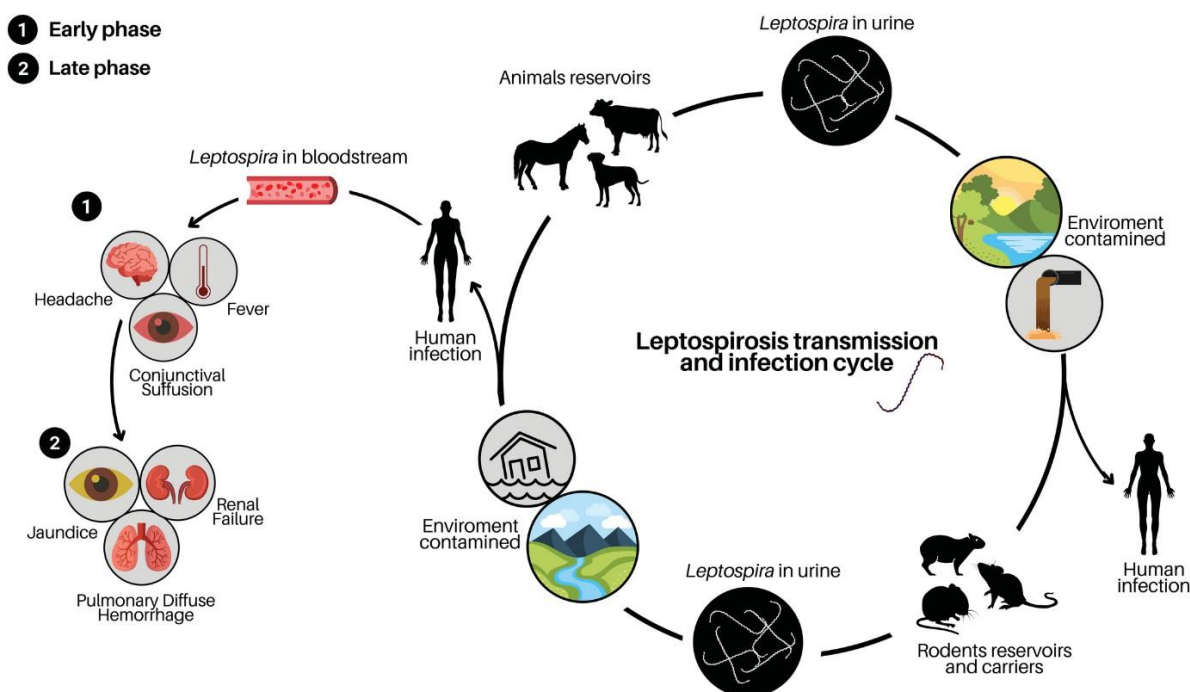


Fig 4: Leptospirosis transmission and infection cycle

In rural areas, livestock and domestic animals like cattle, pigs, and dogs are key reservoirs. In contrast, urban leptospirosis is predominantly linked to rats, which shed leptospires in their urine. Dogs also play a dual role; while they may be reservoirs for specific serovars like *Canicola*, they can also contract and spread other serovars. Dogs, particularly in peri-urban areas, may become infected while roaming, subsequently transmitting the bacteria through their urine in close proximity to human populations.

Ecological Factors

Leptospire are shed into the environment through the urine of infected animals, where they can survive in soil and freshwater for extended periods, especially under neutral to alkaline conditions. The optimal environment for leptospire is one that is warm and humid, which explains why tropical and subtropical regions see cases of leptospirosis throughout the year. In temperate climates, leptospirosis is more seasonal, occurring mainly during the warmer, rainy months.

India, with its vast biodiversity and varied ecosystems, provides ideal conditions for both natural reservoir hosts and the survival of leptospire in the environment following their excretion through urine. There is a biological balance between the species of rodents, the specific

leptospiral serovars they carry, and their persistence in nature. However, ecological disruptions such as earthquakes or floods can upset this balance, leading to the mixing of rodent species and the introduction of multiple serovars in an area. In India, the monsoon season, with its heavy rains and flooding, is closely associated with increased transmission of leptospirosis. Pathogenic leptospires, while sensitive to UV light, chlorine, and detergents, can persist in waterlogged conditions, making outbreaks following floods a common occurrence.

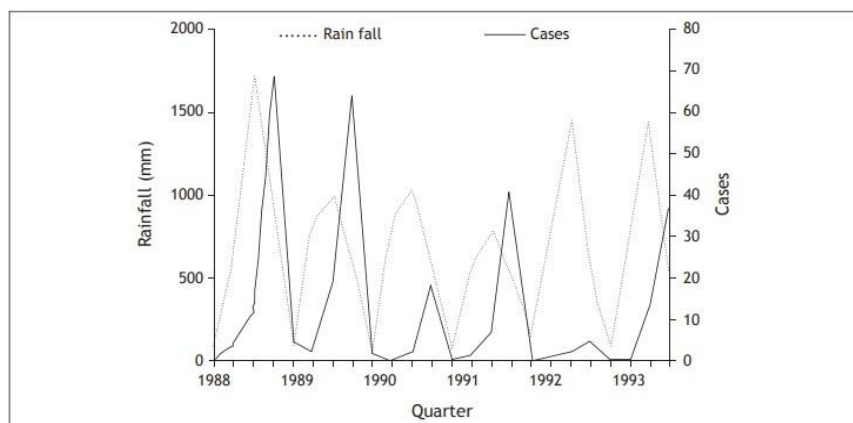


Fig 5: Association of rainfall with occurrence of leptospirosis cases in Andaman

Impact of Climate Change

Warmer annual temperatures promote the growth and activity of *Leptospira* species, extend the infectious period, and expand the geographical range of the bacteria. Increased rainfall and humid conditions also support the survival and proliferation of *Leptospira*. Future climate projections suggest that these factors will likely increase the incidence of the disease. Another critical climate related risk factor for leptospirosis is the rise in extreme weather events. Heavy rains, storms, and flooding heighten human exposure to contaminated water sources. When combined with poor sanitation, limited healthcare, or overcrowded living conditions, the risk of infection escalates. Drought conditions, conversely, can increase recreational activities like swimming or bathing in contaminated water and lead to occupational exposure when farms rely on alternative, possibly contaminated, water sources during water shortages. Both scenarios can result in heightened risks of leptospirosis transmission.

Urban Exposure

In urban and peri-urban areas, leptospirosis transmission is primarily driven by rodent populations, particularly rats (*Rattus norvegicus*), which serve as reservoirs for the serogroup *Icterohaemorrhagiae*. Poor sanitation, unplanned urbanization, and open drainage systems further contribute to the spread of the disease. Urban sewage workers, garbage collectors, and those working in flood affected areas are at heightened risk.

Occupational Exposure

Certain occupations place individuals at higher risk of contracting leptospirosis due to their frequent interaction with animals or contaminated environments. Veterinarians, slaughterhouse workers, dairy farmers, and laboratory scientists working with animals are among the groups most at risk. In India, paddy field workers, particularly in rice cultivation, are frequently exposed to contaminated water, heightening the risk of infection. The extent of exposure and the local prevalence of leptospirosis largely determine the magnitude of the risk.

Recreational Exposure

Leptospirosis is not limited to occupational hazards; recreational activities also pose a risk, especially those involving freshwater sources. Activities such as swimming, rafting, or trekking through waterlogged areas can lead to exposure. In India, the rise of adventure sports like river rafting in places like Rishikesh or trekking in the Western Ghats during the monsoon season increases the likelihood of indirect contact with leptospires. Events like large outdoor competitions can lead to outbreaks, as contaminated water can affect large numbers of participants.

POINTS TO REMEMBER

- High morbidity and mortality rates are concentrated in regions like South and Southeast Asia, Oceania, the Caribbean, and parts of Latin America and Sub-Saharan Africa.
- India is a hotspot for leptospirosis, with outbreaks mainly occurring in southern and western states like Gujarat, Maharashtra, Kerala, Tamil Nadu, Karnataka, and the Andaman and Nicobar Islands.
- The global economic burden of leptospirosis was estimated to cost \$29.3 billion annually, with countries like India, China, and Indonesia bearing the highest financial losses due to lost productivity.
- Rodents, especially rats, are the main reservoirs for *Leptospira* bacteria. They shed large amounts of the bacteria in their urine, contaminating soil and water, which then leads to human infections.
- *Leptospira* bacteria thrive in warm, humid environments and can survive in soil and freshwater. Floods, heavy rains, and other ecological disruptions increase the risk of transmission, especially in tropical regions.
- Leptospirosis transmission is driven by multiple exposures, including occupational (e.g., paddy field workers, sewage workers), urban (due to poor sanitation and rodent infestation), and recreational activities (e.g., water sports in contaminated environments).

Notes

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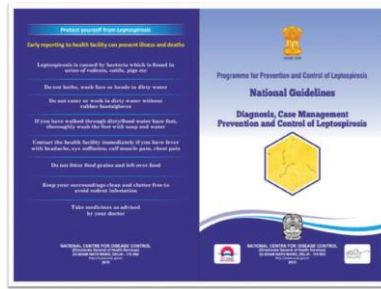
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Indian Scenario

- To combat this, the Government of India launched the Programme for Prevention and Control of Leptospirosis during the 12th Five-year Plan.
- The main objective of this program was to reduce morbidity and mortality due to Leptospirosis.

Endemic Regions - Highest infection rate in southern India; endemic in Gujarat, Maharashtra, Kerala, Tamil Nadu, Karnataka, and Andaman and Nicobar Islands.



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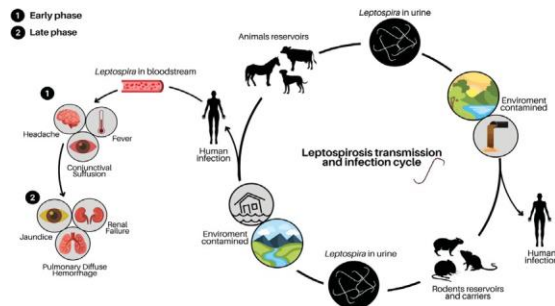
Animal Reservoirs

- Broad Range of Hosts:** Includes both rodents and non-rodent animals; key reservoirs are rodents, foxes, wild cats, and rabbits.
- Rodents as Major Reservoirs:**
 - High capacity to shed leptospires in urine, leading to environmental contamination.
 - Specific serovars endemic to regions reflect local epidemiology.
- Life-Long Infection:** Rodents can be infected for life, significantly contributing to the spread of leptospirosis.
- Other Animal Reservoirs:** Wild and domestic animals, including cattle, pigs, and dogs, expel bacteria through urine.
- Human Infection:** Typically occurs through direct exposure to infected urine or environmental contact. Entry via skin or mucous membranes (eyes, mouth) during chores, work, or recreation.
- Urban vs. Rural Dynamics:**
 - Urban leptospirosis linked to rats.
 - Rural areas involve livestock and domestic animals as key reservoirs.

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Leptospirosis transmission and infection cycle



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Ecological Factors in Leptospirosis Transmission

- Environmental Shedding** - Leptospire excreted through animal urine survive in soil and water.
- Optimal Conditions** - Warm, humid, neutral to alkaline environments support survival.
- Tropical and Subtropical Regions** - Continuous cases; temperate areas see seasonal trends.
- India's Biodiversity** - Offers reservoirs and favorable conditions; monsoon season increases cases.
- Ecological Disruptions** - Natural events like floods and earthquakes mix rodent species, potentially introducing new serovars.

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LEPTOSPIROSIS

Impact of Climate Change and Urban Exposure on Leptospirosis

Impact of Climate Change

- **Warmer Temperatures** - Promote *Leptospira* growth, extend infection period, and expand geographical range.
- **Increased Rainfall & Humidity** - Enhance *Leptospira* survival and spread.
- **Extreme Weather Events** - Heavy rains, floods, and poor sanitation heighten exposure to contaminated water sources.
- **Drought Conditions** - Recreational and occupational exposure to possibly contaminated water increases infection risk.

Urban Exposure

- **Rodent Populations** - Especially rats, act as reservoirs in urban areas.
- **Poor Sanitation & Open Drainage** - Unplanned urban growth and lack of sanitation aid transmission.
- **High-Risk Occupations** - Urban sewage workers, garbage collectors, flood responders are especially vulnerable.

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Occupational Exposure

- Certain occupations place individuals at higher risk of contracting leptospirosis due to frequent interaction with animals or contaminated environments.
- Veterinarians, slaughterhouse workers, dairy farmers, and laboratory scientists working with animals are among the groups most at risk.
- In India, paddy field workers, particularly in rice cultivation, are frequently exposed to contaminated water, heightening the risk of infection.



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Recreational Exposure



Activities such as swimming, rafting, or trekking through waterlogged areas can lead to exposure.

In India, the rise of adventure sports like river rafting in places like Rishikesh or trekking in the Western Ghats during the monsoon season increases the likelihood of indirect contact.



Leptospirosis is not limited to occupational hazards; recreational activities also pose a risk, especially those involving freshwater sources.

Events like large outdoor competitions can lead to outbreaks, as contaminated water can affect large numbers of participants.



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LEPTOSPIROSIS

Session-3

Leptospirosis in Humans

Course No. 003	Session 3: Leptospirosis in Humans
Duration	30 minutes
Learning Objective	• Describe the incubation period and its variability in leptospirosis. • Explain the case fatality rate (CFR) and its association with severe outcomes. • Recognize the clinical presentation of leptospirosis, including key symptoms and complications. • Identify the features of severe leptospirosis, often referred to as Weil's disease. • Outline the recovery phase and its implications for patients post leptospirosis.
Pre-requisite knowledge/skill	• Basic understanding of human physiology and infectious disease progression. • Familiarity with clinical terminology related to fever, organ dysfunction, and systemic infections. • Ability to differentiate between mild and severe manifestations of infectious diseases.
Competencies to be achieved	• Learners will gain insights into the incubation period of leptospirosis and its significance in disease progression. • Acquire knowledge about the range of case fatality rates and risk factors for severe disease. • Develop the ability to recognize and differentiate clinical symptoms of leptospirosis from other febrile illnesses. • Recognize the complications associated with severe leptospirosis, including pulmonary and renal involvement, and their management. • Learn about the recovery phase and potential chronic symptoms in patients after the acute illness.

LEPTOSPIROSIS IN HUMANS

Incubation Period

The incubation period for leptospirosis typically ranges from 5 to 14 days, though it can vary from as short as 2 days to as long as 20 days.

Case Fatality Rate (CFR)

Reported case-fatality rates for leptospirosis vary widely, from less than 5% to as high as 15%. More than 90% of the deaths due to leptospirosis occur because of pulmonary alveolar hemorrhage.

Clinical Presentation

Leptospirosis in humans typically presents with a sudden onset of fever, chills, and headache. These early symptoms are nonspecific and can mimic other acute febrile illnesses, such as influenza, dengue fever, or malaria, making it difficult to diagnose initially.

Fever: Patients experience remittent fever, which can range from moderate to severe.

Headache: The headache associated with leptospirosis is often severe, characterized by bitemporal or frontal throbbing, and may be accompanied by retro-orbital pain and sensitivity to light (photophobia).

Myalgia: Muscle pain and tenderness, particularly affecting the calves, lower back and abdomen, is a common feature of leptospirosis.

Conjunctival suffusion, Subconjunctival haemorrhage and Icterus: One clinical sign that can help distinguish leptospirosis from other febrile illnesses is **conjunctival suffusion**, which refers to redness in the eyes due to dilated blood vessels without pus. Other ocular findings may include subconjunctival hemorrhages and jaundice (icterus), particularly in more severe cases.

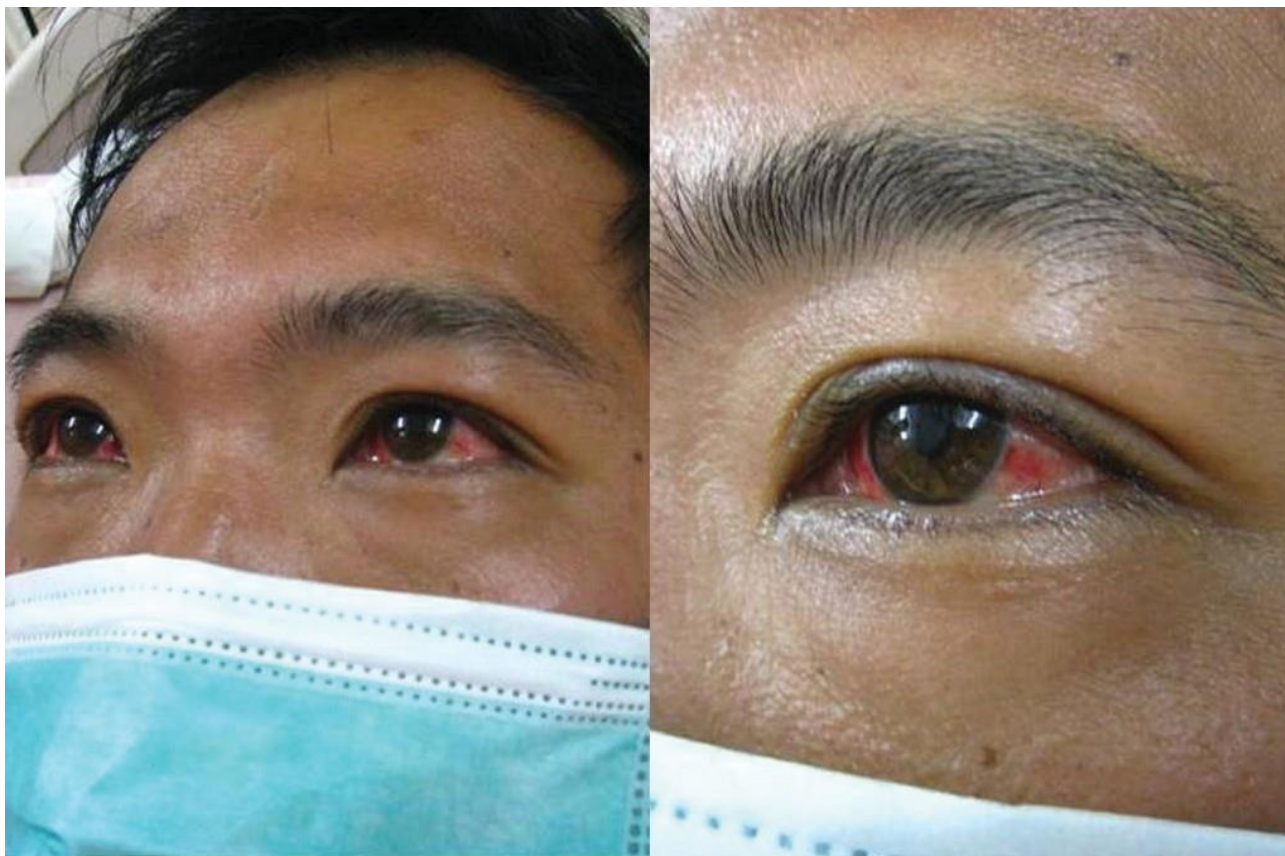


Fig 6: Bilateral Conjunctival Suffusion

Pulmonary Manifestations: Respiratory symptoms are also commonly reported, with up to 57% of patients developing a nonproductive cough, which can sometimes mislead clinicians into suspecting influenza or other respiratory illnesses.

Gastrointestinal symptoms: Gastrointestinal symptoms, including nausea, vomiting, diarrhea, and abdominal pain, are frequent in leptospirosis patients. These symptoms can contribute to dehydration, especially in those experiencing high-output non-oliguric renal failure a common complication of leptospirosis which has been discussed in the subsequent section.

In more severe cases, patients may experience abdominal pain due to conditions like acalculous cholecystitis (inflammation of the gallbladder without gallstones) or pancreatitis. While most cases of pancreatitis associated with leptospirosis are mild and self-limiting, some severe cases can lead to fatal outcomes. It is important to note that impaired renal function can also elevate pancreatic enzyme levels, complicating the diagnosis of pancreatitis in leptospirosis patients.

Severe Leptospirosis (Weil's Disease)

Severe leptospirosis, often referred to as **Weil's disease**, is characterized by multiple organ dysfunction, primarily involving the liver, kidneys, lungs, and brain. Weil's disease is recognized by the combination of jaundice and acute renal failure. Evidence of organ dysfunction may develop suddenly, even in patients who initially present with milder symptoms, and often signals a more advanced stage of infection.

Hepatic involvement: Liver involvement in leptospirosis typically results in jaundice, which can vary in severity depending on the serovar of *LEPTOSPIRA* involved. The *Icterohaemorrhagiae* serogroup is strongly associated with jaundice and elevated bilirubin levels. In some cases, patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency may develop acute hemolytic anemia, contributing to the jaundice. Jaundice is generally accompanied by mild to moderate elevations in liver enzymes, particularly liver transaminases.

Renal involvement: This is also common in leptospirosis, leading to **acute kidney injury (AKI)**, often manifesting as increased serum creatinine and blood urea nitrogen levels. A unique feature of leptospirosis induced kidney injury is the **non-oliguric potassium-wasting nephropathy**, where patients lose potassium while retaining normal urine output. This form of renal failure can become life-threatening in areas with limited access to dialysis.

Hematuria, (dark, cola-coloured urine) and the presence of red blood cell casts in urine microscopy, is a common finding in leptospirosis. In severe cases, this can progress to **acute renal failure**, presenting with **decreased urine output** (oliguria or anuria), **edema** in the face and extremities, and **uremic symptoms** such as breathlessness, convulsions, delirium, and altered consciousness. These symptoms are more pronounced in very severe cases. Renal dysfunction usually worsens during the first week of illness, peaking by the second week, before gradually improving. Complete recovery is generally expected by the fourth week if appropriate renal support is provided. In severe cases of acute renal failure, **dialysis** may be necessary during the acute phase, though most patients recover without lasting renal impairment.

Pulmonary involvement: One of the most serious complications of leptospirosis is **severe pulmonary hemorrhage syndrome (SPHS)**, which is associated with massive hemoptysis (coughing up blood) and has a fatality rate exceeding 50%. It is marked by frank hemoptysis (coughing up blood) and severe respiratory distress, which includes rapid breathing (tachypnea) and difficulty breathing. On a chest X-ray, patients typically exhibit nodular densities, patchy alveolar infiltrates, and occasional consolidation, most commonly in the lower lobes of the lungs. SPHS often progresses to **acute respiratory distress syndrome (ARDS)**, characterized by diffuse lung injury, impaired gas exchange, and widespread hemorrhage within the lungs. SPHS can be mistaken for other respiratory conditions, such as viral pneumonitis, and has been reported in outbreaks worldwide.

Hemorrhagic pneumonitis, characterized by interstitial and intra-alveolar hemorrhage surrounded by focal capillary injury, is a common pathological finding in severe leptospirosis. In extreme cases, death can occur within hours to two days due to massive pulmonary hemorrhage and severe respiratory distress. The pulmonary presentation of leptospirosis varies widely, but **pulmonary complications** are the leading cause of death in leptospirosis.

The manifestation of pulmonary radiologic abnormalities ranges from 11% to 67% and can manifest as early as 24 hours following the onset of respiratory symptoms, but they often appear within a time frame of 3 to 9 days.

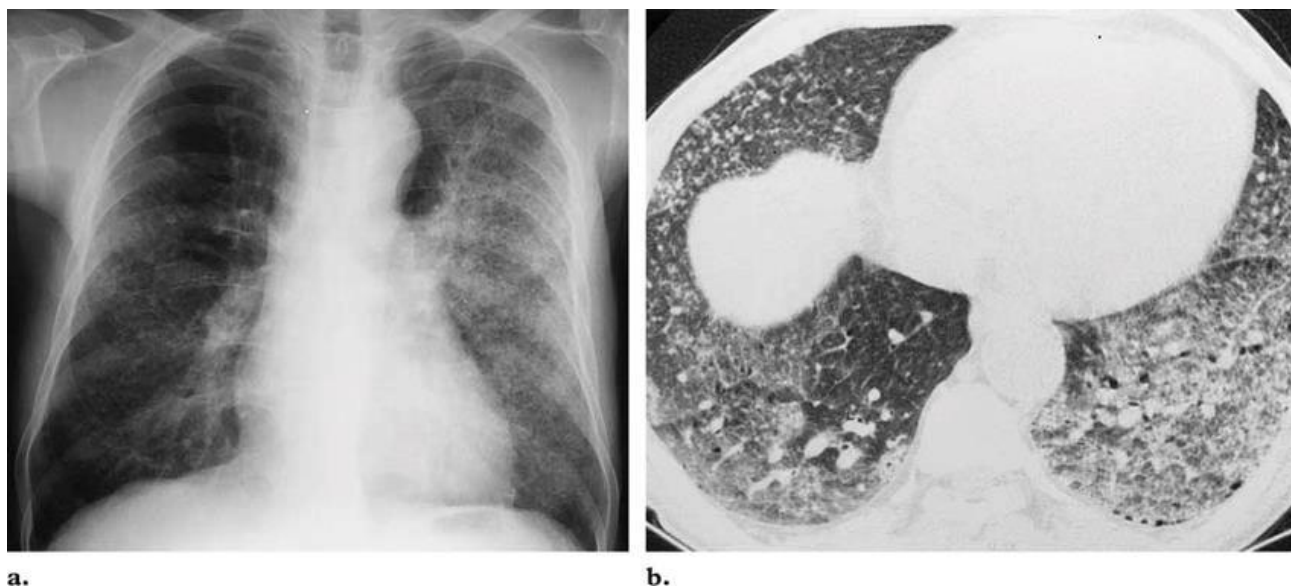


Fig 6: (a). Initial chest radiograph shows fine reticulonodular opacities throughout both lungs.
(b). High-resolution CT scan obtained the same day shows ground-glass attenuation, intralobular interstitial thickening, and ill-defined small nodular hyperattenuating areas.

Central Nervous System: Neurological complications are less common but can include aseptic meningitis, meningoencephalitis, and more severe manifestations such as hemiplegia, Guillain-Barré syndrome, and transverse myelitis. Patients with neurological involvement may present with altered mental status, confusion, or even coma, often signaling a poor prognosis.

Cardiovascular System Involvement: Cardiovascular complications in leptospirosis often manifest as **shock** and **arrhythmias**, including **atrial fibrillation**. Patients may present with one or more of the following features:

- **Shock:** This is characterized by severe **hypotension**, **cold clammy extremities**, and tachycardia. An echocardiogram typically shows normal systolic function of the left ventricle, suggesting that the hypotension is caused by **dehydration** or **peripheral vasodilatation**, rather than a primary cardiac dysfunction.
- **Arrhythmias:** Patients may experience **palpitations**, **syncope**, and an **irregular pulse**. Common arrhythmias include **supraventricular tachyarrhythmia** and various degrees of **A.V. block**, although **ventricular tachyarrhythmias** are less common. Some patients may also present with **segment depression** and **T-wave inversion** on their electrocardiogram (ECG).

Note: All patients with severe, multiple organ involvement should be referred to tertiary care centre.

Risk Factors for Morbidity and Mortality

Several factors have been identified as increasing the risk of severe disease and death from leptospirosis. Severe and life-threatening outcomes are associated with hemodynamic instability, thrombocytopenia, elevated blood creatinine, high serum potassium levels, and lung involvement. The risk of mortality also increases with age, with individuals over 60 years old experiencing a seven-fold increase in mortality compared to younger adults. Other poor prognostic indicators include pulmonary involvement (dyspnea or alveolar infiltrates on chest X-ray), acute renal failure, hypotension, and arrhythmias. Delayed hospital admission is also increasing the likelihood of death.

Recovery Phase

With proper medical care, including supportive treatment such as dialysis and intensive care for multi-organ failure, most patients with leptospirosis recover fully. However, some patients may experience chronic symptoms after the acute phase, a condition known as **post-leptospirosis syndrome**. These patients report persistent fatigue, myalgia, malaise, headache, and weakness, with symptoms lasting for months or even years in some cases.

Ocular involvement, particularly uveitis, is also recognized during the recovery phase of leptospirosis. Uveitis can vary in severity, ranging from mild inflammation of the eye to severe panuveitis (inflammation involving all layers of the eye). Recurrent episodes of uveitis have been reported, often requiring prolonged treatment.

Case Definition of Leptospirosis

The recommended case definitions for the management of a case of leptospirosis is as follows:

Suspected Case

A person having acute febrile illness with headache, myalgia and prostration associated with a history of exposure to infected animals or an environment contaminated with animal urine with one or more of the following –

- Calf muscle tenderness
- Conjunctival suffusion
- Anuria or oliguria and/or proteinuria
- Jaundice
- Hemorrhagic manifestations
- Meningeal irritation
- Nausea, Vomiting, Abdominal pain, Diarrhoea.

Probable Case

Suspected case with positive presumptive laboratory diagnosis.

Laboratory Confirmed Case

A case compatible with the clinical description of leptospirosis with at least one of the following:

- Isolation of leptospirosis from clinical specimen.
- Fourfold or greater rise in the MAT titre between acute and convalescent phase serum specimens run in parallel.
- Positive by any two different types of rapid test.
- Detection of pathogenic *Leptospira* DNA (e.g., by PCR) from a clinical specimen.

Differential Diagnosis

Leptospirosis can present with nonspecific clinical symptoms, making it challenging to differentiate from several other tropical and systemic diseases that share similar features, such as fever, headache, and muscle pain (myalgia). Recognizing the clinical and laboratory distinctions is crucial for accurate diagnosis, especially in endemic regions.

Commonly Confused Diseases

Falciparum Malaria, Dengue, Scrub Typhus, and Typhoid Fever: These tropical diseases are prevalent in regions where leptospirosis occurs and present with overlapping symptoms like fever, headache, and muscle pain. However, certain specific features can help distinguish leptospirosis:

Dengue fever often presents with conjunctival suffusion (red eyes), a symptom shared with leptospirosis. However, the bleeding tendencies and shock in Dengue Hemorrhagic Fever can help differentiate it.

Scrub typhus and Typhoid fever both mimic the febrile presentation of leptospirosis but lack the characteristic muscle tenderness of leptospirosis, especially in the calves and lower back.

Viral Hepatitis: Liver involvement is common in both viral hepatitis and leptospirosis, making them difficult to distinguish. However, liver enzyme patterns are useful:

In leptospirosis, SGOT (AST) and SGPT (ALT) levels are typically normal or mildly elevated (hundreds of IU/L), while in viral hepatitis, SGPT is significantly elevated, often in the thousands. Creatinine Phosphokinase (CPK) is often elevated in leptospirosis, a sign of muscle injury, which is normal in viral hepatitis and alcoholic hepatitis. This elevation in CPK serves as a distinguishing marker.

Rickettsial Infections, and Hemorrhagic Fevers: Leptospirosis shares some epidemiologic and clinical features with Rickettsial diseases (e.g., Scrub Typhus), and other hemorrhagic fevers like Yellow Fever and Rift Valley Fever. These diseases, like leptospirosis, present with systemic symptoms, such as fever, hemorrhage, and organ involvement.

In areas with concurrent infections, dual infections with leptospirosis and other zoonotic diseases have been reported. Therefore, serologic testing for rickettsiae, dengue virus, and hantavirus is advised when leptospirosis is suspected, especially if there is bleeding.

Table 1: Differential Diagnosis of Leptospirosis

Disease	Epidemiological Clues	Key Clinical Differences	Laboratory Tests
Falciparum Malaria	Endemic in tropical regions, mosquito exposure, travel history.	Cyclic fever with chills, no hydrophobia or aerophobia, CNS symptoms only in cerebral malaria.	Hematological: Anemia, thrombocytopenia.
			Biochemical: Normal or mild bilirubin elevation.
			Serology/Special: Blood smear or rapid antigen test positive for <i>Plasmodium</i> .
Dengue Fever	Endemic in urban areas, mosquito exposure (Aedes).	Fever with severe myalgia ("breakbone fever"), bleeding tendencies, no CNS involvement or hydrophobia.	Hematological: Thrombocytopenia, leukopenia.
			Biochemical: Elevated hematocrit in plasma leakage.
			Serology/Special: Dengue NS1 antigen or IgM/IgG positive.
Scrub Typhus	Rural areas, mite exposure, history of outdoor activity.	Fever with eschar (specific to scrub typhus), no CNS excitability or phobic symptoms.	Hematological: Leukocytosis, thrombocytopenia.
			Biochemical: Mildly elevated LFTs.
			Serology/Special: IgM for <i>Orientia tsutsugamushi</i> positive, Weil-Felix test.
Typhoid Fever	Endemic regions, history of contaminated food/water.	Sustained high fever, rose spots, diarrhea, no hydrophobia or aerophobia.	Hematological: Leukopenia, anemia.
			Biochemical: Mild LFT elevation.
			Serology/Special: Blood culture positive for <i>Salmonella</i> .
Viral Hepatitis	Endemic regions, contaminated water or needle sharing.	Jaundice, no CNS symptoms or phobic reactions; markedly elevated ALT/AST differentiates from rabies.	Hematological: Normal or mild anemia.
			Biochemical: ALT/AST > 10x normal.
			Serology/Special: Hepatitis viral markers (HBsAg, HCV Ab).
Meningitis (Bacterial/Viral)	History of upper respiratory infection or recent trauma.	Stiff neck, photophobia, altered mental status; no hydrophobia or aerophobia.	Hematological: Leukocytosis in bacterial; normal in viral.
			Biochemical: Elevated CSF protein, low glucose (bacterial).
			Serology/Special: CSF PCR or Gram stain.

Coinfections

In endemic areas, coinfections with leptospirosis and other tropical diseases such as malaria, dengue, and rickettsial diseases have been reported, further complicating the differential diagnosis. Healthcare providers should maintain a high index of suspicion and consider multiple simultaneous infections.

Case Presentation

Patient Information

Name: C.R.

Age: 16 years

Location: Kerala

Marital Status: Single

Date of Birth: October 7, 2008

First-time admission at local hospital

Informant: Mother [Reliability: 90%]

Chief Complaint - "3-day history of fever"

History of Present Illness - 1 Week History of Wading through Floodwaters

- *Day 1:* (+) Undocumented fever; (+) Myalgia, headache; (+) Abdominal pain, decreased appetite and activity; Self-administered Paracetamol twice, no medical consultation
- *Day 2:* Persistence of above symptoms; (+) Decreased urine output (yellow-orange colour); (+) Calf pain
- *Day 3:* Persistence of symptoms; (+) Loose bowel movements (LBM) and vomiting; Last urine output at 12 noon, < 1ml; Few hours later: (+) Anuria (no urine output); (+) Difficulty of breathing (DOB); Sought consultation at hospital

Review of Systems

- *General:* **(+) Body weakness**, (-) Weight loss, **(+) Decreased appetite**, (-) Chills, (-) fatigue
- *Skin:* **(+) Jaundice**, (-) Pallor, (-) Pruritus, (-) Cyanosis, (-) Rashes, (-) Hematoma
- *Head & Neck:* (-) Nodules, (-) Stiffness, (-) Swelling, (-) Pain, (-) Trauma, **(+) Headache**, **(+) Dizziness**, (-) Light headedness
- *Eyes:* (-) Asymmetry, (-) Infection, **(+) Icteric sclera**, (-) Itchiness, (-) Diplopia, (-) Use of glass/lenses, (-) Lacrimation, (-) Blurred vision
- *Ears:* (-) Hearing problem, (-) Itching
- *Mouth & Throat:* (-) Hoarseness, (-) Sore throat, (-) Dysphagia
- *Respiratory:* (-) Cough (-) Colds (-) Dyspnea (-) Cyanosis (-) Hemoptysis
- *Cardiac:* (-) Palpitation, (-) Chest Pain, (-) Orthopnea, (-) Paroxysmal Nocturnal Dyspnea, (-) Easy Fatigability, (-) Edema
- *Gastrointestinal (GIT):* (-) Pain, (-) Anorexia, (-) Vomiting, (-) Melena, (-) Constipation, (-) Excessive Belching, (-) Bloating, (-) Loss of Appetite, (-) Abdominal Pain, (-) Diarrhea

- *Renal:* (-) Dysuria, (-) Hematuria, (-) Nocturia, (-) Incontinence, (-) Polyuria, **(+) Anuria**, (-) Urgency, (-) Frequency, (-) Gross Hematuria, (-) Tea-Coloured Urine
- *Genitalia:* (-) Pain, (-) Swelling, (-) Discharge, (-) Infection
- *Musculoskeletal:* (-) Stiffness, (-) Numbness, **(+) Joint Pain**, **(+) Muscle Pain (Calf)**, (-) Change in Strength, (-) Backache
- *Hematological:* (-) Pallor, (-) Hematoma, (-) Bleeding, (-) Anemia, (-) Easy Bruising
- *Endocrine:* (-) Weight Loss, (-) Edema, (-) Polyuria, (-) Polyphagia, (-) Polydipsia, (-) Heat Intolerance, (-) Cold Intolerance, (-) Excessive Sweating

Past Medical History

- Completed vaccinations
- No pertinent childhood illnesses
- No previous surgical interventions

Family History

- No history of hereditary diseases
- No history of tuberculosis, asthma, diabetes mellitus, or cardiac disease

Personal and Social History

- Lives with father and two siblings in a well-lit, well-ventilated bungalow with a pour-flush toilet
- Garbage collection 2-3 times per week
- Drinks tap water
- No history of recent travel

Physical Examination

- Awake, conscious, coherent, ambulatory, GCS 15, in cardiorespiratory distress with the following vital signs: **BP: 50/30**, PR: 98 bpm, Temp: 37°C
- *Skin:* Brown complexion, **mild jaundice**, no pallor or lesions, normal skin turgor, **multiple scars on bilateral lower extremities**
- *HEENT (Head, Eyes, Ears, Nose, Throat):* No areas of balding, no swelling, tenderness
 - ◆ **EYES:** pale palpebral conjunctivae, **icteric sclera, conjunctival suffusion**, no cataract, no asymmetry.
 - ◆ **EARS:** at level of lateral canthus of the eyes, symmetrical, non-tender, with no erythema, no discharges, no scaling.
 - ◆ **NOSE:** Nasal mucosa is pink, patent nares, non-deviated septum and no Nasal discharge, non-tender sinuses.
 - ◆ **MOUTH:** pinkish lips, Buccal mucosae is pink, no ulcer, **Dry lips**.
- *Chest and Lungs:* Symmetrical chest wall expansion, No intercostal or subcostal retraction, no tenderness, normal resonant breathing sound.
- *Heart:* Adynamic precordium, Apex beat at 5th ICS left MCL, (-) Thrills, (-) Loud And Palpable P2; Normally Split S2; (-) S3, (-) S4, Normal Rate, (-) Murmur, Tachycardic.

- *Abdomen:*
 - ◆ **Inspection:** No Scars, No Spider Angioma
 - ◆ **Auscultation:** Hypoactive Bowel Sounds at 6 per minute.
 - ◆ **Percussion:** Tympanic, Liver Span 8 cm in Right Midclavicular Line, Non-Palpable Liver Edge.
 - ◆ **Palpation:** (-) Tenderness
- *Musculoskeletal:* **(+) tenderness Gastrocnemius**, No bone nor joint deformity, No joint swelling
- *Extremities:* Full pulses, Warm extremities, CRT 2 seconds, No cyanosis, No edema
- *Neurologic:* Conscious, coherent, oriented to time, place and person, follows commands, GCS 15 (E4V5M6). The rest of the neurologic examinations were unremarkable.

Admitting Diagnosis - Leptospirosis

Hospital Course

- HD/PICU Day 1:
 - Admitted to Pediatric ICU under GREEN service
 - Diagnostics: CBC, BUN, Creatinine, electrolytes, blood cultures, leptospira test, dengue test
- Therapeutics:
 - IV fluids (PNSS)
 - Penicillin (2 million units Q4)
 - Oxygen via face mask (10 LPM)
 - Dopamine drip (10 cc/hr)
 - Norepinephrine infusion
- 5:40 PM:
 - BP: 110/50, no urine output
- HD/PICU Day 2:
 - BP: 100/50, neck vein distention
 - Nephrology Notes: Give furosemide 80mg, intubation explained to patient
- 12 PM:
 - (+) Tachypnea, GCS 15, (+) crackles, refused intubation
- 1:45 PM:
 - HD order initiated: Duration 2 hours
- 2:33 PM:
 - (+) Desaturation, pulse and respiration deteriorated
 - CPR initiated, patient pronounced clinically dead at 3:10 PM

Working Impression - Septic Shock; Acute Kidney Injury secondary to Leptospirosis

Final Diagnosis - Pulmonary Hemorrhage; Weil's Disease (Leptospirosis)

POINTS TO REMEMBER

- The incubation period for leptospirosis typically ranges from 5 to 14 days but can vary from 2 to 20 days.
- The case fatality rate (CFR) can vary widely, from less than 5% to as high as 15%, with most fatalities associated with pulmonary complications.
- Initial symptoms of leptospirosis include sudden fever, chills, severe headache, myalgia, and gastrointestinal disturbances, making early diagnosis challenging.
- Severe leptospirosis, or Weil's disease, is characterized by jaundice, acute renal failure, and multi-organ dysfunction, which can develop suddenly.
- Proper medical care can lead to full recovery in most patients; however, some may experience chronic symptoms like fatigue and uveitis during the recovery phase.
- Differential diagnosis is crucial, as leptospirosis can present similarly to other tropical diseases; laboratory tests are essential for accurate identification.

Leptospirosis in Humans

- **Incubation** - Typically ranges from 5 to 14 days (may be as short as 2 days to as long as 20 days).
- **Case Fatality Rate (CFR)** - < 5% to ≥ 15%.
- More than 90% of the deaths due to leptospirosis occur because of pulmonary alveolar hemorrhage.

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LEPTOSPIROSIS

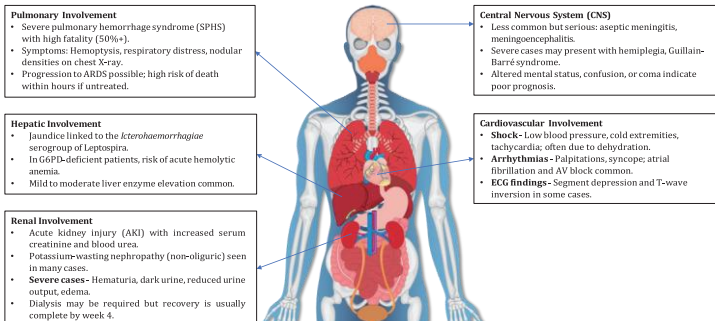
Clinical presentation

- **Fever** - Sudden onset; can be remittent, ranging from moderate to severe.
- **Headache** - Severe, often bitemporal or frontal throbbing, with retro-orbital pain and sensitivity to light.
- **Myalgia** - Intense muscle pain, particularly in calves, lower back, and abdomen.
- **Conjunctival Signs** - Conjunctival suffusion (redness without pus) is distinctive; severe cases may show subconjunctival hemorrhage and jaundice (icterus).
- **Respiratory Symptoms** - Up to 57% experience a nonproductive cough, potentially mimicking flu-like illnesses.
- **Gastrointestinal Symptoms** - Common symptoms include nausea, vomiting, diarrhea, and abdominal pain.
- **Severe GI Complications** - Can cause acalculous cholecystitis or pancreatitis; renal impairment may complicate the diagnosis of pancreatitis.

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LEPTOSPIROSIS

Severe Leptospirosis (Weil's Disease)

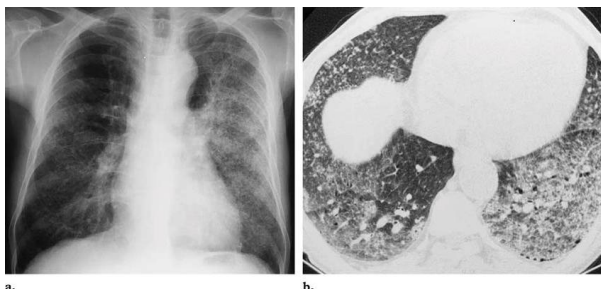


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LEPTOSPIROSIS

Lung involvement - Leptospirosis

(a). Initial chest radiograph shows fine reticulonodular opacities throughout both lungs. (b). High-resolution CT scan obtained the same day shows ground-glass attenuation, intralobular interstitial thickening, and ill-defined small nodular hyperattenuating areas.



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LEPTOSPIROSIS

Risk Factors for Morbidity and Mortality

- **Increased risk of severe outcomes** - Associated with hemodynamic instability, thrombocytopenia, elevated blood creatinine, high serum potassium, and lung involvement.
- **Age-related risk** - Mortality risk increases with age, especially over 60 years (seven-fold increase compared to younger adults).
- **Poor prognostic indicators** -
 1. Pulmonary involvement (dyspnea, alveolar infiltrates)
 2. Acute renal failure
 3. Hypotension
 4. Arrhythmias
- **Delayed hospital admission** - Higher likelihood of mortality.

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LEPTOSPIROSIS

Recovery Phase

- **Full recovery possible** - With proper medical care, including supportive treatments (e.g., dialysis, intensive care).
- **Post-leptospirosis syndrome** -
 - Persistent symptoms like fatigue, myalgia, malaise, headache, weakness.
 - Symptoms may last for months to years.
- **Ocular involvement** -
 - Uveitis is common, ranging from mild inflammation to severe panuveitis.
 - Recurrent uveitis episodes may require prolonged treatment.



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LEPTOSPIROSIS

Differential Diagnosis for Leptospirosis

1. Commonly Confused Diseases

1. *Falciparum Malaria, Dengue, Scrub Typhus, Typhoid Fever*: Share symptoms like fever, headache, muscle pain.
2. **Key Distinguishing Factors**:
 - **Dengue Fever**: Often shows red eyes (conjunctival suffusion); Dengue Hemorrhagic Fever includes bleeding/shock.
 - **Scrub Typhus & Typhoid Fever**: Lack specific muscle tenderness (calves, lower back) seen in leptospirosis.

2. Viral Hepatitis

1. Liver involvement in both diseases, but *liver enzyme patterns* differ:
 - **Leptospirosis**: Mild elevation of SGOT (AST) and SGPT (ALT).
 - **Viral Hepatitis**: Higher SGPT (thousands IU/L).
2. **Creatinine Phosphokinase (CPK)** elevated in leptospirosis (indicates muscle injury).

3. Rickettsial Infections & Hemorrhagic Fevers

1. Similar systemic symptoms, fever, hemorrhage.
2. Recommend *serologic testing* (rickettsiae, dengue, hantavirus) in suspected leptospirosis with bleeding.

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LEPTOSPIROSIS

Differential Diagnosis for Leptospirosis

Disease	Epidemiological Clues	Key Clinical Differences	Laboratory Tests
Falciparum Malaria	Endemic in tropical regions, mosquito exposure, travel history.	Cyclic fever with chills, no hydrophobia or aerophobia, CNS symptoms only in cerebral malaria.	Hematological: Anemia, thrombocytopenia.
			Biochemical: Normal or mild bilirubin elevation.
			Serology/Special: Blood smear or rapid antigen test positive for Plasmodium.
Dengue Fever	Endemic in urban areas, mosquito exposure (Aedes).	Fever with severe myalgia ("breakbone fever"), bleeding tendencies, no CNS involvement or hydrophobia.	Hematological: Thrombocytopenia, leukopenia.
			Biochemical: Elevated hematocrit in plasma leakage.
			Serology/Special: Dengue NS1 antigen or IgM/IgG positive.
Scrub Typhus	Rural areas, mite exposure, history of outdoor activity.	Fever with eschar (specific to scrub typhus), no CNS excitability or phobic symptoms.	Hematological: Leukocytosis, thrombocytopenia.
			Biochemical: Mildly elevated LFTs.
			Serology/Special: IgM for Orientia tsutsugamushi positive, Weil-Felix test.

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LEPTOSPIROSIS

Notes

Differential Diagnosis for Leptospirosis

Disease	Epidemiological Clues	Key Clinical Differences	Laboratory Tests
Typhoid Fever	Endemic regions, history of contaminated water or food/water.	Sustained high fever, rose spots, diarrhea, no hydrophobia or aerophobia.	Hematological: Leukopenia, anemia. Biochemical: Mild LFT elevation. Serology/Special: Blood culture positive for Salmonella.
Viral Hepatitis	Endemic regions, contaminated water or needle sharing.	Jaundice, no CNS symptoms or phobic reactions; markedly elevated ALT/AST differentiates from rabies.	Hematological: Normal or mild anemia. Biochemical: ALT/AST > 10x normal. Serology/Special: Hepatitis viral markers (HBsAg, HCV Ab).
Meningitis (Bacterial/Viral)	History of upper respiratory infection or recent trauma.	Stiff neck, photophobia, altered mental status; no hydrophobia or aerophobia.	Hematological: Leukocytosis in bacterial; normal in viral. Biochemical: Elevated CSF protein, low glucose (bacterial). Serology/Special: CSF PCR or Gram stain.

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LEPTOSPIROSIS

Case Presentation

Patient Information

Name: C.R.

Age: 16 years

Location: Kerala

Marital Status: Single

Date of Birth: October 7, 2008

First-time Admission: Local hospital

Informant: Mother (Reliability: 90%)

Chief Complaint

"3-day history of fever"

History of Present Illness

1 Week History of Floodwater Exposure

Day 1: Fever, myalgia, headache, abdominal pain, decreased appetite/activity; Self-

administered Paracetamol.

Day 2: Continued symptoms; Decreased urine output, calf pain.

Day 3: Loose bowel movements, vomiting, anuria, difficulty breathing; Sought hospital care.

Review of Systems

General: Weakness, decreased appetite, jaundice

Skin: Mild jaundice, scars on lower extremities

HEENT: Headache, icteric sclera, conjunctival suffusion

Musculoskeletal: Calf pain, muscle tenderness

Renal: Anuria, yellow-orange urine

Respiratory/Cardiac: Dyspnea, tachycardia, hypotension

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LEPTOSPIROSIS

Case Presentation

Past Medical & Family History

Fully vaccinated, no major illnesses or surgeries

No family history of chronic diseases

Physical Examination

Vitals: BP: 50/30, PR: 98 bpm, Temp: 37°C

Key Findings: Mild jaundice, tachycardia, normal skin turgor, bilateral calf tenderness, icteric sclera, hypotension, weak pulses

Hospital Course

Day 1 (PICU): Admitted, tests (CBC, BUN, Creatinine, electrolytes, Leptospira test) initiated

Therapy: IV fluids, Penicillin, Oxygen (10 LPM), Dopamine, Norepinephrine

Day 2: BP improved to 100/50, tachypnea; GCS: 15, refused intubation; HD ordered due to anuria

Outcome: Pulmonary hemorrhage, CPR unsuccessful, pronounced dead on Day 2

Final Diagnosis

Septic Shock, AKI secondary to Leptospirosis

Pulmonary Hemorrhage, Weil's Disease (Leptospirosis)



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LEPTOSPIROSIS

Notes

Session-4

Leptospirosis in Animals

Course No. 004	Session 4: Leptospirosis in Animals
Duration	15 minutes
Learning Objective	• Describe the impact of leptospirosis on various animal species, including domestic and wild animals. • Explain the transmission dynamics of <i>Leptospira</i>, emphasizing environmental factors and animal interactions. • Identify clinical manifestations of leptospirosis in different animal species and understand the role of maintenance hosts in disease spread.
Pre-requisite knowledge/skill	• Basic understanding of veterinary microbiology and animal health. • Familiarity with zoonotic disease transmission between animals and humans. • Awareness of environmental factors influencing infectious disease spread among animals.
Competencies to be achieved	• Learners will gain a comprehensive overview of how leptospirosis affects a range of animals, including symptoms and potential complications. • Develop insights into the role of maintenance and incidental hosts in the epidemiology of leptospirosis. • Learn to recognize the varying clinical manifestations of leptospirosis in different species, including cattle, sheep, goats, pigs, dogs, and horses.

LEPTOSPIROSIS IN ANIMALS

Leptospirosis affects both people and animals. This includes household pets and farm animals, as well as wild animals like wild pigs and marine mammals. *Leptospira* has the ability to colonise and persist in the genital tract of infected cows and bulls suggesting that venereal spread may be a factor in transmission. Animals are infected by direct contact with this contaminated water or soil or by drinking contaminated water. Infected animals can carry the bacteria for long periods, shedding them in urine and at birth or abortion, thus contaminating the animals' environment. Many infected animals do not display any illness.

An animal may be infected by serovars maintained by its own species (maintenance host infection or host-adapted infection) or serovars maintained by other species (incidental infection or non-host-adapted infection). Maintenance hosts carry the bacteria and expose other susceptible animals. Maintenance hosts can be cattle, pigs, dogs, rodents or horses. These apparently healthy carriers are the main source of infection for other cattle as well as for humans. There are wide variations in the clinical manifestations of leptospirosis in animals, with some animals not exhibiting any signs and symptoms of the disease.

Animal Leptospirosis

In general, disease in cattle, sheep, goats and swine may include a fever, abortions, reproductive problems/disorders etc.

Cattle: Pyrexia, anorexia, malaise, haemorrhages, anaemia, jaundice, haemoglobinuria, abortion, mastitis etc.

Sheep and Goats: Pyrexia, conjunctivitis, jaundice, anaemia, anuria, hemoglobinuria, diarrhoea, mastitis, haemoagalactia, abortion etc.

Pigs: Pyrexia, weakness, depression, haemoglobinuria, periodic opthalmia, jaundice etc.

Dogs: Pyrexia, weakness, depression, conjunctivitis, vomiting, convulsion, anaemia, haemorrhages, jaundice etc.

Horses: eye is most commonly affected. The eyelids may be reddened, the horse will be sensitive to light and may blink frequently or clouding of the eye may be seen.

Bovine Leptospirosis: In bovine leptospirosis generally associated with clinical signs of agalactia (drop in milk production). Stillbirth or weak calves, abortion at 4-7 months, reduced conception rates, repeat breeding, infertility, failure to thrive, etc., Further, the clinical signs of leptospirosis is dependent on the herd's degree of resistance or immunity, the infecting serovar, and the age of the animal infected.

Leptospirosis is a common cause of an abortion in dairy and beef herds. It can cause milk drop affecting a large proportion of the herd. Infection may cause an increased number of repeat breeder cows, infertility, abortion and poor milk yield. A sudden drop in milk yield may occur two to seven days after infection of susceptible cows.

There is circumstantial evidence of infertility following isolation of *Leptospira Hardjo* from the reproductive tract of a high percentage of repeat breeder cows. *Leptospira Hardjo* may also cause embryonic death. Venereal transmission is also possible but may not significantly affect the pregnancy rate because *Leptospira* is susceptible to uterine defences during oestrus.

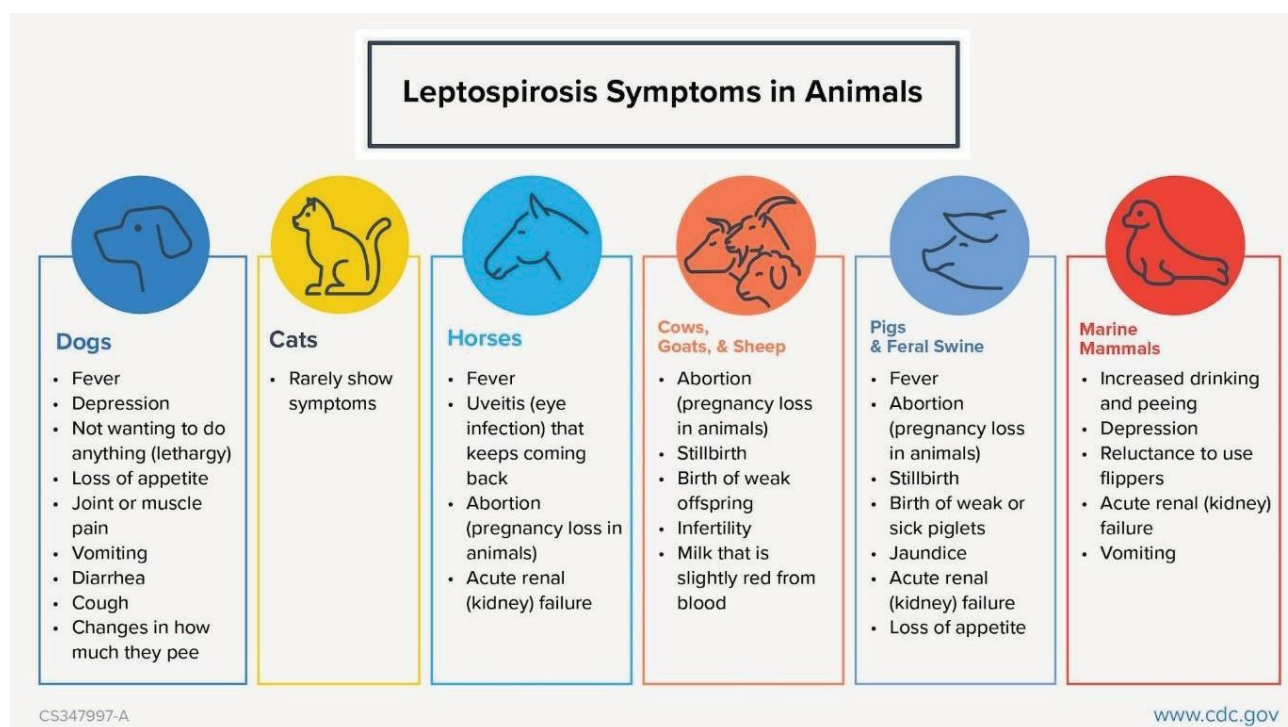
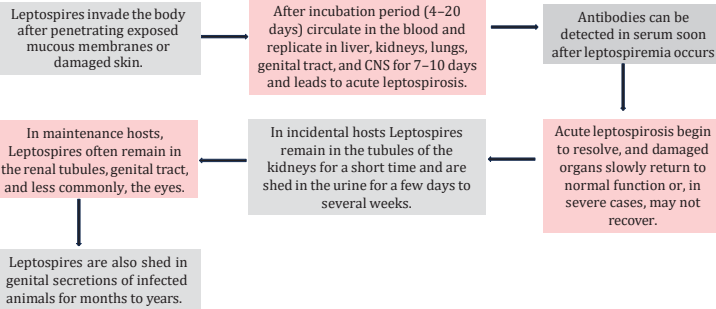


Fig 8: Leptospirosis in different animals

POINTS TO REMEMBER

- Leptospirosis affects a variety of animal species, including pets, farm animals, and wild animals, with infected individuals often remaining asymptomatic while shedding the bacteria in urine and during birthing events, thereby contaminating the environment.
- Transmission occurs primarily through direct contact with contaminated water or soil, with maintenance hosts such as cattle, pigs, dogs, and rodents being crucial for spreading the disease to other susceptible animals and humans.
- Clinical signs of leptospirosis vary by species; in cattle, common symptoms include fever, jaundice, abortion, and reduced milk production, while dogs may exhibit fever, vomiting, and conjunctivitis.
- Infertility, abortion, and decreased milk yield in dairy herds are significant consequences of bovine leptospirosis, with venereal transmission possible but not the primary factor affecting pregnancy rates.

Disease progression of Leptospirosis in Animals



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LEPTOSPIROSIS

Notes

Leptospirosis in Animals



Cattle - Pyrexia, anorexia, malaise, haemorrhages, anaemia, jaundice, haemoglobinuria, abortion, mastitis etc.



Sheep and Goats - Pyrexia, conjunctivitis, jaundice, anaemia, anuria, hemoglobinuria, diarrhoea, mastitis, haemoagallactia, abortion etc.



Pigs - Pyrexia, weakness, depression, haemoglobinuria, periodic ophthalmia, jaundice etc.



Dogs - Pyrexia, weakness, depression, conjunctivitis, vomiting, convulsion, anaemia, haemorrhages, jaundice etc.



Horses - eye is most commonly affected. The eyelids may be reddened, the horse will be sensitive to light and may blink frequently or clouding of the eye may be seen.

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LEPTOSPIROSIS

Session-5

Laboratory Diagnosis

Course No. 005	Session 5: Laboratory Diagnosis
Duration	45 minutes
Learning Objectives	• Describe the key diagnostic methods used for leptospirosis, highlighting their advantages and limitations. • Explain the biphasic nature of leptospirosis and how diagnostic tests are applied at different stages of the disease. • Identify the essential laboratory tests used for organ function assessment in leptospirosis cases.
Pre-requisite knowledge/skill	• Basic knowledge of microbiological and serological diagnostic techniques. • Familiarity with interpreting laboratory test results and their clinical relevance. • Understanding of disease progression and phases in infectious diseases.
Competencies to be achieved	• Learners will acquire detailed knowledge of diagnostic approaches, including PCR, ELISA, MAT, and rapid diagnostic tests. • Gain the ability to select and recommend appropriate tests based on the disease phase and clinical presentation. • Learn to interpret laboratory results related to organ involvement (kidneys, liver, blood) in severe leptospirosis cases.

LABORATORY DIAGNOSIS OF LEPTOSPIROSIS

Leptospire are slow to grow in culture, and recovery rates tend to be low. As the sensitivity of tests for the detection of leptospirosis in the early stages of illness is not great, treatment should not solely rely on tests. If a patient shows symptoms that are suggestive of leptospirosis and has likely exposure related history, it is important to start treatment right away.

Laboratory tests serve two main purposes: confirming the diagnosis and assessing how much the organs are affected and how severe the complications are. Confirmation can be done either by isolating the pathogen or through serologic tests.

Molecular tests like DNA PCR are often used as they are more accessible. Urine is the most reliable fluid to test since leptospire appear in urine from the onset of symptoms up to the third week of infection.

While other body fluids like blood and cerebrospinal fluid (CSF) can also contain the bacteria, the window for detecting them is shorter—typically within the first 7-10 days of symptoms. For suspected leptospirosis, additional lab tests should be done routinely to assess organ involvement after the acute phase. A complete blood count (CBC) is essential and shows:

- In mild cases, there is an elevated erythrocyte sedimentation rate and peripheral leucocytosis ($3,000-26,000 \times 10^9/L$) with a left shift.
- Significant anemia can occur due to pulmonary or gastrointestinal bleeding.
- Low platelet counts may indicate disseminated intravascular coagulation (DIC).
- Blood urea nitrogen and serum creatinine levels can rise dramatically during kidney failure phases.
- Serum creatine kinase (MM fraction) levels are often elevated in those with muscle involvement.
- Coagulation times might be prolonged if there is liver dysfunction or DIC.
- Liver function tests may show high bilirubin levels due to liver capillaritis, though liver enzymes are usually less elevated (below 200 U/L). Jaundice is common, and alkaline phosphatase levels can increase tenfold.
- Urinalysis may reveal proteinuria, leukocytes, erythrocytes, and casts in the sediment. A rapid urine antigen test is being developed using lateral flow assay technology.

CSF analysis is useful mainly for ruling out other causes of bacterial meningitis. When leptospirosis affects the central nervous system, polymorphonuclear leukocytes dominate early on, later replaced by monocytes. CSF protein may be normal or elevated, with normal glucose and pressure, although lumbar puncture can relieve headaches. While leptospire can be isolated from CSF, this doesn't change disease management.

Tissues like liver, muscle, kidneys, skin, and eyes are also potential sources for identification of the bacteria, but they are more difficult to obtain. The most common method for confirming leptospirosis is through paired acute and convalescent serum samples, but this process is delayed. Acute serum is collected 1-2 weeks after symptom onset, and convalescent serum is collected two weeks later.

Imaging studies can help assess organ involvement, such as chest X-rays or CT scans for lung disease and biliary tract ultrasonography for suspected acalculous cholecystitis. ECG abnormalities are common in the leptospiremic phase of Weil's syndrome, and severe cases may lead to congestive heart failure or cardiogenic shock.

Choice of Diagnostic Test

The selection of a diagnostic test for leptospirosis is influenced by several factors, including the accuracy of the test, financial and practical feasibility, and the need for timely results. Leptospirosis can be divided into two distinct stages. The first stage, known as the acute or leptospiremic phase, lasts for 3 to 10 days and is characterized by symptoms like headaches and muscle pain. During this period, leptospires are present in the blood, gradually decreasing in number, and can be detected up to 15 days after symptom onset. To successfully identify leptospires, samples should ideally be collected within two days of starting antibiotics. The likelihood of recovering leptospires from blood or other tissues is highest during this stage. However, failure to detect leptospiral DNA or antigens can result from low leptospiraemia, late sample collection, or early antibiotic treatment.

The second stage, referred to as the immune or convalescent phase, typically begins in the second week after symptoms appear. During this phase, leptospires are excreted in the urine, and antibodies start to form in the blood. Leptospires are cleared from the bloodstream as IgM antibody levels rise, reaching their peak within two to three weeks. These antibodies can persist in humans for years, and in animals, especially reservoir hosts, for even longer periods, sometimes for life.

From the first to the sixth day of infection, PCR testing on blood samples is the most effective diagnostic tool. Between the sixth and tenth days, if PCR is unavailable, ELISA can be used. After the tenth day, PCR testing should be done on cerebrospinal fluid (CSF) or urine, and either ELISA or the Microscopic Agglutination Test (MAT) can be performed. The most definitive diagnosis is achieved by isolating leptospires from clinical samples, although this process can be slow and insensitive, or by identifying leptospiral DNA through PCR or using immunohistochemical staining.

Table 2: Sampling window for Leptospirosis

Time (Days/Weeks)	Sample	Diagnostic Tests
Day 1-7 (Acute Phase)	Blood (serum), urine	Serology (Microscopic Agglutination Test [MAT]), PCR for <i>Leptospira</i> spp.
Day 7-14 (Transition Phase)	Blood (serum)	4-fold rise in MAT antibodies between acute and convalescent samples
Day 14+ (Recovery Phase)	Blood, urine	IgM/IgG serology (indicating acute or past infection), PCR for persistent infection
Post-Mortem	Tissue (liver, kidney)	Histopathology (detection of <i>Leptospira</i> spp. in tissue), PCR, immunohistochemistry

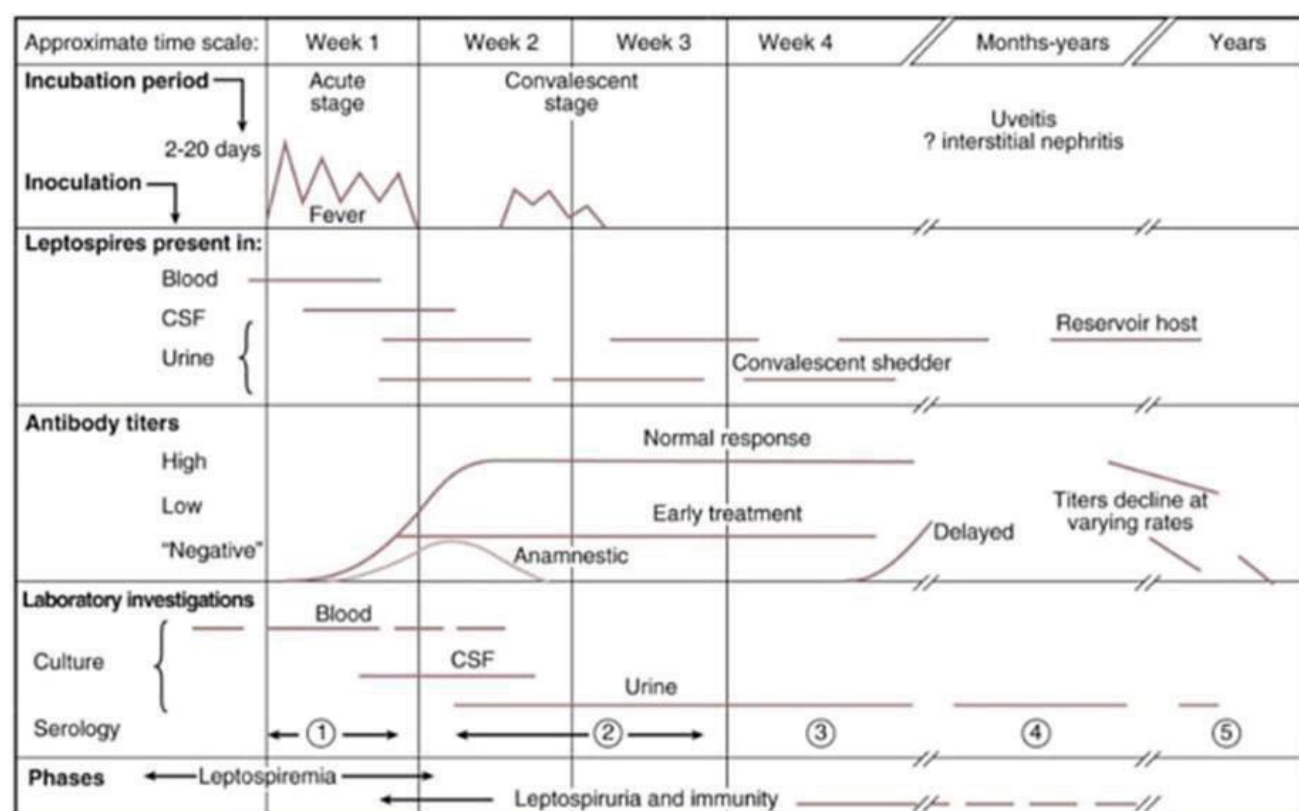


Fig 9: Schematic representation of the biphasic nature of leptospirosis and relevant diagnostic investigations at different stages of disease. For serology specimens 1 and 2 are acute-phase specimens, 3 is a convalescent-phase specimen which may facilitate detection of a delayed immune response, 4 and 5 are follow-up specimens which can provide epidemiological information, such as the presumptive infecting serogroup.

The diagnostic criteria for leptospirosis are categorized into two types: Presumptive and Confirmatory diagnoses.

1. Presumptive Diagnosis:

- A positive outcome from IgM-based immune assays, slide agglutination tests, latex agglutination tests, or immunochromatographic tests.
- A Microscopic Agglutination Test (MAT) titer of 100, 200, or 400 or higher in a single sample, depending on the local endemicity.
- Direct identification of leptospires through various staining techniques.

2. Confirmatory Diagnosis:

- Successful isolation of leptospires from clinical specimens.
- A fourfold or greater increase in MAT titers between acute and convalescent serum samples tested in parallel. Positive results from any two distinct rapid testing methods.
- Evidence of seroconversion using any testing method (MAT or ELISA).
- Confirmation through Polymerase Chain Reaction (PCR) testing.

Diagnostic Tests for Leptospirosis at Various Levels of Care

The diagnostic tests for leptospirosis at different health facilities are as follows, based on national guidelines:

A. At Primary Health Centers/ Ayushman Arogya Mandir - PHC (PHCs/ AAM-PHC)

- Hemoglobin Estimation (Hb)
- Total Leukocyte Count (TLC)
- Differential Leukocyte Count (DLC)
- Platelet Count
- Blood Sugar
- S. Bilirubin (Total)
- Urine Sugar/Albumin
- Rapid Diagnostic Test (RDT)

B. At Community Health Centers (CHCs) and District Hospitals

- Hemoglobin Estimation (Hb)
- Total Leukocyte Count (TLC)
- Differential Leukocyte Count (DLC)
- Platelet Count
- Blood Urea Nitrogen (BUN)
- Serum Creatinine
- Liver Function Tests (SGOT, SGPT, Alkaline Phosphatase)
- Serum Electrolytes (Sodium, Potassium)
- Urine Routine and Microscopic Examination
- Serum Bilirubin (Total and Direct)
- Serum Creatinine Phosphokinase (CPK)
- Rapid Diagnostic Test (RDT)
- ELISA

C. At State-Level Hospitals/ Reference Laboratories

- All tests available at CHCs and District Hospitals
- Isolation of Leptospire
- ELISA
- PCR
- Microscopic Agglutination Test (MAT)

Sample Collection for the Diagnosis of Leptospirosis

The Guidelines on specimen collection for the diagnosis of leptospirosis are presented in the table below:

Table 3: Guidelines on specimen collection for the diagnosis of leptospirosis

Specimen	Timeframe	Procedure
Blood with Heparin (to prevent clotting)	First 10 days of illness	Blood cultures are effective within the first 10 days. Inoculate 1-2 drops of blood into 10 ml semisolid medium with 5-fluorouracil at bedside. Store and transport at ambient temperatures. Multiple cultures improve recovery.
Clotted Blood or Serum for Serology	Collected twice, several days apart	Paired serum samples are necessary to detect rising antibody titres or seroconversion. Negative serology in early phases does not exclude leptospirosis.
Urine for Culture	Process within 2 hours of voiding	Inoculate urine into appropriate medium within 2 hours. Centrifuge, neutralize acidic urine with phosphate-buffered saline, and inoculate into semisolid medium with 5-fluorouracil. Incubate cultures at 28-30°C and examine for up to 13 weeks.
Cerebrospinal Fluid and Dialysate for Culture	First week of illness	Inoculate 0.5 ml cerebrospinal fluid into 5 ml semisolid culture medium. Leptospire may be seen by dark-field microscopy and isolated by culture.
Postmortem Samples	As soon as possible after death	Postmortem samples should be gathered aseptically and as promptly as possible following death, and they should be inoculated into culture media without delay. These samples must be stored and transported at +4 °C to prevent autolysis of cells and a subsequent drop in pH, which helps mitigate the decline in the viability of pathogenic leptospire at lower temperatures. Additionally, fresh or preserved tissues can be tested for leptospire using antibodies tagged with fluorescent markers. Other techniques such as silver staining, immunostaining, and immunohistochemistry may also be employed, though they require advanced technical skills for accurate interpretation.

Laboratory Testing

Laboratory diagnosis can be classified into two main types: direct evidence and indirect evidence. Direct evidence involves the demonstration of leptospire or their DNA, as well as the

isolation of the organism from clinical samples. In contrast, the presence of specific antibodies to leptospires, determined through serological methods, serves as indirect evidence. While numerous techniques have been outlined, this section highlights the most commonly employed procedures along with their respective advantages and disadvantages.

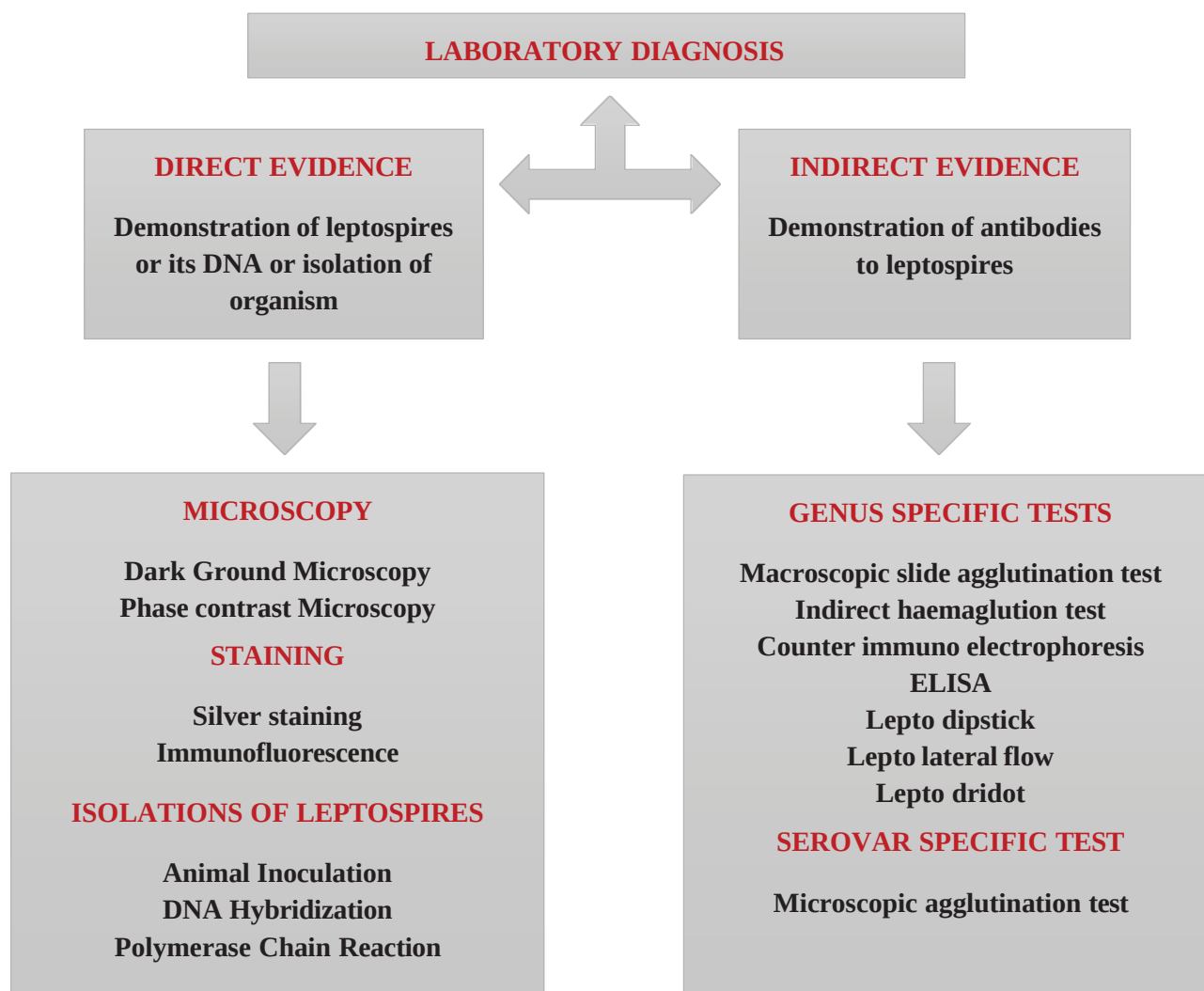


Fig 10: Laboratory diagnosis — Direct and indirect evidences

Rapid Screening for Antibodies

A variety of rapid screening tests are available, such as **latex agglutination** and **dipstick tests**, which are easier to perform and provide quicker results. However, these tests should be confirmed with more accurate methods, such as MAT, to avoid false positives or negatives.

Results are available within minutes, or at most 2 hours

- Samples for RDTs require little or no processing
- Result interpretation is straightforward
- Simple to use and require minimal facilities, equipment, & training
- Stable reagents may be stored under extreme conditions

Variety of different RDT technologies

- **Lateral flow** tests where the user adds the specimen directly onto the strip and reads the results after a specified amount of time has elapsed
- **Flow through** kits of individual cassettes with extraction, wash buffers and a “reveal” reagent to obtain results
- **Agglutination** tests based on agglutination of particles in a sample after the addition of antigenic reagent; agglutination reaction can be visualized with the naked eye

Pros

- Potential for point-of-care diagnostics for quick results
- Easy to use in low-resource settings and in the field

Cons

- Cross-reactive antibodies also have been described in patients with syphilis, relapsing fever, Lyme disease, and legionellosis
- Patients that are immunocompromised, malnourished, or have immune system defects may yield false negative results
- Values for % Sensitivity and % Specificity vary between different RDTs

ELISA and Other Serological Methods

Commercial **ELISA** kits, based on genus-specific antigens, are widely used as an alternative to MAT. These tests are easier to standardize and can detect IgM antibodies, indicating current or recent leptospirosis. However, ELISA is less specific than MAT and may cross-react with antibodies from other diseases. Additionally, since ELISA tests are genus-specific, they cannot identify the causative serovar.

Advantages of ELISA

- Detects IgM early in the infection phase, indicating a recent or ongoing infection.
- Standardizable and easier to implement than MAT.

Disadvantages of ELISA

- Less specificity, with potential for cross-reactivity, particularly with other diseases.
- Does not indicate the specific serovar responsible for infection.

Microscopic Agglutination Test (MAT) for Leptospirosis

The **Microscopic Agglutination Test (MAT)** is a diagnostic method used to detect agglutinating antibodies in a patient’s serum by exposing it to live or formalin-killed leptospires in various dilutions. These antibodies cause the leptospires to aggregate, forming visible clumps, a process known as agglutination. This agglutination is typically observed using dark-field microscopy, which allows for visualization of the clumps. Both **IgM** and **IgG** antibodies can participate in this agglutination process.

Specificity of the MAT

The MAT primarily detects antibodies specific to the infecting serovar, but cross-reactivity with other serovars can occur, especially early in the infection. In the initial stages of leptospirosis, cross-reacting antibodies against non-causative serovars may be more abundant than antibodies targeting the infecting serovar. This phenomenon, known as a **paradoxical** reaction, may result in a false-negative result for the homologous serovar, while the heterologous reaction appears positive. Over time, cross-reactive antibodies tend to diminish, whereas antibodies against the serogroup or serovar specific to the infection can persist for long durations, sometimes even for years.

Factors influencing MAT specificity include:

- Agglutinating antibodies typically target specific serovars or serogroups.
- Multiple serovars may circulate within a given region and be responsible for local infections.
- Changes in local epidemiology, such as the introduction of new hosts or agricultural practices, can alter the prevalence of different serovars.
- New, unidentified serovars may emerge, further complicating serological diagnosis.

To account for these variables, it is essential that **serovar panels** in laboratories are comprehensive, including all locally circulating serovars, or at the very least, a representative range of serogroups. Incomplete panels may lead to inaccurate or false-negative results.

MAT Titers: Interpretation and Clinical Significance

The MAT cannot distinguish between antibodies produced during an acute, recent, or past infection. Ideally, two serum samples should be collected from the patient, with the second sample taken 2–3 weeks after the first to observe a seroconversion or a fourfold rise in antibody titres, which would indicate an active infection. However, single serum samples, especially if taken in the early phase of infection, are often used, and their significance remains debated. In some regions, titres as low as **1:100** are considered positive, while other settings may use higher thresholds, such as **1:200**, **1:400**, or even **1:800**.

Determining MAT Cut-off Points

In regions where leptospirosis is uncommon, a lower titre may be significant. However, in endemic areas, where persistent antibodies from past infections are common, low titres may be challenging to interpret. Determining an appropriate cut-off point requires consideration of the following:

- The prevalence of antibodies from past infections in the general population.
- Cross-reactions with antibodies from other infectious diseases (e.g., **legionellosis**, **hepatitis**, or autoimmune diseases).
- Ideally, cut-off points should be set by comparing serological results from culture-confirmed leptospirosis cases with those from individuals with other confirmed illnesses, though this can be difficult in practice.

Advantages of MAT

- High specificity for identifying the presence of leptospiral antibodies.

Disadvantages of MAT

- Requires specialized laboratory facilities to culture and maintain panels of live leptospires, which are technically demanding and time-consuming to handle.
- Antibodies may not be detectable if the causative strain is not included in the antigen panel or if the serovar in question is not represented.
- The panel cannot be guaranteed to be complete due to the emergence of new or uncharacterized leptospires, which means **false-negative results** may still occur.

MAT Standardization and Variability

MAT cannot be fully standardized because it relies on live leptospires as antigens. While antigenic panels may be standardized within a single batch of leptospires, antigen degradation over time limits this standardization. The test may also vary slightly from day to day, making it preferable to analyze paired serum samples together for consistency.

Serological Identification of Causative Serovars

Although the MAT can indicate antibodies against the infecting serovar, cross-reactions often hinder precise identification of the causative strain. Testing follow-up serum samples several weeks after the onset of symptoms may help improve specificity. Genus-specific ELISAs may detect antibodies earlier in the disease, but they do not provide serovar-specific information.

Sero-epidemiological Investigations

MAT can provide insights into the prevalent serogroups or, in some cases, serovars circulating within a population by testing serum samples from individuals in the region. However, the detection of residual antibodies from past infections may complicate this identification.

Direct Methods for Leptospiral Detection

Direct detection methods for leptospires include **culture, dark-field microscopy, immunostaining, and PCR**. **Culture** is slow and not useful in early diagnosis, but it allows for serovar typing, useful for surveillance and epidemiological studies. **Dark-field** microscopy is useful for observing leptospires in clinical samples, but its sensitivity is limited by the observer's experience and potential artefacts.

PCR for Leptospirosis

Polymerase Chain Reaction (PCR) offers the advantage of detecting leptospiral DNA early in the disease, before antibody levels are detectable. However, PCR is prone to contamination and requires specialized equipment and skilled personnel.

Advantages of PCR

- Rapid detection of leptospiral DNA during the early phase of infection.
- Can confirm the diagnosis before antibodies are detectable.

Disadvantages of PCR

- Requires specialized equipment and is susceptible to contamination.
- May produce false-negative results due to inhibitors in clinical samples.

Isolation of Leptospires from Clinical Specimens

Isolating *Leptospira* from clinical samples provides the most definitive confirmation of infection. This method is crucial for identifying the circulating serovars in specific geographic regions, which can contribute to epidemiological surveillance. Furthermore, locally isolated strains are particularly valuable for use as antigens in the Microscopic Agglutination Test (MAT), as they are often more reactive and sensitive than reference strains. Additionally, these isolates can be used in the development of vaccines tailored to local strains. However, this technique comes with several limitations.

Challenges of Leptospiral Isolation

Leptospira are slow-growing organisms, which necessitates prolonged incubation periods ranging from days to weeks for culture development, and several weeks to months for complete identification. Furthermore, prior antibiotic treatment significantly reduces the likelihood of successful isolation, as the antibiotics may suppress the growth of the organisms.

Blood Culture

- **Ideal Timing:** Within 10 days of symptom onset
- **Culture Media:** EMJH (Ellinghausen-McCullough-Johnson-Harris) and Fletcher's medium

Procedure:

1. Disinfect the venipuncture site with spirit.
2. Draw blood using a sterile syringe and needle.
3. Inoculate 2–4 drops of blood into 5 ml of the prepared culture medium.
4. Incubate the culture at 30°C for 4–6 weeks.
5. Examine the culture using dark-field microscopy at intervals: initially on the 1st, 3rd, and 5th days, followed by 7–10 day intervals until 6 weeks.

To minimize contamination, selective culture media containing:

- 50-1000 µg/ml 5-FU
- Nalidixic acid (50 µg/ml), vancomycin (10 µg/ml), polymyxin B (5 units/ml) or
- Actidione (100 µg/ml), bacitracin (40 µg/ml), 5-FU (250 µg/ml), neomycin sulphate (2 µg/ml), polymyxin B (0.2 µg/ml), and rifampicin (10 µg/ml) should be used.

Subcultures should be performed within 48 hours to reduce inhibitory effects of selective agents on leptospiral growth. Encouraging growth can be achieved by adding 0.1–0.15% agarose and 0.4–1% rabbit serum or fetal calf serum to the medium.

Urine Culture

- **Ideal Time:** 10–30 days post-symptom onset
- **Culture Media:** Same as for blood culture

Procedure:

1. Collect freshly voided midstream urine within 2 hours.
2. Dilute the urine as follows using sterile test tubes and phosphate-buffered saline (PBS, pH 7.2):
 - o Add 0.4 ml of urine to 3.6 ml of PBS (1:10 dilution).
 - o Add 3 ml of this to 3 ml of PBS (1:20 dilution).
 - o Add 2 ml of this to 2 ml of PBS (1:40 dilution).
 - o Add 1 ml of this to 1 ml of PBS (1:80 dilution).
3. Inoculate 0.5 ml of each dilution into separate 5 ml tubes containing medium.
4. Label the tubes with the respective dilution.
5. Incubate at 30°C and examine using dark-field illumination at intervals of 7–10 days up to 6 weeks.

Multiple samples of urine should be collected on different days to increase the probability of detecting leptospires. Filtration through a 0.22 µm filter or inoculation into selective media may help prevent contamination, particularly as urine often has an acidic pH. Collecting urine in tubes containing PBS (pH 7.2) can help neutralize this acidity.

Cerebrospinal Fluid (CSF) Culture

- **Ideal Time:** 5–10 days post-symptom onset
- **Culture Media:** Same as for blood and urine culture

Procedure:

1. Inoculate 0.5 ml of CSF into 5 ml of culture medium.
2. Follow the same procedure as described for blood culture.

Advantages of Isolating Leptospire from Clinical Specimens

- **Definitive Proof of Infection:** Isolation of leptospire provides the most definitive evidence of infection.
- **Serovar Identification:** Circulating serovars can be identified, contributing to local epidemiological monitoring.
- **Use in MAT:** Local isolates can be used as antigens for the MAT, improving sensitivity and specificity.
- **Vaccine Development:** Local isolates can be leveraged to develop vaccines targeted to prevalent serovars in a given area.

Disadvantages of Isolating Leptospire from Clinical Specimens

- **Slow Growth:** *Leptospira* are fastidious organisms and grow slowly, making the process of isolation time-consuming (several days to weeks).
- **Labor-Intensive:** This method is labor-intensive, requires specialized equipment, and is not suitable for small laboratories.
- **Contamination Risks:** Contamination by saprophytic leptospire or other microorganisms is common, making the technique prone to false positives.
- **Antibiotic Interference:** Prior administration of antibiotics, improper sterilization of equipment, and incorrect incubation conditions can significantly hinder the success of leptospiral isolation.

Dark-Field Microscopy

Although Dark Ground Microscopy is often described as a quick and straightforward method for detecting leptospire, its practical application has proven less effective. Despite early references in textbooks suggesting its utility for diagnosing leptospirosis, the organism's concentration in the blood during the acute phase is usually too low for direct microscopic detection. Leptospiral excretion in urine is also sporadic, and serum proteins or cellular debris can resemble leptospire under the microscope, potentially leading to misidentification. Even skilled professionals can be misled by these artefacts, as leptospire in clinical samples may not display characteristic motility due to reactive antibodies or mechanical damage during specimen preparation. Evaluations of DGM have demonstrated that it has relatively low sensitivity (40.2%) and specificity (61.5%).

Reference Laboratories for the Diagnosis of Leptospirosis in India

Assam Medical College, Dibrugarh
LLRM Medical College, Meerut
State Public Health and Clinical Laboratory, Trivandrum
State Public Health Laboratory, Chennai
District Public Health Laboratory, Mangalore, Karnataka
Govt Medical College, Surat, Gujarat

POINTS TO REMEMBER

MSAT/Elisa IgM and other rapid screening tests

PCR

Culture

MAT

- Single positive sample adequate for diagnosis
- Simple, sensitive and specific tests
- Becomes positive earlier than MAT
- Cannot identify the serogroup
- Can be done also in small rural hospitals
- Can be easily done for a large number of patients during an epidemic

Other rapid tests are:

- Latex agglutination test
- Lepto dipstick
- Lepto tek lateral flow Lepto tek Dri-Dot test
- PCR is the only available diagnostic test available in the first week of leptospirosis
- It is a complicated and expensive test
- The serovar cannot be identified by this test
- Isolation of *Leptospira* organism by culture of blood, CSF and urine are the most definite way of confirming leptospirosis
- Culture does not contribute to an early diagnosis as results come late, weeks or even months after inoculation of culture medium.

Standard

- Complicated, DFM required
- Titres peak late (2nd or 3rd week), but persist longer (5 to 10 years)
- Valuable in sero epidemiologic studies
- Less sensitive for current diagnosis
- Repeat samples required for confirming diagnosis Requires 24 live serogroup cultures
- Cut-off titres controversial Interpretation of MAT Single titre – 1:100—significant criteria Diagnostic criteria – Endemic area—1:400 (1:800, 1:1,600) – Nonendemic area—1:100, 1:200 – Serosurvey—1:50 Repeat titre – Four-fold rise/seroconversion

Laboratory Detection and Diagnosis of Leptospirosis

Slow Culture Growth - Leptospire are challenging to culture with low recovery rates.

Early Treatment - Begin treatment immediately if symptoms and exposure history suggest leptospirosis; do not rely solely on test results.

Diagnostic Purposes -

- Confirm diagnosis.
- Assess organ impact and severity of complications.

Diagnostic Methods -

- **Pathogen Isolation** or **Serologic Tests** confirm infection.
- **Molecular Tests** (e.g., DNA PCR) are accessible and effective.

Testing Samples -

- **Urine** - Best for detecting leptospire (from symptom onset to third week).
- **Blood & CSF** - Useful but have a shorter detection window (first 7-10 days).



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Laboratory Detection and Diagnosis of Leptospirosis

Complete Blood Count (CBC) -

- Elevated **ESR** and **leukocytosis** in mild cases.
- **Anemia** from pulmonary or GI bleeding.
- **Low Platelet Counts** could indicate DIC.

Kidney and Muscle Markers -

- High **blood urea nitrogen** and **creatinine** in kidney failure.
- Elevated **creatinine kinase (MM fraction)** with muscle involvement.

Liver Function -

- **High bilirubin** levels (capillaritis); liver enzymes

usually below 200 U/L.

- **Alkaline Phosphatase** may increase tenfold.

Urinalysis -

- Signs of **proteinuria**, **leukocytes**, **erythrocytes**, and **casts**.

CSF Analysis -

- Helps rule out bacterial meningitis; can show polymorphonuclear leukocytes initially.

Serum Testing -

- **Paired acute and convalescent samples** for confirmation (delayed process).

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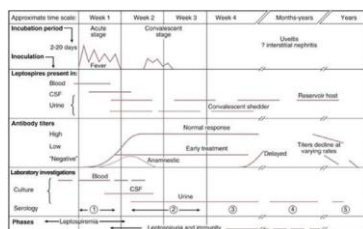
Sampling Window for Leptospirosis

Time (Days/Weeks)	Sample	Diagnostic Tests
Day 1-7 (Acute Phase)	Blood (serum), urine	Serology (Microscopic Agglutination Test [MAT]), PCR for <i>Leptospira</i> spp.
Day 7-14 (Transition Phase)	Blood (serum)	4-fold rise in MAT antibodies between acute and convalescent samples
Day 14+ (Recovery Phase)	Blood, urine	IgM/IgG serology (indicating acute or past infection), PCR for persistent infection
Post-Mortem	Tissue (liver, kidney)	Histopathology (detection of <i>Leptospira</i> spp. in tissue), PCR , immunohistochemistry

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Leptospirosis Diagnostic Stages and Testing



Selection Factors: Test accuracy, cost-effectiveness, practicality, and urgency.

Two Disease Stages:

- **Acute Phase (3-10 days):** Leptospire in blood, symptoms include headache, muscle pain.

- **Best Testing:** Blood PCR (days 1-6); ELISA if PCR is unavailable (days 6-10).

Immune Phase (2nd week onwards): Antibodies in blood, leptospire in urine.

- **Best Testing:** PCR on CSF/urine, ELISA, or MAT after day 10.

Confirmatory Tests:

- Isolation of leptospire (slow but definitive).
- PCR and immunohistochemical staining to detect leptospiral DNA.

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Notes

2. Confirmatory diagnosis



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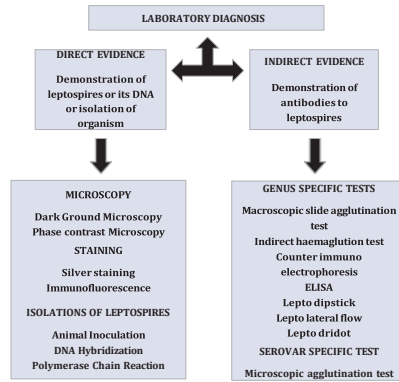
At Primary Health Centres/ Ayushman Aroga Mandir- PHC (PHC/ AAM-PHC) ▪ Hemoglobin Estimation (Hb) ▪ Total Leukocyte Count (TLC) ▪ Differential Leukocyte Count (DLC) ▪ Platelet Count ▪ Blood Sugar ▪ S. Bilirubin (Total) ▪ Urine Sugar/Albumin ▪ Rapid Diagnostic Test (RDT)	Selected CHCs and District Hospital ▪ Hemoglobin Estimation (Hb) ▪ Total Leukocyte Count (TLC) ▪ Differential Leukocyte Count (DLC) ▪ Platelet Count ▪ Blood Urea Nitrogen (BUN) ▪ Serum Creatinine ▪ Liver Function Tests (SGOT, SGPT, Alkaline Phosphatase) ▪ Serum Electrolytes (Sodium, Potassium) ▪ Urine Routine and Microscopic Examination ▪ Serum Bilirubin (Total and Direct) ▪ Serum Creatinine Phosphokinase (CPK) ▪ Rapid Diagnostic Test (RDT) ▪ ELISA	At State-Level Hospitals/ Reference Laboratories ▪ All tests available at CHCs and District Hospitals ▪ Isolation of Leptospires ▪ ELISA ▪ PCR ▪ Microscopic Agglutination Test (MAT)
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- | At Primary Health Centres/
Ayushman Arogya Mandir - PHC
(PHCs/AAM-PHC) | Selected CHCs and District
Hospital | At State-Level Hospitals/
Reference Laboratories |
|--|--|--|
| <ul style="list-style-type: none"> ▪ Hemoglobin Estimation (Hb) ▪ Total Leukocyte Count (TLC) ▪ Total Leukocyte Count (TLC) ▪ Total Leukocyte Count (TLC) ▪ Differential Leukocyte Count (DLC) ▪ Platelet Count ▪ Blood Sugar ▪ S. Bilirubin (Total) ▪ Urine Sugar/Albumin ▪ Rapid Diagnostic Test (RDT) | <ul style="list-style-type: none"> ▪ Hemoglobin Estimation (Hb) ▪ Total Leukocyte Count (TLC) ▪ Differential Leukocyte Count (DLC) ▪ Platelet Count ▪ Blood Urea Nitrogen (BUN) ▪ Serum Creatinine ▪ Liver Function Tests (SGOT, SGPT, Alkaline Phosphatase) ▪ Serum Electrolytes (Sodium, Potassium) ▪ Urine Routine and Microscopic Examination ▪ Serum Bilirubin (Total and Direct) ▪ Serum Creatinine Phosphokinase (CPK) ▪ Rapid Diagnostic Test (RDT) ▪ ELISA | <ul style="list-style-type: none"> ▪ All tests available at CHCs and District Hospitals ▪ Isolation of Leptospirae ▪ ELISA ▪ PCR ▪ Microscopic Agglutination Test (MAT) |

Sample Type	Optimal Timing of Collection	Diagnostic Purpose
Blood (Serum)	Early phase (0-10 days) and convalescent phase (2-4 weeks post-onset)	Detect antibodies via serology tests like MAT and ELISA for confirming immune response over time
Blood (Whole)	Acute phase, within the first 7-10 days of symptoms	Detect active infection through PCR or culture by identifying Leptospira DNA in the bloodstream
Urine	After first week of illness, as bacteria shed intermittently	PCR testing to detect Leptospira DNA, especially if blood results are inconclusive
CSF	Early collection in cases with severe neurological involvement	PCR to confirm presence of Leptospira in cerebrospinal fluid in cases with suspected neuroleptospirosis
Tissue Samples (Post-mortem)	As indicated, particularly in deceased cases with suspected leptospirosis	Histopathology and PCR to confirm presence of Leptospira in organ tissues like liver and kidneys

Sample Type	Optimal Timing of Collection	Diagnostic Purpose
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Tissue Samples (Post-mortem)	As indicated, particularly in deceased cases with suspected leptospirosis	Histopathology and PCR to confirm presence of Leptospira in organ tissues like liver and kidneys

- Laboratory diagnosis can be classified into two main types - direct evidence and indirect evidence.
- Direct evidence involves the demonstration of leptospire or their DNA, as well as the isolation of the organism from clinical samples.
- In contrast, the presence of specific antibodies to leptospire, determined through serological methods, serves as indirect evidence.



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- Rapid screening tests (e.g., latex agglutination, dipstick tests) offer quick results but need confirmation (e.g., MAT).
- Results available within minutes to 2 hours.
- Minimal processing, straightforward interpretation, and requires minimal facilities.
- Stable reagents for varied conditions.

▪ **Types -**

1. **Lateral-flow:** Specimen added to strip, results after a set time.
2. **Flow-through:** Cassette with buffers and reagent for results.
3. **Agglutination:** Visual reaction upon adding antigenic reagent.

- **Pros -** Quick, ideal for low-resource settings.
- **Cons -** Cross-reactivity possible; variable sensitivity and specificity.



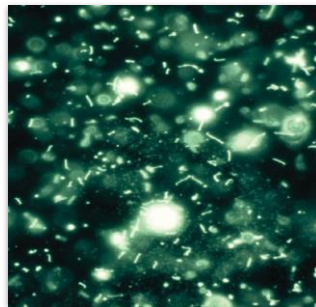
LEPTOSPIROSIS

The diagram illustrates the two-step process of indirect immunofluorescence. In the first step, a patient's sample containing IgM antibody binds to a known antigen. In the second step, a conjugated anti-human IgM antibody binds to the patient's IgM antibody.

- Commercial ELISA kits for leptospirosis detect genus-specific IgM antibodies.
- Easier to standardize than MAT; useful in early infection.
- **Advantages:** Detects IgM early, simple standardization.
- **Disadvantages:** Cross-reactivity with other diseases, cannot specify serovar.

LEPTOSPIROSIS

- **Purpose:** Detects agglutinating antibodies in serum by exposing it to leptospirae in various dilutions, forming visible clumps (agglutination) observed under dark-field microscopy.
- **Specificity:** Primarily detects antibodies specific to the infecting serovar but may cross-react with other serovars early in infection (paradoxical reaction).
 - Cross-reactivity may cause false negatives for the infecting serovar while showing a positive reaction for non-causative serovars.
 - Cross-reactive antibodies typically diminish over time, leaving antibodies specific to the infecting serovar or serogroup.
- **Factors Affecting Specificity:**
 - Target specificity of agglutinating antibodies to serovars or serogroups.
 - Local serovar variation due to epidemiological shifts.
 - Incomplete serovar panels in laboratories may lead to false negatives.



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MAT Interpretation, Limitations, and Applications

MAT Titres -

- Cannot distinguish between acute, recent, or past infection.
- Two serum samples, ideally taken 2–3 weeks apart, indicate active infection through seroconversion or a fourfold rise in titres.
- Cut-off titres vary by region (e.g., 1:100 to 1:800), based on endemic prevalence and antibody persistence.

Advantages & Disadvantages:

- Advantages:** High specificity for leptospiral antibodies.
- Disadvantages:**
 - Requires specialized lab facilities for live leptospire cultures.
 - May yield false negatives if causative strain is missing from the antigen panel.

Standardization Issues:

- MAT relies on live antigens, leading to variability in results.
- Recommended to test paired serum samples together for consistent analysis.

Application in Epidemiology:

- Used to study circulating serovars or serogroups in populations.
- Residual antibodies from past infections may complicate sero-epidemiological findings.

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Polymerase Chain Reaction (PCR)

- PCR is a rapid, sensitive and specific means of diagnosing leptospiral infection, during the first few days when antibodies are not fully detectable in serological tests and symptoms are confusing.

- It involves *in-vitro* amplification of genus-specific target DNA sequence.

- Sample type: Blood, Urine or CSF.

Advantages of PCR:

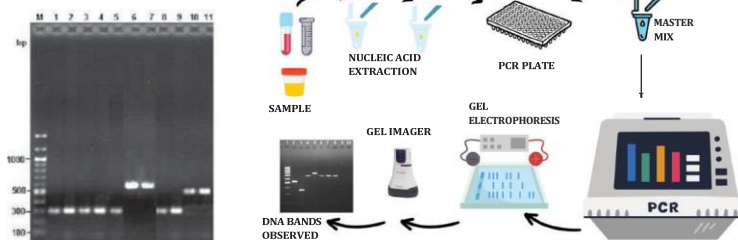
- Rapid detection of leptospiral DNA during the early phase of infection.
- Can confirm the diagnosis before antibodies are detectable.

Disadvantages of PCR

- Requires specialized equipment and is susceptible to contamination.
- May produce false-negative results due to inhibitors in clinical samples.

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Lanes 1-5, 8-9: 285 bp fragment amplified by G1 & G2, Lanes 6-7: 563 bp fragment amplified by B641 & II Lanes 10-11: 474 bp fragment amplified by LipL32

- The amplified PCR products are analysed in 1% - 2% agarose gel with 0.1 µg/ml ethidium bromide in TAE buffer having pH 8.0.
- The gel is visualized in Gel Viewer.

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Isolation of Leptospires

01

Isolation of Leptospires from clinical specimens is the strongest evidence for confirmatory diagnosis and to identify circulating serovars in a particular region.

02

Locally isolated and identified strains are used as antigens in MAT as they are more sensitive and strongly reactive than reference strains and also for developing vaccine.

03

However, Leptospires grow slowly and require several days or weeks to yield cultures and weeks to months for identification.

Isolation

Culture

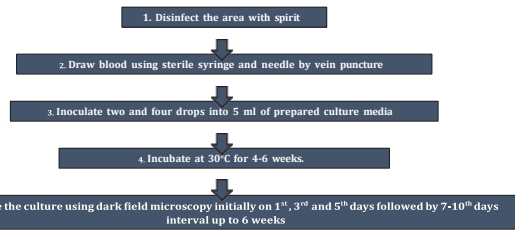
Blood culture
Urine culture
CSF culture

Animal inoculation

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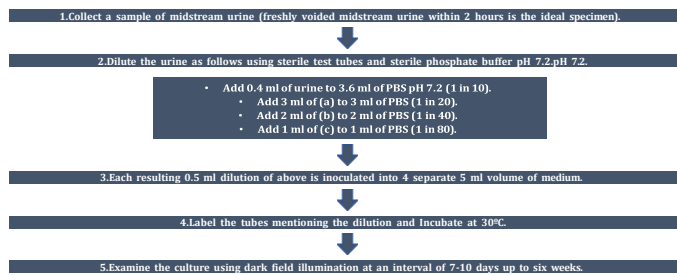
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Media - EMJH (Ellinghausen-Mc Cullough-Johnson-Harris) and **Fletcher's** media. The procedure are as follows:



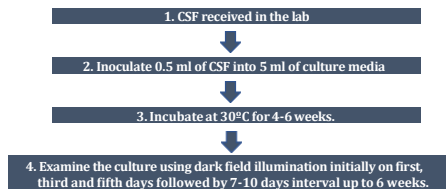
Subculture should be made within 48 hours to minimize the inhibitory effect of the selective agents 0.1% to 0.15% agarose and 0.4% to 1% of rabbit serum or fetal calf serum is added to encourage growth.

Ideal Time - 10 to 30 days after the onset of the disease. **Media** - Same as Blood Culture. The procedure is as follows -



LEPTOSPIROSIS

The procedure are as follows -



- **Slow Growth** - *Leptospira* are fastidious organisms and grow slowly, making the process of isolation time-consuming.
- **Labor-Intensive** - This method is labor-intensive, requires specialized equipment, and is not suitable for small laboratories.
- **Contamination Risks** - Contamination by saprophytic leptospires or other microorganisms is common, making the technique prone to false positives.
- **Antibiotic Interference** - Prior administration of antibiotics, improper sterilization of equipment, and incorrect incubation conditions can significantly hinder the success of leptospiral isolation.

[illegible]

Figure 1 consists of two panels, A and B, showing fluorescence micrographs of the developing chick eye. Panel A shows a normal eye with a clear vitreal space. Panel B shows an eye with a vitreal mass, indicated by a vertical line.

- Quick method but limited practical utility in detecting leptospires.
- Low organism concentration in blood during acute phase hinders direct detection.
- Challenges in detecting leptospiral excretion in urine due to sporadic shedding.
- Serum proteins and cellular debris can resemble leptospires, leading to misidentification.
- Leptospires may not show motility in clinical samples due to reactive antibodies or mechanical damage.
- Sensitivity: 40.2% | Specificity: 61.5% – Limited diagnostic accuracy.

LEPTOSPIROSIS

Assam Medical College, Dibrugarh
LLRM Medical College, Meerut
State Public Health and Clinical Laboratory, Trivandrum
State Public Health Laboratory, Chennai
District Public Health Laboratory, Mangalore, Karnataka
Govt Medical College, Surat, Gujarat

LEPTOSPIROSIS

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Session-6

Management of Leptospirosis

Course No. 006	Session 6: Management of Leptospirosis
Duration	15 minutes
Learning Objectives	• Outline the management protocol for leptospirosis, emphasizing timely intervention. • Identify appropriate antibiotic treatments and their indications based on patient demographics. • Describe the management strategies at different healthcare levels, including primary, secondary and tertiary care.
Pre-requisite knowledge/skill	• Understanding of general principles of infectious disease management and antibiotic use. • Familiarity with patient triaging and referral systems across healthcare levels. • Awareness of basic pharmacology and drug indications across age and risk groups.
Competencies to be achieved	• Learners will gain the ability to promptly initiate antibiotic treatment for leptospirosis based on clinical suspicion and diagnostic confirmation. • Develop skills in managing cases at various healthcare levels, including identification of when to refer patients to higher centers. • Learn to evaluate and manage severe complications associated with leptospirosis.

MANAGEMENT OF LEPTOSPIROSIS

Leptospirosis requires prompt antibiotic treatment, particularly within 7 to 10 days after infection. Timely initiation of therapy, based on clinical suspicion or confirmed diagnosis, is essential to prevent severe complications.

Antibiotic Therapy

- **Benzylpenicillin:** The preferred treatment for leptospirosis is benzylpenicillin administered by injection. The recommended dosage is five million units per day for five days. This antibiotic has proven efficacy against *Leptospira*.
- **Doxycycline:** Alternatively, doxycycline is widely recommended at a dosage of 100 mg twice daily for 10 days. It is a reliable treatment for adults and adolescents.
- **Tetracyclines:** Tetracyclines are also effective, but they are contraindicated in patients with renal insufficiency, children under 8 years, and pregnant women. For these specific groups, alternative treatments should be considered.
- **Pregnant & Lactating Women:** In such cases, **Ampicillin** 500 mg every 6 hours is recommended as a safer option. This avoids the teratogenic risks associated with tetracyclines.
- **Children under 8 years:** For children, **Amoxicillin** or **Ampicillin** is prescribed at 30-50 mg/kg/day in divided doses for 7 days. These antibiotics are safe for young children, unlike tetracyclines, which should be avoided.
- **Penicillin Hypersensitivity:** Patients with a known allergy to penicillin may be treated with alternatives such as **Cephalosporins** (e.g., Ceftriaxone) or Erythromycin (250 mg, four times daily for five days).

Management At Primary Healthcare Centers (PHC)

Step 1: Clinical Suspicion

- Refer to case definitions for leptospirosis.
- Use general guidelines for fever management in the field, paying attention to symptoms such as fever, headache, and muscle pain.

Step 2: Initial Treatment for Suspected Cases

- **Adults:** Administer doxycycline 100 mg twice daily for 7 days.
- **Pregnant & Lactating Mothers:** Provide ampicillin 500 mg every 6 hours.
- **Children under 8 years:** Amoxicillin or ampicillin, 30-50 mg/kg/day, in divided doses for 7 days.

Step 3: Rapid Diagnostic Testing

- Use rapid immunodiagnostic tests for initial screening. While these tests can help identify suspected cases, confirm results with ELISA.

Step 4: Referral to Higher Centers

Patients showing signs of severe infection, including:

- Hypotension
- Decreased urine output
- Hemoptysis or breathlessness
- Bleeding tendencies
- Altered consciousness

These patients must be referred immediately to a higher center for advanced care.

While shifting patients to higher center, individual patient's record should be furnished in the following order-

- Age
- Sex
- Occupation
- Clinical symptoms
- Date of onset of clinical symptoms
- Serological result
- Hospitalization details-treatment given and outcome.

Management at Community Health Centers (CHC) and District Hospitals

Step 1: Clinical Suspicion

Follow case definitions and fever management protocols.

Step 2: Treatment Protocol

- **Adults:** Doxycycline 100 mg twice daily for 7 days.
- **Pregnant & Lactating Women:** Ampicillin 500 mg every 6 hours.
- **Children under 8 years:** Amoxicillin or Ampicillin, 30-50 mg/kg/day in divided doses for 7 days.

Step 3: Laboratory Screening

Rapid diagnostic tests should be conducted, but confirmation via ELISA is necessary for accuracy.

Key laboratory tests include:

- Hemoglobin (Hb)
- Total count (TC), Differential count (DC)
- Platelet count
- Liver and kidney function tests (LFT, RFT)

Step 4: When to Refer to Higher Centres

Patients must be transferred to a higher centre if they exhibit:

- **Renal Complications:** Decreased urine output (<400 ml/day), elevated blood urea (>60 mg/dL), high serum creatinine (>2.5 mg/dL), or signs of uremia.
- **Hepatic Issues:** Jaundice with serum bilirubin >3.0 mg/dL.
- **Pulmonary Symptoms:** Breathlessness, hemoptysis, or chest X-ray showing opacities.

- **Neurological Changes:** Altered level of consciousness.
- **Bleeding Issues:** Spontaneous bleeding, low platelet count.

Management at Tertiary Care Hospital (Medical College)

Step 1: Clinical Suspicion

Any patient with acute febrile illness, muscle pain, or headache—particularly from flood-affected areas—should be suspected of having leptospirosis and treated promptly.

Step 2: Treatment Protocol

- **Adults:** Administer doxycycline 100 mg twice daily for 7 days.
- **Crystalline Penicillin:** For severe cases, inject 15 lacs IU intravenously every six hours. In cases of penicillin sensitivity, alternatives include:
 - o **Ceftriaxone** 1 gm IV every six hours for 7 days.
 - o **Cefotaxime** 1 gm IV every six hours for 7 days.
 - o **Erythromycin** 500 mg IV every six hours for 7 days.
- **Pregnant & Lactating Mothers:** Continue with ampicillin 500 mg every six hours.
- **Children under 8 years:** Administer amoxicillin/ampicillin 30-50 mg/kg/day for seven days. In severe cases, crystalline penicillin at 2–4 lacs IU/kg/day can be used.

Management of Severe Complications

As leptospirosis can affect multiple organs, the management of complications involves:

- **Renal Failure:** Initiate renal replacement therapy (RRT) when necessary.
- **Respiratory Issues:** For patients with acute respiratory distress syndrome (ARDS), manage with non-invasive ventilation or invasive mechanical ventilation based on the severity.
- **Steroids:** Use pulse doses of methylprednisolone (1 gm IV) for cases of multi-organ failure.

Criteria for Critical Care Referral

- Tachypnea (>24 breaths/min)
- Jaundice or altered consciousness
- Oliguria
- Hemorrhagic manifestations

Investigations

Focused diagnostics should assess:

- **Heart:** Rule out myocarditis.
- **Lungs:** Check for ARDS.
- **Liver:** Investigate for hepatitis.
- **Kidneys:** Monitor for acute kidney injury.
- **Blood:** Examine for conditions like rhabdomyolysis and disseminated intravascular coagulation (DIC).

Special Situations

- Pregnant women and immunocompromised patients (e.g., with diabetes, HIV) should be referred immediately to higher centers for specialized care.

POINTS TO REMEMBER

- Initiate antibiotic therapy promptly, ideally within 7 to 10 days post-infection, to prevent severe complications.
- **Preferred Antibiotics:** Benzylpenicillin is the preferred treatment (5 million units daily for 5 days), while doxycycline (100 mg twice daily for 10 days) is a reliable alternative for adults and adolescents.
- **Special Considerations for Populations:**
 1. Use ampicillin for pregnant and lactating women (500 mg every 6 hours).
 2. For children under 8 years, prescribe amoxicillin or ampicillin (30-50 mg/kg/day) to avoid tetracyclines.
- Refer patients to higher centers if they exhibit severe symptoms such as hypotension, decreased urine output, altered consciousness, or bleeding tendencies.
- Conduct clinical assessments based on case definitions and use rapid immunodiagnostic tests for screening, confirming results with ELISA.
- Be prepared to manage complications such as renal failure, respiratory distress, and multi-organ failure, which may require specialized interventions.
- When referring patients, ensure detailed records are provided, including age, sex, occupation, clinical symptoms, serological results, and treatment details.

Treatment – (Leptospirosis requires prompt antibiotic treatment) particularly within 7 to 10 days after infection

ANTIBIOTIC THERAPY

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Treatment Steps at PHC

Step 1 - Clinical Suspicion

Refer to case definitions for leptospirosis, Use general guidelines for fever management in the field, paying attention to symptoms such as fever, headache, and muscle pain.

Step 2 - Initial Treatment for Suspected Cases

- **Adults** - Administer doxycycline 100 mg twice daily for 7 days.
- **Pregnant & Lactating Mothers** - Provide ampicillin 500 mg every 6 hours.
- **Children under 8 years** - Amoxicillin or ampicillin, 30-50 mg/kg/day, in divided doses for 7 days.

Step 3 - Rapid Diagnostic Testing - Use rapid immunodiagnostic tests for initial screening. While these tests can help identify suspected cases, confirm results with ELISA.

Step 4 - Referral to Higher Centres - Patients showing signs of severe infection, including: Hypotension, Decreased urine output, Hemoptysis or breathlessness, Bleeding tendencies, Altered consciousness

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Treatment Steps at CHC/ District Hospital

Step 1: Clinical Suspicion, Follow case definitions and fever management protocols.

Step 2: Treatment Protocol, Adults: Doxycycline 100 mg twice daily for 7 days. **Pregnant & Lactating Women:** Ampicillin 500 mg every 6 hours. **Children under 8 years:** Amoxicillin or Ampicillin, 30-50 mg/kg/day in divided doses for 7 days.

Step 3: Laboratory Screening Rapid diagnostic tests should be conducted, but confirmation via ELISA is necessary for accuracy. Key laboratory tests includes Hemoglobin (Hb), Total count (TC), Differential count (DC), Platelet count, Liver and kidney function tests (LFT, RFT)

Step 4: When to Refer to Higher Centres, Patients must be transferred to a higher centre if they exhibit:

- **Renal Complications:** Decreased urine output (<400 ml/day), elevated blood urea (>60 mg/dL), high serum creatinine (>2.5 mg/dL), or signs of uremia.
- **Hepatic Issues:** jaundice with serum bilirubin >3.0 mg/dL.
- **Pulmonary Symptoms:** Breathlessness, hemoptysis, or chest X-ray showing opacities.
- **Neurological Changes:** Altered level of consciousness.
- **Bleeding Issues:** Spontaneous bleeding, low platelet count.

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Tertiary Care Hospital/Medical College

Step 1: Clinical Suspicion, Any patient with acute febrile illness, muscle pain, or headache—particularly from flood-affected areas—should be suspected of having leptospirosis and treated promptly.

Step 2: Treatment Protocol

- **Adults:** Administer doxycycline 100 mg twice daily for 7 days.
- **Crystalline Penicillin:** For severe cases, inject 15 lacs IU intravenously every six hours. In cases of penicillin sensitivity, alternatives include:
 - **Ceftriaxone** 1 gm IV every six hours for 7 days.
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LEPTOSPIROSIS

Session-7

Prevention and Control of Leptospirosis

Course No. 007	Session 7: Prevention and Control of Leptospirosis
Duration	15 minutes
Learning Objectives	• Describe personal protection strategies to prevent leptospirosis in high-risk environments. • Explain the importance of health education and awareness campaigns in disease control. • Discuss the role of chemoprophylaxis, especially during high-risk periods. • Identify effective rodent control measures to mitigate transmission risks. • Assess the significance of mapping water bodies and drainage systems in preventing contamination. • Recognize the necessity of health impact assessments for developmental projects related to water and sanitation. • Study the role of animal vaccination in controlling leptospirosis in domesticated species.
Pre-requisite knowledge/skill	• Understanding of leptospirosis treatment protocols, prevention, and control measures. • Awareness of zoonotic disease transmission and environmental health strategies. • Familiarity with public health principles, including hygiene, sanitation, vaccination, and chemoprophylaxis
Competencies to be achieved	• Learners will acquire skills in implementing personal protective measures in occupational settings. • Gain insights into the promotion of effective health education campaigns tailored to the community. • Administration of chemoprophylaxis during transmission peaks. • Acquire knowledge on health impact assessments and animal vaccination.

Personal Protection

Maintaining proper hygiene and avoiding direct or indirect contact with animal urine are key strategies for preventing leptospirosis. Individuals working in high-risk environments, such as flooded fields, should be encouraged to minimize contact with contaminated water or mud. Wearing protective gear, like rubber boots and gloves, is crucial in these situations. Furthermore, workers with open wounds or abrasions on their lower limbs should apply antiseptic ointments, such as Betadine, both before and after exposure to potentially contaminated environments.

Health Education

Raising awareness about leptospirosis and preventive measures remains the cornerstone of controlling the disease. Educational campaigns should be tailored to reach various populations through diverse platforms, including print media, audio-visual aids, and outdoor outreach efforts. Utilizing new forms of electronic media, such as social networks and mobile applications, can expand the reach of these initiatives.

Chemoprophylaxis

During high-risk transmission periods, such as the rainy season, chemoprophylaxis can serve as an effective preventative measure for leptospirosis. Agricultural workers, especially those in endemic areas like paddy fields or those involved in canal cleaning, may benefit from a weekly dose of Doxycycline (200 mg). This treatment is typically recommended for up to six weeks but should not be extended beyond eight weeks to prevent potential adverse effects.

Rodent Control

Rodents are the primary reservoirs of *Leptospira* bacteria, with species such as *Rattus rattus* (house rat), *Rattus norvegicus* (Norway rat), *Bandicota bengalensis* (lesser bandicoot), and *Bandicota indica* (larger bandicoot) being the main carriers in India. Effective rodent control strategies are essential to reduce the incidence of leptospirosis in affected areas. A successful rodent control plan should include:

1. Identifying the rodent species responsible for transmission in specific areas.
2. Delineating regions for targeted anti-rodent efforts.
3. Implementing control measures during the pre-monsoon months to limit the rodent population before the peak transmission period.
4. Using appropriate technology and methods for rodent control, ensuring the correct application of interventions.

5. Strengthening community awareness and encouraging participation in these control measures to ensure long-term success.
6. Building capacity in rodent control management, ensuring sufficient resources and knowledge are in place.

Mapping of Water Bodies and Drainage Systems

Mapping all significant water bodies in the area, including rivers, lakes, ponds, and drainage systems and assessing human activity in waterlogged areas can help identify populations at higher risk of leptospirosis. Potential contamination sources near these water bodies, such as agricultural runoff, sewage disposal, and animal grazing areas should be identified. This can involve collecting water samples for testing for leptospiral DNA.

Educating farmers to properly dispose of cattle urine, such as channeling it into a pit rather than allowing it to mix with natural water sources like rivers and ponds, is an important step in preventing contamination. Efforts to collaborate with local communities, agricultural associations, and government agencies should be made to discuss findings. Stakeholder engagement is essential for understanding local practices and gaining support for any recommended changes. Proper drainage systems should be established as that can further reduce the risk of leptospirosis transmission by limiting the accumulation of contaminated water in high-risk areas.

Health Impact Assessment for Development Projects

Making health impact assessments a mandatory component of all developmental projects, alongside environmental impact assessments, can help mitigate the spread of leptospirosis. This requirement ensures that potential public health risks, particularly those related to water and sanitation, are considered before project approval.

Vaccination of Animals

Vaccination plays a critical role in controlling leptospirosis in domesticated animals, though its efficacy varies. In dogs, vaccination is generally administered starting at 8-9 weeks of age, with a booster given at 12 weeks and annual revaccination thereafter. For large animals like cattle and buffalo, vaccination is less common. While vaccines reduce the severity and occurrence of leptospirosis, they do not completely prevent infection or the shedding of *Leptospira* bacteria in urine. Therefore, although vaccination can decrease the excretion of leptospires in cattle urine, it does not eliminate the risk of transmission entirely. The protection offered by these vaccines is typically short-lived, lasting around six months, and the immunity is specific to the strains contained in the vaccine. Therefore, vaccination should be selective and targeted toward areas where the incidence of leptospirosis is high.

POINTS TO REMEMBER

- Maintaining proper hygiene and avoiding contact with animal urine are essential for preventing leptospirosis. Wearing protective gear like rubber boots and gloves is crucial.
- Health education campaigns play a vital role in raising awareness about leptospirosis, utilizing various platforms such as print media, social networks, and mobile applications to reach diverse populations.
- Chemoprophylaxis with Doxycycline (200 mg) can effectively prevent leptospirosis during high-risk periods, particularly for agricultural workers in endemic areas, with a recommended duration of up to six weeks.
- Effective rodent control strategies are necessary, as well as implementing control measures before peak transmission periods.
- Mapping water bodies and assessing human activities in waterlogged areas help identify high-risk populations.
- Health impact assessments should be a mandatory part of developmental projects to address public health risks related to water and sanitation.
- Animal vaccination can reduce the severity of leptospirosis in domesticated animals, although it does not eliminate the risk of transmission entirely.



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Session-8

Risk Communication & Community Engagement

Course No. 008	Session 8: Risk Communication & Community Engagement
Duration	15 minutes
Learning Objectives	• Promote behavioral change through effective risk communication regarding leptospirosis. • Raise awareness about transmission, symptoms, and preventive measures within communities. • Facilitate community engagement for proactive environmental sanitation and rodent control.
Pre-requisite knowledge/skill	• Basic understanding of health communication strategies and community outreach. • Familiarity with principles of behavior change and risk communication. • Awareness of public health education, environmental sanitation, and zoonotic disease prevention.
Competencies to be achieved	• Develop strategies for effective dissemination of information on leptospirosis to various target audiences. • Design tailored communication messages that address the specific needs of high-risk groups and the general public. • Implement participatory approaches for community engagement, fostering collaboration with local leaders and organizations.

RISK COMMUNICATION AND COMMUNITY ENGAGEMENT

An integrated RCCE approach is of particular importance in the Indian context, as diverse ecological conditions and socio-economic disparities exist. This will help to empower communities especially those residing in high-risk areas.

1. Objectives of RCCE for Leptospirosis

The primary goal of risk communication and community engagement for leptospirosis is to promote behavioral change through education and empower communities to take preventive action. The aim is to –

- **Increase awareness** of leptospirosis transmission, symptoms, and prevention.
- **Encourage prompt reporting** of symptoms to healthcare facilities.
- **Motivate community action** for environmental sanitation and rodent control.
- **Promote safe practices** among high-risk groups, including farmers, fishermen, and sewage workers.
- **Ensure trust** between the community and health authorities during outbreak management.

2. Risk Communication Strategies

A. Dissemination of Information

Effective risk communication starts with providing accurate, timely, and relevant information to the community. Information about leptospirosis should include:

- **Modes of transmission**, such as contact with contaminated water or animal urine.
- **Signs and symptoms**, including fever, headache, myalgia, and jaundice.
- **Prevention measures**, such as wearing protective gear (boots and gloves) when working in contaminated water, rodent control, and proper waste disposal.

Health authorities should use multiple channels to disseminate this information, including:

- **Mass media:** Television, radio, and newspapers should regularly broadcast messages on leptospirosis prevention, especially during the monsoon season, when the risk of transmission is highest.
- **Social media:** Platforms like WhatsApp, Facebook, and Twitter are effective for spreading awareness, particularly in urban areas.
- **Pamphlets and posters:** These should be distributed in high-risk areas, including rural communities, farms, and schools.

B. Tailoring Messages to Target Audiences

Communication strategies must be tailored to the needs of different target groups:

- **For high-risk occupational groups** (farmers, fishermen, sewer workers), messages should emphasize the importance of personal protective equipment (PPE) and maintaining hygiene during and after exposure to contaminated environments.
- **For the general public**, messages should highlight the importance of rodent control, proper waste disposal, and avoiding contact with floodwaters.
- **For healthcare workers**, clear guidelines on diagnosing and managing leptospirosis cases, along with information on how to communicate risks to patients, are essential.

C. Overcoming Barriers to Communication

Certain barriers hinder the effectiveness of RCCE in India including –

- **Literacy levels and language differences:** Educational materials should be developed in local languages, and information should be presented in simple, easy-to-understand formats to reach all segments of the population.
- **Cultural and social norms:** Risk communication must consider local beliefs and practices that may affect people's willingness to adopt preventive measures. For example, in rural areas, superstitions regarding the cause of disease may delay seeking medical care. Culturally appropriate messaging would help to dispel myths and encourage prompt treatment seeking behavior.

3. Community Engagement Strategies

A. Involving Local Leaders and Community Groups

Community engagement is more effective when local leaders, such as village heads, religious leaders, and community health workers, are actively involved. These leaders serve as trusted sources of information and can influence behavior change within their communities.

- **Health talks and meetings:** Regular meetings with community leaders, farmers' associations, and other local groups provide an opportunity for open discussions about leptospirosis risks and prevention strategies.
- **Peer education:** Involving trained community members as peer educators can promote knowledge sharing and foster trust within the community. This is particularly effective in rural settings, where formal healthcare services may be limited.

B. Participatory Approach

A participatory approach is key to successful community engagement. WHO emphasizes that communities should not merely be passive recipients of information; rather, they should be actively involved in decision-making and action planning. In India, this approach can be adapted by engaging local communities in identifying specific risk factors, such as stagnant water, poor waste management, or rodent infestations. This enables tailored interventions that address the community's unique needs.

Community members should be involved in planning and implementing environmental management activities, such as cleaning drainage systems and organizing rodent control efforts.

C. Behavior Change Communication (BCC)

Behavior change is essential for effective leptospirosis prevention. BCC strategies should focus on motivating communities to adopt preventive behaviors, such as:

- Educating communities on the importance of waste disposal and eliminating potential rodent breeding sites.
- Encouraging households to use safe rodenticides and maintain clean environments to prevent rodent infestations.
- Promoting the use of protective gear like gloves, boots, and masks in occupations that involve direct contact with contaminated water or soil.

4. Outbreak Communication

During leptospirosis outbreaks, swift and transparent communication is critical to prevent panic and misinformation. WHO recommends the following principles for outbreak communication:

- Health authorities should provide regular updates on the status of the outbreak, the number of cases, and the actions being taken to control the situation. This helps build public trust.
- All the communication from local, state, and national health authorities must be consistent to avoid confusion. Miscommunication or conflicting information can lead to fear and mistrust within the community.
- Health officials should work closely with the media to disseminate accurate information. Press briefings, interviews, and public service announcements can help convey key messages during an outbreak.

POINTS TO REMEMBER

- An integrated RCCE approach is essential for empowering communities, particularly in high-risk areas, to adopt preventive measures against leptospirosis through education and awareness.
- Effective communication strategies should include tailored messaging for different target audiences using diverse channels like mass media, social media, and community outreach.
- Overcoming barriers to communication, such as literacy levels and cultural beliefs, is crucial.
- Active community involvement and collaboration with local leaders can enhance the effectiveness of RCCE initiatives.

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Behavioral change	Promote behavioral change by empowering communities to take preventive actions against leptospirosis.
Awareness	Increase awareness by educating on transmission, symptoms, and prevention (e.g., PPE use, sanitation).
Early reporting	Encourage early healthcare reporting by prompting individuals to seek medical care for symptoms like fever, headache, and jaundice.
Community action	Promote community action focused on environmental sanitation and rodent control in high-risk areas.
Build trust with authority	Build trust with health authorities by fostering transparency during outbreaks to ensure cooperation and effective response.

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Overcoming Barriers

- Use multiple channels: **Mass media** (TV, radio), **Social media** (WhatsApp, Facebook), and **Printed materials** (posters, pamphlets).
- Provide clear information on transmission (contaminated water, animal urine), symptoms, and prevention (PPE, rodent control).
- **High-risk groups** (farmers, sewage workers): Emphasize PPE, hygiene, and sanitation.
- **General public:** Focus on rodent control, avoiding floodwater, and waste management.
- Address literacy, language differences, and cultural beliefs. Use simple language and local dialects to improve accessibility.

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Session-9

Surveillance

Course No. 009	Session 9: Surveillance
Duration	30 minutes
Learning Objectives	• Explain the key components of leptospirosis surveillance under the Integrated Disease Surveillance Programme (IDSP) in India. • Describe the surveillance infrastructure, data collection, and reporting mechanisms for leptospirosis cases. • Outline the outbreak detection, response procedures, and inter-sectoral coordination for effective disease control. • Discuss the importance of laboratory surveillance and public awareness campaigns in managing leptospirosis.
Pre-requisite knowledge/skill	• Basic understanding of public health surveillance systems and disease reporting. • Familiarity with the structure and function of IDSP and outbreak response mechanisms in India. • Awareness of the role of laboratory networks and community engagement in infectious disease control.
Competencies to be achieved	• Learners will acquire detailed knowledge of India's leptospirosis surveillance strategy and the role of IDSP in controlling outbreaks. • Gain skills in recognizing syndromic, presumptive, and confirmed surveillance approaches and their applications in the field. • Ability to identify outbreak situations and initiate Rapid Response Teams (RRTs) for immediate public health interventions. • Develop insights into the coordination required across health, veterinary, and environmental sectors using the One Health approach. • Learn to effectively communicate public health messages to populations at high risk, improving disease reporting and prevention behaviors.

SURVEILLANCE OF LEPTOSPIROSIS

Leptospirosis surveillance in India is a critical component of the Integrated Disease Surveillance Programme (IDSP), under the National Centre for Disease Control (NCDC). The surveillance focuses on early case detection, monitoring trends, controlling outbreaks, and implementing appropriate public health interventions.

Key Elements of Leptospirosis Surveillance

1. Surveillance Infrastructure

The IDSP functions as a nationwide system that collects epidemiological data on 33 priority diseases, including leptospirosis. Surveillance is done through three types of reporting:

- **Syndromic Surveillance:** This involves the collection of early warning signals based on symptoms without laboratory confirmation. Medical officers report cases of fever with specific symptoms indicative of leptospirosis, like myalgia (muscle pain), conjunctival suffusion, and jaundice.
- **Presumptive Surveillance:** Probable cases are identified based on clinical diagnosis and are reported when certain symptoms strongly suggest leptospirosis, even before lab confirmation.
- **Confirmed Surveillance:** Laboratory-confirmed cases are reported based on diagnostic testing like Rapid Diagnostic Tests (RDTs), ELISA, PCR, or Microscopic Agglutination Test (MAT).

2. Data Collection and Reporting

As per IDSP, data is collected at the block, district, state, and national levels. Information is gathered weekly from Primary Health Centres (PHCs), Community Health Centres (CHCs), Sub-district Hospitals (SDHs), District Hospitals (DHs), and other public health facilities/ laboratories. A report is compiled every week which includes:

- **Case incidence:** The number of suspected, probable, and confirmed cases.
- **Outbreak data:** A leptospirosis epidemic is declared when the number of cases detected in a particular area during a given time period exceeds the expected baseline for that region. This is often associated with environmental triggers, such as heavy rainfall, flooding, or other events that lead to increased human exposure to environments contaminated by the urine of infected animals, particularly rodents. Any sudden increase in leptospirosis cases that may signify an outbreak is flagged for further investigation and response.
- **Laboratory results:** Positive test results (PCR, ELISA) are reported to confirm cases and differentiate leptospirosis from other febrile illnesses such as dengue, malaria, and typhoid.

This system supports both routine surveillance and outbreak surveillance. Data is uploaded to the IHIP portal, where health professionals and authorities can monitor trends in real-time. The dashboard shows the number of cases, deaths, age and sex-wise distribution as well as the time trends. This is available for Suspected, Probable and Laboratory confirmed cases according to each state.

3. Outbreak Detection and Response

The IDSP plays a key role in detecting and responding to leptospirosis outbreaks, especially during the monsoon season when cases typically surge. An outbreak is declared when the number of reported cases in a given area exceeds the expected average for that period.

- **Rapid Response Teams (RRTs):** When an outbreak is suspected, RRTs are mobilized at the district level. These teams include epidemiologists, public health officers, and microbiologists.
- In order to identify sites and facilities (such as homes and workplaces) visited by outbreak-related patients during their infectious periods, it is essential to assess the potential risk to public health. This includes checking for factors that encourage rat infestations, such as burrows, traces of urine or droppings, and any issues related to solid waste, wastewater disposal, and water distribution systems. A thorough risk assessment should be conducted at these locations to address any conditions that might contribute to the spread of leptospirosis.
- Information for this assessment can be gathered through interviews with patients, contact tracing, environmental health inspections, medical and public health records, and facility logs. Each of these sources will provide insights into the exposure risks and help identify any environmental or structural concerns that need to be addressed to mitigate the spread of the disease.
- **Laboratory Support:** During outbreaks, confirmed diagnoses of leptospirosis are essential for guiding public health interventions. The IDSP supports laboratory infrastructure, ensuring diagnostic tools like ELISA kits and PCR machines are available in high-burden areas. These tests are critical for confirming suspected cases.

Steps for an outbreak investigation of leptospirosis is given in Annexure – 1.

4. Laboratory Surveillance

At the district and state levels, diagnostic capacity is strengthened to ensure rapid and accurate detection of leptospirosis through:

- **ELISA (Enzyme-Linked Immunosorbent Assay):** Used to detect IgM antibodies to *Leptospira*, providing a presumptive diagnosis.
- **PCR (Polymerase Chain Reaction):** This is more accurate in the early stages of the infection and is essential for detecting leptospiral DNA in clinical samples.
- **Microscopic Agglutination Test (MAT):** Considered the gold standard for confirming leptospirosis, this test helps in detecting the presence of antibodies against *Leptospira* in blood samples.

5. Inter-Sectoral Coordination

Given the zoonotic nature of leptospirosis, collaboration between the human health, veterinary, and environmental sectors is critical. The One Health approach emphasizes coordinated action among various stakeholders to manage, prevent, and control zoonotic diseases.

Zoonotic Disease Committees are formed under the National One Health Programme for Prevention and Control of Zoonoses at the state (State-level Zoonoses Committees) and district (District-level Zoonoses Committees) levels to ensure coordinated surveillance and control activities across human, animal, and environmental health sectors.

6. Public Awareness and Health Education

Public health education is integral to the IDSP's leptospirosis surveillance strategy. Awareness campaigns are conducted through various channels, targeting populations at higher risk, such as agricultural workers and people living in flood-prone areas. The aim is to:

- **Promote the use of protective clothing:** Workers in flooded fields and contaminated water are advised to wear rubber boots and gloves.
- **Encourage prompt medical attention:** Public awareness campaigns encourage early medical reporting in case of symptoms like fever, muscle pain, and eye redness, especially during and after floods.

Although significant progress has been made in controlling leptospirosis, few challenges still remain. Many mild cases go undetected or are misdiagnosed as other febrile illnesses which results in underreporting of the cases. Some regions lack adequate laboratory infrastructure for confirming cases, particularly in rural or remote areas. The NCDC and state health departments are working towards strengthening diagnostic capabilities and improving the training of healthcare workers at the grassroots level to ensure that the cases are not missed out.

POINTS TO REMEMBER

- Leptospirosis surveillance in India is part of the IDSP and includes syndromic, presumptive, and confirmed surveillance methods.
- Outbreaks are declared when leptospirosis cases exceed the expected baseline, typically triggered by environmental factors such as floods or heavy rainfall.
- The RRTs are mobilized during outbreaks to conduct field investigations, risk assessments, and implement control measures, including checking environments for rat infestations.
- The One Health approach ensures collaboration between human, animal, and environmental health sectors through Zoonotic Disease Committees at the state and district levels, crucial for coordinated surveillance and control efforts.

PROGRAMME FOR PREVENTION AND CONTROL OF LEPTOSPIROSIS

Leptospirosis is a major public health concern in India, especially in coastal regions. To address this, a **Pilot Project on Prevention and Control of Leptospirosis** was launched during the **11th Five-Year Plan**, leading to the establishment of a full-scale program during the **12th Five-Year Plan** in endemic states and Union Territories, including Gujarat, Kerala, Tamil Nadu, Maharashtra, Karnataka, and the Andaman & Nicobar Islands. Based on epidemiological data, the program later expanded to **Uttar Pradesh, Assam, Goa, and the UTs of Dadra Nagar Haveli and Daman & Diu**, now covering 114 districts across 10 States/UTs. It is currently approved under **Scheme F of the NCDC Umbrella Scheme** for **FY 2021-22**.

Objective

To reduce morbidity and mortality due to leptospirosis.

Key Components

- Training healthcare personnel in diagnosis, case management, and prevention.
- Strengthening **surveillance** of human leptospirosis cases.
- Enhancing **laboratory capacity** in endemic regions.
- Raising **awareness** for early detection and treatment.
- Improving **inter-sectoral coordination** for outbreak detection, prevention, and control.

Major Activities & Achievements

- Advocacy for **better patient management facilities** in states.
- Training **Master Trainers** in leptospirosis case management.
- Strengthening laboratories through financial assistance to **five medical institutes** for diagnostic support.

Program for Prevention and Control of Leptospirosis (PPCL)

Leptospirosis is a significant health challenge in India, especially in coastal regions.

The Government of India initiated a **Pilot Project on Prevention and Control of Leptospirosis** during the XI Five-Year Plan.

The success of this pilot led to the launch of the **Programme for Prevention and Control of Leptospirosis** in the 12th Five-Year Plan.

Initially implemented in Gujarat, Kerala, Tamil Nadu, Maharashtra, Karnataka, and the Andaman & Nicobar Islands.

Expanded to include Uttar Pradesh, Assam, Goa, and the UTs of Dadra Nagar Haveli, Daman & Diu.

Currently, the program covers **10 States/UTs** across **114 districts**, approved under **SFC for FY 2021-22** under **Scheme F of the NCDC Umbrella Scheme**.

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Programme for Prevention and Control of leptospirosis

Objective

- Reduce **morbidity and mortality** due to Leptospirosis.

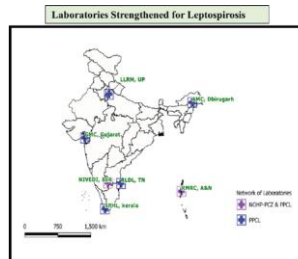
Key Components

- **Training** manpower for diagnosis, case management, prevention, and inter-sectoral coordination.
- **Strengthening surveillance** of Leptospirosis in humans.
- **Enhancing laboratory diagnostic capacity** in endemic states.
- **Raising awareness** for early detection and treatment.
- **Inter-sectoral coordination** at state and district levels for

outbreak detection, prevention,
and control.

Major Activities & Achievements

- **Advocacy** for improved patient management facilities in states.
- **Training of Master Trainers** on case management.
- **Laboratory strengthening** through financial assistance to 5 **medical institutes** for **Leptospirosis** diagnosis.



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Notes

This image shows a single page from a notebook or ledger. The page is white and features approximately 20 evenly spaced horizontal grey lines. There are no margins, text, or other markings on the page.

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Annexure – 1: Steps of the Outbreak Investigation

Leptospirosis is a zoonotic disease caused by bacteria of the genus *Leptospira*. The disease is primarily transmitted through contact with water, soil, or food contaminated by the urine of infected animals. Outbreaks are most common in tropical and subtropical regions, especially after flooding or heavy rainfall. In humans, the disease can range from mild, flu-like symptoms to more severe forms, including jaundice, kidney damage, or even death.

Step 1: Detecting and Verifying the Outbreak

Detection of the outbreak starts with noticing an abnormal increase in the number of reported cases of leptospirosis. This is typically done through routine surveillance or reports from community health workers, hospitals, or even media alerts. Community rumours or unusual case clusters are another red flag. Once suspected, health authorities must **verify the outbreak**.

- **Sources of outbreak detection:** Public rumours, media reports, healthcare institutions, and routine surveillance systems play vital roles in detecting outbreaks. Local health workers, such as Medical Officers (MO) at PHCs (Primary Health Centres), often verify reported cases.
- **Initial verification of the outbreak:** Contact the nearest healthcare facility to check if cases of fever, jaundice, or kidney dysfunction show epidemiological links, clustering in location or time, or other trigger events like heavy rainfall. The verification process may be initiated by the District Surveillance Officer (DSO) or other local health authorities.

Step 2: Formation of the Rapid Response Team (RRT)

Once the outbreak is verified, the **Rapid Response Team (RRT)** should be activated immediately. The RRT usually consists of an epidemiologist, a clinician, and a microbiologist. They are tasked with investigating the outbreak, confirming its cause, and implementing immediate control measures. Their composition, responsibilities, and coordination with local staff are crucial for effective outbreak management.

- **Team composition:**
 - *Epidemiologist:* Leads the epidemiological investigation and identifies sources, transmission routes, and at-risk populations.
 - *Clinician:* Conducts clinical examinations, reviews symptoms, and advises on treatment protocols.
 - *Microbiologist:* Oversees the collection and testing of samples.

The team must be fully prepared with necessary logistical support, including transport, laboratory supplies, and communication tools.

Step 3: Defining and Listing Cases

One of the first tasks of the RRT is to define what constitutes a case of leptospirosis in the current context. This is critical for ensuring accurate data collection and consistency during the investigation. The team should develop a **line-listing** of all cases, which includes:

- **Basic demographic information:** Age, sex, occupation, and location of patients.
- **Exposure history:** Possible sources of contamination (e.g., contact with contaminated water).
- **Clinical features:** Symptoms like fever, conjunctival suffusion, jaundice, muscle aches, and more severe signs such as renal failure and pulmonary haemorrhage.
- **Laboratory results:** Confirmation through serological tests (e.g., detecting IgM antibodies) or isolation of *Leptospira* in samples.

•

Step 4: Epidemiological Investigation

The epidemiological investigation aims to trace the origin of the outbreak, identify high-risk populations, and track the transmission pathways. This process involves the following:

- **Case investigation:** Collect detailed information on individual cases. For leptospirosis, this typically involves assessing contact with potentially contaminated water sources during activities like swimming, working, or during natural disasters such as floods.
- **Environmental sampling:** Investigators may take samples from suspected water sources to test for *Leptospira* contamination. Chlorination levels and water quality are also assessed during this stage.
- Conduct a risk factor analysis based on common activities, geographical locations, and possible contamination points.

Step 5: Laboratory Investigation

Laboratory confirmation is essential to identifying the causative organism. Blood, urine, or cerebrospinal fluid samples are commonly collected for diagnosis. The microbiologist is responsible for advising on which samples to collect, the mode of transportation, and ensuring they reach appropriate laboratories for processing.

- **Sampling protocol:** In outbreaks, samples from the first 10 cases may be sufficient to confirm leptospirosis, minimizing the burden on laboratory resources.
- **Transporting samples:** Samples should be transported in a cold chain to ensure the viability of *Leptospira* until testing is completed.

Step 6: Formulating A Hypothesis

Once enough information is gathered from epidemiological and laboratory investigations, the RRT should formulate a **provisional hypothesis**. The hypothesis addresses the following questions:

- What is the **causal agent**?
- What was the **source of infection** (e.g., contaminated water)?
- What was the **transmission pattern**?
- Who are at **highest risk**?

If the hypothesis is consistent with the findings, specific control measures can be implemented. Otherwise, further analytical studies, such as case-control studies, may be needed.

Step 7: Implementing Immediate Control Measures

Control measures for leptospirosis should be **immediate** and **targeted**. Some of the general interventions include:

- **Public health education:** Inform the population about the risks associated with contaminated water and advise them on protective behaviours such as avoiding standing water and using personal protective equipment (e.g., boots).
- **Water management:** Decontaminate identified water sources, ensure safe water supply, and increase sanitation efforts. Chlorination is a key intervention in affected areas.
- **Isolation of cases:** Severe leptospirosis cases may require hospitalization to manage complications such as renal failure.

In areas with high morbidity or where there is a lack of safe drinking water, temporary water supply measures or mass prophylaxis may be recommended.

Step 8: Monitoring and Containment

Active monitoring of the outbreak is crucial to assess whether control measures are effective. Monitoring includes:

- **Daily trend analysis:** Keep track of new cases, hospital admissions, and deaths.
- **Assessing containment strategies:** Determine the effectiveness of measures such as water sanitation and public health messaging.

Regular feedback should be given to local authorities to ensure that containment efforts are being implemented correctly. In addition, special attention should be paid to high-risk populations.

Step 9: Declaring the Outbreak Over

The outbreak can only be declared over when there have been **no new cases for two incubation periods** following the last confirmed case. For leptospirosis, this could be anywhere from 14 to 28 days. During this time, **active case finding** should continue to prevent any missed cases from going unreported.

Step 10: Final Reporting and Post-Outbreak Evaluation

After the outbreak is officially declared over, the RRT must submit a **comprehensive final report**. The report should include:

- Detailed case summaries, including the demographics and clinical details of all confirmed cases.
- Epidemiological findings on the source, transmission routes, and risk factors.
- A timeline of outbreak progression and containment measures implemented.
-

The report should be reviewed to identify any gaps in the response and make recommendations for preventing future outbreaks.

Outbreak investigations, such as those for leptospirosis, not only help in controlling the current outbreak but also serve as valuable opportunities to strengthen the public health system. A review of response measures often reveals systemic weaknesses—such as inadequate surveillance or poor water management—that can be addressed to improve preparedness for future outbreaks.

The investigation should conclude with a series of **recommendations** that focus on improving water sanitation, enhancing community education, and bolstering epidemiological surveillance in flood-prone areas. This ensures that lessons learned from the outbreak are institutionalized and applied proactively in future scenarios.

Annexure – 2: Leptospirosis Case Investigation Form

Organization/Institution: _____

Date: __/__/____

Interviewer: _____

Interviewer Contact Number: _____

State/UT: _____

District: _____

Section 1: Demographic Information

1. Patient First Name: _____

2. Patient Surname: _____

3. Patient Contact Number: _____

4. Age: _____

5. Sex: M ☐ F ☐ Other ☐

6. Caste/Ethnicity (if applicable): _____

7. Residential Address (Village/Town/City): _____

8. State: _____

9. District: _____

10. Pin code: _____

11. Occupation: _____

12. Has the patient travelled within India or abroad in the last month?

Yes ☐ No ☐ Don't know ☐

- If yes, specify:

Location 1: _____ Arrival Date: __/__/____ Departure Date: __/__/____

Location 2: _____ Arrival Date: __/__/____ Departure Date: __/__/____

Section 2: Clinical Information

1. Date of Symptoms Onset: __/__/__

2. Did you visit a clinic or hospital since symptoms began?

Yes ☐ No ☐

- If yes, name of the physician/hospital: _____

3. Symptoms Experienced (tick all that apply):

- Fever ☐

- Chills ☐

- Headache ☐

- Jaundice ☐

- Muscle pain (myalgia) ☐

- Abdominal pain ☐

- Nausea ☐

- Vomiting ☐

- Diarrhea ☐

- Conjunctival redness ☐

- Hemorrhage ☐

- Breathing difficulty ☐

- Skin rash ☐

- Dark-coloured urine ☐

- Reduced urine output (oliguria/anuria) ☐

- Other (specify): _____

4. Did you take antibiotics in the last month?

Yes ☐ No ☐ Unknown ☐

- If yes, name of antibiotic: _____

5. Hospitalization details (if applicable):

- Date of Admission: __/__/__
- Date of Discharge: __/__/__
- Days of work missed due to illness: _____

6. Resolution of symptoms (if applicable):

- Yes ☐ No ☐
- Date of resolution: __/__/__

Section 3: Exposure History

GENERAL RISK FACTORS:

1. Were you walking barefooted in the last month?

Yes ☐ No ☐

2. Source of drinking water (tick one):

- Tap water ☐
- Borewell ☐
- Hand pump ☐
- Open well ☐
- Stream/river ☐
- Other (specify): _____

3. Presence of skin wounds or cuts in the past month:

Yes ☐ No ☐ Unknown ☐

ANIMAL EXPOSURE:

1. Do you have any domestic animals?

- Yes ☐ No ☐
- If yes, specify:
 - Dog ☐

- Cat ☐
- Cattle ☐
- Other (specify): _____

2. Were you in contact with animals in the last month?

Yes ☐ No ☐

- If yes, which animals? (Tick all that apply):

- Cows ☐
- Buffaloes ☐
- Goats/Sheep ☐
- Rats ☐
- Pigs ☐
- Other (specify): _____
- Type of contact (e.g., feeding, cleaning): _____
- Location of contact (tick one):
 - Home ☐
 - Farm ☐
 - Market ☐
 - Other ☐ (specify): _____

RECREATIONAL ACTIVITIES:

1. Have you been involved in any of the following activities in the last month (tick all that apply)?

- Swimming ☐
- Fishing ☐
- Boating ☐
- Farming ☐
- Walking in mud ☐

- Gardening ☐

- Other (specify): _____

2. Where were these activities conducted?

3. Did you ingest water during these activities?

Yes ☐ No ☐ Unknown ☐

FLOOD EXPOSURE:

1. Were you exposed to floodwaters in the last month?

Yes ☐ No ☐

- If yes, specify exposure:

- Walking through floodwater ☐

- Swimming in floodwater ☐

- Cleaning flood-affected areas ☐

- Exposure of open wounds to floodwater ☐

- Ingestion of water/food contaminated by floodwater ☐

- Date of flood exposure: __/__/__

- Location: _____

Section 4: Diagnostic Information

1. Did you provide any samples for testing (e.g., blood, urine)?

Yes ☐ No ☐

2. Test results (if available):

- Date of sample collection: __/__/__

- Test results: Positive ☐ Negative ☐ Pending ☐

- Laboratory name: _____

Section 5: Public Health Actions (To be Filled by the Investigating Team)

1. Was the patient provided health education on avoiding high-risk exposures?

Yes ☐ No ☐

2. Has the community been alerted about the outbreak?

Yes ☐ No ☐

3. Has water quality in the area been tested or chlorinated?

Yes ☐ No ☐

4. Additional public health measures taken:

NOTE TO FACILITATORS

This guide has been meticulously designed to enhance the understanding and expertise of doctors, veterinarians, paramedical staff, and laboratory personnel in dealing with Leptospirosis cases. Your role is crucial in ensuring the success of this training, so please follow these instructions carefully -

Familiarize Yourself with the Content

Thoroughly review all the materials provided in the Leptospirosis guide. This includes presentations, handouts, case studies and assessment tools.

Tailor the Training to Your Audience

Understand the professional backgrounds of your participants (doctors, veterinarians, paramedics, and lab personnel). Tailor your examples and discussions to make the training relevant to their specific roles.

Set Clear Objectives

Begin each session by clearly stating the objectives participants are expected to achieve by the end. This will give them a sense of direction and purpose throughout the training.

Create an Interactive Learning Environment

Encourage active participation and open discussions. Use real-world scenarios to prompt critical thinking and problem-solving.

Use Multimodal Techniques

Utilize a mix of teaching methods, such as presentations, group discussions and case-based learning. This will cater to different learning styles and keep participants engaged.

Encourage Questions

Welcome questions and create a safe environment for participants to seek clarifications. This fosters deeper understanding and engagement.

Provide Regular Feedback

Throughout the training, provide constructive feedback on participants' performance. This will help them identify areas for improvement and enhance their skills.

Summarize and Review

At the end of each module, summarize key points and takeaways. Conduct a brief review to reinforce learning before moving on to the next topic.

Assessment and Certification

Develop an assessment mechanism, such as quizzes, practical assessments, or case presentations. Issue certificates of completion to participants who meet the training requirements.

Adapt to Participants' Pace

Gauge the participants' pace of learning. Adjust the training speed, accordingly, ensuring that everyone can follow and grasp the content.

Facilitate Networking

Create opportunities for participants to interact and network with each other. This can lead to valuable knowledge exchange and collaboration.

Remember, your role as a trainer or facilitator is to guide participants through this comprehensive Leptospirosis training with expertise, enthusiasm, and a dedication to enhancing their professional skills. Your efforts will contribute to building a more capable and knowledgeable medical workforce prepared to handle Leptospirosis cases effectively.

Course Outline

It is imperative to underscore that the course outline harmonizes with the course schedule. Consequently, any modifications or adaptations made to the course schedule should be duly reflected in this course outline. This synergy between the schedule and the outline ensures consistency and alignment between training plans and their actual implementation.

Note: Make copies of the schedule, one for each participant and include in the training material bag.

TIME	TOPICS/ACTIVITIES	TRAINING/LEARNING METHODS	RESOURCES/MATERIALS
20 min	Welcome participants Facilitate introductions of participants Explore participants' expectations for the course	Open course with a word of welcome by organizers, lead trainers, etc. Facilitate the introductions of all participants and trainers. Explore participants' expectations for the course. Allow participants to freely explore their expectations. In the next session on review of the course objectives, address which expectations can be met and which cannot be met.	Prepare welcome sign, Name badges
20 min	Review course objectives and schedule. Review components of the guide	Review the course goals and objectives; the course design and expected outcomes; Review the course schedule, including starting and ending times and times for breaks and lunch; Review the materials to be used in the course and ensure that participants understand the use of course materials.	Copies of course schedule, one for each participant from Facilitators' Guide (FG). Full set of the guide: Facilitators' Guide (FG) Questionnaire
20 min	Assess participants' pre-course knowledge	Distribute the Pre-course Knowledge Assessment sheet to each participant. Ask them to answer each question. Allow 15 minutes for assessment. Immediately review the correct responses—Have participants grade the papers while the trainer reviews the correct answers with them and collect the papers after reviewing all the answers.	Pre-Training Quiz Sheet for each participant

4-5 hours	Presentation/ Discussion	Use the PowerPoint slides to present information	Power Point slides on the sessions planned as per agenda
20 min	Assess participants' post training knowledge	Distribute the Post Training Knowledge Assessment sheet to each participant. Ask them to answer each question. Allow 15 minutes for the Post Training Knowledge Assessment.	Copies of Post Training Knowledge Assessment Sheets (one for each participant)
15 min	Course Evaluation	Ask questions of the participants and engage them in the presentation of the information.	
15 min	Closing	Closing remarks by training organizers. Distribute certificates to participants.	Certificate for each participant

PRE/POST TRAINING QUIZ

Instructions for the trainer:

- The trainer/instructor will administer the test before the training and collect the response.
- The same test will be given to the trainee after the completion of the training.
- The difference in scores will be recorded for training evaluation purpose.

Trainee Name:

Date: _____

Designation:

Test taken before the training (yes/no):

Test taken after the training (yes/no):

Instructions for the trainee:

- The test quiz carries 30 questions
- Attempt all the questions.
- Put a tick mark on the correct option or fill the blanks with True/ False
- Please check whether all questions are answered before submitting

1. What is the primary mode of transmission of leptospirosis?

- A) Airborne droplets
- B) Water or soil contaminated with urine
- C) Direct person-to-person contact
- D) Ingestion of undercooked meat

2. A 35-year-old man from Mumbai presents with high fever, chills, and muscle pain after working in a flooded area. What is the most likely causative agent?

- A) *Bacillus anthracis*
- B) *Leptospira interrogans*
- C) *Yersinia pestis*
- D) *Rickettsia rickettsii*

3. In which of the following environments is leptospirosis transmission most likely to occur?
- A) Arid deserts
 - B) Snow-covered regions
 - C) Tropical and subtropical areas
 - D) Urban skyscrapers
4. What is the incubation period for leptospirosis?
- A) 13 days
 - B) 514 days
 - C) 1521 days
 - D) 3045 days
5. Which serovar of *Leptospira* is most commonly associated with severe disease and jaundice?
- A) *L. canicola*
 - B) *L. icterohaemorrhagiae*
 - C) *L. pomona*
 - D) *L. hardjo*
6. A farmer presents with conjunctival suffusion, severe headache, and myalgia after working in rice fields during the rainy season. What is the probable diagnosis?
- A) Dengue Fever
 - B) Scrub Typhus
 - C) Leptospirosis
 - D) Malaria
7. Which population is at increased risk of contracting leptospirosis due to occupational exposure?
- A) Office workers
 - B) Sewage workers
 - C) Retail employees
 - D) Teachers

8. What is the most significant consequence of untreated severe leptospirosis?

- A) Mild fever
- B) Acute renal failure
- C) Skin rashes
- D) Headache

9. A 60-year-old patient with a history of diabetes presents with hypotension, hemoptysis, and altered consciousness. What should be the first step in management?

- A) Administer antibiotics
- B) Refer to a tertiary care centre
- C) Start fluid resuscitation
- D) Perform imaging studies

10. Which diagnostic test is considered the gold standard for confirming leptospirosis?

- A) Serology
- B) PCR
- C) Blood culture
- D) MAT

11. During an outbreak investigation, a health officer notes a spike in leptospirosis cases following heavy rainfall. What ecological factor is likely contributing to this increase?

- A) Increased rodent activity
- B) Decreased animal populations
- C) Higher temperatures
- D) Improved sanitation

12. What is the recommended treatment for a suspected case of leptospirosis in a pregnant woman?

- A) Doxycycline
- B) Amoxicillin
- C) Ampicillin
- D) Tetracycline

13. In rural India, which animal is considered the primary reservoir for leptospirosis?
- A) Cattle
 - B) Dogs
 - C) Rats
 - D) Goats
14. A patient presents with hematuria, jaundice, and renal failure. What is the most likely diagnosis?
- A) Hepatitis
 - B) Leptospirosis
 - C) Glomerulonephritis
 - D) Acute renal injury
15. Which laboratory finding is typical in a case of leptospirosis?
- A) Elevated liver enzymes
 - B) Low white blood cell count
 - C) Decreased serum creatinine
 - D) Normal electrolytes
16. In an outbreak setting, what is the purpose of health education campaigns?
- A) To enforce quarantine
 - B) To raise awareness and promote preventive measures
 - C) To conduct mass vaccinations
 - D) To improve sanitation infrastructure
17. A traveller from a tropical region develops fever and muscle pain shortly after returning home. Which action is most appropriate?
- A) Wait for symptoms to resolve
 - B) Seek immediate medical attention
 - C) Self-medicate with over-the-counter drugs
 - D) Report to public health authorities

18. What is the impact of climate change on leptospirosis transmission?
- A) Decreased incidence
 - B) Increased incidence due to changing rainfall patterns
 - C) No impact
 - D) Only affects urban areas
19. In managing a severe case of leptospirosis with multiorgan failure, what is a key intervention?
- A) Oral hydration
 - B) Dialysis
 - C) Antipyretics
 - D) Nutritional support
20. Which of the following best describes the recovery phase in leptospirosis?
- A) Complete absence of symptoms
 - B) Persistent fatigue and myalgia
 - C) Rapid deterioration of health
 - D) Return to baseline function
21. A patient with leptospirosis shows signs of acute respiratory distress syndrome (ARDS). What management strategy is crucial?
- A) Initiate oral antibiotics
 - B) Provide mechanical ventilation
 - C) Administer antihistamines
 - D) Increase fluid intake
22. Which method is least likely to contribute to the prevention of leptospirosis?
- A) Rodent control measures
 - B) Chemoprophylaxis during high-risk periods
 - C) Vaccination of humans
 - D) Public awareness campaigns

23. A 28-year-old man presents with acute renal failure after being exposed to floodwaters. What is the recommended antibiotic treatment?

- A) Doxycycline
- B) Benzylpenicillin
- C) Erythromycin
- D) Ampicillin

24. In which of the following cases would you suspect leptospirosis over other febrile illnesses?

- A) Patient with severe abdominal pain and diarrhea
- B) Patient with myalgia and conjunctival suffusion
- C) Patient with respiratory symptoms and fever
- D) Patient with generalized rash and fever

25. What is a common complication associated with severe leptospirosis?

- A) Myocardial infarction
- B) Acute pulmonary hemorrhage
- C) Chronic obstructive pulmonary disease
- D) Chronic kidney disease

26. Which symptom would most likely prompt a healthcare provider to suspect leptospirosis in a febrile patient?

- A) Fever and vomiting
- B) Severe headache and myalgia
- C) Cough and chest pain
- D) Rash and joint pain

27. What is the typical case fatality rate (CFR) range for leptospirosis?

- A) <1%
- B) 15%
- C) 50%
- D) 25%

28. In terms of geographical distribution, where is leptospirosis most prevalent?

- A) Cold climates
- B) Arid regions
- C) Tropical and subtropical regions
- D) Temperate zones

29. Which characteristic symptom is often associated with severe leptospirosis?

- A) Abdominal cramping
- B) Jaundice
- C) Fatigue
- D) Cough

30. During the recovery phase of leptospirosis, which symptom may persist for weeks to months?

- A) High fever
- B) Hemorrhagic manifestations
- C) Myalgia
- D) Acute renal failure

ANSWER KEY

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