

The human disease leptospirosis

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Leptospirosis: A Neglected Disease

- World most widespread and prevalent zoonotic disease
- Largely under-recognized and under-reported
- 500 000 cases of severe leptospirosis each year (WHO)
- Case-Fatality rate: <5 to 30% (WHO)
- Not yet in the WHO list of NTD
- Lepto: Even more neglected than Neglected Diseases







Clinical manifestations are highly variable

- The majority of cases go unrecognized as the most common presentation is a febrile illness for which medical attention is not called for.
- Typically the disease falls into one of four categories
 - A mild, influenza-like illness
 - Weil's syndrome characterized by jaundice, renal failure, haemorrhage and myocarditis with arrhythmias
 - Meningitis/meningoencephalitis
 - Pulmonary haemorrhage with respiratory failure





Signs and symptoms

CLINICAL MICROBIOLOGY REVIEWS, Apr. 2001, p. 296–326 0893-8512/01/\$04.00+0 DOI: 10.1128/CMR.14.2.296–326.2001 Copyright © 2001, American Society for Microbiology. All Rights Reserved.

Leptospirosis

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TABLE 7. Signs and symptoms on admission in patients with leptospirosis in large case series

Symptom	% of patients								
	China, 1955 (115), n = 75	Puerto Rico, 1963 (18), n = 208	China, 1965 (615), n = 168	Vietnam, 1973 (61) n = 150	Korea, 1987 (442), n = 93	Barbados, 1990 (177), n = 88	Seychelles, 1998 (660), <i>n</i> = 75	Brazil, 1999 (332), n = 193	
Jaundice	72	49	0	1.5	16	95	27	93	
Anorexia	92	a	46		80	85	2007 		
Headache	88.5	91	90	98	70	76	80	75	
Conjunctival suffusion	97	99	57	42	58	54		28.5	
Vomiting	51	69	18	33	32	50	40	(1970) 1970	
Myalgia	100	97	64	79	40	49	63	94	
Arthralgia	51		36		3 <u>1</u> 3	2 <u>000</u>	31		
Abdominal pain	31		26	28	40	43	41		
Nausea	56	75	29	41	46	37			
Dehydration	10 <u></u>		1 <u>1111</u> 2	<u></u> 22		37			
Cough	55	24	57	20	45	32	39		
Hemoptysis	37	9	51		40		13	20	
Hepatomegaly	83	69	28	15	17	27			
Lymphadenopathy	19	24	49	21		21	<u>11 - 1</u> 2	<u>12 - 1</u> 2	
Diarrhea	30	27	20	29	36	14	11		
Rash	0	6		7	×	2		—	

^a —, symptom not recorded.

Vol. 14, No. 2

Atypical presentations

Journal of Infection (1993) 27, 281-283

CASE REPORT

Leptospirosis presenting as atypical pneumonia, respiratory failure and pyogenic meningitis

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Atypical Presentation of Leptospirosis

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Abstract

Leptospirosis, a disease of protean manifestations occurs sporadically throughout the year with a peak seasonal incidence during the rainy season. We hereby present a case that had clinical features of nephrotic syndrome with massive proteinuria. Leptospirosis was detected on ELISA testing. Patient was cured with antibiotics and diuretics.





Severe form

Case-Control study (71 severe vs 105 mild form) in New Caledonia, 2008-2011

Risk factors for severe leptospirosis:

Variable	OR (CI 95%)	p
Smoking	2,94 (1,45-5,96)	0,003
Sérogroup	1,41 (1,08-1,84)	0,011
Icterohaemorrhagiae		
Institution of antibiotic	2,78 (1,31-5,91)	0,008
> 2 days		





Pathogenesis

 Damage to the endothelial lining of small blood vessels by mechanisms that are still poorly understood











Leptospirosis Meeting, November 2011, Suva, Fiji



Virulence

- Virulence factors are poorly understood.
- Some serovars generally tend to cause mild disease and others severe disease (Icterohaemorrhagiae).
- No serovar-specific presentations of infection and any serovar may cause mild or severe disease in different hosts.
- Old age and multiple underlying medical problems are often associated with more severe clinical illness and increased mortality.
- The infection dose may also have an influence on the course of leptospirosis.





Recovery and Sequelae

- Most patients recover completely
- But recovery may take months or even years
- Late sequelae :
 - Chronic fatigue
 - Neuropsychiatric symptoms (headache, paresis, paralysis, mood swings, depression)
 - Uveitis and iridocyclitis



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When should clinicians consider the diagnosis of leptospirosis

- In any patients presenting with an abrupt onset of fever, chills, conjonctival suffusion, headache, myalgia and jaundice
- Diagnosis more difficult when patients present symptoms of cough, dyspnoea, nausea, vomiting, abdominal pain, diarrhoea, arthralgias, skin rash
- Conjonctival suffusion and muscle tenderness, most notable in the calf and lumbar areas, are the most distinguishing symptoms
- Suspicion is further increased if there is a history of occupational or recreational exposure to infected animals or to an environment potentially contaminated with animal
- urine





Differential diagnosis

- Influenza
- Dengue and dengue haemorrhagic fever;
- Hantavirus infection, including hantavirus pulmonary syndrome or other respiratory distress syndromes
- Yellow fever and other viral haemorrhagic fevers
- Rickettsiosis
- Borreliosis
- Brucellosis
- Malaria
- Pyelonephritis
- Aseptic meningitis

- Chemical poisoning
- Food poisoning
- Typhoid fever and other enteric fevers
- Viral hepatitis
- Pyrexia of unknown origin (PUO)
- Primary HIV seroconversion;
- Legionnaire's disease
- Toxoplasmosis
- Infectious mononucleosis
- Pharyngitis.
- + chikungunya







Treatment

- Antibiotics treatment:
 - Severe cases: high doses of intravenous penicillin
 - Less severe cases: oral antibiotics such as amoxycillin, ampicillin, doxycycline, erythromycin
 - Ceftriaxone, cefotaxime and quinolone are also effective

Table 2. Current recommended antibiotics for the treatment of leptospirosis ¹⁴				
Antibiotic	Dose			
Doxycycline	100 mg oral twice daily			
Ceftriaxone	1 g IV once daily			
Cefotaxmine	1 g IV q6hr			
Benzylpenicillin	1.2 g IV q6hr			

- Supportive treatment and haemodialysis
 - Aggressive supportive care with strict attention to fluid and electrolyte balance is essential
 - Peritoneal or haemodialysis is indicated in renal failure









Immunization

- Vaccines are, in principle, suspensions of killed leptospires
- Protection is largely serovar-specific
- Protective antibodies are produced only against the serovars present in the particular vaccine used
- Protection is of relatively short duration, and boosting at regular intervals is necessary to maintain protective titres of antibodies.





Conclusion

Why is there a lack of recognition of leptospirosis

- Leptospirosis may present with a wide variety of clinical manifestations.
- It may also mimic many other diseases, e.g. dengue fever and other viral haemorrhagic diseases.
- The diagnosis is confirmed by laboratory tests, but these are not always available, especially in developing countries.
- For these reasons, leptospirosis is overlooked and underreported in many areas of the world.









FONDS PACIFIQUE



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 Tableau 2. Recommandations pour le traitement et la prophylaxie de la leptospirose (Adapté de réf.²⁰).

Indication	Antibiotique	Dosage	
Chimioprophylaxie	Doxycycline	200 mg PO 1 x/sem.	
Traitement de la leptospirose	Pénicilline G	1,5 million d'unités IV 4 x/j pendant 7 jours	
sévére*	Ceftriaxone	1 g IV 1 x/j pendant 7 jours	
	Ampicilline	0,5-1 g IV 4 x/j pendant 7 jours	
Traitement de la	Doxycycline	100 mg PO 2 x/j pendant 7 jours	
leptospirose non sévère	Amoxicilline	500 mg PO 4 x/j pendant 7 jours	
	Ampicilline	500-750 mg PO 4 x/j pendant 7 jours	

* Présence d'au moins un critère : ictère, insuffisance rénale aiguë, hèmorragie pulmonaire ou syndrome de dêtresse respiratoire aigu, hypotension persistante après remplissage adéquat.







Figure 1. Prototypic antibody response in Leptospirosis against time. Appropriate diagnostic testing for leptospirosis is dependent on accurate timing of infection



