POLICY RECOMMENDATIONS ON THE DIAGNOSIS, MANAGEMENT AND PREVENTION OF LEPTOSPIROSIS

I. On Screening and Diagnosis

1. **Leptospirosis should be suspected among patients with the following clinical manifestations/features:**
   a. acute fever of at least 2 days
   b. residing in a flooded area OR has high-risk exposure (defined as wading in floods and contaminated water, contact with animal fluids, swimming in flood water or ingestion of contaminated water with or without cuts or wounds)
   c. presenting with at least two of the following symptoms:
      - myalgia
      - calf tenderness
      - conjunctival suffusion
      - chills
      - abdominal pain
      - headache
      - jaundice
      - oliguria

   BASIS: Leptospirosis CPG 2010, p. 7

II. On Criteria for Hospital Admission

1. **Any suspected case of leptospirosis associated with the following is BEST managed in a HEALTHCARE / HOSPITAL SETTING**: [Grade A]
   a. unstable vital signs
   b. jaundice/icteric sclerae
   c. abdominal pain
   d. nausea, vomiting and diarrhea
   e. oliguria/anuria
   f. meningismus/meningeal irritation
   g. sepsis/septic shock
   h. altered mental states
   i. difficulty of breathing
   j. hemoptysis

   BASIS: as is, p. 10

2. **Suspected cases of leptospirosis with the following manifestations can be managed on an OUT-PATIENT SETTING**: [Grade A]
   a. stable vital signs
   b. anicteric sclerae
   c. with good urine output
   d. no evidence of meningismus / meningeal irritation
   e. no evidence of sepsis / septic shock
   f. no difficulty of breathing
   g. no jaundice
   h. can take oral medications

.

   BASIS: as is, p. 10

3. Leptospirosis may be classified according to the following:

Table 1. Classification of Leptospirosis

Mild	Moderate	Severe
fever		
headache		
myalgia		
nonproductive cough		
maculopapular rash		
stable vital signs	unstable vital signs	hypotension refractory to fluid resuscitation
no jaundice/anicteric sclerae	jaundice/icteric sclerae	
with good urine output	oliguria/anuria	renal failure
no evidence of meningismus / meningeal irritation	meningismus / meningeal irritation	
no evidence of sepsis / septic shock	sepsis / septic shock	
no difficulty of breathing	difficulty of breathing	
nausea, vomiting and diarrhea		
conjunctival suffusion (red eyes without exudate)		
Severe calf pain		
	abdominal pain	
	altered mental states	
	hemorrhage (most commonly pulmonary)	
		myocarditis

Clinical features associated with increased risk for mortality include altered mental status, respiratory insufficiency (rales, infiltrates), hemoptysis, oliguric hyperkalemic acute renal failure, and cardiac involvement (myocarditis, complete or incomplete heart block, atrial fibrillation).

BASIS: as is, p. 10

III. <u>On Laboratory Tests</u>

Generally, it is not necessary to confirm the diagnosis or wait for the result of the tests before starting treatment. The clinical assessment and epidemiologic history are more important. Early recognition and treatment is MORE important to prevent complications of the severe disease and mortality.

If definitive or confirmatory diagnosis is warranted in suspected cases, these are the locally available diagnostic tests for leptospirosis. Refer to Annex A for the local guidelines for collection and transport of specimens for leptospirosis.

1. Direct Detection Method

a. Culture and isolation - GOLD standard
b. Polymerase Chain Reaction (PCR) has the advantage of early confirmation of the diagnosis especially during the acute leptospiremic phase (first week of illness) before the appearance of antibodies.

2. Indirect Detection Methods

a. Microagglutination Test (MAT) - a four-fold rise of the titer from acute to convalescent sera is confirmatory of the diagnosis. In endemic areas like the Philippines, a single titer of at least 1:1600 in symptomatic patients is indicative of leptospirosis.

b. Specific IgM Rapid Diagnostic Tests like LeptoDipstick®, Leptospira IgM ELISA (PanBio), MCAT and Dridot® False negative results can be a problem if the tests are performed during the early stage of the illness. A second sample should be obtained for suspected cases with initial negative or doubtful results.

BASIS: as is, p. 13

Note: PhilHealth Standards and Monitoring Department (SMD) Consensus: LAATS (Leptospira Antigen-Antibody Agglutination Test) has no value in the confirmation of leptospirosis.

3. **The following are non-specific laboratory tests that can support the diagnosis of leptospirosis and can be used to alert the health practitioner to monitor for the development of complications**:

Table 2. Non-specific laboratory tests and corresponding findings

Laboratory test	Laboratory findings
Complete blood count (CBC) with platelet count	May show peripheral leukocytosis with neutrophilia. Thrombocytopenia is common. Platelet count of < 100,000/cu mm is a risk factor for bleeding and pulmonary hemorrhage. **Severe**: leucocytosis (WBC>12,000 cells/cumm) with neutrophilia and thrombocytopenia (<100,000 cells/cu mm)
Urinalysis	Shows proteinuria, pyuria, and often hematuria. Hyaline and granular casts may also be present during the first week of illness. Findings may sometimes be mistaken for UTI.
Serum creatinine	Can be initially normal and can elevate during the course of the illness. An increasing serum creatinine is indicative of impending acute kidney injury. **Severe**: > 3 mg/dL (or CrCl < 20 ml/min) and BUN > 23 mg/dL
Serum creatine phosphokinase (CPK-MM)	is elevated in patients with severe myalgia.
Liver function tests	Bilirubin, ALT, AST, and alkaline phosphatase may show slight elevation. **Severe**: AST/ALT ratio > 4x, Bilirubin > 190 umol/L
Bleeding parameters (Prothrombin time, partial thromboplastin time PTT)	May be prolonged. **Severe**: prolonged prothrombin time (PT) < 85%
Serum potassium	**Severe**: > 4 mmol/L
Arterial blood gas (ABG)	**Severe**: severe metabolic acidosis(ph< 7.2, HCO3 < 10) and hypoxemia (PaO2 < 60 mmHg, SaO2 < 90%, PF ratio <250)
Chest radiograph	**Severe**: demonstrating extensive alveolar infiltrates
Electrocardiogram	**Severe**: showing signs of heart block, myocarditis, repolarization Abnormalities

BASIS: as is, p. 25

IV. On Treatment

Table 3. Dosage of Antibiotics Recommended for Leptospirosis

Mild Leptospirosis		Moderate-Severe Leptospirosis	
Antibiotic	**Dosage**	**Antibiotic**	**Dosage**
First line agent			
doxycycline hydrochloride, hyclate	100mg bid PO	penicillin G*	1.5 MU q6-8h
Alternative agents			
amoxicillin	500mg q6h or 1g q8h PO	ampicillin IV	0.5-1.0 gm q6h
azithromycin dihydrate**	1 g initially, followed by 500 mg OD for 2 more days PO	azithromycin dihydrate	500 mg OD for 5 days
		ceftriaxone	1 gm q24h
		cefotaxime	1 gm q6h

Step-down therapy can be instituted once patient is clinically stable and able to tolerate oral medication. Any oral antibiotic under mild leptopspirosis can be selected.

** PNDF Vol. 1, 7th Ed. 2008 includes penicillin G benzathine 1.2MU vial and 2.4 MU vial; penicillin G crystalline 500,000 units vial, 1MU vial, and 5MU vial*

*** PNDF Vol. 1, 7th Ed. 2008 includes azithromycin 250 mg capsule,500 mg tablet,200 mg/5 mL powder for suspension, and 500 mg powder, vial as dihydrate*

Antibiotic therapy should be started as soon as the diagnosis of leptospirosis is suspected regardless of the phase of the disease or duration of symptoms. [Grade B]

BASIS: as is, p. 33

V. On Prophylaxis

1. Pre-exposure

The most effective preventive measure is avoidance of high-risk exposure (i.e. wading in floods and contaminated water, contact with animal's body fluid). If high risk exposure is unavoidable, appropriate personal protective measures include wearing boots, goggles, overalls, and rubber gloves. [Grade A]

Pre-exposure antibiotic prophylaxis is NOT ROUTINELY RECOMMENDED. However, in those individuals who intend to visit highly endemic areas AND are likely to get exposed (e.g. travelers, soldiers, those engaged in water-related recreational and occupational activities), pre-exposure prophylaxis may be considered for short-term exposures. [Grade B].

The recommended regimen for pre-exposure prophylaxis for non-pregnant, non-lactating adults is: Doxycycline (hydrochloride and hyclate) 200 mg once weekly, to begin 1 to 2 days before exposure and continued throughout the period of exposure. [Grade B]

Currently, there is NO recommended pre-exposure prophylaxis that is safe for pregnant and lactating women.

BASIS: as is, p. 36

2. Post exposure

Doxycycline (hydrochloride and hyclate) is the recommended post exposure chemoprophylactic agent for leptospirosis. The duration of prophylaxis depends on the degree of exposure and the presence of wounds. Individuals should continue to monitor themselves for fever and other flu-like symptoms and should continue to wear personal protective measures since antibiotic prophylaxis is not 100% effective. The decision to give prophylaxis depends on the risk exposure assessment.

2.1. LOW-RISK EXPOSURE is defined as those individuals with a single history of wading in flood or contaminated water without wounds, cuts or open lesions of the skin.

Doxycycline 200 mg single dose within 24 to 72 hours from exposure [Grade B]

2.2. MODERATE-RISK EXPOSURE is defined as those individuals with a single history of wading in flood or contaminated water and the presence of wounds, cuts, or open lesions of the skin, OR accidental ingestion of contaminated water.

Doxycycline 200 mg once daily for 3-5 days to be started immediately within 24 to 72 hours from exposure [Grade C]

2.3. HIGH-RISK EXPOSURE is defined as those individuals with continuous exposure (those having more than a single exposure or several days such as those residing in flooded areas, rescuers and relief workers) of wading in flood or contaminated water with or without wounds, cuts or open lesions of the skin. Swimming in flooded waters especially in urban areas infested with domestic/sewer rats and ingestion of contaminated water are also considered high risk exposures.

Doxycycline 200 mg once weekly until the end of exposure [Grade B]

BASIS: as is, p. 38

References (Search date: January 2012)

1. The Leptospirosis Task Force. Leptospirosis CPG, 2010
2. Standards and Monitoring Department Consensus. Philippine Health Insurance Corporation, 2012.

DISCLAIMER

These recommendations and restrictions were based on available evidence and may be modified based on the availability of new evidence. Furthermore, they should not replace good, up-to-date clinical judgment based on the present circumstances in each case.

All medicinal products mentioned in the policy statements have an inherent risk profile and have to be used with prudence and caution in the clinical setting. Medicines can cause unexpected and unwanted adverse drug effects and reporting these events to the Food and Drug Administration is recommended in line with public safety. The prescriber should read the product information carefully and help the patient understand these risks in relation to the benefits offered by these medicines. Medicines are safe when used in the proper way.

Annex A. Local guidelines for collection and transport of specimens for leptospirosis

Laboratory test	Specimen to be Collected	Best time to collect the specimen	Transport Requirements	Running Days	Turnaround Time	Where to send the specimen
Culture for leptospira	Blood in EDTA (purple top) Citrated blood (green top) CSF Urine	Blood, CSF within 7 days of illness Urine 2nd week to 4th week of illness	Blood, CSF – room temperature Urine - within 1 hr (protect from excessive heat or cold)	Daily except Saturday Sunday and holidays	6 weeks	1. Philippine General Hospital (PGH) Medical Research Laboratory (MRL) receiving counter 2nd floor, ER complex 2. Research Institute for Tropical Medicine (RITM) Microbiology Dept 9002 Research Drive, Filinvest Corporate City, Alabang, Muntinlupa
PCR for Leptospira	Blood in EDTA (purple top) Whole blood or serum (red top) CSF Urine	Blood, CSF within 7 days of illness Urine 2nd to 4th week	Chilled or with cold packs	Daily except Saturday Sunday and holidays	24-48 hours	RITM Microbiology Dept 9002 Research Drive, Filinvest Corporate City Alabang, Muntinlupa
Microscopic agglutination test (MAT for leptospirosis)	Blood or serum preferably collected twice at an interval of 10 days	> 1 week of illness	With ice if serum Room temperature if newly collected blood	Thursday	Thursday 3 pm	PGH-MRL receiving counter 2nd floor, ER complex
Lepto (IgM) card kit/*Dridot®*	Whole blood, serum or Plasma	> 1 week of illness	With ice	Daily Cutoff time: 3 pm	4 hours	The Medical City Pathology Laboratory
BioRad® macroscopic agglutination test	Serum	> 1 week of illness	With ice	Daily	2 minutes	St Luke's Medical Center Pathology Laboratory