Title: Public Health Reporting and National Notification for Leptospirosis

I. Statement of the Problem
Leptospirosis is considered a re-emerging disease, both among humans and animal species(1). Reports suggest an increasing incidence of human disease in the United States as well as a shift in affected groups(2, 3). Traditionally, leptospirosis has been considered an occupational disease; however, groups at risk have expanded to include urban children and recreationally exposed populations, such as adventure racers(1). Leptospirosis was on the CSTE Nationally Notifiable Conditions (NNC) list until 1994(4-6); due to increasing public health importance referenced below, this position statement proposes to restore leptospirosis to the CSTE NNC list.

II. Background and Justification
Leptospirosis is considered to be one of the most widespread zoonotic diseases in the world, with most cases occurring in warmer climates(7, 8). Leptospira, the causative bacterial agent of leptospirosis, are spread in the environment through the urine of infected animals, contaminating water or soil for weeks to months(7, 9). Leptospira organisms have been found in cattle, pigs, horses, dogs, rodents, and wild animals; animals carrying the bacterium may or may not exhibit signs of illness(7, 10). Infected animals may continue to excrete the bacteria into the environment continuously or sporadically for several years(7, 10). Domesticated canines can be maintenance hosts but can also be susceptible to leptospirosis, while rats are the most common carriers of leptospires and have high carriage rates(7, 10). Leptospirosis has been detected in newly identified host species, such as marine mammals on the Pacific coast of the United States, in the past decade (11).

Human infection may occur following direct contact with urine or other body fluids from an infected animal, or indirectly through contact with contaminated water, soil, or food. Leptospira may enter the body through mucous membranes or abraded skin(7, 8). Person to person transmission is rare.

Disease onset is typically two days to four weeks following exposure(7, 8). About 90% of infections are subclinical or self-limited mild disease(7, 8). Approximately 10% of infections, comprising the majority of recognized cases, are characterized by abrupt onset of fever, headache, muscle aches, vomiting, or diarrhea(7, 8). Cases may experience a biphasic illness, with a short recovery period after the first week of illness followed by more severe symptoms(7, 8). Approximately 10-15% of patients with clinical disease experience severe leptospirosis, a high-mortality syndrome with multi-organ involvement, such as kidney failure, liver failure, pulmonary hemorrhage, or meningitis(7, 8).

The disease has a seasonal occurrence; most cases are diagnosed in summer or fall in temperate climates, or during the wet season in tropical climates(7, 8). Many leptospirosis symptoms can be mistaken for other acute febrile illnesses, thus increased awareness of the disease and use of laboratory diagnostics are important to identify and treat cases.

Leptospirosis is confirmed by laboratory testing of a clinical specimen. The Microscopic Agglutination Test (MAT) is considered the gold standard confirmatory serologic diagnostic test, though MAT primarily detects IgG antibodies. Serum samples should be taken at least 10-14 days apart (acute and convalescent) to identify seroconversion and a confirmatory rise in titers.

Other diagnostic methods are available to diagnose leptospirosis, including isolation, immunofluorescence, darkfield microscopy, other serological tests, and real-time polymerase chain reaction (PCR). Isolation of leptospires from a clinical specimen is confirmatory, though it lacks sensitivity and growth may be slow. Immunofluorescence is a useful diagnostic measure when performed as immunohistochemistry for antigen detection in tissues (direct); however, it is typically performed on tissues obtained at autopsy. Darkfield microscopy is more timely relative to stage of disease; however, it lacks sensitivity and specificity.
Serology to detect IgM antibodies may produce false-positive results due to prolonged elevation of IgM, thus should be used in the context of an acute febrile illness. Real-time PCR of clinical specimens is highly sensitive and specific when the specimen is drawn during the associated clinical phase (e.g., blood: ≤4 days, urine: >7 days); availability of validated tests may be limited.

Antimicrobial drugs including doxycycline, penicillin, and other agents are effective treatments for leptospirosis. No human vaccines are licensed for use in the United States.

Annual incidence rates in the United States ranged from 0.02 to 0.04 per 100,000 population from 1985 through 1994(4, 6). From 1995-2010, 682 case notifications were sent to CDC from 31 of 36 states and territories where leptospirosis remained reportable; 69% were from Puerto Rico (CDC, unpublished data). There appears to be a trend of an increasing number of reported cases in some states. Hawaii has reported a significant increase in annual incidence from 1974 through 2008. The mean annual incidence from 1974 through 1998 was 1.29 per 100,000 with a significant temporal increase seen; the incidence continued to increase from 1.63 to 2.85 per 100,000 during 1999 through 2008(9, 10).

Some occupational groups remain at increased risk for leptospirosis(7, 8). Persons at risk of infection include those who work outdoors or with animals, for example, farmers, sewer workers, veterinarians, fishermen, aquaculturists, dairy farmers, and military personnel. In addition to occupationally-related disease, serosurveys have identified urban children as a risk group, and outbreaks have been identified among those involved in recreational activities in fresh water that may have been contaminated with animal urine. Other risk factors include exposure to wild or domestic animals, wet soil, standing water, or fresh water.

Recreational exposures have included rafting, kayaking, and swimming in fresh water within the United States and in temperate and tropical regions of the world. Since leptospirosis was removed as a NNC, a number of leptospirosis outbreaks have been identified both in the United States and in United States residents returning from a recreational event abroad. An outbreak in 1998 occurred among participants of triathlons in Illinois and Wisconsin(12). Participants were from 44 states and 7 countries; 90 participants met the case definition and 30 were laboratory-confirmed. Another outbreak occurred following an adventure race in Malaysia involving 26 laboratory-confirmed and 54 suspect cases; participants hailed from 27 countries, including the United States(13). In 2005, an outbreak of leptospirosis was identified among participants of an adventure race in Florida(2). Participants were from 32 states and Canada; 44 suspect and 14 laboratory-confirmed cases were identified.

During the 2009-2010 H1N1 influenza pandemic, a number of fatal leptospirosis cases were misdiagnosed as H1N1, and did not receive appropriate antimicrobial treatment for leptospirosis(14). Leptospirosis cases have also been misdiagnosed as dengue fever during dengue outbreaks in Puerto Rico; one study found 10 of 12 suspected dengue deaths were positive for leptospirosis, and 36 of 931 dengue-negative sera samples from suspect dengue cases were positive for leptospirosis(15). In 2010 in Puerto Rico, through enhanced surveillance for fatal dengue, the CDC’s Dengue Branch identified 25 leptospirosis deaths among 126 suspected dengue deaths (unpublished data). In the event of future influenza or dengue epidemics, leptospirosis cases presenting with acute-febrile illness may be misdiagnosed as viral infections, leading to unnecessary fatalities.

Leptospirosis was removed from the list of nationally notifiable conditions in the United States in 1994, although it remains reportable in 36 states and territories. It was removed from the NNC list for several reasons, including the lack of a reliable diagnostic test, underreporting, and the need to add emerging diseases to the NNC list without overburdening health care providers(3). There are multiple reasons of public health importance to reinstate leptospirosis as a NNC. These include the fact that the incidence appears to be increasing, new risk groups have been identified, there is potential for outbreaks to go unrecognized, and technology is no longer a limiting factor. Therefore, the reinstatement of leptospirosis as nationally notifiable is requested. National notification would provide the additional case data and isolate libraries to understand the epidemiologic profile of the disease in the United States, enable CDC to develop targeted education and prevention programs for the public and healthcare providers, enhance surveillance and data sharing between local and state health entities to emerging and re-emerging disease, and improve diagnostic methods.
III. Statement of the desired action(s) to be taken

1. Establish standard reporting and notification methods for leptospirosis and recommend that any State or Territory conducting surveillance for this condition use these standard methods.

2. CSTE recommends that States and Territories conducting surveillance according to these methods report case information to CDC.

3. CSTE recommends that CDC publish data on leptospirosis as appropriate in MMWR and other venues.

4. Leptospirosis should be added to the *Nationally Notifiable Conditions* List as a routinely notifiable condition.

IV. Goals of Surveillance
To provide information on the temporal, geographic, and demographic occurrence of leptospirosis to facilitate its prevention and control.

V. Methods for Surveillance: Surveillance for leptospirosis should use the following recommended sources of data and the extent of coverage listed in Table V.

Table V. Recommended sources of data for case identification and extent of coverage for ascertaining cases of leptospirosis.

<table>
<thead>
<tr>
<th>Source of data for case identification</th>
<th>Coverage</th>
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<tbody>
<tr>
<td></td>
<td>Population-wide</td>
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<tr>
<td></td>
<td>Sentinel sites</td>
</tr>
<tr>
<td>Clinician reporting</td>
<td>X</td>
</tr>
<tr>
<td>Laboratory reporting</td>
<td>X</td>
</tr>
<tr>
<td>Reporting by other entities (e.g., hospitals, veterinarians, pharmacies)</td>
<td>X</td>
</tr>
<tr>
<td>Death certificates</td>
<td></td>
</tr>
<tr>
<td>Hospital discharge or outpatient records</td>
<td>X</td>
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<tr>
<td>Extracts from electronic medical records</td>
<td>X</td>
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<tr>
<td>Telephone survey</td>
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<tr>
<td>School-based survey</td>
<td></td>
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<tr>
<td>Other</td>
<td></td>
</tr>
</tbody>
</table>

VI. Criteria for case identification
Reporting refers to the process of healthcare providers or institutions (e.g., clinical laboratories, hospitals) submitting basic information to governmental public health agencies about cases of illness that meet certain reporting requirements or criteria. The purpose of this section is to provide those criteria that should be used to determine whether a specific illness should be reported.

A. Narrative: A description of suggested criteria that may be for case ascertainment of a specific condition.
Report any illness to public health authorities that meets any of the following criteria:

1. A person with one or more of the following laboratory findings:
   - Isolation of *Leptospira* from a clinical specimen, or
   - Fourfold or greater increase in *Leptospira* agglutination titer between acute- and convalescent-phase serum specimens studied at the same laboratory, or
   - Demonstration of *Leptospira* in a clinical specimen by direct immunofluorescence, or
• *Leptospira* total agglutination titer of ≥ 800 by Microscopic Agglutination Test (MAT) in one or more serum specimens, or
• Detection of pathogenic *Leptospira* DNA (e.g., by PCR) from a clinical specimen.

2. A person with history of fever within the past two weeks and at least two of the following clinical findings: myalgia, headache, jaundice, conjunctival suffusion without purulent discharge, or rash (i.e. maculopapular or petechial); OR at least one of the following clinical findings:
   • Aseptic meningitis
   • GI symptoms (e.g., abdominal pain, nausea, vomiting, diarrhea)
   • Pulmonary complications (e.g., cough, breathlessness, hemoptysis)
   • Cardiac arrhythmias, ECG abnormalities
   • Renal insufficiency (e.g., anuria, oliguria)
   • Hemorrhage (e.g., intestinal, pulmonary, hematuria, hematemesis)
   • Jaundice with acute renal failure;

AND with one or more of the following laboratory findings:
• Demonstration of *Leptospira* in a clinical specimen by indirect immunofluorescence, or
• *Leptospira* total agglutination titer of > 200 but < 800 by Microscopic Agglutination Test (MAT) in one or more serum specimens after onset of symptoms, or
• Demonstration of *Leptospira* in a clinical specimen by darkfield microscopy, or
• Detection of IgM antibodies against *Leptospira* in an in acute phase serum specimen.

3. A person with history of fever within the past two weeks and clinical findings consistent with criteria 2 above AND involvement in an exposure event (e.g., adventure race, triathlon, flooding) with associated laboratory-confirmed cases.

4. A person whose healthcare record contains a diagnosis of leptospirosis.

5. A person whose death certificate lists leptospirosis as a cause of death or a significant condition contributing to death.

**Other recommended reporting procedures**
• All cases of leptospirosis should be reported.
• Reporting should be on-going and routine.
• Timeliness of reporting should follow the state health department’s routine schedule.

**Table VI-B. Table of criteria to determine whether a case should be reported to public health authorities**

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Reporting</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1,4,5</td>
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<tr>
<td><strong>Clinical Evidence</strong></td>
<td></td>
</tr>
<tr>
<td>History of fever &gt; 38.0°C (100.4°F) within two weeks</td>
<td>N</td>
</tr>
<tr>
<td>Myalgia</td>
<td>O†</td>
</tr>
<tr>
<td>Headache</td>
<td>O†</td>
</tr>
<tr>
<td>Jaundice</td>
<td>O†</td>
</tr>
<tr>
<td>Conjunctival suffusion without purulent discharge</td>
<td>O†</td>
</tr>
<tr>
<td>Rash (i.e., maculopapular or petechial)</td>
<td>O†</td>
</tr>
<tr>
<td>Clinical Symptoms</td>
<td>Laboratory Evidence</td>
</tr>
<tr>
<td>-------------------</td>
<td>---------------------</td>
</tr>
<tr>
<td>Aseptic meningitis</td>
<td>O</td>
</tr>
<tr>
<td>GI symptoms (e.g., abdominal pain, nausea, vomiting, diarrhea)</td>
<td>O</td>
</tr>
<tr>
<td>Pulmonary complications (e.g., cough, breathlessness, hemoptysis)</td>
<td>O</td>
</tr>
<tr>
<td>Cardiac arrhythmias, ECG abnormalities</td>
<td>O</td>
</tr>
<tr>
<td>Renal insufficiency (e.g., anuria, oliguria)</td>
<td>O</td>
</tr>
<tr>
<td>Hemorrhage (e.g., intestinal, pulmonary, hematuria, hematemesis)</td>
<td>O</td>
</tr>
<tr>
<td>Jaundice with acute renal failure</td>
<td>O</td>
</tr>
<tr>
<td>Healthcare record contains a diagnosis of leptospirosis</td>
<td>S</td>
</tr>
<tr>
<td>Death certificate lists leptospirosis as a cause of death or a significant condition contributing to death</td>
<td>S</td>
</tr>
</tbody>
</table>

**Laboratory Evidence**

- Isolation of *Leptospira* from a clinical specimen
- Fourfold or greater increase in *Leptospira* agglutination titer between acute- and convalescent-phase serum specimens
- Demonstration of *Leptospira* in a clinical specimen by direct immunofluorescence
- *Leptospira* total agglutination titer of $\geq 800$ by Microscopic Agglutination Test (MAT) in one or more serum specimens
- Detection of pathogenic *Leptospira* DNA (e.g., by PCR) from a clinical specimen
- Demonstration of anti-*Leptospira* antibodies in a clinical specimen by indirect immunofluorescence
- *Leptospira* total agglutination titer of $\geq 200$ but $< 800$ by Microscopic Agglutination Test (MAT) in one or more serum specimens after onset of symptoms
- Demonstration of *Leptospira* in a clinical specimen by darkfield microscopy
- Detection of IgM antibodies against *Leptospira* in an in acute-phase serum specimen

**Epidemiological Evidence**

- Involvement in an exposure event (e.g., adventure race, triathlon, flooding) with associated laboratory-confirmed cases

Notes:

- **S** = This criterion alone is sufficient to report a case
- **N** = This criterion in conjunction with all other “N” and any “O” criteria in the same column is required to report a case.
- **O** = At least one of these “O” (Optional) criteria in each category (e.g., clinical evidence and laboratory evidence) in the same column—in conjunction with all “N” criteria in the same column—is required to report a case.
- **O†** = At least two of these “O” criteria in each category (e.g., clinical presentation and laboratory findings) in the same column—in conjunction with all other “N” criteria in the same column—is required to report a case.

C. Disease-specific data elements

Disease-specific data elements to be included in the initial report are listed below.

**Clinical Information**

Clinical symptoms (mortality, severe manifestations (e.g., hemorrhage, jaundice, renal...
insufficiency, organ failure, meningitis)

Date of diagnosis
Hospitalization

**Laboratory Information**
Microbiological and serological data (serovar or serogroup, if known)

**Epidemiological Information**
Animal Exposures: Specify animal, contact type, and location
  - Wild or domestic animals (including zoo, abattoir, research, vet)
  - Animal products (e.g., excreta, hide, hair, bone, raw meat)
  - Animal bedding, stall material, food contact
Exposure to wet soil or vegetation
Exposure to standing water (e.g., flooding, puddles, runoff)
Occupation
Residence in low-income or congested housing
Residence in rural area
Recreational exposure (e.g., swimming, rafting, boating, fishing, farm, other)
Recent travel (destination, dates of travel)
Walk barefoot or in sandals

**VII. Case Definition for Case Classification**

**A. Narrative: Description of criteria to determine how a case should be classified.**

**Clinical presentation criteria**
An illness characterized by fever, headache, and myalgia, and less frequently by conjunctival suffusion, meningitis, rash, jaundice, or renal insufficiency. Symptoms may be biphasic.

Clinical presentation includes history of fever within the past two weeks and at least two of the following clinical findings: myalgia, headache, jaundice, conjunctival suffusion without purulent discharge, or rash (i.e. maculopapular or petechial); OR at least one of the following clinical findings:
- Aseptic meningitis
- GI symptoms (e.g., abdominal pain, nausea, vomiting, diarrhea)
- Pulmonary complications (e.g., cough, breathlessness, hemoptysis)
- Cardiac arrhythmias, ECG abnormalities
- Renal insufficiency (e.g., anuria, oliguria)
- Hemorrhage (e.g., intestinal, pulmonary, hematuria, hematemesis)
- Jaundice with acute renal failure

**Laboratory criteria**
Diagnostic testing should be requested for patients in whom there is a high index of suspicion for leptospirosis, based either on signs and symptoms, or on occupational, recreational or vocational exposure to animals or environments contaminated with animal urine.

**Confirmatory:**
- Isolation of *Leptospira* from a clinical specimen, or
- Fourfold or greater increase in *Leptospira* agglutination titer between acute- and convalescent-phase serum specimens studied at the same laboratory, or
- Demonstration of *Leptospira* in tissue by direct immunofluorescence, or
• *Leptospira* agglutination titer of \( \geq 800 \) by Microscopic Agglutination Test (MAT) in one or more serum specimens, or

• Detection of pathogenic *Leptospira* DNA (e.g., by PCR) from a clinical specimen.

**Probable/Presumptive:**

• *Leptospira* agglutination titer of \( \geq 200 \) but \(< 800 \) by Microscopic Agglutination Test (MAT) in one or more serum specimens, or

• Demonstration of anti-*Leptospira* antibodies in a clinical specimen by indirect immunofluorescence, or

• Demonstration of *Leptospira* in a clinical specimen by darkfield microscopy, or

• Detection of IgM antibodies against *Leptospira* in an in acute phase serum specimen.

**Criteria for epidemiologic linkage**

Involvement in an exposure event (e.g., adventure race, triathlon, flooding) with associated laboratory-confirmed cases.

**Case classification**

**Confirmed:**
A case with confirmatory laboratory results, as listed above.

**Probable:**
A clinically compatible case with at least one of the following:

- Involvement in an exposure event (e.g., adventure race, triathlon, flooding) with known associated cases, or

- Presumptive laboratory findings, but without confirmatory laboratory evidence of *Leptospira* infection.

**Table VII-B. Classification Tables:** Criteria for defining a case of leptospirosis

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Case Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical Evidence</strong></td>
<td></td>
</tr>
<tr>
<td>History of fever ( &gt; 38.0^\circ\text{C} , (100.4^\circ\text{F}) ) within two weeks</td>
<td>N \ N</td>
</tr>
<tr>
<td>Myalgia</td>
<td>O† \ O†</td>
</tr>
<tr>
<td>Headache</td>
<td>O† \ O†</td>
</tr>
<tr>
<td>Jaundice</td>
<td>O† \ O†</td>
</tr>
<tr>
<td>Conjunctival suffusion without purulent discharge</td>
<td>O† \ O†</td>
</tr>
<tr>
<td>Rash (i.e., maculopapular or petechial)</td>
<td>O† \ O†</td>
</tr>
<tr>
<td>Aseptic meningitis</td>
<td>O \ O</td>
</tr>
<tr>
<td>GI symptoms (e.g., abdominal pain, nausea, vomiting, diarrhea)</td>
<td>O \ O</td>
</tr>
<tr>
<td>Pulmonary complications (e.g., cough, breathlessness, hemoptysis)</td>
<td>O \ O</td>
</tr>
<tr>
<td>Cardiac arrhythmias, ECG abnormalities</td>
<td>O \ O</td>
</tr>
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<td>Renal insufficiency (e.g., anuria, oliguria)</td>
<td>O \ O</td>
</tr>
<tr>
<td>Hemorrhage (e.g., intestinal, pulmonary, hematuria, hematemesis)</td>
<td>O \ O</td>
</tr>
<tr>
<td>Jaundice with acute renal failure</td>
<td>O \ O</td>
</tr>
</tbody>
</table>

**Laboratory Evidence**
| Isolation of *Leptospira* from a clinical specimen | S |
| Fourfold or greater increase in *Leptospira* agglutination titer between acute- and convalescent-phase serum specimens | S |
| Demonstration of *Leptospira* in tissue by direct immunofluorescence | S |
| *Leptospira* total agglutination titer of \( \geq 800 \) by Microscopic Agglutination Test (MAT) in one or more serum specimens after onset of symptoms | S |
| Detection of pathogenic *Leptospira* DNA (e.g., by PCR) from a clinical specimen. | S |
| *Leptospira* total agglutination titer of \( \geq 200 \) but \( < 800 \) by Microscopic Agglutination Test (MAT) in one or more serum specimens after onset of symptoms | O |
| Demonstration of anti-*Leptospira* antibodies in a clinical specimen by indirect immunofluorescence | O |
| Demonstration of *Leptospira* in a clinical specimen by darkfield microscopy | O |
| Detection of IgM antibodies against *Leptospira* in an in acute phase serum specimen | O |
| **Epidemiological Evidence** | |
| Involvement in an exposure event (e.g., adventure race, triathlon, flooding) with known associated cases | N |

Notes:

S = This criterion alone is sufficient to report a case
N = This criterion in conjunction with all other “N” and any “O” criteria in the same column is required to report a case.
O = At least one of these “O” (Optional) criteria in each category (e.g., clinical evidence and laboratory evidence) in the same column—in conjunction with all "N" criteria in the same column—is required to report a case.
O† = At least two of these “O” criteria in each category (e.g., clinical presentation and laboratory findings) in the same column—in conjunction with all other “N” criteria in the same column—is required to report a case.

**VIII. Period of Surveillance**

Surveillance should be on-going.

**IX. Data sharing/release and print criteria**

- Notification to CDC of cases of confirmed and probable leptospirosis is recommended.
- Annual case data on leptospirosis is also summarized in the annual Summary of Notifiable Diseases.
- State-specific compiled data will be published in the weekly reports and annual MMWR Surveillance Summaries.
- The frequency of release of additional publications of these data will be dependent on the current epidemiologic situation in the country. These publications might include annual epidemiologic summaries in the MMWR or manuscripts in peer-reviewed journals.
- Aggregate case data will be shared with WHO as requested.
X. References


XI. Coordination

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