Diphtheria:

Report Immediately

Diphtheria

Disease Plan

Quick Links

✓ WHY IS DIPHTHERIA IMPORTANT TO PUBLIC HEALTH ......................... 2
✓ DISEASE AND EPIDEMIOLOGY ...................................................... 2
✓ PUBLIC HEALTH CONTROL MEASURES ........................................ 5
✓ CASE INVESTIGATION ..................................................................... 6
✓ REFERENCES .................................................................................. 10
✓ UT-NEDSS Minimum/Required Fields by Tab .................................. 11
✓ VERSION CONTROL ....................................................................... 12

Questions about this disease plan?

Contact the Utah Department of Health Bureau of Epidemiology: 801-538-6191.
WHY IS DIPHTHERIA IMPORTANT TO PUBLIC HEALTH

In the pre-vaccine era, diphtheria was recognized as one of the most common causes of illness and death among children. However, since the advent of the vaccine, diphtheria has been well controlled and is infrequently reported in the U.S. Although infrequently reported, public health remains vigilant for cases to control the spread of infection by the implementation of rapid chemoprophylactic interventions.

DISEASE AND EPIDEMIOLOGY

Clinical Description
Respiratory (toxigenic strains)
Diphtheria is caused by infection with toxigenic strains of gram-positive Corynebacterium diphtheriae. Important sites of infection are the respiratory mucosa (respiratory diphtheria) and the skin (cutaneous diphtheria).

Respiratory (nasal, pharyngeal, tonsillar, and laryngeal) diphtheria is typically caused by toxin-producing (toxigenic) strains of C. diphtheria. The respiratory form of the disease is characterized by the presence of a membrane that is usually visible over the tonsils or the throat. The membrane is not easy to remove. Initial symptoms of illness include a sore throat and low-grade fever. Swelling of the neck (“bullneck”) from soft-tissue inflammation can develop and is a sign of severe disease. The membrane may obstruct breathing and can be life threatening. Complications of diphtheria include myocarditis (inflammation of the heart) and nerve paralysis. The respiratory form of diphtheria usually lasts several days, and complications can persist for months.

Respiratory (non-toxigenic strains)
Nontoxigenic C. diphtheriae can also cause membranous pharyngitis; the disease is usually mild, but can lead to endocarditis. The isolation of C. diphtheriae from the throat does not necessarily indicate a pathogenic role in the illness. Although the frequency with which this occurs is unknown, a small percentage of the population may carry nontoxigenic or toxigenic strains of C. diphtheriae without disease symptoms. Respiratory disease caused by nontoxigenic C. diphtheriae should be reported as diphtheria.

Cutaneous
Cutaneous diphtheria, caused by either toxigenic or nontoxigenic strains, is usually mild, typically consisting of non-distinctive sores or shallow ulcers, and only rarely involving toxic complications (1–2% of infections with toxigenic strains). Since 1980, cutaneous diphtheria has not been a nationally reportable disease. Cutaneous diphtheria is not reportable.

Causative Agent
Diphtheria is caused by toxin-producing strains of Corynebacterium diphtheriae, a pleiomorphic, gram-positive, irregularly staining bacterium. Rarely, other Corynebacterium species (C. ulcerans
Diphtheria: Utah Public Health Disease Investigation Plan

or *C. psuedotuberculosis*) may produce diphtheria toxin and can cause classic diphtheria. Whether diphtheria bacteria produce toxin depends on infection by a virus bacteriophage carrying the *tox* gene. There are four strains, or biotypes, of *C. diphtheriae*: gravis, mitis, intermedius, and belfanti. Toxin-producing strains of all biotypes produce an identical exotoxin. There is no consistent difference in pathogenicity or severity of disease among the biotypes; however the order of their likelihood of producing toxin is: gravis, mitis, intermedius, and belfanti.

**Differential Diagnosis**

The primary diagnostic concern is to differentiate diphtheria from *Corynebacterium ulcerans*. This causes a disease that is clinically similar to *C. diphtheriae*. *C. ulcerans* is a zoonotic illness that can be transmitted from dairy animals and other pets. *C. ulcerans* is usually milder, but at least one report has identified *C. diphtheriae* toxins carried by *C. ulcerans*. Other pathogens can cause membranes in the respiratory tract, including *Streptococcus* species, Epstein-Barr virus, cytomegalovirus, *Candida*, and anaerobic organisms (Vincent's angina).

*C. ulcerans* infection in humans frequently has been associated with antecedent contact with farm animals or with consumption of unpasteurized dairy products; human-to-human transmission has not been documented.

**Laboratory Identification**

If diphtheria is strongly clinically suspected, treatment should begin prior to laboratory confirmation. However, laboratory diagnosis is essential for public health purposes.

**Culture**

Bacteriological culture is essential for determining biotype and toxigenicity of the diphtheria isolate. A clinical specimen for culture should be obtained as soon as possible when diphtheria (involving any site) is suspected, even if treatment with antibiotics has already begun (NOTE: only respiratory diphtheria is reportable). Specimens should be taken from the nose and throat and from the membrane. If possible, swabs also should be taken from beneath the membrane. After *C. diphtheriae* has been isolated, the biotype (substrain) should be determined. Only large reference laboratories are likely to be capable of culturing diphtheria. Because special media are required, laboratory personnel should be notified if *C. diphtheriae* is suspected. However, because isolation of *C. diphtheriae* is not always possible (many patients have already received several days of antibiotics by the time a diphtheria diagnosis is considered), and because of the extended time required for the test, PCR testing should always be performed for a faster result. For additional information on the collection of specimens for diphtheria testing, please see **Appendix 1: Collection of Specimens for Isolation of *C. diphtheriae* from the CDC’s Manual for the Surveillance of Vaccine-Preventable Diseases** at: [http://www.cdc.gov/diphtheria/downloads/dip-collection.pdf](http://www.cdc.gov/diphtheria/downloads/dip-collection.pdf).

**PCR**

Specimens for PCR should always be collected at the same time as specimens for culture. Because isolation of *C. diphtheriae* is not always possible (many patients have already received several days of antibiotics by the time a diphtheria diagnosis is considered), PCR can provide
additional supportive evidence for the diagnosis of diphtheria. PCR should not be used as a replacement for culture.

Serology
Serologic results do not provide a clear diagnostic answer. Therefore, serology is not the preferred method for diagnosis.

Submission of C. diphtheria isolates and other Corynebacterium species
All C. diphtheriae isolates should be sent to the CDC Diphtheria Laboratory for reference testing to determine whether the isolate is toxigenic or nontoxigenic, regardless of association with disease, and from any anatomic site. Although uncommon, other diphtheria toxin producing Corynebacterium species (e.g., C. ulcerans or C. pseudotuberculosis) may be isolated from patients. Such isolates should also be sent to the CDC Laboratory. The Utah Department of Health (UDOH) should be contacted to arrange for specimen shipping.

Treatment
If diphtheria is suspected, diphtheria antitoxin should be administered, even before laboratory confirmation. Antitoxin is available through the CDC and requires an approval process for distribution. The UDOH will assist with this process.

A test for sensitivity to diphtheria antitoxin should be carried out each time diphtheria antitoxin is administered. The recommended dosage and route of administration depend on the extent and duration of disease. Antitoxin is only available through an investigational new drug protocol through the CDC. Antibiotics are not a substitute for antitoxin. For more detailed information on antitoxin sensitivity testing and administration, please see the CDC’s Use of Diphtheria Antitoxin (DAT) for Suspected Diphtheria Cases (http://www.cdc.gov/diphtheria/dat.html).

Erythromycin orally or by injection (40 mg/kg/day; maximum, 2 gm/day) for 14 days, or procaine penicillin G (IM) (300,000 units/day for patients ≤10 kg and 600,000 units/day for patients >10 kg) for 14 days has been recommended until the patient can swallow comfortably, followed by oral penicillin V (250 mg four times daily) for a total treatment course of 14 days. Some erythromycin resistant strains have been identified, but they are uncommon and not a public health threat at this time. Newer macrolide antibiotics, including azithromycin and clarithromycin, do not offer any substantial advantage over erythromycin.

Case Fatality
The case fatality rate of 5–10% for respiratory diphtheria has changed little in 50 years. In recent epidemics in the former Soviet Union, the case-fatality rate ranged from 3–23%.

Reservoir
Humans are the only host of C. diphtheriae.

Transmission
Diphtheria is transmitted from person-to-person by respiratory droplets, or by direct contact with the nasopharyngeal secretions of an infected person. Contact with articles soiled with discharges
from cutaneous lesions of infected people can be a source of infection, but this has rarely been documented. Raw milk has served as a vehicle for transmission. Asymptomatic carriers are important in sustaining transmission.

**Incubation period**
Incubation period of diphtheria is 2–5 days (range: 1-10 days).

**Period of communicability**
In untreated persons, the infectious period begins at symptom onset and extends through two weeks after onset in the majority of patients (but may range up to six weeks after onset of symptoms). If patients are treated with antibiotics, communicability usually lasts less than four days. However, chronic carriage may occur, even after antimicrobial therapy. Patients are considered infectious until 2 successive nose and throat cultures (and cultures of skin lesions in cutaneous diphtheria), obtained ≥24 hours apart, and at least 24 hours after completion of antimicrobial therapy, are negative.

**Susceptibility**
Unimmunized and under-immunized individuals are susceptible. Infants born to immune mothers have passive protection, which is usually lost before the sixth month. Disease or unapparent infection usually, but not always, induces lifelong immunity.

**Epidemiology**
Infection can occur in immunized, partially immunized, and unimmunized persons. However, disease is usually less severe in those who are partially or fully immunized. Diphtheria is endemic in many parts of the world, including countries of the Caribbean and Latin America. The incidence of respiratory diphtheria is greatest in the fall and winter, but summer epidemics may occur in warm, moist climates, where skin infections are prevalent.

Most cases of diphtheria reported recently in the U.S. were related to importation. The last known case in Utah occurred in 1960. Since 2004, there have only been two cases reported in the U.S.

**PUBLIC HEALTH CONTROL MEASURES**

**Public health responsibility**
- Immediately contact the epidemiology program at the UDOH for assistance with obtaining laboratory confirmation and antitoxin.
- Investigate all suspect respiratory cases of disease, and fill out and submit appropriate disease investigation forms.
- Provide education to the general public, clinicians, and first responders regarding disease transmission and prevention, and alert them of any events of disease circulation.
- Assure early and appropriate treatment with diphtheria antitoxin and antibiotics.
- Assure appropriate laboratory confirmation is performed.
- Recommend routine immunization against diphtheria.
- Identify clusters or outbreaks of this disease.
Identify and evaluate contacts, and provide necessary antimicrobial prophylaxis to prevent further spread of the disease.

Prevention
The most effective control is widespread active immunization with diphtheria toxoid.

Chemoprophylaxis
Close contacts should be given (preferably) a 7-10 day course of erythromycin (PO, 40 mg/kg/day for children and 1 gram/day for adults) or a single dose of benzathine penicillin (IM) (600,000 units for persons under 6 years and 1.2 million units for persons 6 years or older). If close contacts are culture positive, treat them as patients, not contacts. Household contacts should be prophylaxed regardless of immunization status.

Vaccine
Diphtheria vaccine is complexed with acellular pertussis and tetanus toxoid, also known as DTaP. Immunization should be initiated in infancy. The first three doses are given at 4-8 week intervals beginning at 6-8 weeks of age; a fourth dose should be given 6-12 months after the third dose; and a fifth dose given at 4-6 years of age, prior to school entry. This dose is not necessary if the fourth dose is given at 4 years of age or later.

Adults should receive vaccine specifically formulated with reduced concentration of diphtheria toxoid (Tdap). Active protection for adults should be maintained by administration of this vaccine every 10 years.

Isolation and Quarantine Requirements
Isolation: Non-hospitalized patients with respiratory diphtheria, caused by toxigenic or non-toxigenic strains, and non-hospitalized patients with cutaneous diphtheria, caused by toxigenic strains, should be voluntarily isolated in their house until proven to be culture negative.

Hospital: In addition to standard precautions, use droplet precautions for respiratory diphtheria, and contact precautions for cutaneous diphtheria. Isolation measures should be continued until two negative cultures from both nose and throat are obtained (not less than 24 hours apart, and not less than 24 hours after completion of antibiotic therapy). When culture is impractical, isolation may end following 14 days of appropriate antibiotic therapy.

Quarantine: Adult contacts whose occupations involve handling food (especially milk) or close association with non-immunized children should be excluded from work until treated and bacteriological examinations prove them not to be cases or carriers.

CASE INVESTIGATION

Reporting
All suspected and confirmed cases of diphtheria should be immediately reported to public health.
Table 1: Table of criteria to determine whether a case should be reported

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Reporting</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical Evidence</strong></td>
<td></td>
</tr>
<tr>
<td>Acute respiratory illness</td>
<td>N N N</td>
</tr>
<tr>
<td>Membrane on the tonsil(s) or in the pharynx, larynx or nose</td>
<td>N N N</td>
</tr>
<tr>
<td>Diagnosis of possible diphtheria by a healthcare provider</td>
<td>N</td>
</tr>
<tr>
<td>Death certificate lists the condition as a cause of death or significant</td>
<td>S</td>
</tr>
<tr>
<td>condition contributing to death</td>
<td></td>
</tr>
<tr>
<td><strong>Laboratory Evidence</strong></td>
<td></td>
</tr>
<tr>
<td>Culture of <em>C. diphtheriae</em> from nares, pharynx, tonsil or larynx</td>
<td>N</td>
</tr>
<tr>
<td><strong>Epidemiologic Evidence</strong></td>
<td></td>
</tr>
<tr>
<td>Contact with a laboratory-confirmed diphtheria case</td>
<td>N</td>
</tr>
</tbody>
</table>

Notes:
S = This criterion alone is sufficient to identify a case for reporting.
N = All ―N criteria in the same column are necessary to identify a case for reporting.

Case Definition

Diphtheria (*Corynebacterium diphtheriae*) (CSTE, 2010)

Clinical Description
An upper respiratory tract illness characterized by an adherent membrane of the tonsil(s), larynx, pharynx, and/or nose.

Laboratory Criteria
- Isolation of *Corynebacterium diphtheriae* from the nose or throat, OR
- Histopathologic diagnosis of diphtheria

Case Classification

**Probable:**
In the absence of a more likely diagnosis, an upper respiratory tract illness with:
- an adherent membrane of the nose, pharynx, tonsils, or larynx; AND
- absence of laboratory confirmation; AND
- lack of epidemiologic linkage to a laboratory-confirmed case of diphtheria.

**Confirmed:**
An upper respiratory tract illness with an adherent membrane of the nose, pharynx, tonsil(s), or larynx, and any of the following:
- isolation of *Corynebacterium diphtheriae* from the nose or throat; OR
- histopathologic diagnosis of diphtheria; OR
- epidemiologic linkage to a laboratory-confirmed case of diphtheria.
Note: Only respiratory diphtheria is reportable. A person with suspected or culture confirmed cutaneous diphtheria should not be reported as diphtheria.

Classification Table

Table 2: Table lists the criteria that must be met for a case to be classified

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Confirm</th>
<th>Probable</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical Evidence</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adherent membrane of the nose, pharynx, tonsil(s), or larynx</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Acute respiratory illness</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>A more likely diagnosis other than diphtheria</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td><strong>Laboratory Evidence</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Culture of C. diphtheriae from nares, pharynx, tonsil or larynx</td>
<td>O</td>
<td>A</td>
</tr>
<tr>
<td>Histopathologic diagnosis of diphtheria</td>
<td>O</td>
<td>A</td>
</tr>
<tr>
<td><strong>Epidemiologic Evidence</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epidemiologic link to a laboratory-confirmed diphtheria</td>
<td>N</td>
<td>A</td>
</tr>
</tbody>
</table>

Notes:
N = All —N criteria in the same column are Necessary to classify a case.
A = This criterion must be absent (e.g., NOT present) for the case to meet the classification criteria.
O = At least one of these —O (Optional) criteria in each category (i.e., clinical evidence and laboratory evidence) in the same column—in conjunction with all —N criteria in the same column—is required to classify a case.

Case Investigation Process

All highly suspect cases of diphtheria warrant immediate action until they are shown not to be caused by toxigenic C. diphtheriae. Cases or carriers of toxigenic C. diphtheriae should be managed as follows:

- Local and state public health and the CDC should be immediately notified.
- Appropriate laboratory samples and preliminary clinical and epidemiologic information (including vaccine history) should be obtained.
- Presumptive treatment with antibiotics and antitoxin should be started.
- Strict isolation should be imposed until at least two cultures are negative 24 hours after antibiotics are discontinued.
- All case contacts should be identified and appropriately managed (explained in detail below).
- If case is not imported, the source of infection should be identified.

Outbreaks

A single case of diphtheria without any travel history will be considered an outbreak. Identify all close contacts and define population groups at specific risk and immunize. An epidemiologically-linked case is one in which the patient has had contact with one or more persons who have or had the disease, and transmission of the agent by the usual modes of transmission is plausible. A case
may be considered epidemiologically linked to a laboratory-confirmed case if at least one case in the chain of transmission is laboratory confirmed.

**Identifying case contacts**

Close contacts are defined as persons who have been within three feet (large droplet range) of the patient. This would typically include household members, persons who shared food, drink, or eating/drinking utensils with the patient, and healthcare workers in contact with the patient’s oral or respiratory secretions.Contacts that were in brief contact with the case, but who do not meet the definition for close contact, are not considered significant contacts.

**Case (close) contact management**

Close contact management is necessary for all cases of respiratory diphtheria, caused by toxigenic or non-toxigenic strains, and cutaneous diphtheria, caused by toxigenic strains.

- All close contacts should have cultures taken from their nose and throat and be kept under active surveillance for seven days, **regardless** of vaccination history.
- After culture, all close contacts should receive antibiotic prophylaxis with a single dose of benzathine penicillin G [IM] (600,000 units for children <6 years of age and 1.2 million units IM for individuals ≥6 years of age), or oral erythromycin (40mg/kg/day for children and 1g/day for adults) for 7-10 days.
- Previously immunized contacts should receive a booster dose of diphtheria toxoid if more than 5 years have elapsed since their last dose, and a primary series should be initiated in non-immunized contacts.
- Adult contacts whose occupations involve handling food (especially milk) or close association with non-immunized children should be immediately excluded from work until treated and culture results are negative.
- Treat any confirmed carrier with an adequate course of antibiotic, and repeat cultures at a minimum of two weeks to ensure eradication of the organism. Persons who continue to harbor the organism after treatment with either penicillin or erythromycin should receive an additional 10-day course of erythromycin and should submit samples for follow-up cultures.
- Contact tracing of cases with non-toxigenic cutaneous diphtheria is not necessary.
Centers for Disease Control, Case Definitions for Infectious Conditions Under Public Health Surveillance. MMWR 46 (RR-10), 1997.I.


UT-NEDSS Minimum/Required Fields by Tab

Demographic
- Age
- Area Code
- Birth Gender
- City
- County
- Date of Birth
- Ethnicity
- First Name
- Last Name
- Phone Number
- Race
- State
- Street
- Zip Code
- Name and location of school:

Clinical
- Clinician First Name
- Clinician Last name
- Date Diagnosed
- Date of Death
- Diagnostic Facility (DF)
- DF State
- DF City
- DF County
- Died
- Disease
- Was patient administered antitoxin?
- Onset Date
- Membrane on nose, pharynx, tonsils, or larynx*
- When did treatment start?

Laboratory
- Collection Date
- Lab
- Organism
- Result Value
- Name and location of activity:

- Test Result
- Test Type
- Units

Epidemiological
- Food Handler
- Imported From
- Other Data 1
- Other Data 2
- Did patient travel out of the country in the 30 days prior to onset?
- Were any of the countries known to have endemic disease?
- Did patient travel out of the U.S. in the 25 days before symptom onset?
- Dates and places of travel
- Epi-linkage to a laboratory-confirmed case
- Did patient have contact with any people who recently returned from a country with endemic or epidemic diphtheria? If so, what were the dates of exposure and what were the countries?
- History of vaccination for the indicated disease?
- Year of last known tetanus-diphtheria booster vaccine received
- What is the country of birth?

Contacts
- Does case have workplace contacts? If YES, please fill out contact information below.
- Name and location of workplace:
- Does the case participate in any extra-curricular activities?
Diphtheria: Utah Public Health Disease Investigation Plan

Reporting
- Date first reported to public health

Administrative
- LHD investigation/ intervention started
- State Case Status
- Outbreak Name
- Outbreak Associated

✔ VERSION CONTROL

1.02.16: Updated format as described in current protocol. Epidemiology section was updated to reflect current information. Treatment of cases and close contacts was updated to show current recommendations. Reporting and case classification criteria were changed to match CSTE guidelines.

02.26.16: Updated references and formatting.