Diphtheria

Signs and Symptoms	Diphtheria is a serious infection caused by toxigenic strains of *Corynebacterium diphtheriae*. It can infect any mucus membrane; symptoms of diphtheria depend on the body part that is affected. Early symptoms of toxigenic respiratory infection include malaise, sore throat, anorexia, and low-grade fever (less than 101°F). A bluish-white "pseudomembrane" forms and extends varying in size from covering a small patch on the tonsils to covering most of the soft palate. Non-toxigenic *C. diphtheriae* infections can still cause disease, including wound infections, bacteremia, and sometimes even a less serious respiratory illness. *Complications: pneumonia, myocarditis, endocarditis, neuritis, airway obstruction, septic arthritis, osteomyelitis, and death. The severity of symptoms correlates with the location and extent of the local disease*	
Incubation	For toxigenic diphtheria: 1 to 10 days; average 2 to 5 days.	
Case classification	**Clinical definition:** Upper respiratory tract illness with an adherent membrane of the nose, pharynx, tonsils, or larynx **OR** Infection of a non-respiratory anatomical site (e.g., skin, conjunctiva, ear, genital mucosa)	
	Confirmed case: meets clinical definition **AND** • isolation of toxin-producing *C. diphtheriae* from any anatomical site **OR** • epi-linked to a lab-confirmed case of diphtheria	**Suspected case:** meets clinical definition **AND** absence of laboratory confirmation **AND** lack of epi-linkage to a lab-confirmed case of diphtheria **OR** histopathologic diagnosis
Differential diagnosis	Pharyngitis, Infectious Mononucleosis, Oral Syphilis, Epiglottitis, Oral Candidiasis, Angioedema	
Treatment	Administration of Diphtheria Antitoxin (DAT) and antimicrobial therapy to kill the bacteria	
Laboratory	**Culture:** Clinical specimens for isolation and identification of *C. diphtheriae.* PHL performs this test. **Identification:** *C. diphtheriae* isolates can be confirmed using traditional biochemical methods at PHL. ***Tox* Gene PCR**: All C. diphtheriae isolates are required to be sent to PHL. They will be tested for the presence of the gene that is required to produce diphtheria toxin, and may require testing at CDC. (See Section 4.A.) Note: If *tox* gene is not detected, diphtheria is ruled out, but a positive *Tox* gene PCR result does not confirm diphtheria	
Public Health investigation	• Assess the likelihood of (toxigenic) diphtheria: confirm compatible clinical symptoms, verify vaccination and travel history. Assess exposure risk such as contact with a person with diphtheria or recent visit(s) to a health care facility. • Recommend immediate isolation of case (droplet precautions for suspected respiratory diphtheria and contact precautions for suspected cutaneous diphtheria) until diphtheria is ruled out, or 2 cultures taken at least 24 h apart and 24 h after antimicrobial therapy cessation are negative. • Consult with DOH CD Epi regarding the need for DAT, and specimen collection for confirmatory/toxigenicity testing. If indicated, treatment cannot be delayed until test results are received; presumptive action may be needed. • Recommend appropriate infection control precautions to prevent additional exposures in healthcare facilities, schools, and other public settings. • Identify close contacts and determine their immune status. Close contacts of a confirmed case should have cultures taken from nose and throat regardless immunization status or the presence of symptoms, and they should receive antimicrobial therapy. • Recommend vaccination for all cases during the convalescence period (disease does not always confer immunity), and for any close contact whose last dose was received more than 5 years ago. • **If the infection is non-toxigenic:** public health response is generally not required.	

Diphtheria

1. DISEASE REPORTING

A. Purposes of Reporting and Surveillance

1. To assist in the identification of cases.
2. To assure early and appropriate treatment with diphtheria antitoxin and antibiotics along with isolation to prevent transmission if needed.
3. To identify and evaluate contacts and recommend appropriate antibiotic prophylaxis and/or immunization to prevent further spread of the disease.
4. To alert public health authorities and health care providers to the presence of diphtheria in the community and the potential for additional infections, a particular concern given the large number of susceptible adults.

B. Legal Reporting Requirements

1. Health care providers and Health Care Facilities: **immediately notifiable to local health jurisdiction.**
2. Laboratories: *Corynebacterium diphtheriae* **immediately notifiable to local health jurisdiction**, submission required – isolate within 2 business days; submission on request – specimen associated with positive result, within 2 business days.
3. Local health jurisdictions: if respiratory or other toxigenic diphtheria is suspected, **immediately notifiable to the Washington State Department of Health (DOH) Office of Communicable Disease Epidemiology (CDE) at 877-539-4344 or 206-415-5500.**

C. Local Health Jurisdiction Investigation Responsibilities

1. Begin case investigation immediately. If the health care provider requests antitoxin, contact CDE to facilitate release of the biologic.
2. Facilitate the transport of specimens to assist with the diagnosis.
3. Assess the likelihood of toxigenic diphtheria.
4. Recommend measures to prevent further spread from the case.
5. Identify and evaluate contacts; educate and recommend measures to prevent further spread from contacts.
6. Report all *confirmed* and suspect cases (see Section 3C) to CDE. Complete the diphtheria case report form http://www.doh.wa.gov/Portals/1/Documents/5100/210-056-ReportForm-Diphtheria.pdf and enter the data into the Washington Disease Reporting System (WDRS).

2. THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent

Diphtheria is an acute bacterial disease caused primarily by toxin-producing strains of *Corynebacterium diphtheriae*, though other species of *Corynebacterium* may produce diphtheria toxin. Only detection of *C. diphtheriae* is notifiable in Washington State. The

toxin causes local tissue destruction and membrane formation. It primarily affects the tonsils, pharynx, nose and larynx. Other mucous membranes, skin, and rarely the vagina or conjunctivae can also be involved.

Susceptible persons may acquire toxigenic diphtheria bacilli in the nasopharynx. The organism produces a toxin that inhibits cellular protein synthesis and is responsible for local tissue destruction and formation of the pseudomembrane that is characteristic of this disease. The toxin produced at the site of the membrane is absorbed into the bloodstream and then distributed to the tissues of the body. The toxin is responsible for major complications such as myocarditis, polyneuropathies, nephritis, and thrombocytopenia.

Complications of diphtheria include pneumonia, myocarditis, neuritis, airway obstruction, septic arthritis, osteomyelitis, and death. The case-fatality rate for classic diphtheria is approximately 10%.

For clinical purposes, diphtheria can be classified according to the site of the infection:

1. **Pharyngeal and tonsillar diphtheria (faucial)**

   Pharyngeal and tonsillar diphtheria is the most common type of toxigenic infection (about 70% of cases). It initially presents with an insidious onset of malaise, sore throat, anorexia, and low-grade fever (usually under 102 F). At onset of symptoms, the pharynx is erythematous, but no membrane is present. About a day after onset, small patches of exudate appear in the pharynx. Despite the low-grade fever, patients usually appear quite ill and have tachycardia (“toxic appearance”). Within 2 or 3 days of onset, the patches of exudate spread and become confluent and may form a bluish-white pseudomembrane that can extend to the entire pharynx, including the nasopharynx, tonsillar areas, soft palate, and uvula. This membrane becomes grayish, thick, firmly adherent, and may have patches of green or black necrosis. Attempts to remove the pseudomembrane can cause bleeding.

   Enlargement and tenderness of the anterior cervical lymph nodes is common. With severe disease, patients can develop edema of the soft tissues in the anterior neck, giving a characteristic “bullneck” appearance, which can cause respiratory stridor and is associated with a higher morbidity and mortality.

   The severity of symptoms correlates with the location and extent of the membrane. In untreated patients, the membrane begins to soften about a week after onset and gradually detaches, usually in pieces. As the membrane detaches, acute systemic symptoms disappear. However, at any point during the course of the illness, if a significant amount of toxin is absorbed into the blood stream, patients may develop pallor and a rapid pulse which can progress to coma and even death.

2. **Laryngeal diphtheria**

   Laryngeal diphtheria occurs in about 25% of cases and is more likely to occur in children younger than 4 years. When the infection involves the larynx, it may occur either as an extension of the pharyngeal form, or as laryngeal involvement alone. Patients can present with fever, hoarseness, dyspnea, respiratory stridor, and a barking cough. In this form, also, the pseudomembrane can cause potentially fatal airway obstruction and a greater degree of toxin absorption if the membrane is extensive.

3. Anterior nasal diphtheria

Anterior nasal diphtheria usually presents with mucopurulent discharge from the nose, which may be bloody, and is often associated with a white pseudomembrane on the septum. External nares and upper lip may also be involved. Anterior nasal diphtheria as the only manifestation is uncommon (about 2% of cases).

The differential diagnosis of respiratory diphtheria (i.e. pharyngeal, laryngeal, anterior nasal) includes infection with other pathogens that can cause similar symptoms including: other Corynebacterium species, *Arcanobacterium haemolyticum*, as well as Streptococcus spp., Epstein-Barr virus and cytomegalovirus (both of which cause infectious mononucleosis syndrome). *Candida albicans*, syphilis, bacterial anaerobes (such as the organisms associated with Vincent's angina). Some viruses may cause a membrane of the throat and tonsils as well.

4. Cutaneous (skin) diphtheria

Cutaneous diphtheria, caused by toxin-producing *C. diphtheriae* is usually mild, typically consisting of indistinct sores or shallow ulcers. Toxigenic strains appear to result in less systemic complications compared to other forms of diphtheria.

Cutaneous diphtheria may act as a reservoir for transmission and result in respiratory or cutaneous infections in other susceptible hosts. Thorough cleansing of the lesion with soap and water and appropriate antimicrobial therapy are recommended.

Other possible sites of infection include the conjunctiva, vulvovaginal area, and external auditory canal. Severe disease is more likely to occur in people who are unimmunized or under immunized.

5. Carrier

In some people, infection with diphtheria-causing bacteria causes only a mild illness, or no obvious signs and symptoms at all. Infected people who are asymptomatic are known as carriers because they can spread the infection without being sick themselves.

6. Non-toxigenic *C. diphtheriae* infection

Non-toxin-producing (non-toxigenic) strains of *C. diphtheriae* have been increasingly isolated from wounds, blood, and respiratory sites. These non-toxigenic strains can cause an infection which is generally less severe and does not resemble diphtheria disease. Two forms of non-toxigenic *C. diphtheriae* are known to be present in the United States: non-toxigenic strains which lack the diphtheria toxin gene entirely, and *tox*-gene-bearing strains which do not produce toxin. The latter are known as Non-Toxigenic Tox gene-Bearing (NTTB) isolates. The two forms of non-toxigenic infection will have different testing outcomes at PHL, see section 4.

Wound infections are the most common source of non-toxigenic *C. diphtheriae* isolates. Typically, these wound cultures are polymicrobial, usually containing *Staphylococcus aureus*, *Streptococcus pyogenes*, or, frequently, both. The contribution of non-toxigenic *C. diphtheriae* to the wound infection is not clear at this time since *Corynebacterium* species may be present as commensal organisms, but

may also contribute to pathogenesis. Non-toxigenic respiratory infections have also been reported, associated with milder symptoms such as a sore throat and, rarely, membranous pharyngitis in the respiratory tract. Invasive illnesses, including bacteremia, septic arthritis, and endocarditis, have also been reported. Amputations and death have been reported as outcomes of severe disease.

An increase in non-toxigenic *C. diphtheriae* was first noted in Washington State in 2018, and a much larger, sustained increase began toward the end of 2021. Currently, over 100 *C. diphtheriae* isolates are reported and submitted to WA PHL per year. The last toxigenic infection was detected in 2017.

B. Reservoir

Humans

C. Modes of Transmission

Transmission is most often person-to-person spread from the respiratory tract. Rarely, transmission may occur from skin lesions or articles soiled with discharges from lesions of infected persons (fomites).

D. Incubation Period

The incubation period is usually 2–5 days (range, 1–10 days) for respiratory diphtheria.

E. Period of Communicability

Once infected, untreated persons can shed bacteria from the respiratory tract or from skin lesions for 2–6 weeks. Once an effective antibiotic has been initiated, persons are communicable for up to 4 days. Isolation should be maintained until two cultures have shown an absence of the organism (See Section 6.A.3). A carrier may shed organisms for 6 months or more, but effective antibiotic therapy eliminates shedding.

F. Treatment

The treatment for toxigenic diphtheria is prompt administration of diphtheria antitoxin (DAT). If toxigenic diphtheria is strongly suspected on the basis of clinical and epidemiologic findings, specimens for bacteriologic testing should be collected, then antitoxin given as soon as possible, without waiting for test results. Toxigenicity test results can take 2 weeks or longer to be finalized, so waiting for results before treatment is not possible.

CDC maintains a supply of DAT at Port Health Stations around the country, including the one located at SeaTac airport. DAT is currently available for treatment of respiratory diphtheria under an FDA-approved Investigational New Drug (IND) protocol. Since the antitoxin is of equine origin, a test to rule out hypersensitivity should be performed before administration. Antitoxin may only be administered in an inpatient environment.

Healthcare providers of a patient with suspected diphtheria should contact their local health jurisdiction immediately. The local health jurisdiction, in collaboration with DOH, will arrange a consultation with CDC, and subsequent transport of antitoxin if needed. For additional information regarding DAT, see: https://www.cdc.gov/diphtheria/hcp/dat/

There is a lack of information available to support recommendations for specific

antibiotics, so clinicians may use their best clinical judgement when selecting antibiotics. The currently recommended antibiotics for diphtheria are erythromycin or penicillin G because these are the only antibiotics with clinical evidence showing effectiveness *in vivo*; however, these studies were conducted decades ago, and CDC has reported that penicillin resistance is increasingly being identified in *C. diphtheriae*. The selection of antibiotics can be aided by antimicrobial susceptibility testing. Antibiotics must be initiated as soon as possible for the eradication of the organism, help limit the toxin released into the system, quicken the recovery phase in the patient, and prevent the spread of the infection to close contacts. In the case of antibiotic resistance, linezolid or vancomycin can be used.

Treatment of cutaneous toxigenic diphtheria with antibiotics is usually sufficient, so antitoxin is typically not needed.

Appropriate isolation precautions should remain in place until diphtheria is ruled out or until the patient is off antimicrobial treatment and tests culture-negative (See Section 6.A.3).

If not immunized, carriers should receive active immunization and measures should be taken to ensure completion of the immunization schedule. If a carrier has been immunized previously but has not received a booster of diphtheria toxoid within 5 years, a booster dose of age-appropriate vaccine should be administered.

Carriers of toxigenic strains should receive antimicrobial treatment. Two follow-up cultures should be performed after completing antimicrobial treatment to detect persistence of carriage, which occurs following erythromycin treatment in some cases. The first culture should be performed 24 hours after completing treatment. If results of cultures are positive, an additional 10-day course of oral erythromycin should be administered, and follow-up cultures should be performed again.

G. Immunity

A protective level of antitoxin (defined as greater than 0.1 IU of antitoxin/mL) is reached in more than 95% of vaccine recipients. Diphtheria toxoid-containing vaccine has been estimated to have an efficacy of 97%. After a primary series of 3 properly spaced doses of diphtheria toxoid-containing vaccines in infants and a booster dose at age 15 through 18 months or 3 properly spaced doses in adults.

Use of Tetanus Toxoid, Reduced Diphtheria Toxoid, and Acellular Pertussis Vaccines: Updated Recommendations of the Advisory Committee on Immunization Practices — United States, 2019 | MMWR (cdc.gov)

Diphtheria disease might not confer immunity. Unvaccinated or incompletely vaccinated persons recovering from diphtheria should begin or complete active immunization with diphtheria toxoid during convalescence.

3. CASE AND CONTACT DEFINITIONS

A. Clinical description

Classic (toxigenic) diphtheria is an upper-respiratory tract illness characterized by sore throat, low-grade fever, and an adherent pseudomembrane on the tonsil(s), pharynx, larynx, and/or nose. However, disease can involve almost any mucous membrane. For clinical purposes it is convenient to classify diphtheria depending on the site of disease:

- anterior nasal diphtheria

- pharyngeal and tonsillar diphtheria
- laryngeal diphtheria
- cutaneous (skin) diphtheria

B. Laboratory criteria for diagnosis

Confirmatory laboratory evidence:

- Isolation of *Corynebacterium diphtheriae* from a clinical specimen, AND
- Confirmation of toxin-production by Elek test or by another validated test capable of confirming toxin-production

Supportive laboratory evidence:

Histopathologic diagnosis of diphtheria

C. Case definition (2019)

1. Suspect: In the absence of a more likely diagnosis, an upper respiratory tract illness with each of the following:
   - 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;

   OR

   - Histopathologic diagnosis

2. Confirmed:
   - An upper respiratory tract illness with an adherent membrane of the nose, pharynx, tonsils, or larynx, and any of the following:
     - isolation of toxin-producing C. diphtheriae from the nose or throat, OR
     - epidemiologic linkage to a laboratory-confirmed case of diphtheria;

   OR

   - An infection at a non-respiratory anatomical site (e.g., skin, wound, conjunctiva, ear, genital mucosa) with isolation of toxin-producing *C. diphtheriae* from that site.

An epidemiologically linked case requires direct contact with a laboratory-confirmed case of diphtheria.

D. Comment

All *C. diphtheriae* isolates, regardless of association with disease, should be submitted to the Washington State Public Health Laboratories (PHL) for toxigenicity testing.

Rarely, respiratory diphtheria may result from infection with other *Corynebacterium* species (*C. ulcerans* or *C. pseudotuberculosis*). These bacteria, if isolated from someone

with a diphtheria-like illness, should also be forwarded to PHL as it is possible for them to produce diphtheria toxin, and they can be tested for toxigenicity.

4. DIAGNOSIS AND LABORATORY SERVICES

A. Diagnosis

The initial diagnosis of diphtheria should be based on the clinical presentation and epidemiologic risk factors because it is imperative to begin presumptive therapy quickly.

Culture and toxigenicity testing: Diphtheria is confirmed by isolation of *Corynebacterium diphtheriae* followed by toxigenicity testing. When diphtheria is suspected, the clinical laboratory receiving specimens for testing should be advised so that culture medium that provides a selective advantage for the growth of *C. diphtheria* can be used, if available.

When *C. diphtheriae* is submitted to PHL, the laboratory will run a *Tox* gene PCR assay to quickly determine if the gene required to produce diphtheria toxin is present. The PCR results can be interpreted as follows:

- If the *Tox* gene PCR test result is negative: the gene required to produce diphtheria toxin is not present; therefore, **diphtheria is ruled out**.
    - >99% of isolates since 2018 have lacked the *tox* gene entirely and are quickly ruled out with this single test.
- If the *Tox* gene PCR test result is positive: **toxigenicity has not yet been established**. The presence of the *Tox* gene does not necessarily indicate that the toxin is being produced. These isolates will be forwarded to CDC for the Elek Test: A culture-based functional test which shows whether the bacteria is actively producing toxin.
    - <1% of isolates since 2018 have been positive for the *tox* gene, but all of them have been shown to be non-toxigenic at CDC. These isolates are termed Non-Toxigenic *Tox* gene-bearing (NTTB) isolates.

Serologic testing: Serum antibody levels can assist with assessing the likelihood of the diagnosis whenever diphtheria is suspected. Specimens must be collected prior to the administration of DAT. When antibiotics were administered prior to collection of specimens for culture, health care providers should be strongly encouraged to obtain a serum specimen.

- Serum antibody levels less than 0.01 IU/ml – likely susceptible to diphtheria
- Serum antibody levels between 0.01–0.09 IU/ml – indicates basic immunity.
- Serum antibody levels ≥0.10 IU/ml – considered fully protective.

Testing for serum antibody levels is available at commercial laboratories.

B. Tests Available at Washington State Public Health Laboratories (PHL)

Upon receipt of a *C. diphtheriae* isolate, the PHL Special Bacteriology lab confirms the identification of *C. diphtheriae* isolates using matrix-assisted laser desorption/ionization-time-of-flight mass spectrometry (MALDI-TOF).

PHL can also perform the initial culture to see if *C. diphtheriae* is present in a clinical specimen. All requests for primary diphtheria culture to be done at PHL must have

approval from an CDE epidemiologist prior to specimen submission.

Toxigenicity testing is initiated at PHL through the use of a *Tox* gene PCR assay. If the *tox* gene is not present, toxigenicity is ruled out and diagnostic testing is complete for diphtheria. If the *tox* gene is detected, further testing is required at CDC before toxigenicity status is established—a delay will occur for these specimens to allow for shipment to CDC and further testing. Detection of the *tox* gene does **not** indicate that diphtheria toxin is being produced. Over 99% of *C. diphtheriae* isolates received since 2018 have lacked the *tox* gene entirely. See the above section for more information.

Note that PHL requires all clinical specimens have two patient identifiers, a name **and** a second identifier (e.g., date of birth) both on the specimen label and on the submission form. Due to laboratory accreditation standards, specimens will be rejected for testing if not properly identified. Include specimen source and collection date.

C. Specimen Collection

Information on specimen collection and submission instructions for *C. diphtheriae* culture and identification can be found at PHL Microbiology testing menu.

Culture specimens: Obtain a culture from the nose and throat of all persons with suspected diphtheria (nasopharyngeal swab preferred). If possible, swabs should also be taken from beneath the adherent pseudomembrane, and a portion of the pseudomembrane collected in a sterile container. For suspected cutaneous diphtheria, a swab of the infected area is the preferred specimen. Specimens for culture should be obtained as soon as diphtheria (involving any site) is suspected, even if treatment with antibiotics has already begun.

Clinical specimens should reach the PHL as quickly as possible after collection.

If no diphtheria isolate can be obtained from a patient receiving DAT, a clinical specimen should be sent to PHL for direct testing at CDC for the presence of the tox gene using PCR.

Collection of clinical specimens for isolation of *C. diphtheriae* from close contacts (potential carriers) of a highly suspected diphtheria case can also aid in the presumptive diagnosis.
Presumptive *C. diphtheriae* isolates and clinical specimens are required to be submitted according to PHL requirements:
https://doh.wa.gov/public-health-provider-resources/public-health-laboratories/lab-test-menu

For additional information regarding laboratory testing for diphtheria, see:
https://www.cdc.gov/surv-manual/php/table-of-contents/chapter-1-diphtheria.html

5. ROUTINE CASE INVESTIGATION

A. Evaluate the Diagnosis

Review the clinical presentation, risk factors for exposure, and immunization status to determine the likelihood of the diagnosis.

The following three factors can be used to assess the risk of toxigenic diphtheria. If

feasible, assess these factors for all individuals with *C. diphtheriae* isolates:

1. **Clinical presentation.** Is the clinical presentation highly suggestive of diphtheria? For example, is there a pseudomembrane in the back of the patient's throat? If so, is it adherent? In diphtheria, attempts to remove the membrane cause bleeding. Note that with a cutaneous infection, toxigenicity may be difficult to distinguish based on clinical features alone.

2. **Recent international travel.** Has the individual recently returned from international travel, especially to an endemic location? Refer to the Yellow Book for information about endemicity.

3. **Un- or under-vaccinated status.** Has it been longer than 10 years since the individual's last diphtheria toxoid-containing vaccine, or are they known to be unvaccinated? People who are up to date on diphtheria vaccine are far less likely to have toxigenic diphtheria.

If the patient lacks all three risk factors, the likelihood of a toxigenic infection is extremely low. However, if the patient has one or more of these risk factors, a public health response may be required. Please consult with the DOH VPD Program if there is any concern for toxigenic diphtheria.

CDC has published a list of key questions to consider when assessing suspected respiratory diphtheria cases: CDC has published a guide to assessing clinical risk of respiratory diphtheria: https://www.cdc.gov/diphtheria/media/pdfs/dip-key-questions-508.pdf.

If toxigenic diphtheria is highly suspected, do the following:

- Assure that the patient is in an isolation room with standard plus droplet precautions.
- Immediately consult with CDE regarding the need for testing and treatment with diphtheria antitoxin. CDE will facilitate CDC consultation as needed. Treatment cannot be delayed until test results are received.
- Request collection of specimens for confirmation of the diagnosis at PHL. Collect serum to be held for serologic testing, if needed.
- Recommend the initiation of antibiotic treatment. Treatment should not be delayed pending laboratory confirmation when the diagnosis of diphtheria is strongly suspected. Erythromycin or penicillin G are the recommended antibiotics.
- Facilitate the transportation of specimens to PHL.

If the suspicion of toxigenic diphtheria is low, specimens can be sent to a commercial laboratory.

B. Identify Source of Infection

Ask the patient about potential sources of infection in the 10 days prior to onset including:

- Travel out of the country, especially to an area where diphtheria is still endemic.
- Contact with persons from a country where diphtheria is still endemic; and
- Working, visiting, or volunteering in a healthcare setting.

Please note: Using nose and throat cultures to search for diphtheria carriers, other than among close contacts, is not ordinarily useful or indicated.

C. Identify Close Contacts

Identify all close contacts, particularly household members and others who were directly exposed to respiratory secretions of the case and determine their immunization status. See section 6.B. for managing contacts.

D. Environmental evaluation

None

6. CONTROLLING FURTHER SPREAD

A. Infection Control Recommendations/Case Management

1. Persons with highly suspected pharyngeal diphtheria should be cared for using standard plus droplet precautions until they have completed antimicrobial therapy and two cultures taken at least 24 hours apart, and at least 24 hours after cessation of antimicrobial therapy, fail to show diphtheria organisms.
2. Persons with cutaneous diphtheria should be cared for using standard plus contact precautions until they have completed antimicrobial therapy and two cultures taken at least 24 hours apart, and at least 24 hours after cessation of antimicrobial therapy, fail to show diphtheria organisms. Wounds should remain covered until drainage stops or can be contained by a dressing.
3. Persons with confirmed diphtheria should avoid close contact with others until two cultures taken 24 hours apart, and at least 24 hours after cessation of antimicrobial therapy, fail to show diphtheria organisms.
4. Persons with diphtheria should be vaccinated with diphtheria toxoid during convalescence because clinical disease does not necessarily confer immunity.

B. Contact Management

An investigation is required for all highly suspected diphtheria cases. Cases of cutaneous or respiratory diphtheria caused by infections with nontoxigenic strains of *C diphtheriae* are not nationally notifiable and do not require routine investigation or prophylaxis of contacts; however, some case investigation is recommended to determine the likelihood of the infection being toxigenic (e.g., case had international travel or respiratory symptoms like diphtheria). Close contacts of a person suspected to have diphtheria should be identified, and the following are recommended:

1. Contact tracing usually can be limited to household members and people with direct, habitual close contact or health care personnel exposed to nasopharyngeal secretions, people sharing kitchen facilities, or people caring for infected children.

2. Close contacts with symptoms compatible with diphtheria should be referred to a health care provider for evaluation immediately.
3. Surveillance for evidence of disease in all is necessary for 7- 10 days from last exposure to an untreated patient.
4. Culture all close contacts for *C. diphtheriae*. Specimens should be obtained from nares and throat or any mucosal or cutaneous lesion.
5. Close contacts, regardless of their immunization status, should receive erythromycin or penicillin as prophylaxis. Follow-up cultures of pharyngeal specimens should be performed after completion of therapy for contacts proven to be carriers. If cultures are positive, an additional 10-day course of erythromycin should be administered, and follow-up cultures of pharyngeal specimens again should be performed.
6. For compliance reasons, if the health department cannot maintain surveillance of close contacts, the close contacts should receive a dose of intramuscular benzathine penicillin. and if not fully immunized or if immunization status is not known, they should be immunized with diphtheria-containing vaccine as appropriate for age.
7. Asymptomatic, previously immunized close contacts should receive a booster dose of an age-appropriate diphtheria toxoid-containing vaccine if they have not received a booster dose of a diphtheria toxoid-containing vaccine within 5 years.
8. Asymptomatic close contacts who have had fewer than 3 doses of a diphtheria toxoid-containing vaccine, children younger than 7 years in need of their fourth dose of DTaP (or DT), or people whose immunization status is not known should be immunized with an age-appropriate diphtheria toxoid-containing vaccine.
9. Use of equine diphtheria antitoxin in unimmunized close contacts is not recommended, because there is no evidence that antitoxin provides additional benefit.
10. Close contacts should watch for symptoms of diphtheria during the period from the day after the first possible exposure through 10 days after the last known exposure. Daily symptom check by public health should be considered for contacts that were unimmunized when exposed shown to be nontoxigenic, the health department can discontinue investigation of contacts.

    For additional information regarding case investigations, see the CDC VPD Surveillance Manual available at: https://www.cdc.gov/surv-manual/php/table-of-contents/chapter-1-diphtheria.html

C. Environmental measures

None

7. MANAGING SPECIAL SITUATIONS

Special situations will be handled on a case-by-case basis. Please consult with Office of Communicable Disease Epidemiology.

8. ROUTINE PREVENTION

A. Immunization Recommendations

Diphtheria, tetanus, and acellular pertussis vaccination is recommended across the lifespan. Children younger than 7 years of age receive DTaP or DT, while older children and adults receive Tdap and Td.

- Infants and children receive 5 doses of DTaP. Give one dose at each of these ages: 2 months, 4 months, 6 months, 15 through 18 months, and 4 through 6 years. Use DT for infants and children who should not receive acellular pertussis-containing vaccines.
- Adolescents receive a single dose of Tdap, preferably at 11 to 12 years of age.
- A single dose of Tdap is given during every pregnancy, preferably during the early part of gestational weeks 27 through 36.

Routine booster doses of Td or Tdap vaccine should be given at 10-year intervals.

The full routine vaccination schedule and catch-up recommendations are available at: https://www.cdc.gov/vaccines/hcp/imz-schedules/child-adolescent-age.html

For additional information regarding use of the diphtheria vaccines, adverse reactions and contraindications see the most recent CDC Pink Book available at: https://www.cdc.gov/pinkbook/hcp/table-of-contents/chapter-7-diphtheria.html

B. Prevention Recommendations

Immunization is the best way to prevent diphtheria.

ACKNOWLEDGEMENTS

This document is a revision of the Washington State Guidelines for Notifiable Condition Reporting and Surveillance published in 2002 which were originally based on the Control of Communicable Diseases Manual (CCDM), 17th Edition; James Chin, Ed. APHA 2000. We would like to acknowledge the Oregon Department of Human Services for developing the format and select content of this document.

UPDATES

January 2011: The Legal Reporting Requirements section has been revised to reflect the 2011 Notifiable Conditions Rule revision. Updated to include the 2010 CSTE case classification changes.

March 2016: Clinical presentation and Epidemiology sections were reviewed and updated according to the most recent medical literature available. Specimen collection section was updated to reflect current testing available at PHL and CDC. Immunization section was updated for consistency with current ACIP recommendations.

December 2022: For 2023 WAC revision combined provider and facility reporting requirement, updated laboratory submission (Section 1B)

September 2023: CSTE case definition was updated in 2019, updating guideline to reflect this update. Expanded information provided for cutaneous diphtheria. Updated recommendations for close contacts. Updated information on cutaneous infection and the definition of a carrier. Updated vaccination information

December 2023: For 2024 WAC revision updated laboratory submission.

June 2024: CDC links updated

October 2024: Multiple content revisions were made as follows:

- Cover page was edited for clarity and to include *tox* gene PCR information.
- Section 2.A. was edited to clarify that other *Corynebacterium* species can produce diphtheria toxin.
- Section 2.A.6. about non-toxigenic infections was expanded with information from recent surveillance data and updates from 2023 Epi-Aid.
- Section 2.F. was updated to clarify antibiotic selection.

- Section 4.A. was updated to include guidance for interpreting diphtheria *tox* gene PCR results.
- Section 4.B. was updated to include diphtheria *tox* gene PCR information.
- Section 5.A. was updated to clarify the three primary risk factors for toxigenic diphtheria.
- Minimal edits were made in Sections 2.D., 3.A., 3.D., 6.A., and 6.B. for clarity.