

Diphtheria Quicksheet

October 2023



Background

Diphtheria is caused by gram-positive *Corynebacterium diphtheriae* bacteria that produce diphtheria toxin (toxigenic strains). Important sites of infection are the respiratory mucosa (respiratory diphtheria) and the skin (cutaneous diphtheria). Respiratory diphtheria cases are very uncommon in the United States—six cases were reported during 2000-2018.

Diphtheria is endemic in countries throughout Africa, Latin America, Asia, the Middle East, and parts of Europe where toxoid-containing vaccines are not in widespread use, or where there have been historic gaps in vaccination. See [WHO's webpage](#) with a list of cases reported by country.

Rarely, other mucosa—the eye, ear, or genitals—may be infected. Both respiratory and non- respiratory disease caused by diphtheria toxin- producing *Corynebacteria* require immediate public health follow-up. Non-toxigenic infections are much more common than toxigenic infections. Non-toxigenic infections are typically less severe and are not vaccine-preventable, as vaccines target diphtheria toxin rather than the bacteria.

Mode of transmission

Spread by respiratory droplets and/or by contact with discharges from skin lesions.

Incubation period

2-5 days (range, 1-10 days).

Communicability

In people with untreated diphtheria, *C. diphtheriae* can be present in nose, throat, eye, and skin lesion discharges for 2-6 weeks. Chronic carriers may shed *C. diphtheriae* for 6 months or more. Effective antibiotic therapy typically terminates shedding within 48 hours.

Alternate diagnoses

Health departments may receive inquiries about patients with exudative pharyngitis and what appears to be an adherent pharyngeal membrane. Given the rarity of respiratory diphtheria, alternate diagnoses should be considered, especially in patients who have been immunized and who have not recently traveled to diphtheria- endemic countries. More common causes of membranous pharyngitis include Group A β - hemolytic *Streptococcus*, *Staphylococcus aureus*, *Arcanobacter hemolyticum*, *Candida albicans*, *Borellia vincenti* (Vincent's angina), *H. influenzae* (acute epiglottitis), Epstein Barr virus, cytomegalovirus, adenovirus, herpes simplex, and Toxoplasma. In addition, some anti-neoplastic agents such as methotrexate may induce a pharyngeal membrane.

Symptoms

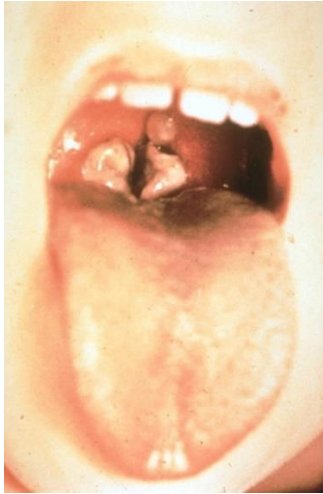
Respiratory diphtheria usually presents as membranous nasopharyngitis or obstructive laryngotracheitis. Initial symptoms include a sore throat, difficulty swallowing, malaise, and low- grade fever. The hallmark of respiratory diphtheria is the presence of a tough, grayish-white pseudomembrane over the tonsils (Figure 1, left), the pharynx, or larynx. The pseudomembrane is strongly adherent and attempts to dislodge it

Diphtheria Quicksheet

usually result in bleeding. The membrane may progressively extend into the larynx and trachea and cause airway obstruction, which, if left untreated, can be fatal. Swelling of the cervical lymph nodes and soft tissue can lead to a “bullneck” appearance in moderate to severe disease (Figure 1, right). Absorption of diphtheria toxin from the site of infection can cause systemic complications, including damage to the myocardium, nervous system, and kidneys. See [CDC webpage](#) for a list of considerations when respiratory diphtheria is suspected.

Figure 1. Images of symptoms

Pseudomembrane over the tonsils



“Bullneck” appearance



From immunize.org

Case definition

Clinical Criteria

- 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, wound, conjunctiva, ear, genital mucosa)

Laboratory Criteria

Confirmatory laboratory evidence:

- Isolation of *C. diphtheriae* from any site **AND**
- Confirmation of toxin-production by Elek test or by another validated test capable of confirming toxin production.

Supportive laboratory evidence:

- Histopathologic diagnosis

Epidemiologic linkage requires direct contact with a laboratory-confirmed case of diphtheria.

Case classification

Confirmed:

- An upper respiratory tract illness with an adherent membrane of the nose, pharynx, tonsils, or larynx **AND** any of the following:

Diphtheria Quicksheet

- isolation of toxin-producing *Corynebacterium 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.

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.

Suspected non-respiratory diphtheria

There has been increasing recognition of cutaneous diphtheria in the U.S.; 4 toxigenic cutaneous cases were identified from 2015 to 2018 among travelers to areas with endemic diphtheria. The incidence of respiratory diphtheria is greatest during fall and winter, but summer epidemics of cutaneous diphtheria may occur in warm climates where skin infections are prevalent.

Health departments may receive inquiries about non-respiratory (usually wound/cutaneous) cultures growing *C. diphtheriae*. Diphtheria in non-respiratory sites became reportable in 2019. These specimens are very unlikely to be toxigenic; however, testing should be performed to rule out toxin production (see page 5 this document). Toxin-producing *C. diphtheriae* in non-respiratory sites may serve as reservoirs for respiratory and non-respiratory diphtheria in susceptible contacts but are unlikely to cause systemic disease. **Antitoxin is not generally indicated for non-respiratory diphtheria.**

Cutaneous diphtheria, is usually mild, typically consisting of sores or shallow ulcers. Antibiotic treatment as above is recommended.

Conjunctival infection may be mild, resembling a viral conjunctivitis, but the more typical infection is that of membranous conjunctivitis. Infiltration of the conjunctival surface leads to extreme edema and erythema of the eyelids with increasing stiffness of the lids. Membrane formation occurs over the conjunctivae, which ultimately becomes necrotic.

Treatment

Diphtheria antitoxin (DAT)

DAT should be administered promptly to patients with suspected respiratory diphtheria, without waiting for results of toxin testing. DAT can only be obtained through the CDC. If respiratory diphtheria is suspected and a request for DAT is considered, an infectious disease consult can be helpful in determining whether the level of suspicion is high enough to consult CDC for DAT. If you wish to consult CDC, **please contact CDPH first**. To contact CDPH during office hours, contact the Immunization Branch at VPDReport@cdph.ca.gov or 510-620-3737. Outside of office hours, contact the CDPH Duty Officer. For more information, please see [CDC's DAT webpage](#).

Antibiotic treatment for 14 days is also indicated:

- Until the patient can swallow comfortably, administer:
 - IM procaine penicillin G (units/dose q 12 hours: 300,000 if weight \leq 10 kg, 600,000 units if >10 kg), or

Diphtheria Quicksheet

- IV erythromycin (10 mg/kg/dose, q 6 hours, up to maximum of 500 mg/dose).
- Once swallowing comfortably, may substitute oral doses every 6 hours:
 - erythromycin (10 mg/kg/dose, up to maximum of 500 mg/dose), or
 - penicillin V (250 mg per dose).

For toxigenic cases, elimination of the organism should be documented 24 hours after completion of treatment by two consecutive negative nose and throat cultures taken 24 hours apart. If cultures remain positive after treatment, a second antibiotic course should be given, and follow-up cultures performed. Because disease does not necessarily confer immunity, DTaP or Tdap should be administered during convalescence per ACIP recommendations for age.

Infection control for confirmed or suspected diphtheria cases

Appropriate infection control precautions should be instituted until proven that the patient is not infected with toxin-producing *C. diphtheriae*. For respiratory diphtheria, droplet precautions, in addition to standard precautions, are indicated until elimination of the bacteria is documented 24 hours after the completion of antimicrobial therapy by 2 consecutive negative culture sets of both nose and throat collected 24 hours apart. For cutaneous diphtheria, contact precautions are indicated.

Close contact management

Contact tracing and post-exposure prophylaxis (PEP) for **confirmed toxigenic** diphtheria cases is usually limited to household members and other people with a history of direct, habitual close contact (including kissing or sexual contacts), healthcare workers exposed to nasopharyngeal secretions, people sharing utensils or kitchen facilities, and people taking care of children.

Decisions regarding whether to undertake contact tracing and PEP for suspected diphtheria cases while confirmatory lab testing is pending should be made on a case-by-case basis. For suspected cases in whom *C. diphtheriae* has been detected in a blood or skin culture, if the person has:

- No exudative pharyngitis, and
- No history of travel to or contact with travelers from countries endemic for diphtheria, then public health personnel may defer contact tracing and management, including chemoprophylaxis.
- Additional reassurance is provided if the patient received one or more doses of diphtheria toxoid (e.g., DTaP, DT, Td, Tdap) in the last 10 years.

Management of close contacts includes:

- Surveillance for 7 days for evidence of disease
- Nose and throat cultures for *C. diphtheriae*
- Immunization, as appropriate (complete primary series if <3 doses; booster if last dose >5 years ago)
- Antibiotics: See table below for options. Persons who cannot be relied upon to complete a multiday course or who cannot be kept under surveillance should receive penicillin G and a dose of DTaP or Tdap as appropriate for their age and according to the CDC algorithm on page 6.

Antibiotic options for close contacts

Antibiotic	Dose
Penicillin G benzathine, IM, one dose	Children weighing <30 kilos should receive 600,000 units, and children and adults weighing ≥30 kilos should receive 1.2 million units.
Erythromycin, oral, 7 -10 days	Children: 40-50 mg/kg per day in divided doses, maximum 1g/day Adults: 1 g per day in divided doses

Laboratory testing

If respiratory diphtheria is strongly suspected, treatment with antitoxin should occur whether or not laboratory testing has been completed. The diagnosis should be confirmed with lab testing.

Specimen collection: For respiratory diphtheria, swab the underside of the pharyngeal membrane with a cotton or synthetic swab, or submit a portion of the membrane. For cutaneous diphtheria, swab the lesion.

Clinical lab testing: *C. diphtheriae* can be isolated from culture of nasal or throat swabs, membrane tissue, and/or swabs or tissue from other sites. Isolation of *C. diphtheriae* requires culture media containing tellurite. Clinical lab testing cannot determine whether *C. diphtheriae* is toxigenic.

Public health laboratory testing: Please send samples from all isolates of *C. diphtheriae* (regardless of suspected or known toxigenicity) to CDPH MDL for potential additional toxigenicity testing at CDC.

- Place all swabs in transport media such as Amies and ship overnight with ice packs. Dry swabs submitted in silica gel sachets are also acceptable. Store pieces of membrane or other tissue in sterile saline (not formalin) and ship overnight with ice packs. Alert the receiving laboratory to the suspicion of diphtheria so that tellurite-containing culture media is used.
- Please see [specimen submission information](#), or contact the CDPH Microbial Diseases Lab at 510-412-3903.

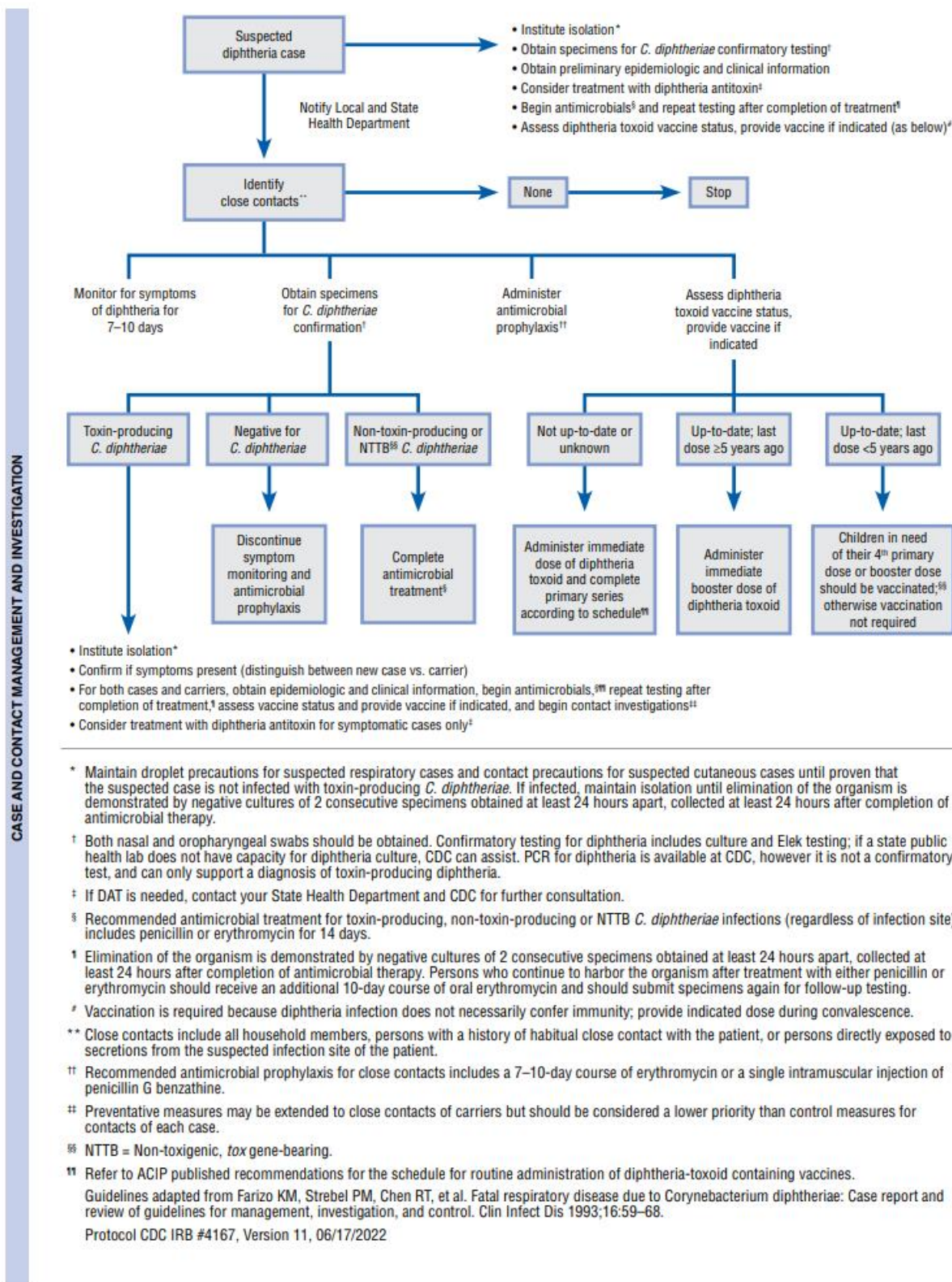
Laboratory detection of *C. diphtheriae*

With the advent of technologies such as MALDI- TOF mass spectrometry, *C. diphtheriae* strains are being detected more frequently. These bacteria are unlikely to be toxigenic, but all specimens positive for *C. diphtheriae* should be submitted to CDPH MDL for toxin testing per laboratory testing guidance above.

Non-toxigenic strains of *C. diphtheriae* have been detected in:

- healthy individuals;
- persons with pharyngitis (unclear if causal or colonizing);
- persons with skin and soft tissue infections, including in persons experiencing homelessness (skin infections may be polymicrobial); and
- persons with invasive disease, including endocarditis.

Figure 2. Case Management Flow Diagram From CDC



From [CDC Webpage](https://www.cdc.gov).