California Department of Public Health – May 2017

Respiratory Diphtheria: Public Health Recommendations

Background: CDPH receives inquiries about cases of exudative pharyngitis where the diagnosis of diphtheria is being considered. Although endemic elsewhere, respiratory diphtheria is rare in the U.S; the last reported case occurred in 2014.

The onset of respiratory diphtheria can be insidious. 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, the pharynx, or larynx. The pseudomembrane is strongly adherent, and attempts to dislodge it 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.

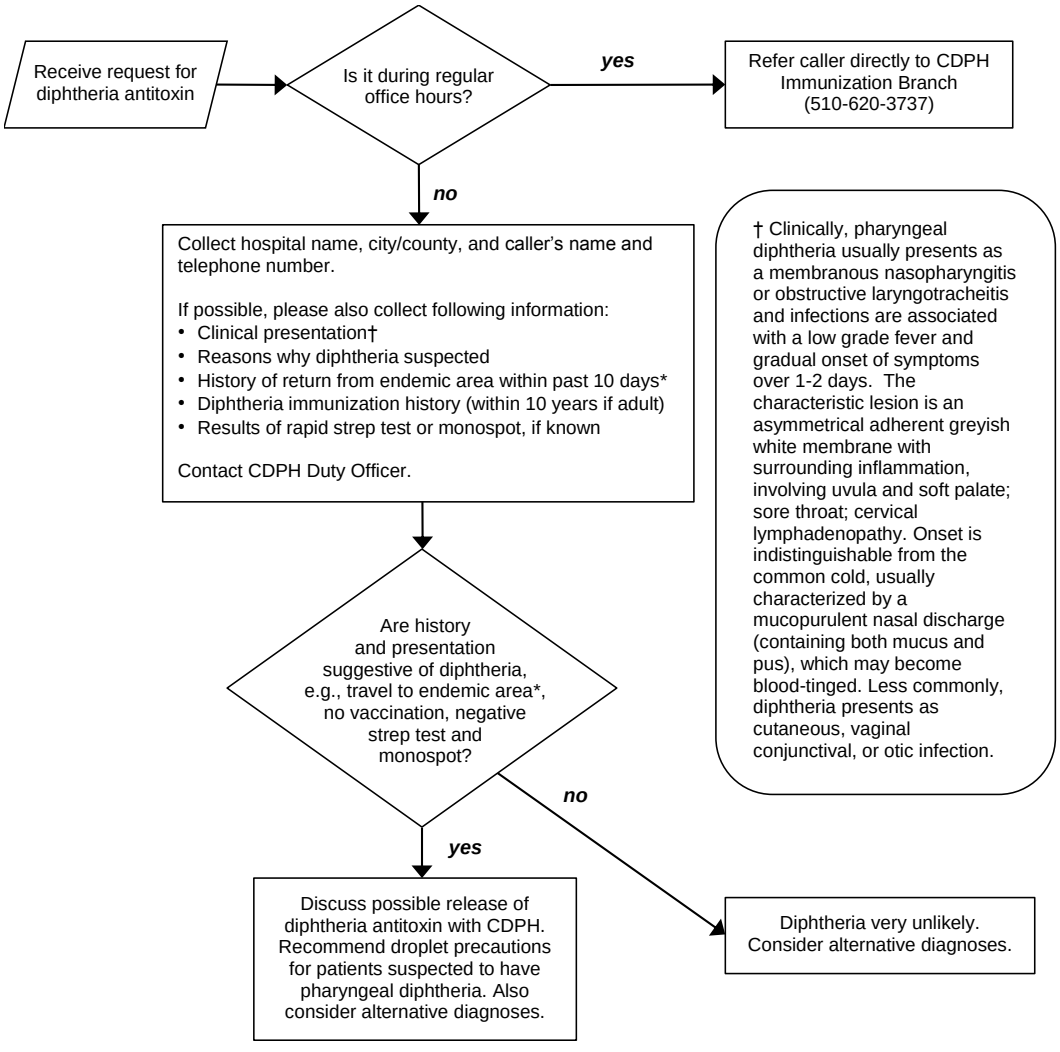
Inflammation of cervical lymph nodes and surrounding soft-tissue swelling of the neck result in the "bull-neck" appearance of moderate to severe diphtheria. Absorption of diphtheria toxin from the site of infection can cause systemic complications, including damage to the myocardium, nervous system and kidneys.

Mode of transmission: *C. diphtheriae* organisms are spread by respiratory droplets and/or by contact with discharges from skin lesions.

Incubation period: 2-5 days (range 1-10).

Communicability: In untreated people, virulent bacilli usually persist 2 weeks or less, and seldom more than 4 weeks. Chronic carriers may shed organisms for 6 months or more. Effective antibiotic therapy typically terminates shedding within 4 days.

Please use the following algorithm to assess the need for diphtheria antitoxin:



To obtain diphtheria antitoxin (DAT): Please contact the CDPH Duty Officer who will contact the CDC Duty Officer to authorize the release of DAT through the San Francisco or Los Angeles Quarantine Stations. Before intravenous administration of DAT, tests for sensitivity to antitoxin should be performed. Complete instructions for sensitivity testing will accompany the antitoxin. If the patient is sensitive to antitoxin, desensitization is necessary. Allergic reactions can be expected in 5-20% of patients. For more information, please see CDC's DAT webpage: http://www.cdc.gov/diphtheria/dat.html.

Treatment of infected people: Although diphtheria antitoxin is the primary therapy, antimicrobial therapy is also indicated. Treatment with erythromycin orally or by injection (40 mg/kg/day; maximum, 2 gm/day) for 14 days, or procaine penicillin G daily, intramuscularly (300,000 U/day for those weighing 10 kg or less, and 600,000 U/day for those weighing more than 10 kg) for 14 days. Monitor closely for airway obstruction.

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 culture positive, a second course of oral erythromycin should be given and follow-up cultures performed. Because disease does not necessarily confer immunity, DTaP or Tdap as appropriate, is recommended during convalescence.

Laboratory testing: A presumptive diagnosis is usually based on clinical features. If diphtheria is suspected, treatment with antitoxin should occur whether or not laboratory testing has been completed.
Local testing: Diagnosis is confirmed by isolating *C. diphtheriae* from culture of nasal or throat swabs or membrane tissue. Isolation of *C. diphtheriae* requires special culture media containing tellurite
Public health laboratory testing: The CDC laboratory can confirm toxin production by performing a modified Elek test and can detect the *tox* gene responsible for production of diphtheria toxin by PCR. For information, please contact the CDPH Microbial Diseases Laboratory at: (510) 412-3903.
Specimen collection: Swab the underside of the pharyngeal membrane with a cotton or synthetic swab, or submit a portion of the membrane. Place 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 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.

For more specific information, please see CDC laboratory testing guidance available at: http://www.cdc.gov/vaccines/pubs/surv-manual/chpt22-lab-support.html.

Other pathogens that may also cause 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 may also result in formation of a pharyngeal membrane, e.g., methotrexate; and long term use of corticosteroids (e.g., prednisolone) can cause oral candidiasis.

Infection control: Droplet precautions, in addition to standard precautions, are indicated until elimination of the organism 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.

Care of close contacts: Close contacts of a person suspected to have respiratory diphtheria should be identified promptly. Contact tracing should begin in the household and can usually be 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.
For close contacts (regardless of their immunization status) the following measures should be taken:
Surveillance for 7 days for evidence of disease;
Nose and throat cultures for *C. diphtheriae;* and
Oral erythromycin‡ (40-50 mg/kg/day) for 10 days (maximum 2g/day) or a single IM injection of benzathine penicillin G (600,000 U for children <30 kg and 1.2 million U for children ≥30 kg and adults).
Immunization, as appropriate (complete primary series if <3 doses and give booster if last dose >5 years ago).

‡Persons who cannot be relied upon to complete the oral course of erythromycin or who cannot be kept under surveillance should receive benzathine penicillin G and a dose of DTaP or Tdap depending on their age.

Treatment of carriers: Close contacts found by culturing to be carriers should have received antibiotics and vaccine as per the recommendations for close contacts above. Those who need to complete the vaccine series should receive follow-up to ensure completion of the series. Follow-up cultures should be performed as per the recommendations for the cases above.

CDC 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, tonsils, 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.

***Areas with endemic diphtheria**

COUNTRIES	
Africa	Algeria, Angola, Egypt, Eritrea, Ethiopia, Guinea, Niger, Nigeria, Sudan, Zambia, and other sub-Saharan countries
Americas	Bolivia, Brazil, Colombia, Dominican Republic, Ecuador, Haiti, and Paraguay
Asia/South Pacific	Bangladesh, Bhutan, Burma (Myanmar), Cambodia, China, India, Indonesia, Laos, Malaysia, Mongolia, Nepal, Pakistan, Papua New Guinea, Philippines, Thailand, and Vietnam
Middle East	Afghanistan, Iran, Iraq, Saudi Arabia, Syria, Turkey, and Yemen
Eastern Europe	Albania, Armenia, Azerbaijan, Belarus, Estonia, Georgia, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Moldova, Russia, Tajikistan, Turkmenistan, Ukraine, and Uzbekistan

Although diphtheria disease is rare in the United States, it appears that *C. diphtheriae* continues to circulate in areas of the country with previously endemic diphtheria. In 1996, 10 isolates of *C. diphtheriae* were obtained from persons in a Native American community in South Dakota. Eight of these isolates were toxigenic.

Check list for assessing a patient with suspected diphtheria

	SYMPTOM OR EVENT	YES/NO
Suspect case	Pharyngitis, nasopharyngitis, tonsillitis, laryngitis, tracheitis (or any combination of these), absent or low-grade fever	
	Grayish adherent pseudomembrane present	
	Membrane bleeds, if manipulated or dislodged	
Probable case	Suspect case above + 1 or more of the following	
	• Stridor	
	• Bull-neck (cervical edema)	
	• Toxic circulatory collapse	
	• Acute renal insufficiency	
	• Sub-mucosal or sub-cutaneous petechiae	
	• Myocarditis	
	• Death	
	Recently returned (<2 weeks) from travel to area with endemic diphtheria?	
	Recent contact (<2 weeks) with confirmed diphtheria case or carrier?	
	Recent contact (<2 weeks) with visitor from area with endemic diphtheria?	
	Recent contact with dairy or farm animals? Domestic pets?	
	Immunization status: Up to date - any DTaP/DT/Tdap/Td within 10 years?	
Laboratory Confirmed case	Positive culture of *C. diphtheriae (or C. ulcerans)* **AND**	
	- Positive Elek test **OR**	
	- PCR for *tox* gene (Positive for subunit A and B)	

Available at: https://www.cdc.gov/diphtheria/downloads/dip-cklist-diag.pdf