

Diphtheria Outbreak Control Guidelines

Infectious agent

Bacteria: *Corynebacterium diphtheriae* (*C. diphtheriae*)

Clinical manifestations

Infection with *C. diphtheriae* can involve any mucous membrane. A toxin produced by bacteriophage-infected strains is associated with increased disease severity. Disease classification is based on the site of infection as follows:

Tonsillar and pharyngeal

- ◆ This is the most common primary site of infection (> 90% of symptomatic cases).
- ◆ Initial symptoms include: sore throat, low-grade fever, membrane formation and throat/neck edema.
- ◆ A blue-white membrane forms on the tonsils, extends and may cover the soft palate.
- ◆ The membrane may also extend to the pharynx and larynx. There is a minimal amount of mucosal erythema surrounding the membrane.
- ◆ The membrane is adherent to the tissue, and forcible attempts to remove it cause bleeding.
- ◆ Extensive membrane formation may result in respiratory obstruction. This infection site may be associated with substantial systemic absorption of toxin and compromised breathing.

Laryngeal

- ◆ Symptoms are similar to tonsillar/pharyngeal site of infection.
- ◆ Symptoms include fever, hoarseness, barking cough and loss of voice.
- ◆ Membrane forms on the larynx as a primary site or as an extension of tonsillar/pharyngeal infection.
- ◆ The membrane can lead to airway obstruction, coma, and death.

Anterior nasal

- ◆ Symptoms are indistinguishable from that of the common cold and are usually characterized by a mucopurulent nasal discharge (containing both mucus and pus) which may become blood-tinged.
- ◆ A white membrane usually forms on the nasal septum. The disease is usually fairly mild because of apparent poor systemic absorption of toxin in this location.

Cutaneous

- ◆ In the U.S. this type is most often associated with homeless persons or poor hygiene.
- ◆ It is more common in tropical climates.
- ◆ Symptoms include a scaling rash or ulcers with demarcated edges and a membrane. Symptoms may persist for weeks to months.
- ◆ Ocular and genital manifestations also occur.

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- ◆ The non-toxigenic form has minimal transmission and has generally been isolated in recent cases in the U.S.
- ◆ The severity of skin disease with the toxigenic strains appears to be less than in other forms of the disease.

Complications

- ◆ Most complications and deaths are attributable to the presence of toxin. The severity of complications is also generally related to the extent of local disease.
- ◆ The toxin can affect organs and tissue distant from the site of infection.
- ◆ Toxin absorption may lead to complications in all forms of disease; however, these complications are more common in tonsillar, pharyngeal and laryngeal disease than in other forms.

Complications include:

Respiratory

- ◆ Patients with severe disease may develop marked cervical lymphadenopathy creating a characteristic "bullneck" appearance.
- ◆ Neck swelling may cause airway obstruction which untreated may lead to pallor, stupor, coma, and death.
- ◆ Extensive laryngeal membrane formation may lead to airway obstruction and respiratory insufficiency.
- ◆ Diaphragmatic paralysis can lead to secondary pneumonia.

Other complications

- ◆ Myocarditis: occurrence early in infection carries an increased risk of heart failure and death.
- ◆ Neuritis: paralysis of the soft palate, eye muscles, limbs and/or diaphragm can occur.
- ◆ Otitis media can occur.

Mortality

- ◆ Respiratory case fatality rate is 5-10%, with rates up to 20% in those < 5 and > 40 years of age.
- ◆ Complications and deaths are much less frequent with cutaneous diphtheria.

Incubation period

- ◆ 2-5 days (range 1-10 days).

Period of communicability

- ◆ Without antimicrobial treatment, communicability may range from 2 to 6 weeks from the time of infection.
- ◆ With antibiotic treatment, patients may be infectious for fewer than 4 days.
- ◆ Chronic carriers may shed organisms for over 6 months.

Transmission

- ◆ Respiratory transmission through droplets, nose, throat and eye discharges are most common.

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- ◆ Contacts with skin lesion discharge and fomite transmission are rare.

Basic epidemiology

- ◆ Diphtheria occurs worldwide.
- ◆ Human carriers, who are asymptomatic, are the reservoir for this bacterium.
- ◆ Before the vaccination era, children were at the highest risk for respiratory diphtheria.
- ◆ Recently, diphtheria has primarily affected adults who did not receive diphtheria toxoid booster vaccinations and who traveled to disease-endemic regions.
- ◆ The highest incidence in temperate regions is in winter and spring.
- ◆ Vaccinated individuals may be asymptomatic carriers or have a mild sore throat.

Case definition

Approved by CSTE 1995 and 2010

Clinical description

- ◆ An upper respiratory tract illness characterized by sore throat, low-grade fever, and an adherent membrane of the tonsil(s), pharynx, and/or nose.

Laboratory criteria

- ◆ Isolation of *C. diphtheriae* from a clinical specimen, 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, tonsils, or larynx; and any of the following:

- ◆ isolation of *C. diphtheriae* from the nose or throat; OR
- ◆ histopathologic diagnosis of diphtheria; OR
- ◆ epidemiologic linkage to a laboratory-confirmed case of diphtheria.

Testing and Diagnosis

- ◆ Diagnosis of diphtheria is usually made on the basis of clinical presentation since it is imperative to begin presumptive therapy quickly. Isolation of *C. diphtheriae* by bacteriological culture is essential for confirming diphtheria.

*Note: Other pathogens can cause a membrane of the throat and tonsils, including Streptococcus, Epstein-Barr virus and cytomegalovirus (both of which cause infectious mononucleosis syndrome), Arcanobacter hemolyticum, Candida albicans; anaerobic organisms (Vincent's angina), and some viruses. The patient's healthcare provider should be encouraged to perform appropriate laboratory tests to rule out these conditions.

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- ◆ Diagnostic tests used to confirm infection include isolation of *C. diphtheriae* on culture and toxigenicity testing. Although no other tests for diagnosing diphtheria are commercially available, Wadsworth Center and CDC can perform a PCR test on clinical specimens to confirm infection with a potentially toxigenic strain. PCR can detect nonviable *C. diphtheriae* organisms from specimens taken after antibiotic therapy has been initiated.

The diphtheria membrane has been described as a bluish-white membrane, varying in size from covering a small patch on the tonsils to covering most of the soft palate. Often by the time a physician is contacted, the membrane is grayish-green, or black if bleeding has occurred. The membrane is adherent to the tissue, and forcible attempts to remove it cause bleeding.

Culture

- ◆ Culture of the lesion is done to confirm the diagnosis.
 - Alternatively, isolation of *C. diphtheriae* from a close contact may confirm the diagnosis of the case, even if the patient's culture is negative.
- ◆ Nasopharyngeal, pharyngeal membrane and lesion swabs should be obtained.
- ◆ Alert the laboratory that diphtheria is suspected, so that tellurite-containing media will be used.
 - All isolates from any body site (respiratory or cutaneous) should be sent to the CDC for reference testing.
 - The CDC can perform a PCR test on clinical specimens to quickly confirm an infection with a toxigenic strain.
- ◆ Contact the NYSDOH Bureau of Immunization or Wadsworth Center for the procedure for submitting specimens to CDC.
- ◆ **Do not wait for culture confirmation before initiation of therapy and case investigation.**

Serology

- ◆ Before administering antitoxin, obtain serum antibodies to assess for a low nonprotective diphtheria antibody titer, which can aid in presumptive diagnosis.

Specimen collection

Specimen

- ◆ Nasopharyngeal and pharyngeal specimens should both be taken from all cases and close contacts.
- ◆ Samples from cases should also be taken from the membrane and if possible from beneath the membrane.

Procedure

- ◆ Throat swab
 - Pharynx should be clearly visible and well illuminated.
 - Depress tongue with an applicator and swab the throat without touching the tongue or inside the cheek.

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- Rub vigorously over any membrane, white spots, or inflamed areas.
- If a membrane is present, lift the edge and swab beneath it to reach the deeply located organisms.
- ◆ Nasopharyngeal specimen
 - Insert the swab into the nose through one nostril beyond the anterior nares.
 - Gently swab along the floor of the nasal cavity, under the middle turbinate until the pharyngeal wall is reached.
 - Do NOT use force to overcome any obstruction.
- ◆ Skin diphtheria and other lesions
 - Lesions should be cleaned with sterile normal saline and crusted material removed.
 - Press the swab firmly into the lesion to obtain specimen.

Transport

- ◆ Store in cold room or refrigerator until shipping.
- ◆ Ship immediately and by overnight delivery.
 - Avoid shipping on Fridays and weekends.
 - If samples must be shipped on a Friday, arrangements must be made with Wadsworth Center for specimen receipt.

Case investigation

Demographics

- ◆ Name
- ◆ Address
- ◆ DOB/Age
- ◆ Gender
- ◆ Race
- ◆ Ethnicity
- ◆ Country of birth
- ◆ Occupation/Setting
- ◆ Length of time in the U.S.

Outcome

- ◆ Recovered/deceased
- ◆ Date of death, postmortem examination results, cause of death

Reporting

- ◆ Source
- ◆ County
- ◆ Date reported

Clinical information

- ◆ Date of symptom onset
- ◆ Site of infection (nose, throat, larynx, etc.)
- ◆ Hospitalizations (dates and duration of stay)
- ◆ Signs (neck edema, stridor, tachycardia)

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- ◆ Complications (e.g. myocarditis or neuritis)

Laboratory results

- ◆ Antibody results
- ◆ Culture results
- ◆ Bio-type and toxigenicity test
- ◆ PCR results
- ◆ Molecular typing

Treatment

- ◆ Anti-toxin: date of administration, number of units given
- ◆ Antibiotic, antibiotic dosage and duration of therapy

Vaccination history

- ◆ Type
- ◆ Manufacturer
- ◆ Number of doses, dates and lot numbers
- ◆ Reason, if not vaccinated

Epidemiology

- ◆ Contact with confirmed or probable case
- ◆ Travel history (last 6 weeks)
- ◆ Contact with immigrants or travelers to endemic areas
- ◆ Number of contacts cultured
- ◆ Results of contact cultures

Control measures

Since toxigenic diphtheria strain infections occur rarely in the United States, please consult with the NYSDOH Bureau of Immunization as soon as possible after the report of any suspect, probable, or confirmed case.

Patient

- ◆ Impose strict respiratory and droplet isolation until at least 2 cultures are negative, collected 24 hours after antibiotic therapy is completed.
- ◆ All suspected cases should be treated with diphtheria antitoxin without waiting for culture confirmation.
 - Diphtheria antitoxin is currently available only through the CDC.
 - Contact the NYSDOH Bureau of Immunization for assistance with arranging transport of antitoxin.
- ◆ Initiate early presumptive antibiotic treatment of suspected cases with erythromycin or penicillin.
- ◆ A 14-day course of antibiotics (erythromycin or penicillin) is necessary to eradicate carriage of *C. diphtheriae* regardless of the use of treatment with antitoxin.

Respiratory contacts

- ◆ Identify close contacts, especially household members and other persons directly exposed to oral secretions of the patient.

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- ◆ Culture all close contacts, regardless of their immunization status. Ideally, culture should be from both throat and nasal swabs.
- ◆ Based on culture results, treat any carrier with antibiotics. A repeat culture to ensure eradication of the organism must be performed.
- ◆ All contacts should receive erythromycin or penicillin antibiotic prophylaxis.
- ◆ Treat any contact presumptively at the first sign of illness.
- ◆ Unimmunized contacts should start a course of vaccine and be closely monitored for symptoms of diphtheria for 7 days.
- ◆ Inadequately immunized contacts should receive an age-appropriate diphtheria vaccine dose and continue according to schedule. See current vaccine schedules at:
<http://www.cdc.gov/vaccines/recs/schedules/default.htm>.
- ◆ If > 5 years have elapsed since administration of diphtheria-containing vaccine, a booster dose should be given. The Tdap vaccine is preferred for adolescents and adults.

Cutaneous contacts

- ◆ Give diphtheria vaccine booster if > 10 years have elapsed from last dose.
 - The Tdap vaccine is preferred for adolescents and adults.
- ◆ If toxigenic, close contacts should be monitored for respiratory symptoms for about 7 days (not required for non-toxigenic *C. diphtheria*).
- ◆ HCP involved in wound care, changing of linens, etc. should be encouraged to have a diphtheria vaccination every 10 years (not mandatory).

Reporting

- ◆ A Confidential Case Report Form (DOH-389) must be submitted.
- ◆ The LHD must be notified immediately by telephone as soon as a diagnosis of diphtheria, including cutaneous diphtheria, is suspected.
- ◆ The LHD must notify the NYSDOH Bureau of Immunization within 24 hours of their notification, but preferably by telephone, as soon as the case is reported to them.
- ◆ Cutaneous diphtheria is not nationally reportable. No CDESS report should be generated for cutaneous diphtheria.