

Diphtheria

Diphtheria

IMMEDIATELY REPORTABLE DISEASE

Per N.J.A.C. 8:57, health care providers and administrators shall immediately report **by telephone** confirmed and suspected cases of diphtheria to the health officer of the jurisdiction where the ill or infected person lives, or if unknown, wherein the diagnosis is made. The health officer (or designee) **must immediately institute the control measures listed below in section 6, “Controlling Further Spread,”** regardless of weekend, holiday, or evening schedules.

Directory of Local Health Departments in New Jersey and

Directory of After Hour Emergency Contact Phone Numbers for Local Health Departments in New Jersey, both available at:

<http://www.nj.gov/health/lh/community/index.shtml#1>

If the health officer is unavailable, the health care provider or administrator shall make the report to the New Jersey Department of Health by telephone to 609.826.5964, between 8:00 A.M. and 5:00 P.M. on non-holiday weekdays or to 609.392.2020 during all other days and hours.



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1 THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent

Diphtheria is caused by toxigenic strains of *Corynebacterium diphtheriae* and, rarely, *Corynebacterium ulcerans*. *C. diphtheriae* is an irregularly staining, gram-positive, non-spore-forming, nonmotile, pleomorphic bacillus with three biotypes (mitis, intermedius, and gravis). All biotypes of *C. diphtheriae* may be either toxigenic or nontoxigenic. Toxigenic strains possess the toxin gene, *tox*, which is carried by a family of related corynebacteria phages. The toxin inhibits protein synthesis in all cells, including myocardial, renal, and peripheral nerve cells.

B. Clinical Description

Diphtheria has two forms: respiratory and cutaneous. Respiratory (nasal, pharyngeal, tonsillar, and laryngeal) diphtheria is typically caused by toxin-producing (toxigenic) strains of *C. diphtheriae*. Cutaneous disease can be caused by either toxigenic or nontoxigenic strains. In the respiratory form of the disease, a membrane is formed; this membrane is usually visible on the throat or tonsils. Respiratory diphtheria begins two to seven days after infection. Initial symptoms of illness include a sore throat and low-grade fever; swelling of the neck (“bull-neck”) from inflammation can develop and is a sign of severe disease. Persons may die from asphyxiation when the membrane obstructs breathing. Other complications of respiratory diphtheria are caused by systemic effects of the absorbed diphtheria toxin; these include myocarditis (inflammation of the heart) and nerve paralysis. Case fatality rates of 5 to 10% for respiratory diphtheria have changed little in 50 years. The respiratory form of diphtheria usually lasts several days; complications can persist for months.

Membranous pharyngitis from nontoxigenic *C. diphtheriae* is also reportable, although disease is usually mild and cannot cause systemic complications. 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. Rarely, other *Corynebacterium* species (*C. ulcerans* or *C. pseudotuberculosis*) may produce diphtheria toxin and lead to classic respiratory diphtheria.

NOTE: Other pathogens, including *Streptococcus* species; Epstein-Barr virus and cytomegalovirus; *Candida*; and anaerobic organisms (Vincent’s angina), can cause a membrane of the throat and tonsils. Isolation of *C. diphtheriae* from a clinical specimen or histopathologic diagnosis of diphtheria establishes a laboratory diagnosis of diphtheria.

Cutaneous diphtheria, caused by either toxigenic or nontoxigenic strains, is usually mild, typically consisting of nondistinctive 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 and is also not a reportable disease in New Jersey.

C. Reservoirs

Humans are the only host of *C. diphtheriae*. Human carriers are usually asymptomatic and constitute a disease reservoir.

D. Modes of Transmission

Diphtheria is transmitted person-to-person by droplet or 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, but this has rarely been documented. Raw milk has served as a vehicle for transmission.

E. Incubation Period

The incubation period is usually 2 to 5 days (range, 1-10 days) but may occasionally be longer.

F. Period of Communicability or Infectious Period

The infectious period begins at symptom onset and typically lasts two to six weeks after infection. 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 two successive pairs of nose and throat cultures (and cultures of skin lesions in cutaneous diphtheria) obtained ≥ 24 hours after completion of antimicrobial therapy and ≥ 24 hours apart are negative. Asymptomatic chronic carriers are important in sustaining transmission.

G. Epidemiology

Diphtheria was one of the most common causes of death among children in the prevaccine era. Infection can occur in immunized, partially immunized, and unimmunized persons. However, it is usually less severe in those who are partially or fully immunized. In the United States, although cases can occur across all age groups, most cases occur in children <10 years of age and adults over 50 years of age. Diphtheria is endemic in many parts of the world, including countries of the Caribbean and Latin America. The incidence of respiratory diphtheria is greatest during autumn and winter, but summer epidemics may occur in warm moist climates in which skin infections are prevalent. Large epidemics of diphtheria, primarily in adolescents and adults, have occurred in the former Soviet Union, Algeria, and Ecuador. In the states of the former Soviet Union (including Russia, the Ukraine, and Central Asian Republics), over 150,000 cases and 5,000 deaths due to diphtheria occurred between

1990 and 1997. In recent epidemics in the former Soviet Union, the case fatality ratio has ranged from 3% to 23%.

Generally, fewer than five cases of diphtheria are reported annually in the United States. Between 2004 and 2017, 2 cases of diphtheria were recorded in the U.S. While most cases of diphtheria reported recently in the United States were related to importation, enhanced surveillance in a previously endemic area (a Northern Plains Indian community) has revealed ongoing circulation of a toxigenic strain of *C. diphtheriae* first identified in that region in the 1970s. The last known cases in New Jersey occurred in 1963. It is estimated that more than 40% of U.S. adults lack protective levels of circulating antitoxin.

2 CASE DEFINITION

A. New Jersey Department of Health Case Definition

Diphtheria cases are reported by states to CDC through the National Notifiable Diseases Surveillance System (NNDSS). The New Jersey Department of Health (NJDOH) Communicable Disease Service (CDS) follows the most current case definition as published on the CDC NNDSS website. For the most recent case definition please visit:

<http://wwwn.cdc.gov/NNDSS/script/conditionsummary.aspx?CondID=43>

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)

Case Classification (as of 2019)

SUSPECTED/POSSIBLE

- 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

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 *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 *Corynebacterium diphtheriae* from that site

Case Classification Comments

- Cases of laboratory-confirmed, non-toxin-producing *C. diphtheriae* (respiratory or non-respiratory) should not be reported by state or local health departments to CDC as diphtheria cases.
- Negative laboratory results may be sufficient to rule-out a diagnosis of diphtheria; however, clinicians should carefully consider all lab results in the context of the patient's vaccination status, antimicrobial treatment, and other risk factors.
- PCR (polymerase chain reaction) and MALDI-TOF (matrix assisted laser desorption/ionization-time of flight mass spectrometry) diagnostics for *C. diphtheriae*, when used alone, do not confirm toxin production. These tests, when used, should always be combined with a test that confirms toxin production, such as the Elek test.

3

LABORATORY TESTING SERVICES AVAILABLE

Bacteriological **culture** (isolation of *C. diphtheriae*) and **toxigenicity testing** of the resulting isolate are essential for confirming diphtheria. The NJDOH Public Health and Environmental Laboratories (PHEL) is not currently equipped to test for *C. diphtheriae*. However, all diphtheria isolates, with prior approval from NJDOH CDS staff, should be sent to PHEL for subsequent forwarding to the CDC Pertussis and Diphtheria Laboratory.

Because respiratory diphtheria is very uncommon in the U.S. and other pathogens can cause a membrane in the throat and over the tonsils, the patient's healthcare provider should be encouraged to consider other conditions in the differential diagnosis and perform appropriate laboratory tests to rule out these conditions and organisms. A list of other biological disease agents which may also cause a membranous pharyngitis can be found on CDC's Checklist

for Assessing a Patient with Suspected Diphtheria, available here:
<https://www.cdc.gov/diphtheria/downloads/dip-cklist-diag.pdf>

When diphtheria (involving any site) is suspected, clinical specimens for culture should be obtained as soon as possible from the nose or nasopharynx and throat, even if treatment with antibiotics has already begun. If possible, swabs also should be taken from beneath the membrane, or a piece of the membrane should be removed. Except in situations where the index of suspicion is low, close contacts should be cultured as well. The laboratory should be alerted to the suspicion of diphtheria because isolation and identification of *C. diphtheriae* is aided by special culture media containing tellurite.

Although no other tests for confirming diphtheria are commercially available, CDC can perform a polymerase chain reaction (PCR) test on clinical specimens to confirm infection with a potentially toxigenic strain. While this PCR assay allows for detection of the diphtheria toxin gene (*tox*), it does not confirm whether the organism is producing the toxin. The PCR test may be able to detect nonviable *C. diphtheriae* organisms from specimens taken after antibiotic therapy has been initiated. Although, PCR (performed by the CDC) provides supportive evidence for the diagnosis, data are not yet sufficient for PCR to be accepted as a criterion for laboratory confirmation. A case that is PCR positive without isolation of the organism or histopathologic diagnosis and without epidemiologic linkage to a laboratory-confirmed case should be classified as a probable case. Please note: CDC does not perform PCR to rule out diphtheria unless diphtheria anti-toxin (DAT) has been requested to treat the patient.

Similarly, serologic testing cannot be used to confirm a case of *C. diphtheriae*. If acute antibody levels are low, diphtheria cannot be ruled out; if acute levels are high, diphtheria is unlikely to be the cause of illness. Please note: at this time, CDC does not test sera for antibodies to *C. diphtheriae*.

Attachment A (at the end of this chapter) describes the procedures for collecting specimens for culture and subsequent toxigenicity testing. Attachment B (at the end of this chapter) gives an overview of available diagnostic tests.

4 PURPOSE OF SURVEILLANCE AND REPORTING AND REPORTING REQUIREMENTS

A. Purpose of Surveillance and Reporting

To alert public health authorities to the circulation of *C. diphtheriae* and the possibility of other cases developing in the area, particularly given the large number of susceptible adults

To ensure early and appropriate treatment with diphtheria antitoxin and antibiotics

To obtain necessary laboratory specimens before antibiotic or antitoxin treatment

To identify and evaluate contacts and provide necessary antimicrobial prophylaxis to prevent further spread of the disease

B. Laboratory Reporting Requirements

The New Jersey Administrative Code (N.J.A.C. 8:57-1) stipulates that a positive test of diphtheria must be reported immediately by telephone to the local health department (LHD) where the patient resides. If the laboratory director or his/her designee is unable to reach the LHD where the patient resides, call the NJDOH at 609.826.5964 (weekdays) or 609.392.2020 (nights/weekends). Telephone reports shall be followed by a report via the Communicable Disease Reporting and Surveillance System 2.0 (CDRSS), or in writing to the health officer of the jurisdiction in which the patient lives or, if unknown, to the health officer in whose jurisdiction the healthcare provider requesting the laboratory examination is located. Please refer to the list of reportable diseases at <https://www.nj.gov/health/cd/reporting/> for information.

C. Healthcare Provider Reporting Requirements

The N.J.A.C. 8:57-1 stipulates that a confirmed or suspect case of diphtheria must be immediately reported by telephone to the health officer of the jurisdiction where the patient resides or, if unknown, wherein the diagnosis was made. If the health officer is unavailable the report shall be made to the NJDOH at 609.826.5964 (weekdays) or 609.392.2020 (nights/weekends).

D. Health Officer Reporting Requirements and Follow-up Responsibilities

As specified in the N.J.A.C. 8:57-1 each health officer pursuant to the provisions of N.J.A.C. 8:57-1 shall within 24 hours of receipt of a report initiate or update case information in CDRSS 2.0. If the initial report is incomplete, the health officer shall seek complete information and provide all available information to the NJDOH CDS within five days of receiving the initial report. Refer to the health officer’s Reporting Timeline at <https://www.nj.gov/health/cd/reporting/> for information on prioritization and timelines requirements of reporting and case investigation.

E. Entry into CDRSS 2.0

The mandatory fields in CDRSS include disease, name, county, municipality, gender, race, ethnicity, case status, and report status. The following table can be used as a quick reference guide to determine CDRSS fields to be completed for accurate and complete reporting of *C. diphtheriae* cases.

CDRSS Topic	Required Information
Disease Info	Enter the disease name (“DIPHTHERIA”), illness onset date, and the date the case was reported to the State or LHD. There are no subgroups for <i>C. diphtheriae</i> .
Patient Personal Info	Enter patient demographic information. Verify date of birth and spelling of name. Please also document race and ethnicity.

CDRSS Topic	Required Information
Addresses	Enter patient’s primary address and any additional alternate address (e.g., a daycare or workplace address). Use the Comments section in this screen to record any pertinent information about the alternate address (e.g., the times per week the case-patient attends day care). Entering an alternate address will allow other disease investigators access to the case if the alternate address falls within their jurisdiction.
Laboratory and Diagnostic Information	For positive culture results select “MICROORGANISM IDENTIFIED”. Specimen type/source, specimen collection date, test result, and, if applicable, test value should also be recorded. If isolate is being sent to PHEL, please enter the date and method by which it will be sent. NOTE: diphtheroid results are NOT reportable
Clinical Status	Enter appropriate clinical info in this section. Confirm mortality of the patient. If the patient died, date of death should be recorded under the Mortality section.
Contact Tracing	Information regarding close contacts is required for this disease (household and other close contacts). Identify susceptible high-risk contacts (e.g., pregnant women, immunocompromised or unvaccinated persons, infants <12 months of age). Document any vaccine or travel history of contacts, as well as any PEP administered (e.g., antibiotics or diphtheria booster) in this section.
Immunization Info	Obtain diphtheria immunization info and document within this section.
Medical Facility and Provider Info	Record the names of the medical facilities and provider(s) involved in the patient’s care. If the patient received care from two or more hospitals, be sure that all are entered so the case can be accessed by all infection preventionists (IPs) covering these facilities. Ensure admission and discharge dates are entered for medical facilities.
Pregnancy Info	Indicate pregnancy status in this section.

CDRSS Topic	Required Information
Risk Factors	Enter complete information about risk factors to facilitate study of <i>C. diphtheriae</i> disease in New Jersey, including whether vaccination status is known (if unvaccinated, indicate reason). Please document travel history of patient or any visitors to patient (e.g., domestic/international within past 12 days), document additional details in the Comments section.
Signs/Symptoms	Answer “yes” for any of the signs and symptoms that are present and indicate an onset date. Make every effort to get complete information by interviewing the provider, patient, family members, IP, or others who might have knowledge of the patient’s illness. Also, information regarding the resolution of signs and symptoms should be entered, if available.
Treatment	Enter any treatment that the patient received for diphtheria in this section (e.g., antibiotics or antitoxin). If antitoxin is administered, enter any additional information about the acquisition of the antitoxin in the Comments section.
Case Comments	Enter general comments (i.e., information that is not discretely captured by a specific topic section or drop-down menu) in the Comments section. NOTE: Select pieces of information entered in the Comments section CANNOT be automatically exported when generating reports. Therefore, whenever possible, record information about the case in the data fields that have been designated to capture this information; information included in these fields CAN be automatically exported when generating reports.
Disease Specific Questionnaire: Z. Diphtheria Complications	If the individual is classified as case of diphtheria, please add this section and answer the questions regarding complication from diphtheria.

5 CASE INVESTIGATION

- a. It is the health officer’s responsibility to investigate the case by interviewing the patient and others who may be able to provide pertinent information.
- b. The NJDOH CDS will provide technical assistance and consultation to the LHD, as needed.
- c. Case investigation should document such epidemiologic information around a suspected case as (a) clinical symptoms, (b) Site of infection (e.g., nose, throat,

- larynx), (c) diphtheria immunization history, (d) country of origin and length of time in United States, (e) travel history (to where and dates), (f) whether there were any recent out-of-town visitors (from where and dates), (g) whether there was any recent contact with anyone with similar symptoms, etc., (h) hospitalization dates, (i) risk factors for exposure and transmission (e.g., food handling, healthcare setting), (j) other clinical and/or epidemiologic information, as requested by CDS staff.
- d. Institution of disease control measures is an integral part of case investigation. It is the local health officer's responsibility to understand and, if necessary after consultation with the NJDOH, institute the control guidelines listed below.

6 CONTROLLING FURTHER SPREAD

A. Isolation and Quarantine Requirements (N.J.A.C. 8:57-1)

Minimum Period of Isolation of Patient

The case is usually not contagious 48 hours after antibiotic treatment begins. Document elimination of the organism using two consecutive negative cultures obtained 24 or more hours after completion of antimicrobial therapy and 24 or more hours apart. If there was no antimicrobial therapy, these two sequential pairs of cultures should be taken after symptoms resolve and two or more weeks after their onset. If an avirulent (nontoxigenic) strain is documented, isolation is not necessary.

Minimum Period of Quarantine of Contacts

Contacts (both symptomatic and asymptomatic) whose occupations involve handling food must be excluded from that work until two successive pairs of nose and throat cultures obtained two or more weeks after completion of antimicrobial prophylaxis (if any) and 24 or more hours apart are negative. These requirements may be extended to other contacts who work in high-risk transmission settings, as determined by NJDOH.

B. Protection of Contacts of a Case

Close contacts are defined as those who sleep in the same house or who share food, drink, or eating/drinking utensils with the case-patient, as well as healthcare workers in contact with the case-patient's oral or respiratory secretions. Those contacts who were in brief contact with the case but do not meet the definition for close contact are not considered significant contacts.

Below, management of cases and contacts is divided into three categories: (a) case-patient(s) and symptomatic close contacts, (b) asymptomatic close contacts, and (c) nonsignificant contacts. It is important to follow the sequence of actions given, as administration of antibiotics, diphtheria antitoxin (DAT), and diphtheria toxoids will interfere with interpretation of diagnostic testing. CDC recommendations for diagnosis, treatment, and

follow-up can be found in diagram form here:

<https://www.cdc.gov/diphtheria/downloads/close-contacts.pdf>

Cases and Symptomatic Close Contacts

1. Isolate the confirmed or suspect respiratory case on droplet precautions, until two cultures from both the nose and the throat are negative for toxigenic *C. diphtheriae*. Cultures should be taken two or more weeks after cessation of antimicrobial therapy and 24 or more hours apart. If there was no antimicrobial therapy, the cultures should be taken after symptoms resolve, two or more weeks after their onset, and 24 or more hours apart.
2. Collect cultures as described in Attachment A (located at the end of this chapter). If antibiotics have been started, it is still useful to collect specimens which are described in Attachment B (at the end of this chapter).
3. Cases and symptomatic close contacts should be evaluated for initiation of therapy with DAT. **DAT can be obtained only through an Investigational New Drug (IND) protocol from CDC. Information regarding DAT can be found on CDC's diphtheria website <https://www.cdc.gov/diphtheria/dat.html>**
4. After lab study specimens are collected, case-patients and symptomatic close contacts should begin antibiotic treatment as follows (<https://www.cdc.gov/diphtheria/clinicians.html#antibiotics>):
 - Erythromycin, orally or by injection (40 mg/kg/day; maximum, 2 gm/day) for 14 days, or
 - Procaine penicillin G daily, intramuscularly (300,000 units every 12 hours for those weighing 10 kg or less, and 600,000 units every 12 hours for those weighing more than 10 kg) for 14 days.
5. If case-patients or symptomatic close contacts are culture-positive, they will need two repeat pairs of nose and throat cultures taken two or more weeks after antibiotics have been discontinued and 24 or more hours apart. If a case or symptomatic close contact has not received antibiotics, two successive pairs of nose and throat cultures taken after symptoms resolve, two or more weeks after the onset of symptoms and 24 or more hours apart are needed.
 - If both sets of cultures are negative, the individual is considered free of infection.
 - If any of the repeat cultures is positive, an additional ten-day course of oral erythromycin should be administered, and follow-up cultures will need to be repeated as described.
6. Case-patients and symptomatic close contacts who are not-up-to-date for diphtheria toxoid-containing vaccines should be immunized with a diphtheria toxoid-containing preparation appropriate for age during convalescence. Remember, if serum is to be collected, do this before vaccinating.

7. Close contacts should be monitored for symptoms daily for at least seven days after their last exposure. Active surveillance for suspect cases in the affected settings should take place for at least two incubation periods (ten days).

Asymptomatic Close Contacts

1. Where diphtheria is confirmed or highly suspected in the case, all asymptomatic close contacts should have cultures collected as described in Attachment A.
2. Assess and monitor daily for signs and symptoms of diphtheria for at least seven days after their last exposure. Active surveillance for suspect cases in the affected settings should take place for at least two incubation periods (10 days).
3. Assess diphtheria toxoid vaccination status and administer a diphtheria toxoid booster, appropriate for age, to close contacts, especially household contacts if they are not up to date with diphtheria vaccination.
4. All close contacts, *regardless of their culture result or immunization status*, should begin antibiotic prophylaxis with a 7- to 10-day course of oral erythromycin (40 mg/kg/day for children and 1 g/day for adults). For compliance reasons, if surveillance of contacts cannot be maintained, they should receive benzathine penicillin (600,000 units for persons younger than 6 years old and 1,200,000 units for those 6 years or older).
5. All asymptomatic close contacts who were initially culture-positive will need two repeat pairs of nose and throat cultures taken two or more weeks after antibiotics have been discontinued and 24 or more hours apart. If an asymptomatic contact has not received antibiotics, two successive pairs of nose and throat cultures taken 24 or more hours apart are needed. If any of the repeat cultures is positive, an additional ten-day course of oral erythromycin should be given and the cultures repeated as described above.

Nonsignificant Contacts

Contacts who do not sleep in the same house as the case-patient; do not share food, drink, or eating/drinking utensils with the case-patient; and are not healthcare workers in contact with the case-patient's oral or respiratory secretions should be immunized with the appropriate diphtheria toxoid-containing preparation. They do not need to be cultured or placed on antibiotic prophylaxis.

C. Preventive Measures

Personal Preventive Measures/Education

Vaccination, including routine childhood vaccination, catch-up vaccination of adolescents, and targeted vaccination of high-risk adult groups, is the best preventive measure against diphtheria. CDC recommends diphtheria, tetanus, and acellular pertussis vaccination across the lifespan. Children younger than 7 years of age receive DTaP or DT, while older children and adults receive Tdap and Td. Please refer to the most current recommendations from CDC's Advisory Committee on Immunization Practices (ACIP) statement on diphtheria,

pertussis, and tetanus, summarized here <https://www.cdc.gov/vaccines/vpd/dtap-tdap-td/hcp/recommendations.html>

Additional Information

A Diphtheria Fact Sheet can be obtained at the NJDOH Web site at <https://www.state.nj.us/health/cd/topics/>

Click on the “Diseases & Health Topics A-Z List” and scroll down to “Diphtheria.”

References

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Attachment A: Collection of Specimens for Isolation of *C. diphtheriae* (1 page)

Attachment B: Overview of Requirements for Laboratory Testing for Diphtheria (1 page)

Attachment C: Algorithm for Diagnosis, Treatment, and Follow-Up of Suspect Diphtheria Cases and Infected Contacts (1 page)

Collection of Specimens for Isolation of *C. Diphtheriae*

Clinical specimens for culture should be obtained as soon as possible when diphtheria (involving any site) is suspected, even if treatment with antibiotics has already begun. Unless the index of suspicion is low, close contacts of suspected cases also should have specimens taken from the nose and throat. (Culture of *C. diphtheriae* from close contacts may confirm the diagnosis of the case, even if the patient's culture is negative.) Use a dry, sterile swab.

Throat Swabs

1. Pharynx should be clearly visible and well illuminated.
2. Depress tongue with an applicator and swab the throat without touching the tongue or inside of the cheek.
3. Rub vigorously over any membrane, white spots, or inflamed areas; slight pressure with a rotating movement must be applied to the swab.
4. If any membrane is present, lift the edge and swab beneath it to reach the deeply located organisms. A portion of the membrane may also be submitted for testing.

Nasopharyngeal Specimens

1. Insert the swab into the nose through one nostril beyond the anterior nares.
2. Gently introduce the swab along the floor of the nasal cavity, under the middle turbinate until the pharyngeal wall is reached. Force must not be used to overcome any obstruction. Leave swab in place for ten seconds. Remove the swab slowly. Polymerase chain reaction specimens should be taken at the same time as those for culturing. Place swabs in sterile, dry tube or vial.
3. Ship immediately at + 4°C (with cold packs in a sterile container or in silica gel sachets), so that specimen arrives at the laboratory as soon as possible after collection.

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- Place swabs in a currette swab transport system. If transport time is anticipated to be less than 24 hours, Amies or Modified Stuart's medium is recommended. If transport time is to be 24 hours or more, silica gel is recommended.
 - Notify the lab that specimens for diphtheria culture are on the way, since isolation of *C. diphtheriae* requires special tellurite-containing media.
 - If *C. diphtheriae* is isolated, regardless of association with disease, CDS staff will help facilitated shipment of isolates to the CDC Pertussis and Diphtheria Laboratory (with prior approval from CDC).

Attachment B: Overview of Requirements for Laboratory Testing for Diphtheria

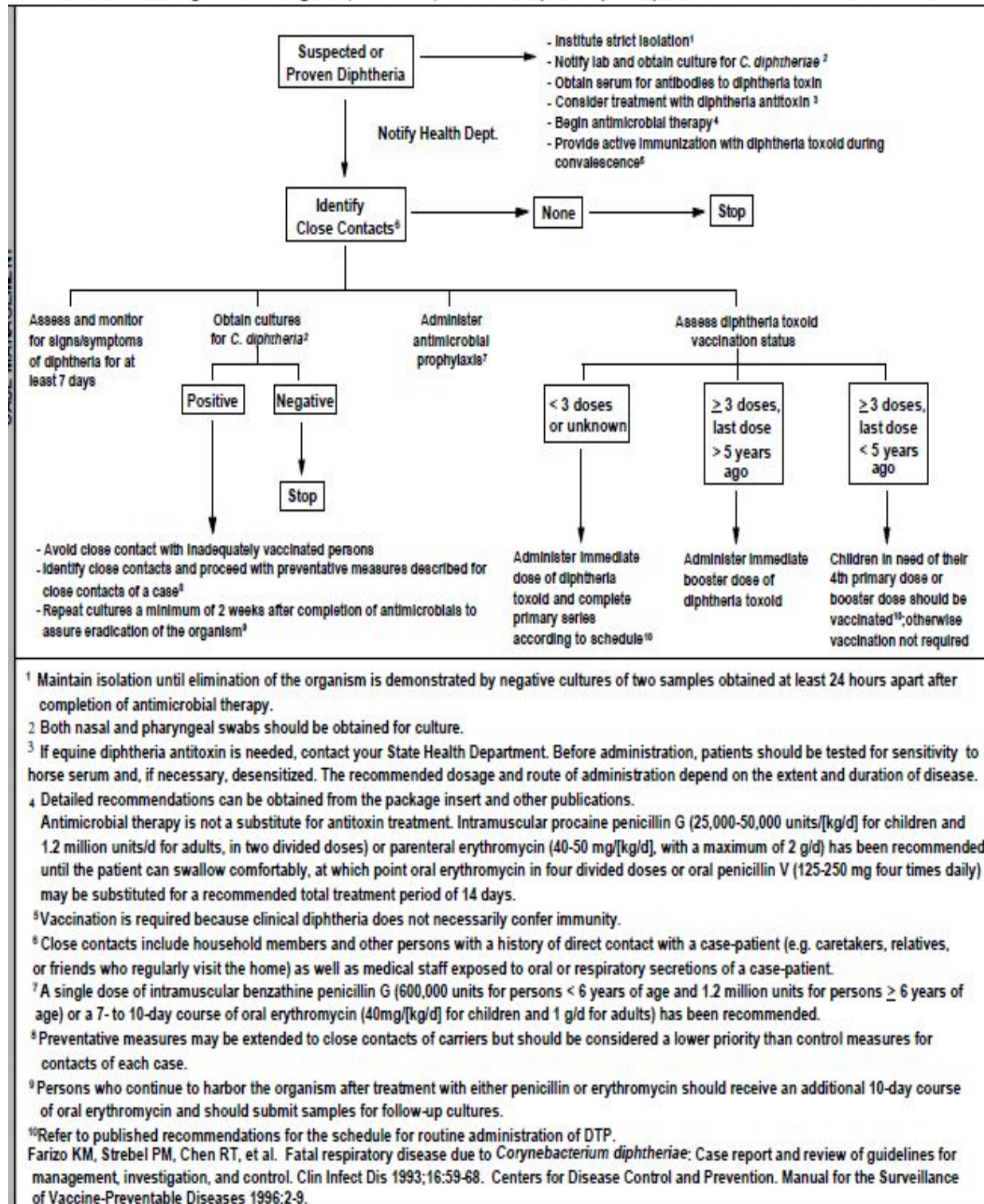
Test name	Specimens to take	Timing for specimen collection	Transport requirements	Collection & notification requirements	Notes
Culture	<ul style="list-style-type: none"> Swabs of nose, throat, and membrane (or other infected body site) of case Swabs of nose and throat of close contacts 	As soon as possible, when diphtheria is suspected	<p>< 24 hours: Amies or modified Stuart's medium</p> <p>≥ 24 hours: silica gel sachets</p>	<p>Providers/labs may call NJDOH CDS 609.826.5964 regarding suspect case, if LHD is not available.</p> <p>NJDOH may call CDC diphtheria lab at 404.639.1231 or 404.639.1239</p>	Alert lab that diphtheria is suspected to ensure that tellurite-containing media is used. After isolation, biotype (strain) and toxigenicity can be determined.
PCR	Swabs (as above), or pieces of membrane or biopsy tissue of case	As soon as possible (same time as those for culture), when diphtheria is suspected	<p>Swabs, silica gel sachet; or a sterile dry container at 4°C.</p> <p>Membrane/tissues – container with sterile saline without formalin at 4°C.</p>	Contact as above	Available only at CDC – approval required from NJDOH CDS staff. Alert lab that diphtheria is suspected so that specific PCR assay is used. Can detect nonviable organisms and toxin gene. Provides supportive evidence for, but not confirmation of, diagnosis.
Toxigenicity testing (Elek test)	Isolate from culture of case (above)	After <i>C. diphtheriae</i> has been isolated	Transport medium such as Amies medium or silica gel sachets	Contact as above	Available at CDC – approval required from NJDOH CDS staff prior to submission.
Serology (antibodies to diphtheria toxin)	Serum of case	Before administration of antitoxin or vaccine	Frozen (-20°C)		Not currently available at CDC. If acute antibody levels are low, diphtheria can't be ruled out; if acute levels are high, diphtheria is unlikely to be cause of illness.

Adapted from *Manual for the Surveillance of Vaccine-Preventable Diseases*. Centers for Disease Control and Prevention, Atlanta, GA, 2008. Current version available online at: <https://www.cdc.gov/vaccines/pubs/surv-manual/index.html>

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Attachment C: Algorithm for Diagnosis, Treatment, and Follow-Up of Suspect Diphtheria Cases and Infected Contacts



Accessed from <https://www.cdc.gov/diphtheria/downloads/close-contacts.pdf>