Diphtheria

IMMEDIATELY REPORTABLE DISEASE

Per NJAC 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. A directory of local health departments in New Jersey is available at [http://www.state.nj.us/health/lh/directory/lhdselectcounty.shtml](http://www.state.nj.us/health/lh/directory/lhdselectcounty.shtml).

If the health officer is unavailable, the health care provider or administrator shall make the report to the Department 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.
Diphtheria

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-sporo-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 two to seven 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. 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 and Senior Services Case Definition

**Case Definition for Diphtheria (as defined by Centers for Disease Control and Prevention (CDC), 1999)**

**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.

**Case Classification**

**PROBABLE**

A clinically compatible case that is not laboratory-confirmed and is not epidemiologically linked to a laboratory-confirmed case.

**CONFIRMED**

A clinically compatible case that is either laboratory-confirmed or epidemiologically linked to a laboratory-confirmed case.

Laboratory criteria for diagnosis

- Isolation of *C. diphtheriae* from a clinical specimen
• Histopathologic diagnosis of diphtheria

Comment

Cutaneous diphtheria should not be reported. Respiratory disease caused by nontoxigenic *C. diphtheriae* should be reported as diphtheria. All diphtheria isolates, regardless of association with disease, should be sent initially to the New Jersey Department of Health and Senior Services (NJDHSS), Public Health and Environmental Laboratories (PHEL) for subsequent forwarding to the Diphtheria Laboratory, National Center for Infectious Diseases, CDC.

### 3 LABORATORY TESTING SERVICES AVAILABLE

Bacteriological culture and toxigenicity testing of the resulting isolate are essential for confirming diphtheria. Both of these procedures are available at the NJDHSS PHEL. The NJ Vaccine Preventable Disease Program (VPDP) and/or PHEL staff must be consulted before a specimen is being submitted. 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. Except in situations where the index of suspicion is low, close contacts should be cultured as well.

Although no other tests for diagnosing diphtheria are commercially available, CDC can perform a polymerase chain reaction (PCR) test on clinical specimens to confirm infection with a toxigenic strain. The PCR test can detect nonviable *C. diphtheriae* organisms from specimens taken after antibiotic therapy has been initiated. PCR for the diphtheria toxin gene and its regulatory element provides supportive evidence for the diagnosis; however, a case that is PCR positive without the isolation of the organism or histopathologic diagnosis and without epidemiological linkage to a laboratory-confirmed case should be classified as a probable case. 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.

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 (NJAC 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 NJDHSS VPDP at 609.826.4860 (weekdays) or 609.392.2020 (nights/weekends). Telephone reports shall be followed by a report via confidential fax, over the Internet using the Communicable Disease Reporting and Surveillance System (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 [http://www.state.nj.us/health/cd/documents/reportable_diseases.pdf](http://www.state.nj.us/health/cd/documents/reportable_diseases.pdf) for information.

C. Healthcare Provider Reporting Requirements

The New Jersey Administrative Code (NJAC 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 NJDHSS VPDP at 609.826.4860 (weekdays) or 609.392.2020 (nights/weekends).

D. Health Officer Reporting Requirements and Follow-up Responsibilities

As specified in the New Jersey Administrative Code (NJAC 8:57-1) each health officer pursuant to the provisions of NJAC 8:57-1 shall within 24 hours of receipt of a report initiate or update case information in CDRSS. If the initial report is incomplete, the health officer shall seek complete information and provide all available information to the NJDHSS VPDP within five days of receiving the initial report. Refer to the health officer’s Reporting Timeline at [http://www.state.nj.us/health/cd/reporting.shtml](http://www.state.nj.us/health/cd/reporting.shtml) for information on prioritization and timelines requirements of reporting and case investigation.
E. Entry into CDRSS

The mandatory fields in CDRSS include disease, last name, county, municipality, gender, race, ethnicity, case status, and report status.

The following table can be used as a quick reference guide to determine which CDRSS fields need to be completed for accurate and complete reporting of *C. diphtheriae* cases. The “Tab” column includes the tabs that appear along the top of the CDRSS screen. The “Required Information” column provides detailed explanations of what data should be entered.

<table>
<thead>
<tr>
<th>CDRSS Screen</th>
<th>Required Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Info</td>
<td>Enter the disease name (“DIPHTHERIA”), patient demographic information, illness onset date, and the date the case was reported to the LHD. There are no subgroups for <em>C. diphtheriae</em>.</td>
</tr>
<tr>
<td>Addresses</td>
<td>Enter any 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.</td>
</tr>
<tr>
<td>Clinical Status</td>
<td>Enter any treatment that the patient received and record the names of the medical facilities and physician(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 control professionals (ICPs) covering these facilities. Enter any treatment provided in the Treatment selection section (e.g., antibiotics or antitoxin). If antitoxin is administered, enter any additional information about the acquisition of the antitoxin in the Comments section. Indicate pregnancy status under Clinical Status section. If immunization status is known, it should also be entered under Immunizations section. If the patient died, date of death should be recorded under the Mortality section.</td>
</tr>
<tr>
<td>Signs/Symptoms</td>
<td>Check appropriate boxes for signs and symptoms and indicate their onset date. Make every effort to get complete information by interviewing the physician, family members, ICP, or others who might have knowledge of the patient’s illness. Also, information regarding the resolution of signs and symptoms should be entered.</td>
</tr>
<tr>
<td>CDRSS Screen</td>
<td>Required Information</td>
</tr>
<tr>
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</tr>
<tr>
<td><strong>Risk Factors</strong></td>
<td>Enter complete information about risk factors to facilitate study of <em>C. diphtheriae</em> disease in New Jersey. If patient has not received immunizations due to a medical or religious exemption, please check risk factor in [Risk factor(s)] section. Please document travel history of patient or any visitors to patient (e.g., domestic/international within past 12 days) in the [Comments] section.</td>
</tr>
<tr>
<td><strong>Laboratory Eval</strong></td>
<td>For positive culture results select “MICROORGANISM IDENTIFIED” when culture was performed. Specimen type, specimen collection date, test result, and, if applicable, test value should also be recorded.</td>
</tr>
<tr>
<td><strong>Contact Tracing</strong></td>
<td>Information regarding contacts is required for this disease including information on any household and other close contacts. Identify susceptible high-risk contacts (e.g., pregnant women, immunocompromised or unvaccinated persons, infants &lt;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 [Comments] section.</td>
</tr>
<tr>
<td><strong>Case Comments</strong></td>
<td>Enter general comments (i.e., information that is not discretely captured by a specific topic screen or drop-down menu) in the [Comments] section. <strong>NOTE:</strong> 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 fields that have been designated to capture this information; information included in these fields CAN be automatically exported when generating reports.</td>
</tr>
<tr>
<td><strong>Epidemiology</strong></td>
<td>Indicate method of import in the [Epidemiology] section. Under the [Other Control Measures] section, indicate if the patient falls into any of the categories listed under [Patient Role(s)/Function(s)] (e.g., “HEALTHCARE WORKER,” “DAYCARE PROVIDER”). Record name of and contact information for case investigators from other agencies (e.g., CDC, out-of-state health departments). Document communication between investigators in the [Comments] section.</td>
</tr>
<tr>
<td>CDRSS Screen</td>
<td>Required Information</td>
</tr>
<tr>
<td>--------------</td>
<td>----------------------</td>
</tr>
<tr>
<td><strong>Case Classification</strong>&lt;br&gt;<strong>Report Status</strong></td>
<td>Case status options are “REPORT UNDER INVESTIGATION (RUI),” “CONFIRMED,” “PROBABLE,” “POSSIBLE,” and “NOT A CASE.”&lt;br&gt;• All cases entered by laboratories (including LabCorp electronic submissions) should be assigned a case status of “REPORT UNDER INVESTIGATION (RUI).”&lt;br&gt;• Cases still under investigation by the LHD should be assigned a case status of “REPORT UNDER INVESTIGATION (RUI).”&lt;br&gt;• Upon completion of the investigation, the LHD should assign a case status on the basis of the case definition. “CONFIRMED,” “PROBABLE,” and “NOT A CASE” are the only appropriate options for classifying a case of <em>C. diphtheriae</em> (see section 2A).&lt;br&gt;Report status options are “PENDING,” “LHD OPEN,” “LHD REVIEW,” “LHD CLOSED,” “DELETE,” “REOPENED,” “DHSS OPEN,” “DHSS REVIEW,” and “DHSS APPROVED.”&lt;br&gt;• Cases reported by laboratories (including LabCorp electronic submissions) should be assigned a report status of “PENDING.”&lt;br&gt;• Once the LHD begins investigating a case, the report status should be changed to “LHD OPEN.”&lt;br&gt;• The “LHD REVIEW” option can be used if the LHD has a person who reviews the case before it is closed (e.g., health officer or director of nursing).&lt;br&gt;• Once the LHD investigation is complete and all the data are entered into CDRSS, the LHD should change the report status to “LHD CLOSED.”&lt;br&gt;• “LHD CLOSED” cases will be reviewed by DHSS and be assigned one of the DHSS-specific report status categories. If additional information is needed on a particular case, the report status will be changed to “REOPENED” and the LHD will be notified by e-mail. Cases that are “DHSS APPROVED” cannot be edited by LHD staff.&lt;br&gt;If a case is inappropriately entered (e.g., a case of dengue was erroneously entered as a case of <em>C. diphtheriae</em>) the case should be assigned a report status of “DELETE.” A report status of “DELETE” should NOT be used if a reported case of <em>C. diphtheriae</em> simply does not meet case definition. Rather, it should be assigned the appropriate case status, as described above.</td>
</tr>
</tbody>
</table>
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 NJDHSS, VPDP 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) and (g) whether there was any recent contact with anyone with similar symptoms, etc., (h) hospitalization dates, and (i) risk factors for exposure and transmission (e.g., food handling, healthcare setting).
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 NJDHSS, institute the control guidelines listed below.

6 CONTROLLING FURTHER SPREAD

A. Isolation and Quarantine Requirements (NJAC 8:57-1)

The current recommendations of CDC and NJDHSS (as of 2000) are as follows:

Minimum Period of Isolation of Patient

Maintain isolation until two successive pairs of nose and throat cultures obtained 24 or more hours after completion of antimicrobial therapy and 24 or more hours apart are negative. 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 NJDHSS.

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. Attachment C (at the end of this chapter) presents recommendations for diagnosis, treatment, and follow-up in diagram form.

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. Continue as described in Section 2 immediately below.

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 for PCR and serology as well, which are described in Attachment B (at the end of this chapter). Blood for serology specimens should be collected before administration of DAT or diphtheria toxoid.

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. Healthcare providers treating a case of suspect diphtheria can contact the diphtheria duty officer directly at the CDC Child Vaccine-Preventable Disease Branch, Epidemiology and Surveillance Division, National Immunization Program in Atlanta. (See Attachment D at the end of this chapter for important telephone numbers.) If serology specimens are to be collected, this should be done before administration of DAT.

4. After lab study specimens are collected, case-patients and symptomatic close contacts should begin antibiotic treatment as follows:
   - Erythromycin, orally or by injection (40–50 mg/kg/day; maximum, 2 gm/day) for 14 days or
   - Procaine penicillin G daily, intramuscularly or intravenously (25,000–50,000 U/kg/day for mild to moderate infection, 250,000–400,000 U/kg/day for severe infection; maximum, 24 million U/d) 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 (located at the end of this chapter).

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 vaccinate as outlined below:
   - If fewer than three doses or unknown, administer a dose of diphtheria toxoid (DTaP, DT, or Td or Tdap as appropriate) and complete primary series according to schedule.
   - If three or more doses and last dose was more than five years ago, administer a booster dose of diphtheria-containing toxoid.
   - If three or more doses and last dose was less than five years ago, children needing their fourth primary dose or booster dose should be vaccinated; otherwise vaccination is not required.

4. All close contacts, regardless of their culture result or immunization status, should begin antibiotic prophylaxis with
   - Oral erythromycin (40–50 mg/kg/day for ten days, maximum 2 g/day) or
   - Intramuscular benzathine penicillin G (600,000 U for children weighing less than 30 kg and 1.2 million U for children weighing 30 kg or more and adults). This regimen is preferred for contacts who cannot be kept under surveillance since it is not dependent on adherence to an oral regimen.

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. Please refer to the most current versions of the Advisory Committee on Immunization Practices (ACIP) statement on diphtheria, pertussis, and tetanus (listed under References, below). These as well as other relevant resources are available through the NJDHSS VPDP at 609.826.4860.

**Additional Information**

Additional information about diphtheria can be obtained at the NJDHSS Web site at http://www.state.nj.us/health. Click on the “Health Topics A-Z” and scroll down to “Diphtheria.”

**References**


Attachment A: Collection of Specimens for Isolation of \textit{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)

Attachment D: Important Telephone Contacts for Diphtheria Control (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.

- Place swabs in a culturette 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. Send specimen with the attached submission form to the New Jersey Department of Health and Senior Services (NJDHSS) Public Health and Environmental Laboratories (PHEL).
- Call the NJDSS PHEL at 609.984.2514 to notify them 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, PHEL staff will arrange for shipment of isolates to the Diphtheria Laboratory, National Center for Infectious Diseases, Centers for Disease Control and Prevention (CDC), as directed by the CDC.

*Last Updated April 2010*
### Overview of Requirements for Laboratory Testing for Diphtheria

<table>
<thead>
<tr>
<th>Test name</th>
<th>Specimens to take</th>
<th>Timing for specimen collection</th>
<th>Transport requirements</th>
<th>Collection &amp; notification requirements</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Culture</td>
<td>• Swabs of nose, throat, and membrane (or other infected body site) of case</td>
<td>As soon as possible, when diphtheria is suspected</td>
<td>&lt; 24 hours: Amies or modified Stuart’s medium</td>
<td>Physicians or labs call NJDHSS PHEL at 609.984.2514 and</td>
<td>Available at PHEL and elsewhere. Alert lab that diphtheria is suspected to ensure that tellurite-containing media is used. After isolation, biotype (strain) and toxigenicity can be determined.</td>
</tr>
<tr>
<td></td>
<td>• Swabs of nose and throat of close contacts</td>
<td></td>
<td>≥ 24 hours: silica gel sachets</td>
<td>NJDHSS VPDP at 609.826.4860 regarding suspect case. NJDHSS may call CDC diphtheria lab at 404.639.1730 or 404.639.4057</td>
<td></td>
</tr>
<tr>
<td>PCR</td>
<td>Swabs (as above), or pieces of membrane or biopsy tissue of case</td>
<td>As soon as possible, when diphtheria is suspected</td>
<td>Silica gel sachet, or a sterile dry container at 4°C</td>
<td>Contact as above</td>
<td>Available only at CDC. 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.</td>
</tr>
<tr>
<td>Toxigenicity testing (Elek test)</td>
<td>Isolate from culture of case (above)</td>
<td>After <em>C. diphtheriae</em> has been isolated</td>
<td>Transport medium such as Amies medium or silica gel sachets</td>
<td>Contact as above</td>
<td>Available at NJDHSS PHEL, CDC, and elsewhere.</td>
</tr>
<tr>
<td>Serology (antibodies to diphtheria toxin)</td>
<td>Serum of case</td>
<td>Before administration of antitoxin or vaccine, collect paired sera, taken 2-3 weeks apart</td>
<td>Frozen (-20°C)</td>
<td></td>
<td>Available only 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.</td>
</tr>
</tbody>
</table>

Algorithm for Diagnosis, Treatment, and Follow-up of Suspect Diphtheria Cases and Infected Contacts

1. Institute strict isolation
2. Notify lab and obtain nasal & pharyngeal cultures for *C. diphtheriae*
3. Obtain serums for antibodies to diphtheria toxoid
4. Consider treatment with diphtheria antitoxin (DAT)
5. Begin antimicrobial therapy
6. Provide active immunization with tetanus diphtheria toxoid
7. Take two repeat pairs of nasal and pharyngeal cultures (≥ 24 hours apart) at least 24 hours after completion of antibiotic therapy. If cultures are not taken, cultures should be done after symptoms resolve and ≥ 2 weeks after the onset.

Identify Close Contacts

Obtain cultures for *C. diphtheriae*

Administer antimicrobial prophylaxis

Assess diphtheria toxoid vaccination status

Positive

Negative

< 3 doses or unknown

≥ 3 doses, last dose ≥ 5 years ago

≥ 3 doses, last dose < 5 years ago

- Avoid close contact with inadequately vaccinated persons
- Identify close contacts and proceed with preventive measures described for close contact of a case
- Take two repeat pairs of nasal and pharyngeal cultures (≥ 24 hours apart) at ≥ 2 weeks after completion of antibiotic therapy

Administer immediate dose of diphtheria toxoid and complete primary series according to schedule

Administer immediate booster dose of diphtheria toxoid

Children in need of their fourth primary dose or booster dose should be vaccinated; otherwise vaccination not required

1. Maintain isolation until elimination of the organism is demonstrated by negative cultures of two samples obtained at least 24 hours apart and taken ≥ 2 weeks after completion of antimicrobial therapy. If antibiotic therapy is not taken, cultures should be done after symptoms resolve and it is ≥ 2 weeks since their onset.
2. Both nasal and pharyngeal swabs should be obtained for culture.
3. If acute diphtheria antitoxin is needed, contact your state health department. Before administration, patients should be tested for sensitivity to horse serum and, if necessary, desensitized. The recommended dosage and route of administration depend on the extent and duration of disease. Detailed recommendations can be obtained from the package insert and other publications.
4. Antimicrobial therapy is not a substitute for antitoxin treatment. Antimicrobial: Erythromycin, orally or by injection (40-50 mg/kg/day; maximum, 2 g/day) for 14 days or procaine penicillin G daily, intramuscularly or intravenously (25,000-50,000 U/kg/day for mild to moderate infection; 250,000-400,000 U/kg/day for severe infection; maximum, 24 million U/day) for 14 days.
5. Vaccination with diphtheria toxoid is required because clinical diphtheria does not necessarily confer immunity.
6. Persons who continue to harbor the organism after treatment with either penicillin or erythromycin should receive an additional 10-day course of oral erythromycin and should submit samples for follow-up cultures.
7. Close contacts include household members and other persons with a history of direct contact with a case-patient (e.g., caretakers, relatives, or friends who regularly visit the home) as well as medical staff exposed to oral or respiratory secretions of a case-patient.
8. Antimicrobial prophylaxis: oral erythromycin (40-50 mg/kg/day for 10 days, maximum 2 g/day) or intramuscular benzathine penicillin G (600,000 U for children weighing < 30 kg and 1.2 million units for children weighing ≥ 30 kg and adults); intramuscular is preferred for contacts who cannot be kept under surveillance since it is not dependent on adherence to an oral regimen.
9. Preventive measures may be extended to close contacts of carriers but should be considered a lower priority than control measures for contacts of each case.
10. Refer to published recommendations for the schedule for routine administration of diphtheria-containing vaccines.

Important Telephone Contacts for Diphtheria Control

New Jersey Department of Health and Senior Services (NJDHSS)
P.O. Box 369
Trenton, NJ 08625-0369

NJDHSS Vaccine Preventable Disease Program 609.826.4860
(Monday through Friday, 8:30 am to 5:00 pm)

NJDHSS Infectious and Zoonotic Diseases Program 609.826.5964
(Monday through Friday, 8:30 am to 5:00 pm)

NJDHSS CDS On-Call Answering Service 609.392.2020
(nights, weekends, holidays)

NJDHSS Public Health & Environmental Laboratories 609.984.2514
(Bacteriologists available Monday through Friday, 8:00 am to 5:00 pm)

Centers for Disease Control and Prevention (CDC)
Bacterial Vaccine-Preventable Disease Branch
Epidemiology and Surveillance Division (MS E-61)
National Immunization Program
Diphtheria Duty Officer 404.639.3158 or 404.639.8257
(Monday through Friday, 8:00 am to 4:30 pm ET)

CDC Emergency Operations Center 770.488.7100