Diphtheria

BASIC EPIDEMIOLOGY

Infectious Agent
Toxin-producing strains of *Corynebacterium diphtheriae*

Transmission
Direct person-to-person transmission by intimate respiratory and physical contact. Cutaneous skin lesions are also important in transmission.

Incubation Period
Usually 2-5 days (range 1-10 days)

Communicability
Untreated individuals generally shed bacteria from the respiratory tract or from skin lesions for 2-4 weeks after infection. Infected individuals are infectious for up to 4 days after antibiotic treatment has been initiated. A chronic carrier state is extremely rare, but known to exist, and such a carrier may shed organisms for up to 6 months or longer.

Clinical Illness
Classic diphtheria is an upper respiratory tract illness characterized by sore throat, low-grade fever, and an adherent membrane of the tonsils, pharynx, and/or nose. The disease can involve almost any mucous membrane. Growth of the adherent membrane can cause a potentially fatal airway obstruction. Patients with severe disease can develop a “bullneck” appearance caused by edema of the anterior neck.

Cutaneous diphtheria is either caused by toxigenic or non-toxigenic strains of *C. diptheriae*. The disease is usually mild, typically consisting of non-distinctive sores or shallow ulcers, and rarely causes toxic complications. Cutaneous infections represent 1-2% of infections with toxigenic strains. Cutaneous diphtheria is not reportable but should be promptly investigated to determine whether the strain is toxigenic.

DEFINITIONS

Clinical Case Definition
An upper respiratory tract illness typically characterized by sore throat, low-grade fever, and an adherent membrane of the tonsil(s), pharynx, larynx, and/or nose with an adherent membrane of the nose, pharynx, tonsils, or larynx **OR** an infection of non-respiratory anatomical site (e.g., skin, wound, conjunctiva, ear, genital mucosa)

Laboratory Criteria for Diagnosis
- Isolation of toxin-producing *Corynebacterium diphtheriae* from any site, **AND**
- Confirmation of toxin-production by Elek test or by another validated test capable of confirming toxin-production

Case Classification
- **Confirmed:**
  - A clinically compatible case that is:
    - Laboratory confirmed **OR**

        - Epidemiologically linked to a laboratory-confirmed case
    - An infection of a non-respiratory anatomical site (e.g., skin, wound, conjunctiva, ear, genital mucosa) with:
        - Isolation of toxin-producing *Corynebacterium diphtheriae* from any site
- **Probable:** No probable case definition

Note: PCR (polymerase chain reaction) and MALDI-TOF (matrix-associated 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, which can be performed at the CDC through submission to the DSHS Lab in Austin.

SURVEILLANCE AND CASE INVESTIGATION

Case Investigation
Local and regional health departments should immediately investigate any reported suspect cases of diphtheria.

****If a provider suspects respiratory diphtheria, the provider should be instructed to call the Texas Department of State Health Services EAIDU to discuss the case and determine whether diphtheria antitoxin is needed. During business hours, the provider should call 512-776-7676, after hours the number is 512-221-6852****

EAIDU will evaluate and determine the need for antitoxin prior to contacting the Centers for Disease Control and Prevention (CDC) for diphtheria antitoxin, if still required. The current CDC Emergency Operations Center (EOC) protocol has been revised to redirect medical care providers requesting DAT (for treatment of suspected diphtheria) to contact their respective state health departments and discuss their case, if they have not previously done so.

If the CDC releases antitoxin, the following control measures should be implemented immediately. If the CDC does not feel antitoxin is warranted, the control measures can be implemented after laboratory/pathological confirmation.

Case Investigation Checklist
- ☐ If not done already, notify DSHS EAIDU immediately and discuss possible release of antitoxin for respiratory diphtheria. Antitoxin is not recommended for cutaneous diphtheria, unless there are signs of systemic toxicity.
- ☐ If deemed to be a candidate for antitoxin by EAIDU, refer provider to CDC for antitoxin.
- ☐ Isolate patient (for respiratory infections, standard + droplet precautions; if cutaneous, contact).
- ☐ Confirm that laboratory results meet the case definition.
- ☐ Verify that the laboratory has forwarded the specimen to the DSHS laboratory. See Laboratory Procedures.
- ☐ Review medical records or speak to an infection preventionist or physician to verify case definition, underlying health conditions, course of illness, vaccination status and travel history.
    - Request copies of admission and discharge summaries and laboratory results.
- ☐ Determine vaccination status of the case. Sources of vaccination status that should be checked include:
    - Case (or parent), ImmTrac, school nurse records, primary care provider, etc.
- ☐ Identify and follow-up with all close contacts. See Managing Close Contacts below.
    - Collect specimens and send to the DSHS laboratory.
    - Provide prophylaxis (see Prophylaxis Guidelines).

- Monitor for 7 days.
- Give vaccination or booster as appropriate for age and vaccination status.

- ☐ Submit specimens from case and close contacts to the DSHS laboratory.
- ☐ All confirmed case investigations must be entered and submitted for notification in the NEDSS Base System (NBS). Please refer to the *NBS Data Entry Guidelines* for disease specific entry rules.

Control Measures

- ☐ Reports of suspected diphtheria should be investigated **immediately**.
- ☐ Universal vaccination with a diphtheria toxoid containing vaccine is the best prevention and control measure.
- ☐ Identify and follow-up with close contacts of confirmed cases.
  - Only close contacts of a patient with culture-confirmed or suspected diphtheria should be considered at increased risk for acquiring secondary disease. Such contacts include all household members and other persons with a history of habitual close contact with the patient, as well as those directly exposed to oral secretions of the respiratory patient or wound of the cutaneous patient.
  - Treat any contact with antitoxin at the first sign of respiratory illness. **CONTACT EAIDU**.
- ☐ Patient should be kept in strict isolation until two cultures from both throat and nose, taken at least 24 hours apart and at least 24 hours after cessation of antimicrobial therapy, are negative for diphtheria bacilli. If cultures are not possible, patient should be kept in isolation for 14 days following appropriate antibiotic treatment.
- ☐ Treat any confirmed carrier with an adequate course of antibiotic and repeat cultures at a minimum of 2 weeks to ensure eradication of the organism. Persons who continue to harbor the organism after treatment with either penicillin or erythromycin should receive an additional 10-day course of erythromycin and should submit samples for follow-up cultures. Cases should be monitored until hospital discharge, even if all investigation and control measures have been completed.

Managing Close Contacts

- ☐ Close contacts include household members and other persons directly exposed to oral secretions of a respiratory diphtheria case or the wound of a cutaneous diphtheria case.
- ☐ Close contacts should be cultured regardless of their immunization status, receive prompt antimicrobial chemoprophylaxis, and be examined daily for seven days for evidence of disease.
  - Submit specimens from close contacts to the DSHS laboratory.
  - Do not wait for culture results before treating contacts.
- ☐ After culture, all contacts should receive antibiotic prophylaxis (see below).

Prophylaxis Guidance

- ☐ **Inadequately immunized contacts should receive DTap/DT/Td/Tdap boosters.**
- ☐ All close contacts who have received fewer than 3 doses of diphtheria toxoid or whose vaccination status is unknown should receive an immediate dose of a diphtheria toxoid-containing preparation appropriate for their age and should complete the primary series according to the recommended schedule.
- ☐ If more than 5 years have elapsed since administration of diphtheria toxoid-containing vaccine, a booster dose should be given.
- ☐ If the most recent dose was within 5 years, no booster is required.
- ☐ Unimmunized contacts should start a course of DTap/DT/Td vaccine and be monitored closely for symptoms for 7 days.
- ☐ Recommended prophylaxis is a 7-10-day course of oral erythromycin (children 40 mg/kg/day and adults 1 g/day).
- ☐ Identified carriers of *C. diphtheriae* should be cultured after they complete antimicrobial

therapy. Those who continue to carry the organism should receive an additional 10-day course of oral erythromycin and follow-up cultures.

Treatment
The mainstay of treatment of a case of suspected respiratory diphtheria is prompt administration of diphtheria antitoxin. This should be given without waiting for laboratory confirmation of a diagnosis. Antitoxin is only available from the CDC, usually through the Quarantine Station in Houston. To determine whether or not the case-patient is approved for antitoxin release, call EAIDU at 512-776-7616 or 512-221- 6892 (after hours).

Cutaneous diphtheria should have the wound thoroughly cleaned with soap and water and the patient given appropriate antibiotics for 10 days.

Exclusion
Patient should be excluded until released from isolation by provider.

MANAGING SPECIAL SITUATIONS

Outbreaks
If an outbreak of diphtheria is suspected, notify the regional DSHS office or EAIDU at **(800) 252-8239 or (512) 776-7676**.

REPORTING AND DATA ENTRY REQUIREMENTS

Provider, School & Child-Care Facilities, and General Public Reporting Requirements
Clinically suspected diphtheria cases are required to be reported **immediately** to the local or regional health department or to DSHS EAIDU at **(800) 252-8239 or (512) 776-7676**.

Local and Regional Reporting and Follow-up Responsibilities
Local and regional health departments should:

- Enter the case into NBS and submit an NBS notification on all **confirmed** cases to DSHS within 30 days of receiving a report of a confirmed case.
  - Please refer to the *NBS Data Entry Guidelines* for disease-specific entry rules.
  - A notification can be sent as soon as the case criteria have been met. Additional information from the investigation may be entered upon completing the investigation.
- Fax, send a secure email, or mail a completed investigation form within 30 days of completing the investigation.
  - **In the event of a death, copies of the hospital discharge summary, death certificate, and autopsy report should also be sent to DSHS EAIDU.**
  - Investigation forms may be faxed to **512-776-7616**, securely emailed to VPDTexas@dshs.texas.gov or mailed to:

Infectious Disease Control Unit
Texas Department of State Health Services Mail Code: 1960
PO Box 149347
Austin, TX 78714-9347

When an outbreak is investigated, local and regional health departments should:

- Report outbreaks within 24 hours of identification to the regional DSHS office or to EAIDU at (800) 252-8239 or 512-776-7676.

LABORATORY PROCEDURES

Isolation and identification of *Corynebacterium diphtheriae* is available through the DSHS

Laboratory. Specimens should be sent to DSHS from cases and all close contacts. Before shipping specimens, be sure to notify DSHS EAIDU VPD staff at **(512) 776-7676.**

Please refer to the TAC Title 25, Ch 97, Subchapter A, Rule §97.3 “What Condition to Report and What Isolates to Report or Submit”.

Specimen Collection

- Use a cotton-tipped or polyester-tipped swab.
- Swabs should be taken below the membrane, if possible. (A portion of the membrane may be submitted for culture, but does not always yield *C. diphtheriae* well.)
- Ship swabs in Amie’s or Stuarts Transport or transfer to a Loeffler’s Slant for transport to DSHS Labs.

Submission Form

- Use DSHS Laboratory G-2B form for specimen submission.
- Make sure the patient's name and date of birth or social security number match exactly what is written on the transport tubes.
- Fill in the date of collection, date of onset, and diagnosis/symptoms.

Specimen Shipping

- Transport temperature: Keep at 2° - 25°C.
- Ship specimens via overnight delivery on cold packs or wet ice (double bagged) within 48 hours of collection.
- DO NOT mail on a Friday or a day before a state holiday unless special arrangements have been pre- arranged with DSHS Laboratory.
- Ship specimens to:

Laboratory Services Section, MC-
1947 Texas Department of State
Health Services Attn. Walter
Douglass (512) 776-7569 1100 West
49th Street
Austin, TX 78756-3199

Causes for Rejection:

- Incorrect source of specimen
- Specimen > 24 hours not in transport medium
- Missing or discrepant information on form/specimen

REVISION HISTORY

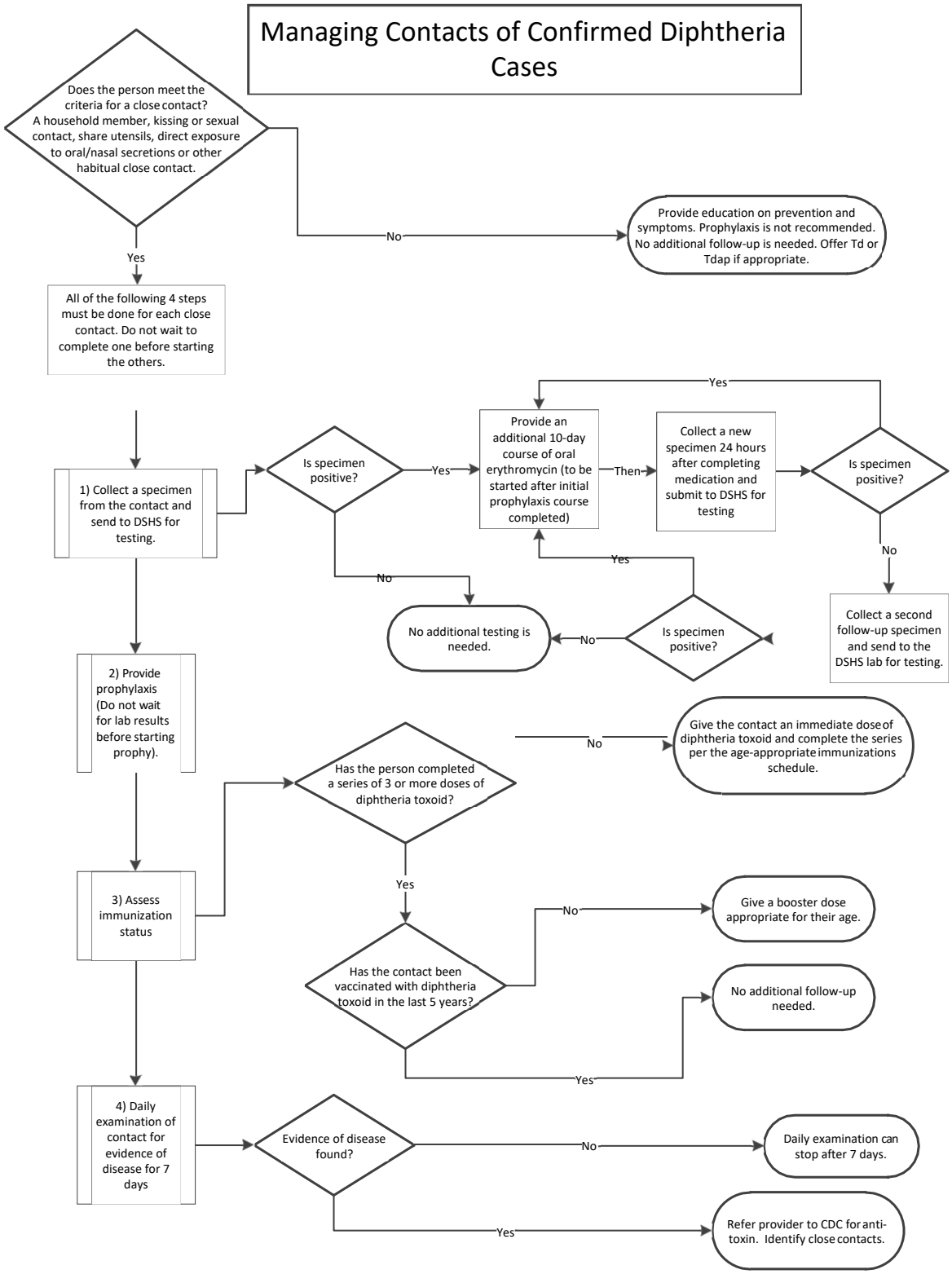
January 2021

- Updated case classification
- Updated Managing Close Contacts
- Added Prophylaxis Guidelines section
- Updated throughout to add cutaneous diphtheria

December 2022

- Updated Case Investigation Checklist
- Updated Case Classification section

FLOW CHART


Managing Contacts of Confirmed Diphtheria Cases
Does the person meet the criteria for a close contact? A household member, kissing or sexual contact, share utensils, direct exposure to oral/nasal secretions or other habitual close contact.
No
Provide education on prevention and symptoms. Prophylaxis is not recommended. No additional follow-up is needed. Offer Td or Tdap if appropriate.
Yes
All of the following 4 steps must be done for each close contact. Do not wait to complete one before starting the others.
1) Collect a specimen from the contact and send to DSHS for testing.
Is specimen positive?
Yes
Provide an additional 10-day course of oral erythromycin (to be started after initial prophylaxis course completed)
Then
Collect a new specimen 24 hours after completing medication and submit to DSHS for testing
Is specimen positive?
Yes
No
Collect a second follow-up specimen and send to the DSHS lab for testing.
Yes
No
Is specimen positive?
No
No additional testing is needed.
2) Provide prophylaxis (Do not wait for lab results before starting prophy).
No
Give the contact an immediate dose of diphtheria toxoid and complete the series per the age-appropriate immunizations schedule.
Has the person completed a series of 3 or more doses of diphtheria toxoid?
Yes
3) Assess immunization status
No
Give a booster dose appropriate for their age.
Has the contact been vaccinated with diphtheria toxoid in the last 5 years?
No additional follow-up needed.
Yes
4) Daily examination of contact for evidence of disease for 7 days
Evidence of disease found?
No
Daily examination can stop after 7 days.
Yes
Refer provider to CDC for anti-toxin. Identify close contacts.