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EPI-NEWS

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IN THIS ISSUE: *CORYNEBACTERIUM DIPHTHERIAE*

Toxin & Non-Toxin-Producing *C. diphtheriae*: Recognition, Risks, and Reporting

Background

Diphtheria is a rare but potentially serious disease caused by the bacterium *Corynebacterium diphtheriae* (*C. diphtheriae*). While respiratory diphtheria remains the best-known form, cutaneous diphtheria is an emerging issue in the United States and globally.[1, 2] There have been no cases of diphtheria reported in Washoe County in at least the last 25 years. Cutaneous cases are most common in individuals with disrupted skin barriers and in communities with overlapping social vulnerabilities.

Epidemiology & Transmission

Diphtheria is an acute, bacterial disease caused by toxin-producing strains of *C. diphtheriae.*[3] Toxigenic strains, usually acquired in the nasopharynx, produce diphtheria toxin that inhibits cellular protein synthesis, destroying local tissue and forming a pseudomembrane that makes it difficult to breathe or swallow.[3] This form is responsible for major complications, including myocarditis and fatal airway obstruction, but it is vaccine-preventable (e.g. DTaP, Td, Tdap, etc.).[3] Nontoxigenic strains of *C. diphtheriae* do not produce toxin but can still lead to localized and invasive disease, including endocarditis and bacteremia.[1, 2] Non-toxin-producing strains of the organism are not counted as diphtheria for reporting purposes because the severe manifestations and complications of diphtheria are caused by the diphtheria toxin produced by the bacteria; non-toxigenic strains may still cause illness but are generally less severe and not considered classic diphtheria.[4]

Humans are believed to be the sole reservoir of *C. diphtheriae*. Transmission occurs via respiratory droplets or through contact with wound secretions. In untreated people, organisms can be present in discharges from the nose and throat and from eye and skin lesions for two to six weeks after infection.[2] The incubation period is two to five days (range of one to 10 days).[2, 3] Disease can involve almost any mucous membrane but is classified by anatomic site infected: respiratory (pharyngeal, tonsillar, laryngeal, nasal) and non-respiratory (cutaneous and other mucus membranes) disease.[3] Diphtheria used to be one of the most common causes of illness and death among children, but now diphtheria is well controlled primarily due to vaccination, with the last U.S. case of confirmed respiratory diphtheria in 1997.[5] A small number of toxigenic cutaneous cases associated with international travel have been reported since (4 toxigenic cases identified from 2015 to 2018 among travelers to areas with endemic diphtheria).[2]

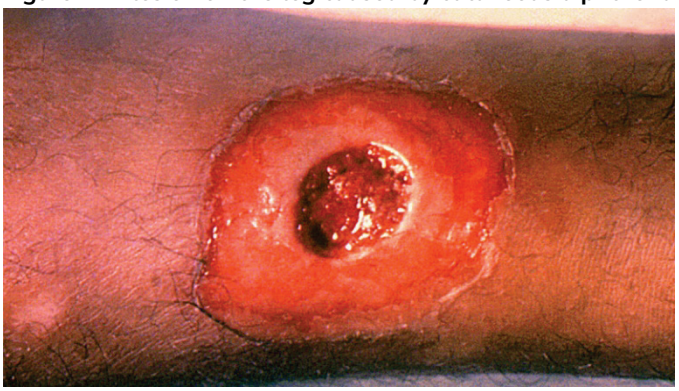
Understanding nontoxigenic forms of *C. diphtheriae* is also important because diphtheria toxoid-containing vaccines create immunity to the toxin itself but cannot protect against infection or illness caused by nontoxigenic *C. diphtheriae.*[6] Unfortunately, as nontoxigenic cutaneous *C. diphtheriae* is not nationally notifiable and cutaneous diphtheria was not notifiable in the United States from 1980 to 2018, U.S. disease incidence and trend data are limited.[4] However, there have been increased nontoxigenic cutaneous *C. diphtheriae* cases reported in Washington State since 2018 among unhoused individuals and people who use drugs.[6, 7] Between 2018 and 2023, Washington State reported 176 patients with nontoxigenic *C. diphtheriae*, of which 78% were from a cutaneous wound culture, 97% of those were polymicrobial, 63% were from persons experiencing unstable housing or recently used illicit substances, 12% had bacteremia, 4% were diagnosed with endocarditis, 8% died, and none had clinical findings suggestive of diphtheria.[6]

Clinical Presentation

Respiratory diphtheria has a gradual onset and is characterized by mild fever, sore throat, and a pseudomembrane over the mucous lining of the

tonsils, pharynx, or larynx. \Cutaneous diphtheria typically presents as non-healing or shallow wounds with grayish membranes or erythematous borders and may present as a scaling rash or ulcers with clearly demarcated edges [Fig. 1].[2, 8] Lesions are frequently polymicrobial (most often *S. aureus* and *S. pyogenes)* and may be indistinguishable from other chronic wounds.[2, 6, 9] Systemic complications such as bacteremia and endocarditis have occurred even in nontoxigenic infections.[6]

Figure 1: A lesion on the leg caused by cutaneous diphtheria.



Source: https://www.cdc.gov/diphtheria/hcp/clinical-signs/index.html

Diagnosis & Testing

Diagnosis of respiratory diphtheria is usually based on clinical presentation because it is imperative to begin presumptive therapy quickly. However, cutaneous diphtheria may not be clinically suspected; therefore, diagnosis is typically based on the laboratory finding.[3] Culture is the gold standard for detecting *C. diphtheriae*.[1, 2] Specimen collection for diphtheria culture of the nose, throat, or wounds can be conducted using standard swab materials.[10] It is critical to take a swab of the affected area, especially any ulcerations or pseudomembranes, prior to antibiotic treatment if possible.[3] The organism can be cultured on common laboratory media; however, further biochemical tests are required to fully identify an isolate as *C. diphtheriae*. If *C. diphtheriae* is isolated, it must be tested for toxin production. Clinical laboratories are required to submit an isolate to the Nevada State Public Health Lab (NSPHL) to confirm the organism identification and for forwarding to the Diphtheria Laboratory at the National Center for Immunization and Respiratory Diseases where it can be determined if the strain is toxigenic (Elek test).[10, 11]

Treatment & Infection Control

If respiratory diphtheria is suspected, a single dose of diphtheria (equine) antitoxin (DAT) should be administered before culture results are available. This must be done in consultation with NNPH as DAT is not available from any commercial source.[2] However, if cutaneous diphtheria is suspected, DAT is generally not recommended as it is not typically recommended in cases of nonrespiratory diphtheria.[2] Acceptable therapy for respiratory and nonrespiratory *C. diphtheriae* infections (regardless of toxigenicity status) is 14 days of erythromycin, administered orally or parenterally, or penicillin administered orally, intravenously, or intramuscularly.[2] If cutaneous, an appropriate antimicrobial agent for 10 days is acceptable with additional, thorough wound care.[2]

Patients with suspected cutaneous diphtheria should be placed on contact precautions until two negative cultures (≥24 hours apart and ≥24 hours after antibiotics) confirm clearance.[2] Patients treated with an appropriate antimicrobial agent usually are not infectious beginning 48 hours after treatment is initiated.[2] Follow-up testing to confirm elimination is not required for nontoxigenic *C. diphtheriae* infections.[2] Unvaccinated or partially vaccinated persons recovering from diphtheria should begin or complete active immunization with diphtheria toxoid during convalescence.[3]

At-Risk Populations & Prevention

Nearly all diphtheria cases in the United States are associated with international travel with people who aren't up to date with their diphtheria vaccines at increased risk. However, recent international and U.S. clusters of cutaneous *C. diphtheriae*, particularly nontoxigenic, which are not preventable through vaccination, have disproportionately impacted individuals experiencing homelessness or substance use disorder.[12, 13] Education about wound hygiene, handwashing, not sharing personal items or drug paraphernalia, and seeking early care for infections is critical.[14] Vaccination with diphtheria toxoid-containing products remains essential to prevent toxigenic disease.

NOTE: Attached are two printable flyers that can be used to help provide information on wound infections to vulnerable populations and patients, including the unhoused and those with substance use disorders.

Reporting

All suspected or confirmed cases of toxigenic *C. diphtheriae*, including cutaneous cases, should be reported to NNPH immediately.[11, 15] Specimens must be forwarded for confirmatory testing to NSPHL. Toxigenicity testing remains critical given the potential for non-toxigenic strains to acquire the toxin gene.[1, 7]

The list of reportable communicable diseases and reporting forms can be found at: **http://tinyurl.com/WashoeDiseaseReporting**

Report communicable diseases to Northern Nevada Public Health. To report a communicable disease, please call 775-328-2447 or fax your report to the NNPH at 775-328-3764.

Acknowledgement

Thank you to all health care providers, infection control practitioners, and laboratory staff, for their reporting and collaboration to make this work possible.

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WOUND INFECTIONS

If you're facing housing instability or inject or use drugs, you are at higher risk.

Wound infections can spread easily among unhoused individuals. Wounds that are not kept clean and covered can become infected. Infection can lead to serious illness.

Here's how you can prevent infections & complications

TREATMENT

Get treatment for wounds, lice, bed bugs or itchy skin, especially if you have a fever. Keep wounds covered with a clean bandage.

BATHING & CLEANING

Bathe and wash clothing as regularly as possible.

HAND WASHING

Wash hands frequently with soap and water. Soap and water is best, but if unavailable, use hand sanitizer.

VACCINES

Make sure you are up to date on all vaccines, especially those that protect against tetanus and diphtheria.

CHECK WOUNDS

Check, clean, and cover wounds until healed. Red, swollen, or painful wounds should be checked by a health care provider as soon as possible.

HOW TO AVOID GETTING SICK:

DO NOT SHARE personal items like bars of soap, toothbrushes, razors, combs, unwashed clothing, towels, etc.

DO NOT SHARE food, drinks, dishes, or utensils

DO NOT SHARE cigarettes or items used to inject, smoke, or snort drugs (needles, cookers, water, tourniquets, pipes, etc.)

If you have skin or a wound that is painful or has swelling, pus, redness or red streaks, or is not healing, see a doctor or healthcare provider *as soon as possible*.

Wound Infections Prevention & Treatment

For people facing housing instability and substance use

KEEP WOUNDS CLEAN AND COVERED TO PREVENT INFECTION

- Wound infections can spread easily among **people living homeless**.
- Wounds that are **not kept clean and covered** can become infected.
- Infection can lead to **serious illness**.
- People **living homeless or who inject drugs** are at higher risk of wound infections.

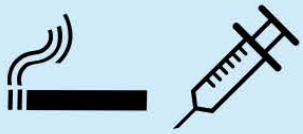
HOW TO PREVENT WOUNDS FROM GETTING INFECTED

- Get treatment for wounds, lice, bed bugs or itchy skin, especially if you have a fever. Keep wounds covered with a clean bandage.
- Regularly check, clean, and cover wounds until healed. Red, swollen, or painful wounds should be checked by a health care provider **as soon as possible.**
- Wash hands frequently with soap and water, especially after toileting, before meals, after coughing/sneezing, and after touching wounds. Soap and water is best, but if unavailable, use hand sanitizer.
- Bathe and wash clothing as regularly as possible.
- Make sure you are up to date on all vaccines, especially those that protect against tetanus and diphtheria.

AVOID SHARING

Personal care items (bar soap, toothbrushes, razors, combs, unwashed clothing, towels, etc.)

Food, drinks, dishes, or utensils



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If you have skin or a wound that is painful or has swelling, pus, redness or red streaks, or is not healing, see a doctor or healthcare provider as soon as possible.