Kansas
Department of Health and Environment
Division of Health

Diphtheria

Investigation Guideline

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Fact Sheet (vs. 12/2014)

Revision History:

Date	Replaced	Comments
05/2018	**12/2014**	Notification Section and Isolation...Restriction Section modified with requirements of revised regulations. Additional guidance provided on management of cutaneous case and contact management. Epidemiology section updated. Guidance added in data management on classification of cutaneous cases and asymptomatic (carrier) cases.
12/2014	**02/2012**	Updated Laboratory and Case Management Section. More details added to Investigators Responsibilities and Data Management. Reformatted Standard Case Investigation section to assist with EpiTrax system data entry. Reformatted fact sheet.
02/2012	**03/2009**	Revised format. Added diphtheria worksheet. Replaced BSE with BEPHI. Added notification section. Removed references to KS-EDSS. Revised case definition with CDC 2010 version.

Diphtheria
Disease Management and Investigative Guidelines

CASE DEFINITION (CDC 2010)

Case Classification:

- **Confirmed:**
  An upper respiratory tract illness with an adherent membrane of the nose, pharynx, tonsils, or larynx; and any of the following:
  - isolation of *Corynebacterium diphtheriae* from the nose or throat; or
  - histopathologic diagnosis of diphtheria; or
  - epidemiologic linkage to a laboratory-confirmed case of diphtheria.
- **Probable:**
  In the absence of a more likely diagnosis, an upper respiratory tract illnesswith:
  - 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.

Comment: Cutaneous diphtheria is not reported to CDC is still investigated by the local health jurisdiction.

LABORATORY ANALYSIS

Services available from the Kansas Health and Environmental Laboratories (KHEL):

- KHEL is not equipped to test for *C. diphtheriae*.
- KHEL will assist in the forwarding of isolates and specimens to the CDC Diphtheria Laboratory for testing:
  - KHEL's responsibility is to contact the CDC Diphtheria Laboratory and make arrangements for testing.
  - CDC will perform culture, toxigenicity testing, and polymerase chain reaction (PCR) tests on clinical specimens forwarded by KHEL.
    - CDC does not test sera for antibodies to *C. diphtheriae*.
- KHEL will only forward specimens to CDC that have been approved by the KDHE Infectious Disease and Epidemiology Response (IDER) unit.

Because respiratory diphtheria is very uncommon in the US, the medical provider must first review the attached Checklist for Assessing a Patient with Suspected Diphtheria and consider other agents in the differential diagnosis.

Other biological disease agents which may cause a membranous pharyngitis:

1. Group A β-hemolytic *Streptococcus*
2. *Staphylococcus aureus*
3. *Arcanobacter hemolyticum*
4. *Candida albicans*
5. *Borellia vincenti* (Vincent's angina)
6. *H. influenzae* (acute epiglottitis)
7. Viruses – EBV (Infectious mononucleosis), adenovirus, Herpes simplex
8. Other agents - *Toxoplasma*

Use of some anti-neoplastic agents may also result in formation of a pharyngeal membrane and the long-term use of corticosteroids can cause oral candidiasis.

If diphtheria is still suspected, the medical provider should contact the KDHE-IDER at 1-877-427-7317, and:

- Institute strict isolation.
- Arrange for antibody testing for diphtheria toxin though a commercial laboratory.
- Arrange for *C. diphtheriae* culture, and toxigenicity testing of any isolates, through a commercial laboratory.
    - Both nasal and pharyngeal swabs should be obtained for culture.
    - If a commercial laboratory cannot assist with the culture and toxigenicity testing, work with KDHE- IDER to use KHEL for forwarding to the CDC's Diphtheria Laboratory for testing.
- Consider treatment with diphtheria toxin (DAT). [*Suspect cases of pharyngeal diphtheria should receive diphtheria antitoxin immediately after bacteriologic specimens are taken without waiting for lab results.*] Refer to guidance in the:
    - Case Management section of this document and
    - CDC's Use of DAT for Suspected Diphtheria Cases—Protocol
- For pharyngeal diphtheria, arrange with KDHE-IDER for *C. diphtheriae* PCR testing at CDC.
    - Obtain additional clinical specimens for PCR testing when specimens are obtained for culture.
    - Ship specimens to KHEL for forwarding to CDC.
    - CDC will not perform PCR to rule out diphtheria unless diphtheria anti-toxin (DAT) has been requested to treat a patient.

Additional notes on Laboratory Testing:

- Testing of isolates: For *C. diphtheriae* and any other diphtheria toxin-producing *Corynebacterium* species (*C. ulcerans* or *C. pseudotuberculosis*), ***CDC requests that all isolates of these types be sent to the CDC Diphtheria Laboratory***.
- Serology: Measurement of serum antibodies to diphtheria toxin before administration of antitoxin helps to assess the probability of diphtheria.
    - <0.01 IU/ml, immunity is likely to be absent
    - >0.1 IU/ml, considered protective and diphtheria is unlikely the cause
    - Levels between 0.01 IU/ml to 0.09 IU/ml, indicate the presence of some or limited immunity
- PCR: If a patient has received antibiotics, PCR can still be used to detect the toxin production gene (dtxR) and the toxin gene (tox). It does not confirm a case for surveillance as the test does not show toxin is being actively produced.

For additional information on laboratory testing for confirmation of diphtheria, see:

- CDC's Diphtheria Laboratory web page: www.cdc.gov/diphtheria/laboratory.html
- CDC's Manual for the Surveillance of Vaccine-Preventable Diseases, Chapter 22: "Laboratory Support for the Surveillance of Vaccine-Preventable Diseases."

EPIDEMIOLOGY

Diphtheria occurs worldwide, particularly in tropical countries. It is a rare disease in industrialized countries with active immunization programs. In the U.S., from 1995 to 2015, 14 cases were reported; the median age was 28 years (range: 8 months–86 years) and the majority of cases (92%) were among persons 15 years of age or older.

Diphtheria epidemics can occur in susceptible populations. Contributing factors include increased susceptibility among adults due to waning of vaccine-induced immunity; and failure fully to immunize children because of unwarranted contraindications, anti-vaccine movements, and declining socioeconomic conditions. Outbreak control is achieved through mass immunization campaigns.

While rarely developing into systemic disease or being transmitted to others, cutaneous diphtheria still has the potential to result in respiratory or cutaneous infections in other susceptible hosts. While more common in tropical climates, it is associated with homeless persons or those with poor hygiene in the U.S.

DISEASE OVERVIEW

A. Agent:
Diphtheria is caused by toxin-producing biotypes of *C. diphtheriae*, a gram-positive bacillus. The 4 biotypes, in order of likelihood of producing toxin, are: *gravis*, *mitis*, *intermedius*, and *belfanti*.

B. Clinical Description:
A toxin mediated, upper respiratory tract illness characterized by sore throat, low-grade fever, and an adherent grayish membrane of the tonsil(s), pharynx, and/or nose. Symptoms also include large tender cervical lymph nodes, and marked swelling and edema of neck ("bull neck"). Upper airway obstructions may be caused by extensive membrane formation. Late effects of the toxin include cranial and peripheral motor and sensory nerve palsies, myocarditis, and nephropathy. Cutaneous diphtheria usually appears as a localized ulcer that is non-healing.

C. Reservoirs:
Humans are the only reservoir of *C. diphtheria.*

D. Mode(s) of Transmission:
Person-to-person transmission by respiratory droplets or direct contact with respiratory secretions, discharges from skin lesions or, rarely, fomites. Raw milk may serve as a vehicle of transmission.

E. Incubation Period:
Average, 2-5 days (range 1-10 days).

F. Period of Communicability:
Transmission may occur as long as virulent bacilli are present in discharges and lesions. Usually < 2 weeks and rarely > 1 month. Effective antibiotic therapy can reduce communicability to < 4 days. Carriers may shed organisms for ≥ 6 months.

G. Susceptibility and Resistance:
Infants born of immune mothers are relatively immune; protection is usually lost before the 6th month. Lifelong immunity is usually, but not always, acquired after infection. Prolonged active immunity can be induced by toxoid.

H. Treatment: **

- Suspect cases of pharyngeal diphtheria should receive diphtheria antitoxin (DAT) immediately after bacteriologic specimens are taken without waiting for lab results. Appropriate antibiotic therapy with erythromycin or penicillin should then be given in conjunction with antitoxin to eradicate the organism and reduce the period of communicability.
    - Antibiotics are not substitutes for antitoxin which is the primary treatment.
- Suspect cases of cutaneous diphtheria should receive appropriate antibiotic therapy with erythromycin or penicillin immediately after bacteriologic specimens are taken prior to lab results.

NOTIFICATION TO PUBLIC HEALTH AUTHORITIES

All confirmed or ***suspected*** diphtheria cases shall be reported within **4 hours by phone** **:

1. Health care providers and hospitals: report to local health jurisdiction
2. Laboratories: report to KDHE - BEPHI
3. Local health jurisdiction: report to KDHE - BEPHI

Kansas Department of Health and Environment (KDHE)
Bureau of Epidemiology and Public Health Response (BEPHI)
Phone: 1-877-427-7317

****** ***Suspected cases of respiratory diphtheria should be reported promptly by telephone to CDC so that diphtheria antitoxin can be obtained patient.***

- U.S. physicians caring for patients with suspected respiratory diphtheria can obtain DAT by contacting the CDC's Emergency Operations Center at 770-488-7100. The diphtheria duty officer at CDC's Meningitis and Vaccine Preventable Diseases Branch (MVPDB) in the Division of Bacterial Diseases (DBD) of the National Center for Immunization and Respiratory Diseases (NCIRD) will discuss the case and protocol for DAT release with the physician.

Further responsibilities of state and local health departments to the CDC:
As a nationally notifiable condition, all respiratory diphtheria cases even before classification require an IMMEDIATELY NOTIFIABLE, URGENT report to the Center of Disease Control and Prevention (CDC).

1. *IMMEDIATELY NOTIFIABLE, URGENT* reporting requires a KDHE epidemiologist to call the CDC EOC at 770-488-7100 within 24 hours of a case meeting the notification criteria, followed by submission of an electronic case notification in next regularly scheduled electronic transmission.
    - KDHE-BEPHI will notify the CDC immediately by phone of all confirmed or suspected cases and will file electronic reports weekly with CDC.
2. **Local public health jurisdiction** will report information requested on the supplemental form as soon as possible, completing the form within 3 days of receiving a notification of a report.

INVESTIGATOR RESPONSIBILITIES

1) Report all suspected or confirmed diphtheria cases to the KDHE.

2) Initiate the case investigation within1 day of notification of a report.
- Complete the investigation within 3 days of the notification.
- Use the CDC *Diphtheria Worksheet* as a guide for data collection.

3) Contact medical provider to collect additional information and confirm diagnosis using the current case definition.
- Collect all information requested in Step 1) of case investigation.
- Verify that laboratory testing has occurred or is underway for a of *C. dipththeriae* culture and serology for antibodies to dipththeria toxin
- Ensure isolates of any toxin-producing *Corynebacterium species* are sent KHEL for transport to CDC.
- For pharyngeal diphtheria, what is the status of DAT release?
- Ensure patient isolation and antimicrobial therapy has begun.
- Ensure that the patient is aware of his/her diagnosis.

4) Conduct a case investigation to determine the individual's risks of exposure and potential geographical location of exposure.
- If there is no known exposure (low suspicion) and no high-risk transmission setting (unvaccinated contacts), wait for laboratory results to confirm and a final diagnosis prior to starting the contact investigation.
- If there is a possible exposure (high suspicion) or a potential high-risk transmission setting (unvaccinated contacts), the investigator should immediately start the contact investigation.

5) Situations of high suspicion or potential high-risk situations include:
- Suspected case is reported from a group objecting to vaccination.
- Suspected case traveled internationally within his/her exposure period.
- Suspected case was exposed to a diphtheria case or carrier or to an international traveler or immigrant.
- Suspected case interacted with unimmunized or under-immunized individuals during his/her infectious period or a healthcare setting, school/daycare or food facility is involved.

6) Conduct contact investigation to locate additional cases and/or contacts.

7) Control and prevention measures will include case management and contact management with restrictions on activity, collecting of specimens for culture, antibiotic treatment, and vaccinations.
- Contacts of cutaneous cases require no restrictions, unless they are later identified as diphtheria carriers or cases.
- Cutaneous infections with non-toxigenic strains require no close contact management.

8) Record data, collected during the investigation, in the KS EpiTrax system under the data's associated [tab] in the case morbidity report (CMR).

9) As appropriate, use the disease fact sheet to notify individuals or groups.

STANDARD CASE INVESTIGATION AND CONTROL METHODS

Case Investigation

1) Contact the medical provider who ordered testing and obtain the following information. (This includes medical records for hospitalized patients.)
   - Collect patient's demographics and contacting information (address, birth date, gender, race/ethnicity, primary language, and phone number(s)) [Demographic]
   - Obtain clinical information on:
     - Date of illness onset [Clinical]
     - Date diagnosed-presumptive [Clinical]
     - Date of final diagnosis, what was diagnosed, and how was the final diagnosis confirmed. [Clinical]
     - Symptoms & signs: type of wound (if present), fever, sore throat, difficulty swallowing, change in voice , shortness of breath, weakness, fatigue, membrane present (specify anatomical site of membrane), soft tissue swelling around membrane, neck edema (specify: bilateral or side of swelling and extent of swelling), stridor, wheezing, palatal weakness, tachycardia, and EKG abnormalities) [Investigation-Symptoms]
     - Complications and date of complication onset for pharyngeal symptoms: airway obstruction, myocarditis, polyneuritis, or other (describe) [Investigation-Complications]
     - Examine the laboratory testing that was done, especially:
       - Culture, biotype and toxigenicity test*, PCR, molecular typing.
     - Determine if further laboratory testing is needed.
       - If not yet done, coordinate testing for symptomatic, highly suspected cases.
   - Record treatment, including: [Clinical]
     - Antibiotics prescribed, date started and duration of therapy [Clinical]
     - DAT administration, including amount antitoxin [Investigation-Follow Up]
   - Request history of immunization against diphtheria, post-vaccine antibody titers, or information on why the patient, if less than 18 years of age, is not immunized or fully immunized. [Investigation-Vaccination History]
     - If not available from the medical records, attempt to collect the information from another credible source.
   - Record hospitalizations: location, duration of stay, and reason [Clinical]
   - Record outcomes: "Recovered, no residual", "Recovered, residual", or Death (with date of death) [Clinical]

** All cases of pharyngeal diphtheria require close contact management. Only toxigenic strains of cutaneous diphtheria will require close contact management. (Pink Book, 2015)*

2) Interview the patient to determine source, risk factors and transmission settings.
   - Travel History:
     - If not US resident, record date of US arrival. [Investigation-Exposure]
     - Record any travel outside of Kansas 14 days before illness began; specify whether travel was inside the US and/or international (include dates and locations) [Investigation-Exposure]
     - Noting travel dates and locations record where the infection was most likely imported from. (Indigenous / out-of-county, state, or U.S.) [Epidemiological]
   - Investigate potential exposures: [Investigation-Exposure]
     - Exposure to diphtheria case or carrier; include dates and locations
     - Exposure to international travelers; include dates and locations
     - Exposure to immigrants; include dates and locations
   - Examine potential transmission settings, include:
     - Patient's occupation: food handler, health care worker, group living, day care attendee / worker, or school attendee / employee; specifically list patient's occupation [Epidemiological]
       - Obtain name of school and grade of patient (if applicable).
     - Examining occupation, record any Place Exposure(s) (where illness could have been transmitted). [Epidemiological]
3) Examine the epidemiological information, record where the infection was most likely imported from. (Indigenous or out-of-county, state, or U.S.). [Epidemiological]
4) Collect information from case for the Contact Investigation. (See below).
5) Investigate epi-links among cases (clusters, household, co-workers, etc).
   - If the patient had contact with person(s) who have/had diphtheria, determine if the other "cases" have been reported to the state:
     - Search the state electronic surveillance for the possible case.
     - If found, record the previously reported record number in the record of the case you are investigating [Notes]
   - Highly suspected illness in persons that have not previously been reported should be investigated as a suspect case and reported to KDHE-BEPHI:
     - Enter the symptomatic contact of the case on the [Contact] Tab of the CMR and save.
     - After the CMR has updated successfully, click 'Show' beside the contact on the listing.
     - With the View Contact open in show mode, select 'Promote to CMR'; update, as needed.
   - For suspected outbreaks refer to Managing Special Situations section.

Contact Investigation

1) Review the patient's occupation and activities collected during the case investigation and recorded on [Epidemiological] and [Investigation-Exposure] tabs:
   - Examine activities from onset date to 2 weeks after onset. (The period can be shortened to 4 days after the completion of antibiotic therapy if therapy was considered effective.)
   - Verify patient's household address and telephone number(s) [Demographics]
   - Verify addresses of places of exposure, dates the patient was at the location, and ways to identify potential contacts at the locations. [Epidemiological]
   - Consider the locations the patient sought medical care. [Clinical]
2) Consider the following types of contacts during the contact investigation:
   - Household members or those who regularly visit the home.
   - Other persons with a history of close direct contact with a case-patient in manner that would have allowed exposure to oral or respiratory secretions for pharyngeal case or lesion discharge for cutaneous. (e.g. caretakers)
     - Close contact with oral or respiratory secretions are those persons within large droplet range of 3 feet including those who shared food, drink or eating utensils.
   - Medical staff exposed to oral or respiratory secretions of a case-patient.
3) Create a line listing of contacts. [Contact]
   - Obtain name, address, and telephone of contacts
   - Collect contact's immunization status and note any diphtheria symptoms
   - Collect information on the contact's occupation.
   - Note any school or daycare attendance. (Include facility name and location.)
   - Note any healthcare associations. (Include facility name and location)
   - Note any high risk situations or medical conditions
4) Follow-up symptomatic contacts as suspect cases.
   - Report and manage as diphtheria case and refer for medical care. *(On the* [Contact] *Tab of the CMR, click 'Show' beside the contact on the listing. When View Contact Event opens in show mode, select 'Promote to CMR.)*
   - A contact meeting the clinical case definition is considered a confirmed case if epi-linked to a laboratory confirmed case.
   - If a symptomatic contact is laboratory confirmed – the primary case that was not laboratory confirmed is confirmed based on the epi-link.
5) Institute control measures for infected persons and close contacts.
   - Contacts of cutaneous diphtheria may require a vaccine booster and monitoring, but no work or daycare restrictions are required.
6) Follow-up close contacts as recommended under Contact Management.
   - Cutaneous cases resulting from non-toxigenic strains require no further contact management. (Pink Book, 2015)

Isolation, Work and Daycare Restrictions

K.A.R 28-1-6 for Diphtheria:

Control of Cases with Cutaneous Diphtheria

- For each person hospitalized with a case, contact precautions shall be followed until:
  - Two consecutive negative cultures from lesion specimens are obtained at least 24 hours apart and at least 24 hours after completion of appropriate antimicrobial therapy, ***OR***
  - Two sequential pairs of cultures are obtained after symptoms resolve and greater than 14 days after onset of symptoms if appropriate antimicrobial therapy is not followed.
- Each person with a case shall remain in home isolation until:
  - Two consecutive negative cultures from lesion specimens are obtained at least 24 hours apart and at least 24 hours after completion of appropriate antimicrobial therapy, ***OR***
  - Two sequential pairs of cultures are obtained after symptoms resolve and greater than 14 days after onset of symptoms if appropriate antimicrobial therapy is not followed.

Control of cases with Pharyngeal Diphtheria

- For each person hospitalized with a case, droplet precautions shall be followed until:
  - Two consecutive negative cultures are obtained from both nose and throat specimens collected at least 24 hours apart and at least 24 hours following completion of appropriate antimicrobial therapy, ***OR***
  - Two sequential pairs of cultures are obtained after symptoms resolve and greater than 14 days after onset of symptoms if appropriate antimicrobial therapy is not followed.
- Each person with a case shall remain in home isolation until:
  - Two consecutive negative cultures from both nose and throat specimens are attained at least 24 hours apart and at least 24 hours after completion of antimicrobial therapy, ***OR***
  - Two sequential pairs of cultures shall be obtained after symptoms resolve and greater than 14 days after onset of symptoms if appropriate antimicrobial therapy is not followed.

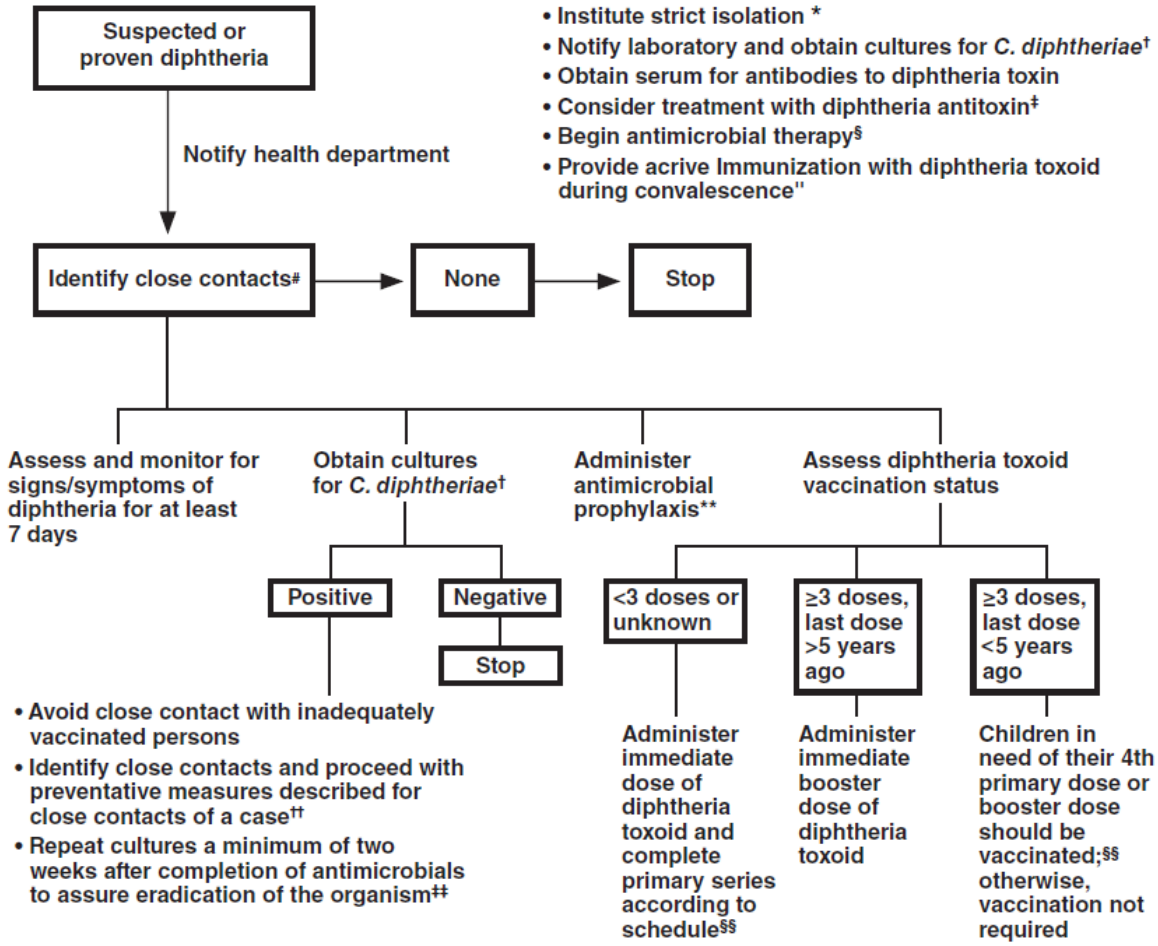
Control of Contacts of Pharyngeal Diphtheria

- All contacts, regardless of their immunization status, shall be monitored for seven days for evidence of disease and shall have specimens collected from both nose and throat for culture.
- Each contact found to be a carrier shall be considered a person with a case and shall be kept in isolation until requirements in control of cases are met.
- Each contact shall be excluded from working as a food employee, health care worker, and attending or working in a child care facility and attending or working in a school, child care facility, or adult day care:
  - For 28 days from the last exposure to a case, ***OR***
  - Until treated with appropriate antimicrobial therapy and two consecutive negative cultures are obtained from both nose and throat specimens collected at least 24 hours apart and at least 24 hours following completion of any antimicrobial therapy

Case Management

1) Prompt administration of DAT is needed for pharyngeal diphtheria.
   - DAT is currently available only through the CDC under an FDA-approved Investigational New Drug protocol; important epidemiologic and clinical data are needed prior to its release.
     - Physicians caring for patients with suspected respiratory diphtheria can obtain DAT by contacting the CDC's Emergency Operations Center at 770-488-7100. The diphtheria duty officer will discuss the case and protocol for DAT release with the physician.
     - KDHE disease reporting hotline (877-427-7317) should be contacted to assist with any laboratory specimens that will be sent to the CDC.
   - Patients should be tested for sensitivity to horse serum and, if necessary, desensitized before administration of the antitoxin.
   - The recommended dosage and route of administration depends on the extent and duration of disease; refer to the package insert.
   - Antimicrobial therapy (penicillin or erythromycin) is not a substitute for antitoxin treatment but is administered to eradicate the organism, prevent further production of toxin and decrease chance of further transmission.
2) Strict isolation continues until two sequential pairs of negative cultures are obtained (lesion swab for cutaneous or nose and throat swabs for pharyngeal).
   - Swabs are to be collected >24 hours apart and ≥24 hours from the completion of antimicrobial therapy.
   - If illness onset was ≥2 weeks prior and symptoms have resolved without antimicrobial therapy, collect the first specimens for culture immediately.
3) If a repeat culture is positive, an additional 10-day course of oral erythromycin is administered with follow-up cultures again repeated as described.
4) Provide active immunization with diphtheria toxoid during convalescence, as disease does not confer immunity.
5) Record whether or not DAT was administered. [Investigation-Exposure]
6) Conduct a follow-up as needed to assure compliance with control measures.
7) Conduct a follow-up interview to determine outcome of illness. [Clinical]
8) As an additional reference, see Figure 1 for pharyngeal diphtheria.

Figure 1. Diphtheria: Recommendations for Case Management and Investigation of Close Contacts



* Maintain isolation until elimination of the organism is demonstrated by negative cultures of two samples obtained at least 24 hours apart after the completion of antimicrobial therapy.
† Both nasal and pharyngeal swabs should be obtained for culture.
‡ Contact the state health department to make arrangements for antitoxin from the CDC.
§ Antimicrobial therapy is not a substitute for antitoxin treatment in clinical diphtheria but may eliminate the organism. Procaine penicillin G or parenteral erythromycin is used until patient can swallow comfortably, and then oral erythromycin or oral penicillin V is used.
" Vaccination is required because clinical diphtheria does not necessarily confer immunity.
Close contacts include household members and other persons with a history of direct contact with a case-patient (e.g. caretakers, relatives, or regular visitors to home) and medical staff exposed to oral or respiratory secretions of the case-patient.
** Prophylaxis includes a single dose of benzathine penicillin G or a 7- to 10- day course of oral erythromycin.
†† Preventive measures may extend to close contacts of carriers but should be a lower priority than control measures for contacts of a case.
‡‡ 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.
§§ Refer to published recommendations for the schedule for routine administration of DTP.

(Source: Appendix 2-6 of the CDC Manual for the Surveillance of Vaccine-Preventable Diseases)

Contact Management

1) Maintain notes on all contacts: symptoms screenings, immunization histories, culture results, prophylaxis recommended/completed (antibiotics and booster doses), and the disposition of the contact after 10 days of active surveillance, including any missing or gone explanations (MOGE). [Contact- 'Edit Contact']
2) Refer to Figure 1 and complete the following steps for all pharyngeal close contacts and for those cutaneous close contacts of toxigenic strains.
   - Obtain nose and throat swabs for culture.
   - Initiate antibiotic prophylaxis of contacts regardless of immunization status:
     - After specimens for culture are collected.
     - Recommend a single dose of benzathine penicillin or a 7-10 day course of erythromycin.
     - Single penicillin dose is used when the contact's compliance in doubt.
   - Assess diphtheria toxoid vaccination status and vaccinate as needed.
     - Previously immunized contacts should receive a booster dose of diphtheria toxoid if >5 years have elapsed since their last dose.
     - Non-immunized contacts (those with <3 doses or unknown histories) should begin and/or continue with a primary series according to published recommendations for routine immunizations.
     - Report any adverse event that occurs after the administration of a vaccine to Vaccine Adverse Events Reporting System at https://vaers.hhs.gov/index.html
3) Carryout work, school, and daycare restrictions of pharyngeal contacts only as instructed in K.A.R. 28-1-6.
4) Assess and monitor contacts (active surveillance) for signs and symptoms of diphtheria for 10 days after last contact with an infectious case.
   - Symptomatic contacts are treated as cases and reported to the National Notifiable Disease Surveillance System (NNDSS)
   - Asymptomatic contacts that are culture-positive are carriers, not reportable cases to NNDSS but are managed as cases.
5) Management of culture-positive secondary cases and carriers:
   - Treat and manage as described in Case Management, including the strict isolation for two weeks or until two consecutive sets of nose and throat swabs, collected >24 hours apart, are culture negative for *C. diphtheriae.*
   - Close contacts of carriers are managed as close contacts of cases but:
     - Assign close contacts of persons with clinical diphtheria highest priority.
     - Contacts of carriers should be given secondary priority.

   Note: *The risk of developing diphtheria is sevenfold higher after household exposure to clinical diphtheria case than after household exposure to a carrier.*
6) Initiate active surveillance for suspect cases in the affected settings for at least 2 maximum incubation periods (a total of 20 days).

Environmental

- Disinfect fomites and discharges from lesions.
- Use pasteurized milk.

Education

1) Provide education that includes basic information about the disease and its complications and ways to treat and prevent transmission of illness.
2) Instruct cases on the necessary isolation.
3) Cases, carriers and contacts should be instructed to pay strict attention to personal hygiene by:
   - Covering nose and mouth with tissue when coughing.
   - Placing all contaminated tissues directly into garbage containers.
   - Washing hands with soap and water every time there is contact with respiratory secretions or infected wounds.
4) Instruct cases and contacts to be aware of the high risk that infection poses to certain individuals, especially unvaccinated or inadequately vaccinated persons such as infants under 2 months of age.
5) Counsel contacts to watch for signs or symptoms for 10 days after exposure.
   - Should symptoms develop, medical care should be sought promptly and appropriate specimens taken. Treatment should be considered for persons with any of the signs or symptoms that are compatible with pertussis.

MANAGING SPECIAL SITUATIONS

A. Outbreak Investigation:

- A single case of suspected diphtheria should be treated with urgency.
- Notify KDHE immediately, 1-877-427-7317.
- Active case finding will be an important part of any investigation; especially when there is no history of international travel or contact with visitors who have been to an area endemic for diphtheria.
- All epidemiologic data will be reported and managed through the Kansas outbreak module of the electronic surveillance system.
- Recommendations will be made based on the CDC's Manual for the Surveillance of Vaccine-Preventable Diseases.

DATA MANAGEMENT AND REPORTING TO THE KDHE

A. Accept the case assigned to the LHD and record the date the LHD investigation was started on the [Administrative] tab.

B. Organize and collect data, using appropriate questionnaires, case listings (spreadsheets), and investigation forms, including the Diphtheria Investigation Worksheet and Diphtheria Contact Investigation Worksheet.

- Investigators can collect and enter all required information directly into EpiTrax [Investigation], [Clinical], [Demographics], and [Epidemiological] tabs without using the paper forms.
- During outbreak investigations, refer to guidance from a KDHE epidemiologist for appropriate collection tools.

C. Report data collected during the course of the investigation via EpiTrax**.**

- Verify that all data requested on the applicable forms has been recorded on an appropriate EpiTrax [tab], or that actions are completed for a case lost to follow-up as outlined below.
- Some data that cannot be reported on an EpiTrax [tab] may need to be recorded in [Notes] or scanned and attached to the record.
- Paper report forms do not need to be sent to KDHE after the information is recorded in EpiTrax. The forms should be handled as directed by local administrative practices.

D. If a case is lost to follow-up, after the appropriate attempts to contact the case have been made:

- Indicate 'lost to follow-up' on the [Investigation] tab with the number of attempts to contact the case recorded.
- Record at least the information that was collected from the medical records.
- Record a reason for 'lost to follow-up' in [Notes].

E. After the requirements listed under Case Investigation have been completed, record the "Date LHD investigation completed" field located on the [Administrative] tab.

- Record the date even if the local investigator's Case or Contact Management for the contact is not "Complete".

F. Once the entire investigation is completed, the LHD investigator will click the "Complete" button on the [Administrative] tab. This will trigger an alert to the LHD Administrator, so they can review the case before sending to the state.

- The LHD Administrator will then "Approve" or "Reject" the CMR.
- Once a case is "Approved" by the LHD Administrator, BEPHI staff will review the case to ensure completion before closing the case.

Notes on case classification of **Diphtheria (Corynebacterium diphtheriae)**:

- Case investigation and management is required for cutaneous diphtheria cases and diphtheria carriers, but the events are not nationally notifiable disease events to CDC.
- Cases in EpiTrax that are identified as cutaneous cases or culture positive, asymptomatic cases will be closed as "Not a case" for data reporting purposes.

ADDITIONAL INFORMATION / REFERENCES

A. Treatment / Differential Diagnosis: American Academy of Pediatrics. Red Book: Report of the Committee on Infectious Disease, 29th Edition. Illinois, Academy of Pediatrics, 2014.

B. Epidemiology, Investigation and Control: Heymann, D., ed., Control of Communicable Diseases Manual, Washington, DC, American Public Health Association, 2010.

C. Case Definitions: wwwn.cdc.gov/nndss/

D. Quarantine and Isolation: Kansas Community Containment Isolation/ Quarantine Toolbox Section III, Guidelines and Sample Legal Orders www.kdheks.gov/cphp/operating_guides.htm#coc

E. Kansas Regulations/Statutes Related to Infectious Disease: www.kdheks.gov/epi/regulations.htm

F. Pink Book: Epidemiology and Prevention of Vaccine-Preventable Diseases. Available at: www.cdc.gov/vaccines/pubs/pinkbook/index.html

G. Manual for the Surveillance of Vaccine-Preventable Diseases: Available at: www.cdc.gov/vaccines/pubs/surv-manual/index.html.

H. Additional Information (CDC): www.cdc.gov/health/default.htm

ATTACHMENTS

To view attachments in the electronic version:

1. Go to <View>; <Navigation Pane>; <Attachments> – OR – Click on the "Paper Clip" icon at the left.
2. Double click on the document to open.

Diphtheria Worksheet (Edited CDC Worksheet)

PATIENT INFORMATION

Date of Request (Month / Day / Year)

Name (Last, First)

Birth Date (Month / Day / Year)

Age (Unk = 999)

Age Type
0 = 0-120 years
1 = 0-11 months
2 = 0-52 weeks
3 = 0-28 days
9 = Age unknown

Sex
M = Male
F = Female
U = Unknown

Pregnant?
Y = Yes
N = No
U = Unknown

Race
N = Native Amer./Alaskan Native
A = Asian/Pacific Islander
B = African American
W = White
O = Other
U = Unknown

Ethnicity
H = Hispanic
N = Not Hispanic
U = Unknown

Address (Street and No.)

Date First Diagnosis

County

State

Zip

Phone

Date Symptom onset (Month / Day / Year)

Date Hospitalized (Month / Day / Year)

History of immunization against diphtheria

Childhood primary series
Y = Yes
N = No
U = Unknown

If < 18 years old, number of doses

Boosters as adult
Y = Yes
N = No
U = Unknown

Date of last dose (Month / Day / Year) Or U = Unk

Description of Clinical Picture

Outcome
N = Recovered, No Residua
R = Recovered, Residua
D = Died
U = Unknown

CLINICAL INFORMATION

Enter Y = Yes, N = No, or U = Unknown in the boxes below unless otherwise indicated

Symptoms

- Fever
- Sore throat
- Difficulty swallowing
- Change in voice
- Shortness of breath
- Weakness
- Fatigue
- Other

If Yes, Temp _____ °F / C

Membrane present?

If Yes, Sites
- Tonsils
- Soft Palate
- Hard Palate
- Larynx
- Nares
- Nasopharynx
- Conjunctiva
- Skin

Signs

- Soft tissue swelling (Around membrane)
- Neck edema?
  - If Yes, (B = Bilateral, L = Left side only, R = Right side only)
  - If Yes, Extent (S = Submandibular only, M = Midway to clavicle, C = To clavicle, B = Below clavicle)
- Stridor
- Wheezing
- Palatal weakness
- Tachycardia
- EKG abnormalities

Complications

- Airway obstruction — Date of onset (Month / Day / Year)
- Intubation required
- Myocarditis — Date of onset (Month / Day / Year)
- (Poly)neuritis — Date of onset (Month / Day / Year)
- Other — Describe:

LABORATORY

Specimen for diphtheria culture obtained
Y = Yes
N = No
U = Unknown

If Yes, date specimen obtained (Month / Day / Year) Or U = Unk

Culture result
P = Positive
N = Negative
U = Unknown

Specify lab performing culture

If culture positive, biotype
M = Mitis
G = Gravis
I = Intermedious
B = Belfanti

If culture positive, results of toxigenicity testing
X = Not done
P = Positive
N = Negative
U = Unknown

Specimen sent to CDC Diphtheria Lab for confirmation/molecular typing
Y = Yes
N = No
W = Will be Sent

Type of specimen (Check all that apply)
- Clinical swab
- Piece of membrane
- *C. diphtheria* isolate

Serum Specimen for Diphtheria Antitoxin Antibodies Obtained?
Y = Yes
N = No
U = Unknown

PCR Result
P = Positive
N = Negative
U = Unknown
X = Not Done

ANTIBIOTICS

Treated with Antibiotics?
Y = Yes
N = No
U = Unknown

As an Outpatient
If Yes, Date Initiated (Month / Day / Year)

Antibiotic (See Codes Below)

Duration of Therapy (Days)

Antibiotic Therapy in Hospital?
Y = Yes
N = No

As an Inpatient
If Yes, Date Initiated (Month / Day / Year)

Antibiotic (See Codes Below)

Duration of Therapy (Days)

Were Antibiotics Given in the 24 Hours Before Culture?
Y = Yes
N = No
U = Unknown

Antibiotic Codes

1 = Erythromycin (incl. Pediazole, ilosone)
2 = Penicillin (Bicillin, Pfizerpen-AS, Wycillin)
3 = Amoxicillin/Ampicillin/Augentin/Ceclor/Cefixime
4 = Clarithromycin/azithromycin
5 = Cotrimoxazole (bactrim/septra)
6 = Tetracycline/Doxycycline
7 = Other
9 = Unknown

EXPOSURE

Country of Residence
☐ U = US
O = Other

If Other, Country Name:

Date of U.S. Arrival
Month Day Year
OR ☐ U = Unknown

History of International Travel? (2 Weeks Prior to Onset)
☐ Y = Yes
N = No
U = Unknown

City,Country(s) Visited

From Month	From Day	From Year	To Month	To Day	To Year

History of Interstate Travel? (2 Weeks Prior to Onset)
☐ Y = Yes
N = No
U = Unknown

City,State(s) Visited

From Month	From Day	From Year	To Month	To Day	To Year

Known Exposure to Diphtheria Case or Carrier?
☐ Y = Yes
N = No
U = Unknown

Known Exposure to International Travelers?
☐ Y = Yes
N = No
U = Unknown

Known Exposure to Immigrants?
☐ Y = Yes
N = No
U = Unknown

REPORTING INFO

Has this Suspected Case been Reported to the State or Local Health Department?
☐ Y = Yes
N = No
U = Unknown

Date Reported to State or Local Health Department
Month Day Year

Person Informed: Phone: Fax:

Reporting Physician: Phone: Fax:

REQUESTING PHYSICIAN

Name

Institution

Street

City State Zip code

Phone: Fax:

Name of Investigator under the IND
(If different from requesting physician)
Phone: Fax:

SHIP DRUG TO:

Name

Attn:

Institution

Street

City State Zip code

Phone: Fax:

DOSE

Amount of DAT Administered: ☐☐☐,☐☐☐ IU DAT

DISPOS.

Final Diagnosis:

How was the final diagnosis confirmed?

Final Case Disposition
☐ C = Confirmed
P = Probable
N = Not a Case

Information for Close Contacts*
Diphtheria

*Close Contact = Household members and others with a historyof direct contact with a case-patient, and medical staff exposed to oral or respiratory secretions of a case-patient

CONTACT INFORMATION

Name | **Age** | **Relation to Case**

Vaccinated? (Y = Yes, N = No, U = Unknown)	If Vaccinated, Number lifetime of Doses (U = Unknown, L = < 3 Doses, U = Unknown)	If Vaccinated, Last Dose (L = = 5 Years Ago, G = > 5 Years Ago)	Nasopharyngeal Culture Obtained? (Y = Yes, N = No, U = Unknown)	Oropharyngeal (Throat) Culture Obtained? (Y = Yes, N = No, U = Unknown)	Date of Culture (Month / Day / Year)	Results (P = Positive, N = Negative, U = Unknown)	Antibiotic Prophylaxis (See Codes Below)
☐	☐	☐	☐	☐	☐☐ ☐☐ ☐☐	☐	☐

Name | **Age** | **Relation to Case**

Vaccinated? (Y = Yes, N = No, U = Unknown)	If Vaccinated, Number lifetime of Doses (U = Unknown, L = < 3 Doses, U = Unknown)	If Vaccinated, Last Dose (L = = 5 Years Ago, G = > 5 Years Ago)	Nasopharyngeal Culture Obtained? (Y = Yes, N = No, U = Unknown)	Oropharyngeal (Throat) Culture Obtained? (Y = Yes, N = No, U = Unknown)	Date of Culture (Month / Day / Year)	Results (P = Positive, N = Negative, U = Unknown)	Antibiotic Prophylaxis (See Codes Below)
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☐	☐	☐	☐	☐	☐☐ ☐☐ ☐☐	☐	☐

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☐	☐	☐	☐	☐	☐☐ ☐☐ ☐☐	☐	☐

Name | **Age** | **Relation to Case**

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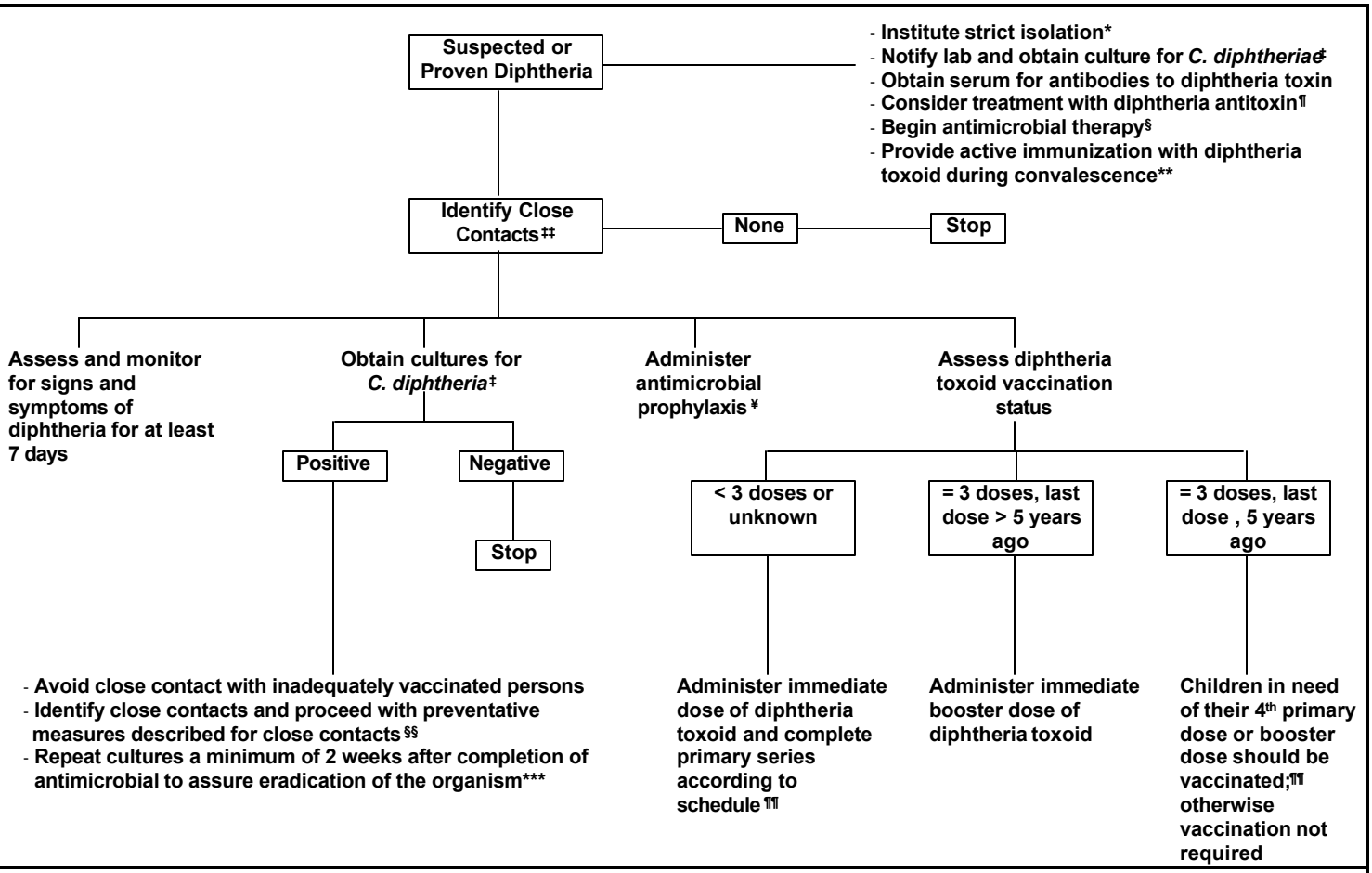
☐	☐	☐	☐	☐	☐☐ ☐☐ ☐☐	☐	☐

Antibiotic Codes

1 = Erythromycin (inc. Pediazole, ilosone)
2 = Penicillin (Bicillin, Pfizerpen-AS, Wycillin)
3 = Amoxicillin/Ampicillin/Augmentin/Ceclor/Cefixime
4 = Clarithromycin/azithromycin
5 = Cotrimoxazole (bactrim/septra)
6 = Tetracycline/Doxycycline
7 = Other

vs. 02/2012

CONTACT INFORMATION



* Maintain isolation until elimination of the organism is demonstrated by negative cultures of two samples obtained at least 24 hours apart after completion of antimicrobial therapy.

‡ Both nasal and pharyngeal swabs should be obtained for culture.

¶ If equine 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.

§ Antimicrobial therapy is not a substitute for antitoxin treatment. Intramuscular procaine penicillin G (25,000–50,000 unites/[kg/d] for children and 1.2 million units/d for adults, in two divided doses) or parenteral erythromycin in four divided doses or oral penicillin V (125–250 mg four times daily) may be substituted for a recommended total treatment period of 14 days.

** Vaccination is required because clinical diphtheria does not necessarily confer immunity.

‡‡ 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.

¥ A single dose of intramuscular benzathine penicillin G (600,000 units for persons < 6 years of age and 1.2 million units for persons = 6 years of age: or a 7- to 10-day course of oral erythromycin (40 mg/[kg/d]) for children and 1 g/d for adults) has been recommended.

§§ Preventative measures may be extended to close contacts of carriers but should be considered a lower priority than control measures for contacts of each case.

***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.

¶¶ Refer to published recommendations for the schedule for routine administration of DTP.

Farizo KM, Strebel PM, Chen RT, et al. Fatal respiratory disease due to *Corynebacterium diphtheriae*: Case report and review of guidelines for management, investigation, and control. *Clin Infect Dis* 1993;16:59-68.