Diphtheria

CLINICAL CASE DEFINITION

An upper-respiratory tract illness characterized by sore throat, difficulty in swallowing, malaise, low-grade fever, and a tough, grayish-white adherent pseudo-membrane over the tonsils, pharynx, larynx, or nose.

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 toxin-producing *Corynebacterium diphtheriae* from the nose or throat **OR**
  - epidemiologic linkage to a laboratory-confirmed case of diphtheria.

OR

- An infection at a non-respiratory anatomical site (e.g., skin, wound, conjunctiva, ear, genital mucosa) with isolation of toxin-producing *C. diphtheriae* from that site

♦ **Suspected**

- In the absence of a more likely diagnosis, an upper respiratory tract illness with each of the following:
  - an adherent membrane of the nose, pharynx, tonsils, or larynx **AND**
  - absence of laboratory confirmation **AND**
  - lack of epidemiologic linkage to a laboratory-confirmed case of diphtheria.

OR

- Histopathologic diagnosis

Comments:

- An epidemiologically linked case is one in which the patient has had contact with one or more persons who have or had the disease, and transmission of the agent by the usual modes of transmission is plausible. A case may be considered epidemiologically linked to a laboratory-confirmed case if at least one case in the chain of transmission is laboratory confirmed.

- Cultures positive for *C. diphtheriae*, should be sent to the state laboratory for confirmation of the organism's identification; the state will then send the isolate to CDC Pertussis and Diphtheria Laboratory for determination of toxin-production.

- Cases of laboratory-confirmed, non-toxin-producing C. diphtheriae (respiratory or non-respiratory) do not meet the surveillance case definition requirements and should not be reported to CDC as part of NNDSS.

- Rarely, respiratory diphtheria-like illness may result from infection with other Corynebacterium species (e.g., C. ulcerans, C. pseudotuberculosis). While not reportable, if a non-diphtheria Corynebacterium species is identified, jurisdictions are asked to submit available specimens or isolates to the CDC Pertussis and Diphtheria Laboratory for further characterization.

TRANSMISSION

Transmission is most often person-to-person via respiratory secretions.

On rare occasions, transmission may occur from skin lesions or articles (fomites) soiled with

discharges from lesions of infected persons.

INCUBATION PERIOD

2 – 5 days, range 1 -10 days. See Diphtheria Timeline, below.

REPORTING/INVESTIGATION

Health care providers should report immediately any cases/suspect cases of diphtheria to the local health department serving the residence of the case.

Local health department responsibilities:

- Contact case/guardian and health care provider;
- Determine if case meets clinical case definition;
- If definition met (probable or confirmed cases), investigate using report form/surveillance worksheet and control guidelines given below.
- Notify MDHHS Immunization Division Vaccine-Preventable Disease (VPD) Surveillance Coordinator at 517-335-8159.
- Report/ensure reporting of case to the Michigan Disease Surveillance System (MDSS). CDC Diphtheria Surveillance Worksheet may be helpful in field investigation to collect and capture data; CDC guidelines for managing a diphtheria case and close contacts may also be helpful. Obtain immunization history information from provider record or MI Care Improvement Registry (MCIR - state immunization registry).
- Update the MDSS record in a timely manner with new or additional info as it becomes available. Finalize MDSS record when case investigation is complete.
- In the event of death, obtain and send copies of hospital discharge summary, death certificate, and autopsy report to MDHHS Immunization Division.

LABORATORY CONFIRMATION

Laboratory criteria for diagnosis

- Isolation of *Corynebacterium diphtheriae* from a clinical specimen; or
- Histopathologic diagnosis of diphtheria.

See **LABORATORY SPECIMENS: PROCEDURES AND CONSIDERATIONS,** below for more details

IMMUNITY/SUSCEPTIBILITY

- Lifelong immunity is usually but not always acquired after infection.
- Immunization with toxoid produces prolonged, but not lifelong, immunity.
- Serosurveys in the U.S. indicate that 40 percent of adults may lack protective levels of circulating antitoxin (antibodies able to neurtralize diphtheria toxin).

- Antitoxin immunity protects against systemic disease but not against possible colonization of the organism in the nasopharynx, which may result in a chronic carrier state.

CONTROL MEASURES

Patient-related measures:

- Reports of suspect diphtheria should be investigated immediately.

- Suspect cases should be reported promptly by telephone to MDHHS VPD Surveillance Coordinator so that arrangements can be made to obtain diphtheria antitoxin (DAT) for the patient from CDC and the MDHHS Laboratory can be notified to set up for cultures.

  Contact information:
  MDHHS VPD Surveillance Coordinator: 517-335-8159
  MDHHS Communicable Disease Epidemiology Office: 517-335-8165
  MDHHS After hours emergency: 517-335-9030
  MDHHS Laboratory: 517-335-8067
  CDC consultation - *Meningitis and Vaccine-Preventable Diseases Branch,* 404-639-3158
  CDC after-hours: 770-488-7100 or 404-639-7100 or 404-639-2888
  CDC laboratory: 404-639-1231

- The patient should be placed in strict isolation, which should be maintained until elimination of the organism is demonstrated by negative cultures of two samples obtained at least 24 hours apart after completion of antimicrobial therapy.

- Obtain both nasal and pharyngeal swabs for culture, if this has not yet been done, to confirm the diagnosis. Ideally these should be collected prior to initiation of antibiotic treatment.

- Obtain serum for serology studies of antibodies to diphtheria toxin.

- Obtain, if possible, a consultation from an Infectious Disease physician on the patient; consider treatment with diphtheria antitoxin in consultation with MDHHS and CDC authorities.

- Begin/assure antimicrobial therapy (antimicrobial therapy is not a substitute for diphtheria antitoxin treatment). Per the AAP Red Book, the following constitute acceptable therapy though consultation with CDC and an infectious disease physician is advised:

  - Erythromycin given orally or parenterally for 14 days, OR
  - Penicillin G given intramuscularly or intravenously for 14 days, OR
  - Penicillin G procaine given intramuscularly for 14 days

- Administer/assure active immunization with diphtheria toxoid during convalescence, because clinical diphtheria does not necessarily confer immunity.

- Obtain repeat nasal and pharyngeal specimens for culture a minimum of two weeks after completion of antimicrobial treatment to assure 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 oral erythromycin and should submit samples for follow-up cultures.

Contact management:

- Identify close contacts:
  - household members;
  - persons with a history of direct contact with a case-patient (e.g., caretakers, relatives, or friends who regularly visit the home);
  - medical staff exposed to case-patient's oral or respiratory secretions.

- Assess and monitor contacts for signs and symptoms for diphtheria for at least 7 days.

- Obtain nasal and pharyngeal swab specimens from contacts for *C. diphtheriae* cultures.

- Administer/assure antimicrobial prophylaxis for contacts. Recommended prophylaxis (for all close contacts, regardless of immunization status):

  - A single dose of intramuscular benzathine penicillin G (600,00 units for children weighing less than 30 kg, 1.2 million units for persons weighing 30 kg or more); - this course is preferable to erythromycin for any contacts who cannot be kept under surveillance.

  OR

  - A 7- to 10-day course of oral erythromycin (40 mg/[kg/d]) for children and 1 g/d for adults).

- Any persons found to be carriers or 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.

- Assess diphtheria toxoid vaccination history status of contacts:

  - If < 3 doses: Administer immediate dose of diphtheria toxoid and complete primary series according to schedule.
  - If ≥3 doses with last dose >5 years ago: Administer immediate booster dose of diphtheria toxoid.
  - If ≥ 3 doses with last dose <5 years ago: Children in need of their fourth primary dose should be vaccinated; otherwise vaccination not required.

- Provide information about diphtheria to persons at risk and/or the general public. A Question-&-Answer diphtheria information sheet in **.PDF** format is available from the Immunization Action Coalition (www.immunize.org/catg.d/p4203.pdf)

- 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.

LABORATORY SPECIMENS: PROCEDURES AND CONSIDERATIONS

Guidelines for Collection of Specimens for Isolation of *C. diphtheriae* (source: World Health Organization):

Throat Swabs

- Pharynx should be clearly visible and well illuminated.

- Depress tongue with an applicator and swab the throat without touching the tongue or inside of the cheek.

- Rub vigorously over any membrane, white spots, or inflamed areas; slight pressure with a

rotating movement must be applied to the swab.

- If any membrane is present, lift the edge and swab beneath it; diphtheria organisms are often deeply embedded.

Nasopharygeal specimens

- Insert the swab into the nose through one nostril beyond the anterior nares.
- 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.

Skin Diphtheria and Other Lesions

- Lesions should be cleansed with sterile normal saline and crusted material removed.
- Press the swab firmly into the lesion.

Diphtheria testing may not be available in most clinical laboratories. Contact MDHHS Microbiology Laboratory (517-335-8067) and MDHHS VPD Surveillance Coordinator (517-335-8159) for further direction.

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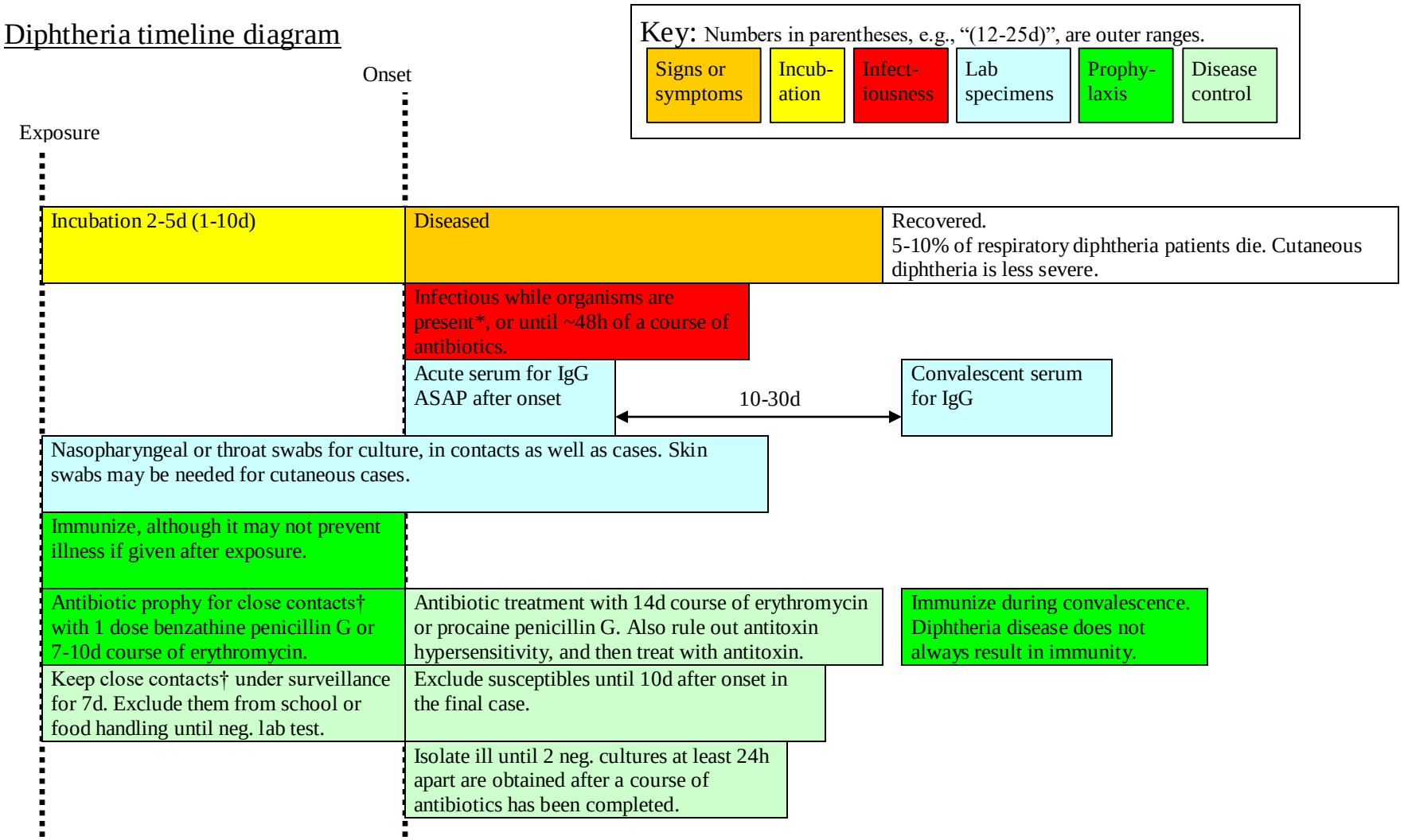
Diphtheria timeline diagram



* Rarely, chronic carriers may shed bacteria for ~6 months.
† This applies to both immunized and nonimmunized close contacts.

Sources: APHA Control of Communicable Diseases Manual, AAP Red Book, CDC Pink Book, CDC VPD surveillance manual