Diphtheria

Manitoba
Health
Public Health

Communicable Disease Control Unit

Case Definition

Confirmed Case: Laboratory identification of toxigenic *C. diphtheriae*, epidemiologic link (contact within two weeks before onset of symptoms) to a laboratory-confirmed case, or histopathologic diagnosis of diphtheria, **plus** one of the following:

- upper respiratory tract infection (nasopharyngitis, laryngitis, or tonsillitis) with or without a nasal, tonsillar, pharyngeal and/or laryngeal membrane, with or without gradually increasing hoarseness or stridor, cardiac (myocarditis) and/or neurologic involvement (motor and/or sensory palsies) one to six weeks after onset, or death with no other known cause;
- systemic manifestations compatible with diphtheria in a person with an upper respiratory tract infection or infection at another site.

Probable case: Upper respiratory tract infection (nasopharyngitis, laryngitis, or tonsillitis) with or without a nasal, tonsillar, pharyngeal and/or laryngeal membrane, plus at least one of the following:

- gradually increasing hoarseness or stridor;
- cardiac (myocarditis) and/or neurologic involvement (motor and/or sensory palsies) one to six weeks after onset;
- death, with no other known cause.

Suspect case: Upper respiratory tract infection (nasopharyngitis, laryngitis, or tonsillitis) with a nasal, tonsillar, pharyngeal and/or laryngeal membrane.

A carrier is defined as a person who harbours and may disseminate toxigenic *C. diphtheriae* but who manifests no upper respiratory tract (pharyngitis or laryngitis) or systemic symptoms. Carriers include persons with otitis media, nasal or cutaneous infections and asymptomatic pharyngeal infections due to *C. diphtheriae*.

Reporting Requirements

- All positive isolates of toxigenic *C. diphtheriae* are reportable by laboratory.
- All confirmed, probable and suspect cases of diphtheria are reportable by attending health care professional.
- The laboratory should be notified as soon as the diagnosis is suspected since the successful isolation of *C. diphtheriae* depends on the rapid inoculation of special culture media.

Clinical Presentation/Natural History

An acute bacterial disease involving primarily tonsils, pharynx, larynx, nose, occasionally other mucous membranes or skin and sometimes the conjunctivae or genitalia. The characteristic lesion, caused by liberation of a specific cytotoxin, is marked by a patch or patches of an adherent grayish membrane with surrounding inflammation. The throat is moderately sore in faucial or pharyngotonsillar diphtheria, with cervical lymph nodes somewhat enlarged and tender; in severe cases, there is marked swelling and edema of the neck.

Laryngeal diphtheria is serious in infants and young children, while nasal diphtheria is mild, often chronic, and marked by one-sided serosanguinous nasal discharge and excoriations. Inapparent infections outnumber clinical cases. The lesions of cutaneous diphtheria are variable and may be indistinguishable from, or a component of, impetigo. Late effects of absorption of toxin, appearing after two to six weeks, include cranial and peripheral motor and sensory nerve palsies and myocarditis (which may occur early) and are often severe. Case-fatality rates of 5-10% for noncutaneous diphtheria have changed little in 50 years.

Etiology

Corynebacterium diphtheriae of gravis, mitis or intermedius biotype. Toxin production results when the bacteria are infected by corynebacteriophage containing the diphtheria toxin gene tox. Nontoxigenic strains rarely produce local lesions; however, they have been increasingly associated with infective endocarditis.

Epidemiology

Reservoir and Source: Other persons with disease or asymptomatic infection.

Transmission: Contact with the nasopharyngeal secretions of a patient or carrier; more rarely, contact with articles soiled with discharges from lesions of infected persons. Raw milk has served as a vehicle.

Occurrence:

General: A disease of colder months in temperate zones, involving primarily nonimmunized children less than 15 years of age; often found among adults in population groups whose immunization was neglected. Most common in low socioeconomic groups living under crowded conditions. In the tropics, where seasonal trends are less distinct, inapparent, cutaneous and wound diphtheria cases are much more common. In the United States, from 1980 to 1992, an average of fewer than four cases were reported annually; two thirds of the affected people were 20 years of age or older. In the early 1980s, diphtheria incidence began to increase in the former Soviet Union because of disruption of immunization programs for children and adults and, by the beginning of the 1990s, it reached epidemic proportions in Russia and Ukraine. In 1994, more than 39,000 cases of diphtheria, and 1,100 deaths, were reported from the Russian Federation, and almost 3,000 from Ukraine. The majority of patients were over 15 years of age. In Ecuador, an outbreak of diphtheria occurred in 1993-1994, with about 200 cases, half of whom were 15 years of age or older. Control was achieved by mass immunization activities.

Canada: There were two cases in 1994 (the latest year for which national data have been published).

Manitoba: Most recent infection was a 73 year-old unimmunized carrier diagnosed in January 1997.

Incubation period: Usually two to five days, occasionally longer.

Susceptibility and Resistance: Infants born to immune mothers have transient immunity; protection is passive and usually lost before the sixth month. Recovery from a clinical attack is not always followed by lasting immunity; immunity can be acquired through inapparent infection. Prolonged active immunity can be induced by toxoid. Serosurveys in the United States indicate that more than 40% of adults lack protective levels of circulating antitoxin. Decreasing immunity levels have also been found in Canada, Australia and several European countries. Antitoxic immunity protects against systemic disease but not against local infection in the nasopharynx.

Period of Communicability: Variable, until virulent bacilli have disappeared from discharges and lesions; usually two weeks or less and seldom more than four weeks. Effective antibiotic therapy promptly terminates shedding (less than four days). The rare chronic carrier may shed organisms for six months or more.

Diagnosis

See **Case Definition** above. Diphtheria should be considered in the differential diagnosis of bacterial (especially streptococcal) and viral pharyngitis, Vincent's angina, infectious mononucleosis, oral syphilis and candidiasis. Presumptive diagnosis is based on observation of a whitish membrane, especially if extending to the uvula and soft palate, in association with tonsillitis, pharyngitis or cervical lymphadenopathy, or a serosanguinous nasal discharge. The diagnosis is confirmed by a positive

culture. If diphtheria is strongly suspected, specific treatment with antibiotics and antitoxin should be initiated while studies are pending, and should be continued even in the face of a negative laboratory report. **When multiple throat swabs will be taken to document cure or identify carriers, please notify Cadham Provincial Laboratory in advance so that appropriate quantities of culture materials can be arranged to be available.**

Key Investigations

- Check immunization histories of case/carrier and contacts.
- Determine if there is a high risk for the person to transmit infection through his/her work, i.e., foodhandling/processing, work with children less than seven years of age, or health care workers with hands-on patient contact.

Control

Management of Cases:

Treatment:

- If diphtheria is strongly suspected, antitoxin (only antitoxin of equine origin is available) should be given immediately after bacteriologic specimens are taken, without waiting for results.
- After completion of tests to rule out hypersensitivity, a single dose of 20,000-100,000 units is given IM, depending on the duration of symptoms, area of involvement and severity of the disease (see Table 1 below). Intramuscular administration usually suffices; in severe infections, both IV and IM administration may be indicated. **The administration of equine antitoxin under the protection of a desensitization procedure must be continuous because protection from desensitization is lost once administration is interrupted. Therefore, all efforts should be made to obtain sufficient antitoxin before treatment is started.**
- Refer to the *Red Book: Report of the Committee on Infectious Diseases* or other clinical texts for a guide on sensitivity tests.
- **To obtain diphtheria antitoxin, please contact the local Medical Officer of Health; after regular hours contact the Medical Officer of Health on call at 945-0183.**
- Both erythromycin and penicillin are effective against the organism, and either should be administered after cultures have been obtained, in conjunction with, but not as a substitute for, antitoxin.
- Procaine penicillin G (IM) (25,000 to 50,000 units/kg/d for children and 1.2 million units/d for adults, in two divided doses) or parenteral erythromycin (40-50 mg/kg/d, with a maximum of 2 g/d) has been recommended until the patient can swallow comfortably, at which point erythromycin PO in four divided doses or penicillin V PO (125-250 mg four times daily) may be substituted for a recommended total treatment period of 14 days.
- Persons convalescent from diphtheria should be given a complete primary course of toxoid, as indicated by age, unless serologic testing indicates protective levels of antitoxin, since diphtheria infection does not necessarily confer immunity.
- **Carriers** should be given oral erythromycin 40 to 50 mg/kg/d for seven days (maximum 2 g/d), or a single dose of benzathine penicillin G 600,000 to 1,200,000 U, intramuscularly (the lower dose is for patients weighing less than 30 kg). Carriers who have not completed a primary immunization series should be immunized promptly and complete the series. For carriers who have completed a

primary series with or without booster doses, a booster dose should be given if one has not been received within the last year.

- Droplet precautions for pharyngeal diphtheria.
- Contact precautions for hospitalized cutaneous diphtheria.
- Cases and carriers should have two cultures of both nose and throat (skin lesions in cutaneous diphtheria) following antibiotic therapy. The cultures should be taken not less than 24 hours apart, and not less than 24 hours after cessation of antimicrobial therapy. If any of these cultures are positive, additional therapy with erythromycin for 10 days should be provided, followed by additional cultures.

Public Health Measures

- Individuals who are carriers 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;
  - cleaning wounds and skin lesions vigorously with soap and water.
  - keeping all infected wounds covered.

Management of Contacts:

- Public Health will identify contacts and coordinate surveillance, immunization, cultures and prophylaxis as necessary.
- All household contacts and other community contacts with frequent, close contact to a case or carrier should be traced to determine immunization status, symptomatology and occupation (e.g., friends, relatives, and caretakers who regularly visit the home; kissing and/or sexual contacts; those who share the same room at school or work; health care staff exposed to oropharyngeal secretions of the infected person). Health care staff members who have taken appropriate isolation precautions need not be considered contacts. All contacts should be advised to contact a physician or nurse practitioner for assessment and possible treatment if a sore throat and/or fever occurs within seven days following last exposure to the case/carrier prior to treatment.
- High risk contacts who: are foodhandlers/ processors (especially of milk); work with children less than seven years of age, the elderly, or members of religious groups who do not accept immunizations; or are symptomatic health care workers, should be excluded from work until throat cultures are shown to be negative.
- Contacts who have received a primary immunization series and have had a booster dose of vaccine within the last five years do not require any further immunization. Those who have not begun/completed a primary immunization series should immediately begin or complete it. Those who have completed a primary series but have not had a booster within the last five years should receive a booster.
- All contacts, irrespective of their immunization status, should receive a nasal and throat swab and then be placed on a prophylactic antibiotic regimen, consisting of oral erythromycin 40 to 50 mg/kg/d (maximum 2g/d) for seven days or a single dose of benzathine penicillin G 600,000 to 1,200,000 U intramuscularly (lower dose of penicillin is for patients weighing less than 30 kg; penicillin may fail). For reasons of compliance, benzathine penicillin G is preferred for contacts who cannot be kept under surveillance. Administration of prophylactic antitoxin (with antibiotics as above) should be considered only for the rare, exposed person who cannot be kept under surveillance (5,000 units to 10,000 units intramuscularly).

- If a positive culture is obtained in a contact, two cultures of both nose and throat should be obtained following antibiotic prophylaxis (see bullet on follow-up cultures for cases and carriers under **Management of Cases** above).

Management of Outbreaks:

- Immunize the largest possible proportion of the population group involved, with emphasis on protection of infants and preschool children.
- In an epidemic involving adults, immunize groups that are most affected and at high risk. Repeat immunization procedures one month later to provide at least two doses to the recipients.

Preventive Measures:

- All persons should receive a primary immunization series with diphtheria toxoid.
- Adults should continue to receive 10-year boosters. **Booster doses of tetanus toxoids provided after wound exposure should include diphtheria toxoid.**