4.2 Diphtheria

Etiology

Diphtheria is an acute, toxin mediated disease caused by the bacteria toxigenic strains of *Corynebacterium (C.) diphtheria* of gravis, mitis or intermedius biotypes. Toxigenic strains express an exotoxin that inhibits cellular protein synthesis and is responsible for local tissue destruction and membrane formation. The toxin produced at the membrane site is absorbed into the bloodstream and then distributed to the tissues. The most severe disease is associated with the gravis biotype, but any biotype may produce the toxin. Non-toxin producing strains generally produce milder illness.

Case Definitions

Confirmed Case

Clinical illness[1] or systemic manifestations compatible with diphtheria in a person with an upper respiratory tract infection, or at another site (e.g. wound, cutaneous) PLUS at least one of the following:

Laboratory confirmation of infection:

- isolation of *Corynebacterium diphtheria* with confirmation of a toxin from an appropriate clinical specimen **OR**
- isolation of other *Corynebacterium s*pecies (*C. ulcerans* or C*. pseudotuberculosis*) from an appropriate specimen including the exudative membrane **OR**
- histopathologic diagnosis of diphtheria **OR**
- epidemiologic link (contact within 2 weeks prior to an onset of symptoms) to a laboratory-confirmed case

Probable Case

Clinical Illness[1] in the absence of laboratory confirmation or epidemiologic link to a laboratory-confirmed case.

Suspected Case

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

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[1] Clinical illness is characterized as an upper respiratory tract infection (nasopharyngitis, laryngitis, or tonsillitis) with or without an adherent nasal, tonsillar, pharyngeal and/or laryngeal membrane, plus at least one of the following:

- gradually increasing stridor
- cardiac (myocarditis) and or neurologic involvement (motor and/or sensory palsies) 1-6 weeks after onset
- death, with no known cause

Clinical Presentation

Diphtheria is an acute bacterial disease that can involve almost any mucous membrane. The characteristic lesion, caused by liberation of a specific cytotoxin, is marked by a patch or patches of an adherent grayish-white membrane with surrounding inflammation. The infection most often manifests as membranous naso-pharyngitis or obstructive laryngotracheitis. The toxin produced by some strains can cause severe damage to the throat or other tissues.

Occasionally, *C. diphtheriae* disseminates from the skin or respiratory tract and causes invasive systemic infections including bacteremia, endocarditis and arthritis. Diphtheria can be classified based on site of infection:

Pharyngeal/tonsillar: This is the most common site of infection and is associated with the absorption of toxin. The onset is insidious. Early symptoms include malaise, sore throat, anorexia and low-grade fever. Two to three days later the membrane appears in the pharyngeal/tonsillar area. The membrane initially appears white and glossy, but evolves into a dirty gray color with patches of green or black necrosis. The extent of the membrane correlates with the severity of symptoms (i.e., with posterior pharynx, soft palate and periglottal area involvement, profound malaise and obstructed breathing may occur). In cases of severe disease the individual may also develop edema of the submandibular areas and the anterior neck, along with lymphadenopathy, giving the characteristic “bullneck” appearance. The individual may recover or, depending on the amount of toxin absorbed, develop severe illness, pallor, rapid pulse, stupor and coma with death occurring in six to 10 days.

Nasal: Infection limited to the anterior nares presents with a serosanguinous or seropurulent nasal discharge often associated with a subtle whitish mucosal membrane, particularly on the septum. Signs indicating toxin effect are rare.

Laryngeal: This may be either an extension of the pharyngeal form or be the only site involved. Symptoms include fever, hoarseness and a barking cough. Development of the membrane may lead to airway obstruction, coma, and death.

Cutaneous: *C. diphtheriae* can cause clinical skin infections characterized by a scaling rash or by chronic non-healing ulcers with a dirty gray membrane and are often associated with Staphylococcus aureus and group A streptococci. This type of diphtheria is often associated with overcrowding, impoverished groups and homeless persons. Cutaneous sites of *C. diphtheriae* have been shown both to contaminate the inanimate environment and to induce throat infections in others. Bacterial shedding from cutaneous infections continues longer than from the respiratory tract. Because *C. diphtheriae* is usually isolated in association with other known skin pathogens, and because the ulcers do not respond to antitoxin therapy, there is debate as to whether or not the isolates are actually causing clinical illness.

Invasive Disease: Complications are predominantly attributable to the effects of the toxin. The two most common complications are myocarditis and neuritis. In most cases, the cardiac manifestations appear during the latter part of disease progression. The more extensive the local lesion and the more delayed the initiation of antitoxin therapy, the more frequently myocarditis occurs. Neuritis most often affects motor nerves and

usually resolves completely. Other complications include otitis media and respiratory insufficiency due to airway obstruction, especially in infants.

Diagnosis

Diagnosis is usually made based on history and clinical presentation as it is essential to begin therapy as soon as possible. Diagnosis is confirmed by bacteriologic examination of specimens. 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.
Prior to specimen collection call the Provincial Public Health Laboratory (PHL) for guidance on specimen collection and transport recommendations at 709-777-6583.

Epidemiology

Occurrence

Diphtheria occurs worldwide and is endemic in many developing countries as well as in Albania, Russia and other countries of the former Soviet Union. In other countries, occasional cases of imported diphtheria are identified. Resurgence of diphtheria has been reported in countries with low vaccine coverage. A total of 4,187 cases of diphtheria were reported to the World Health Organization (WHO) in 2010. The potential for re-emergence of diphtheria if immunization levels decline was demonstrated during the 1990s in the Commonwealth of Independent States (former Soviet Union) when over 140,000 cases and 4,000 deaths were reported.

In Canada, immunization has resulted in a dramatic decline in diphtheria cases. A small number of toxigenic strains of diphtheria bacilli are detected each year (0 to 5 isolates), although classic diphtheria is rare. Serosurveys of healthy adult populations in Canada indicate that approximately 20% (higher in some age groups) do not have protective concentrations of antibody to diphtheria; adult booster doses are required. In recent years there have been very few cases in Canada with none reported since 2000, and a total of 12 cases seen since 1991.
In Newfoundland and Labrador there have been no cases of diphtheria reported through the surveillance system from 1990 – 2012; the last death from diphtheria was recorded in 1964.

Reservoir

Humans.

Transmission

Diphtheria is transmitted by person-to-person spread from the respiratory tract or, rarely, by contact with articles soiled with excretions of infected persons.

Incubation Period

The incubation period is about 2 to 5 days (range, 1 to 10 days).

Communicability

The infectious period in untreated persons is usually 2 weeks or less and, rarely, more than 4 weeks. Chronic carriers are asymptomatically colonized with *C. diphtheria* on the skin or in the nasopharynx and may shed organisms for 6 months or more.

Control Measures

Management of Cases

Investigations

- Confirm the diagnosis and strain
- Notify the Medical Officer of Health (MOH) and the PHL
- Identify if person had recent contact with a case or carrier, or contact with articles soiled with the discharges from lesions of infected individuals
- Review the travel history
- Determine immunization history
- Identify close contacts

Treatment

- Treatment should begin as soon as possible based on clinical symptoms
  - Therapy should not be delayed until bacteriologic confirmation is obtained

- Diphtheria antitoxin (DAT) is considered the mainstay of treatment
  - The antitoxin blocks or neutralizes the effects of the toxin
  - Delayed administration increases the risk of late effects such as myocarditis and neuritis
  - Currently there is no licensed product made in Canada. An antidiphtheria serum is made available from Health Canada's Special Access Program (SAP)
  - Contact the Chief Medical Officer of Health or the MOH for assistance in obtaining the product diphtheria antitoxin accessed through the Department of Health and Community Services (DH&CS) by calling 709-729-3430 or the MOH after hours 1-866-270-7437

- Antibiotic therapy is required to eradicate the organism, to stop toxin production and prevent transmission
  - Antibiotic treatment is not a substitute for antitoxin.
  - Laboratory specimens should be collected before antibiotics are started
  - Elimination of *C. diphtheriae* should be confirmed by two negative cultures of throat and nasopharyngeal swabs taken at least 24 hours apart and a minimum of 2 weeks after antibiotic treatment is completed

Immunization

Cases 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.

Exclusion

- Hospitalized cases should be on Droplet and Contact Precautions
  - Discontinue precautions only in consult with the Infection Control Practitioner
- Non-Hospitalized (Community) Case
  - Minimal contact with other persons in the home is recommended until proof of elimination of *C. diphtheriae* organism is demonstrated

Management of Contacts

Contact tracing should be initiated promptly and should begin in the household of the suspected or confirmed case, as the risk of infection is directly related to the closeness and duration of contact and the intensity of exposure.

Definitions

Contacts

All persons who have been in contact with a case of diphtheria caused by toxigenic *C. diphtheriae* in the previous 7 days should be considered at risk.

Close contacts include

- Household members
- Friends, relatives, and caretakers who regularly visit the home
- Kissing and/or sexual contacts
- Those who share the same room at school or work
- Healthcare workers exposed to the respiratory secretions of the infected person (staff who have taken appropriate isolation precautions need not be considered contacts)

Carrier

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

Immunoprophylaxis

- Close contacts of a diphtheria case should receive a dose of a diphtheria toxoid-containing vaccine as appropriate for age unless the contact is known to have been fully immunized and the last dose of diphtheria toxoid-containing vaccine was given within 10 years

- The diphtheria toxoid-containing vaccine series should be completed for previously unimmunized or incompletely immunized contacts

Chemoprophylaxis

- Antibiotic prophylaxis should be given to all contacts regardless of vaccination status
- Diphtheria antitoxin is not recommended for prophylaxis of immunized or unimmunized close contacts of diphtheria cases, given the substantial risk of allergic reaction to equine serum and lack of evidence of additional benefit of antitoxin for contacts who have received antimicrobial prophylaxis

Exclusion

- Regardless of vaccination status, all close contacts should be kept under daily surveillance for 7 days from the date of last contact with the case and assessed clinically for signs and symptoms of diphtheria, and samples for culturing should be taken from nasal and pharyngeal swabs before antibiotic treatment is started
- Contacts whose occupations involve handling food (especially milk) or involve close contact with unimmunized persons (including children, the elderly, or members of religious groups who do not accept immunizations) should be excluded from their work until bacterial examination proves them not to be carriers
- Non-hospitalized carriers should be excluded from the workplace or school until two negative cultures are obtained after completion of antibiotics. Contact with other persons in the home should be minimized when appropriate. Individuals who are carriers should be instructed to pay strict attention to personal hygiene by
  - Covering the nose and mouth with tissue when coughing
  - Placing all contaminated tissues directly into garbage containers
  - Cleaning hands with soap and water every time there is contact with respiratory secretions or infected wounds
  - Keeping all infected wounds covered

Management of Outbreaks

An outbreak management team should be established to address infection prevention and control measures.

Education and Preventive Measures

- Education measures are important. Inform the public, particularly parents of young children, of the hazards of diphtheria and the need for vaccination
- The most effective preventive measure is widespread vaccination with diphtheria toxoid
- Maintain continual improvements in childhood and adult vaccination coverage rates
- Special efforts should be made to ensure that people at higher risk of exposure eg., health care workers, are fully vaccinated

- Travelers should be vaccinated if they have not had a booster dose of diphtheria in the last 10 years.

Reporting Requirements and Procedures

- The laboratory (hospital or public health laboratories) report case/s to the attending physician, the Chief Medical Officer of Health and the Medical Officers of Health (MOH)
- MOH office will notify, as required, local physicians, nurse practitioners, environmental health officers, community health nurses, communicable disease control nurses (CDCNs) and Infection control practitioners (ICP), in the particular region as required for follow-up and case investigation
- The CDCN in collaboration with the ICP (if necessary) will collect case details
- The CDCN will enters the case details into the electronic reporting system and utilize the Canadian Network for Public Health Intelligence (CNPHI) tool, if indicated, for alerts or outbreak summaries

Provincial Disease Control

- Reports the aggregate case data to Public Health Agency of Canada
- Provides an analysis of the case/s with reports in the Quarterly Communicable Disease Report (CDR), also posted on the Public Health website http://www.health.gov.nl.ca/health/publichealth/cdc/informationandsurveillance.html
- Coordinates the response if an outbreak occurs across RHAs.

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