DIPHTHERIA

Pharyngeal And Cutaneous Diphtheria[1]

Associated Documents

Case Report Form:

- Y:\CFS\ProtectionTeam\FinalDocs\NotifiableConditions\Diphtheria\FormsStdLettersQuest\Generic2016CRF230908.pdf

Referral letters to GP:

- https://cdhbintranet.cdhb.health.nz/communitypublichealth/cphpoliciesandprocedures/Documents/Diphtheria%20Contact%20Referral%20Form.aspx
- https://cdhbintranet.cdhb.health.nz/communitypublichealth/cphpoliciesandprocedures/Documents/Diphtheria%20Contact%20Vaccine%20Referral%20Form.aspx

Introduction

Diphtheria can be either pharyngeal or cutaneous and is caused by toxigenic strains of *Cornybacterium diphtheriae* (or rarely *Cornybacterium ulcerans*). A swab that cultures *Cornybacterium diphtheriae* will be forwarded to Canterbury Health Laboratories for toxigenicity testing, with results available within 24hrs of CHL receiving the isolate. Both forms of the disease are notifiable.

The Illness[2-5]

Pharyngeal diphtheria is a serious, often fatal disease caused by *Corynebacterium diphtheriae* bacillus. The disease characteristically involves membranous inflammation of the upper respiratory tract, with involvement of other tissues, especially the myocardium and peripheral nerves. *C. diphtheriae* is rarely invasive, but causes tissue damage through local and systemic actions of a potent exotoxin produced by some strains.

Cutaneous diphtheria, is typically less severe and characterised by secondary infection of other skin conditions or formation of a chronic ulcer with a gray membrane. While toxic sequelae in cutaneous cases are uncommon, transmission can result in pharyngeal disease (see Clinical description below).

Other **extra-respiratory** presentations have also been described, including septic arthritis, conjunctivitis, and vaginal and external auditory canal infections.

In 1858 there was a sudden widespread appearance of severe diphtheria, and within a year it had spread all over the world, including New Zealand. Already before the introduction of immunisation the incidence of diphtheria had been declining, and with the introduction of the vaccine the decline accelerated.

Although immunisation is more effective at preventing disease than preventing infection, it does create herd immunity and reduces carriage and therefore transmission. To prevent major community outbreaks it has been suggested that 70 percent or more of the childhood population must be immune to diphtheria. This may explain the control of diphtheria in New Zealand despite relatively poor coverage. A larger dose of diphtheria vaccine is recommended for children (signified by capital D - DTaP) than for adults (signified by a small d - Tdap). The 2005–07 National Serosurvey of Vaccine Preventable Diseases found that only 47% of adults $\geq$ 24 years old had presumed protective levels of diphtheria antibody [2].

Isolation of the toxigenic strain of *C. diphtheriae* is rare in New Zealand and when it is isolated it is more likely to be from a cutaneous lesion rather than from a pharyngeal infection. Diphtheria remains endemic in many areas of the developing world including South East Asia and PNG and an article in the NZMJ in 2012 referred to ongoing transmission in Pacific countries [3]. Large outbreaks occurred in the early 1990s in Russia and other former Soviet states, where vaccination rates were low. A case in Auckland in 2015 was acquired in Indonesia and the Christchurch case in 2016 developed cutaneous diphtheria in Samoa.

However, non-toxigenic isolates are more common. They are mainly obtained from cutaneous lesions and are usually acquired in the Pacific Islands. Non-toxigenic strains may result in sore throat, but rarely produce membranous lesions. However they may be associated with infective endocarditis.

Clinical description
Respiratory diphtheria is characterised by infection primarily involving the tonsil(s), pharynx and/or larynx, low-grade fever, with or without an asymmetrical greyish-white adherent membrane of the tonsil(s), pharynx and/or nose. In moderate to severe cases there can be marked neck swelling (enlarged anterior cervical lymph nodes and oedema of the surrounding tissues), resulting in a 'bull neck' appearance. Toxic effects can arise, including cardiac and neurological symptoms (for example, myocarditis and neuropathies).

Cutaneous diphtheria is characterised by secondary infection of other skin conditions or chronic ulcers with a grey membrane. Toxic sequelae in cutaneous cases are uncommon. Cutaneous diphtheria can act as a reservoir of bacteria capable of causing pharyngeal disease:
i) cutaneous sites of *C. diphtheriae* have been shown to contaminate both the inanimate environment and to induce throat infections more efficiently than does pharyngeal colonisation [4]
ii) 20% to 40% of patients with cutaneous diphtheria carry *C. diphtheriae* in their upper respiratory tract
iii) Cutaneous diphtheria may be as contagious as the respiratory form of the disease among school children [5].

Other **extra-respiratory** presentations have also been described, including septic arthritis, conjunctivitis, and vaginal and external auditory canal infections.

Incubation: Usually 2-5 days, occasionally longer.

Transmission: Contact with respiratory droplets or infected skin of a patient or carrier or, more rarely, contaminated articles. Unpasteurised milk has also been a source of infection.

Communicability: Variable; usually 2 weeks or less, seldom more than 4 weeks. Effective antimicrobial therapy promptly terminates shedding.

Prevention: Immunisation is the key prevention strategy with five vaccinations in childhood between 6 weeks and 11 years, and at 45 and 65 years of age.

Notification Procedure

All isolates of C. diphtheriae and C. ulcerans are notifiable until toxigenicity is determined, including cutaneous isolates. If the isolate is determined to be nontoxigenic, the case should be denotified.

- Suspected diphtheria must be notified immediately by the attending medical practitioner. **Inform the MOH immediately**. If non-toxigenic or toxin status unknown discuss with the Medical Officer of Health.
- The MOH is to report the notification of toxigenic or pharyngeal diphtheria to the Ministry when they are received.
- A person from whom *C. diphtheria* has been cultured from the pharynx or a person with a cutaneous lesion from which *C. diphtheriae* or *C.ulcerans* has been cultured, requires public health action while awaiting the laboratory report on toxicity.

Case Classification
Under investigation - A case which has been notified but information is not yet available to classify it as probable or confirmed.

Probable - A clinically compatible illness (see **Clinical descriptions** above) that is not laboratory confirmed.

Confirmed - A clinically compatible illness that is laboratory confirmed.

	Not a case - A case that has been investigated, and subsequently has been shown not to meet the case definition.

Laboratory Testing

- Laboratory confirmation requires isolation of diphtheria toxin-producing corynebacteria from a clinical specimen such as nasopharyngeal[6], throat and skin swabs.
- Laboratories must be informed that the sample is from a suspected case of diphtheria as selective media are required.
- Diphtheria is caused by toxigenic strains of *Corynebacterium diphtheriae* and very rarely *C. ulcerans*.
- There are four biotypes of *C. diphtheriae: gravis, mitis, intermedius* and *belfanti.*
- Toxin production results when bacteria are infected with corynebacteriophage containing the diphtheria toxin gene *tox*.
- Isolates are sent to ESR and CHL to test toxigenicity. CHL will generate a result within 24 hours of sample receipt and will trigger an e-notification if toxogenic strains are identified. Health Connect South will need to be checked if no e-notification has been received within 24 hours – 48 hours.
- The final ESR result should also be followed up.
- Antibiotic sensitivities are also required.

Management of Case

Assessment
The level of public health response while awaiting case confirmation will depend on the assessment of risk on a case-by-case basis. If there are known risk factors for a toxigenic cutaneous infection such as recent travel to a disease-endemic area, then a more proactive public health response may be warranted.

Investigation
Obtain history of vaccination, possible contacts, travel, any cutaneous lesions or existing skin conditions and consumption of unpasteurised milk from the notifying doctor and case and enter on the Generic Case Report form.

- Ensure the laboratory has been aware that diphtheria is suspected and that confirmation has been attempted from clinical specimen(s) by nasopharyngeal and throat swabs for all cases and in addition skin swabs if cutaneous diphtheria.
- Ensure toxigenicity testing of *C diphtheriae* or *C. ulcerans* isolates has been done. Awanui Laboratories send diphtheria isolates to Canterbury Health Laboratories for rapid turnaround diphtheria toxin testing as well as to ESR for reference laboratory testing (which may take several days). CHL requests and results can be checked online.
- Inform MOH immediately of the:
  - notification
  - toxigenic status (inform the Ministry if positive (see **Reporting** section))
  - antibiotic sensitivities
- One toxigenic case is an outbreak (consider responding under a CIMS structure).
- To date, most isolates in New Zealand have been non-toxigenic. The extent of public health action while awaiting laboratory confirmation should be based on available information and the judgement of the local medical officer of health.

Restriction

- Apply Standard and Droplet precautions for toxigenic pharyngeal diphtheria, and
- Standard and Contact precautions (refer to links above to infection prevention and control documents) for toxigenic cutaneous diphtheria until microbiological clearance has been documented: IPC policies and procedures.
- Exclude case from early childhood service, school, work and close contact with previously unexposed people until microbiologically cleared. See Health (Infectious Notifiable Diseases) Regulations 1966.

Microbiological clearance
Swabs from both throat and nasopharynx in all cases and if cutaneous diphtheria, from skin lesions as well, taken not less than 24 hours apart and not less than 24 hours after finishing antimicrobials, fail to show *C. diphtheriae* or *C. ulcerans*.

Treatment
All cases should be under the care of an infectious diseases physician or paediatrician. Advice should be sought from an Infectious Diseases Physician.

Respiratory diphtheria
- Treatment consists of antibiotic therapy and diphtheria antitoxin for severe cases. Antitoxin is usually indicated before laboratory confirmation when there is strong clinical suspicion.

Cutaneous diphtheria
- Antibiotic treatment (eg, erythromycin) to cover toxigenic strains, and hygienic ulcer care. (Cover the skin lesion, double bag soiled dressings and place in rubbish bin, and ensure thorough hand washing after the wound is dressed.)

Immunisation
- Case should be immunised in the convalescent stage because clinical infection does not always induce adequate levels of antitoxin (particularly if pharyngeal diphtheria).

Counselling
Advise the case and their caregivers of the nature of the infection and its mode of transmission. Te Whatu Ora information is available:
https://info.health.nz/conditions-treatments/infectious-diseases/diphtheria

Management of Contacts

Outbreak control measures should be instituted for each case. Every effort should be made to locate contacts and unreported cases of toxigenic diphtheria (including cutaneous infections). Person-to-person transmission of *C. ulcerans* is rare but contacts still require the same management as *C. diphtheriae*.

Definition
Regardless of vaccination status, all those with a history of close contact during the 7 days before onset of illness or during the subsequent period of communicability should be considered potentially at risk. Risk is directly related to the closeness and duration of contact. In most cases, those at greatest risk will be:
- household contacts
- kissing and/or sexual contacts
- students in a hall of residence in the same corridor and/or who share kitchen and/or bathroom facilities
- child minders and children regularly being supervised by the case
- healthcare staff exposed to the oro-phayrngeal secretions or infected wound (staff who have taken appropriate infection control precautions need not be considered contacts)

Depending on duration of contact and immunisation status of contact, others at risk of being contacts may include anyone:
- regularly visiting the case's residence
- in the same workplace space, class or early childhood service room.

Contacts on public transport or on an aircraft are thought to be low risk, especially if the journey is less than 8 hours.

Investigation
- Refer to GP for swabs, antibiotics and vaccinations using letter found here https://cdhbintranet.cdhb.health.nz/communitypublichealth/cphpoliciesandprocedures/Documents/Diphtheria%20Contact%20Referral%20Form.aspx

- All contacts identified as at risk (regardless of immunisation status) should have a nasopharyngeal swab (Southern Community Lab [SCL]: Blue wire swab into charcoal gel) and a throat swab ([SCL]: Purple swab with white shaft) taken for diphtheria culture.
- All close contacts should also have any skin lesions swabbed, regardless of whether there is clinically apparent infection.
- All contacts should receive follow-up checks for 7 days from the date of last contact. Such checks may be conducted daily, or the contact may be provided with an information sheet that includes a full and clear list of symptoms and a phone number to call if they become unwell.
- The primary health care practitioner should be kept informed of the management of contacts and laboratory results.

Restriction
Contacts who have a positive laboratory result should be isolated as if they are a case until proven bacteriologically negative.

Prophylaxis
All contacts, after cultures have been taken and regardless of immunisation status:

- A single dose of intramuscular benzathine penicillin (600,000 units or 400 mg) for contacts under 6 years of age and 1.2 million units (900 mg) for contacts 6 years of age or over). Benzathine penicillin is preferred for contacts who cannot be kept under surveillance.

Or

- Oral Azithromicin, treat for total 5 days
  - Children: 10 mg/kg as a single dose on the first day followed by 5 mg/kg/day on days 2-5. For children weighing >45 kg, dose as adult.
  - Adults: Total dose of 1.5g taken as 500mg on day 1, then 250mg daily on days 2-5 or alternatively 500mg for 3 days

Or

- Oral erythromycin, treat for 7 to 10 days
  - children: 30-50 mg/kg/day in equally divided doses four times daily (every 6 hours). Can be also given twice daily if needed.
  - adults 1,600 mg/day in equally divided doses 400mg four times daily (every 6 hours). Can be also given twice daily if needed.

Microbiological clearance for contacts with a positive culture: Two follow-up cultures (nasopharynegeal and throat swabs) obtained at least 24 hours apart and not less than 24 hours after finishing antimicrobials. If cultures are still positive discuss further management with an infectious diseases physician.

Immunisation

- Diphtheria vaccinations are funded for all contacts (contact Immunisation Coordinator if necessary)
- All close contacts should also be offered either a complete course of vaccine or a booster according to the following schedule:
- Fully immunised children (refers to the primary course, currently given at 6 weeks, 3 months and 5 months; the 4-year-old dose is a booster) up to and including 6 years of age who have only received three doses of diphtheria toxoid-containing vaccine within the last 5 years: give one injection of DTaP-IPV.
- Fully immunised individuals aged 7 years and older who have not received a booster dose of a diphtheria toxoid-containing vaccine within the last 5 years: If aged 7–15 years, give one injection of Tdap; if aged over 15 years, give one injection of Td or Tdap.
- Unimmunised individuals: Refer to the schedules in the *Immunisation Handbook* (Ministry of Health 2014) (2)

Counselling
Advise all contacts to seek early medical attention if symptoms develop. Health NZ | Te Whatu Ora information is available online:
https://info.health.nz/conditions-treatments/infectious-diseases/diphtheria

Other Control Measures

Identification of source
Check for other cases in the community. Notify doctors of the potential for outbreaks.

Disinfection
Disinfect all articles in contact with the case.

Health education
In early childhood services or other institutional situations, ensure that satisfactory facilities and practices are in place for hand cleaning; nappy changing; toilet use and training; food preparation and handling; and cleaning of sleeping areas, toys and other surfaces.

Disinfection
- Disinfect all articles in contact with the patient or soiled by discharges of the patient. Discuss with the MOH about involving the Infection Control officer from either Canterbury Health/Timaru/Grey Hospital or one of the private pathology laboratories.

Health education
- Consider a media release and direct communication with local parents, early childhood services, schools and health professionals to encourage prompt reporting of symptoms. Also encourage immunisation of children and the routine administration of a diphtheria booster at 11, 45 (using Td) and 65 years of age (using Td).
- Encourage early childhood services to keep up-to-date immunization records of children (see the Health (Immunisation) Regulations 1995).
- In communications with doctors, include recommendations regarding diagnosis, notification, treatment and infection control.

Reporting

- Ensure complete case information is entered into EpiSurv.
- On receiving a notification of a toxigenic case, medical officers of health should immediately notify the Ministry of Health Communicable Diseases Team and liaison staff at ESR, and complete the Outbreak Report Form (one case is regarded as an outbreak).
- File.

References and further information

1. Health NZ | Te Whatu Ora. Communicable Diseases Control Manual, Diphtheria 2023
2. Health NZ | Te Whatu Ora. Immunisation Handbook 2025
3. A Sears, M McLean, D Hingston, et al., Cases of cutaneous diphtheria in New Zealand: implications for surveillance and management. NZ Med J. 125: 1350, 24 Feb 2012. https://www.nzma.org.nz/journal/read-the-journal/all-issues/2010-2019/2012/vol-125-no-1350/article-sears
4. Mandell, Douglas and Bennett's Principles and practice of infectious diseases. 7th ed. 2010. *Corynebacterium diphtheriae*. page 2691.

5. Mandell, Douglas and Bennett's Principles and practice of infectious diseases. 7th ed. 2010. Cellulitis, necrotizing fasciitis and subcutaneous tissue infections. Page 1298.

6. A. Werno. Email communication, 19 Dec 2016. Consensus opinion of microbiology colleagues that nasopharynx preferable to nose swab for diphtheria cases.

Further information

Baker M, Taylor P, Wilson E, et al. 1998. A case of diphtheria in Auckland – implications for disease control. *New Zealand Public Health Report* 5(10): 73–6.

Bonnet JM, Begg NT. 1999. Control of diphtheria: guidance for consultants in communicable disease control. *Communicable Disease and Public Health* 2: 242–9.

Communicable Disease Report. 2000. Three cases of toxigenic *Corynebacterium ulcerans* infection. *CDR Weekly* 10(6). ISSN 1350-9357.

Farizo KM, Strebel PM, Chen RT, et al. 1993. Fatal respiratory disease due to *Corynebacterium diphtheriae*: case report and review of guidelines for management, investigation, and control. *Clinical Infectious Diseases* 16(1): 59–68.

Heymann DL (ed). 2015. *Control of Communicable Diseases Manual* (20th edition). Washington: American Public Health Association.

Miller LW, Bickham S, Jones WL, et al. 1974. Diphtheria carriers and the effect of erythromycin therapy. *Antimicrobial Agents and Chemotherapy* 6(2): 166–9.

Ministry of Health. 2007. *Direct Laboratory Notification of Communicable Diseases: National guidelines.* Wellington: Ministry of Health.

MMWR. 1997. Case definitions for public health surveillance. *Morbidity and Mortality Weekly Report* 46(RR10): 1–55. URL: www.cdc.gov/mmwr/preview/mmwrhtml/00047449.htm.

Tejpratap SP, Tiwari MD. 2011. Diphtheria. In *VPD Surveillance Manual* (5th edition). 1 Chapter 1-1. http://www.cdc.gov/vaccines/pubs/surv-manual/chpt01-dip.html.

Wagner J, Ignatius R, Voss S, et al. 2001. Infection of the skin caused by *Corynebacterium ulcerans* and mimicking classical cutaneous diphtheria. *Clinical Infectious Diseases* 33: 1598–600.

Document Control

Protocol review task	Responsibility	Date completed
Minor update v4: correction to contacts definition, updated contact prophylaxis guidelines (addition of azithromycin, adjustment to ciprofloxacin dose) as per updates to Communicable Disease Control Manual	PHS	V4, 11/04/2024
Minor update v5: reflecting CHL's ability to provide a prompt result (within 24hrs) for toxigenicity testing, links updated.	PHMR/PHS	V5, 19/03/2025