NSW Health

Diphtheria

NSW Control Guideline for Public Health Units

Response summary

Public health priority: Urgent

Case management: Isolate case with appropriate precautions. Treat case with antibiotics and consider diphtheria antitoxin urgently. Exclude from high-risk settings during infectious period.

Contact management: Conduct nasopharyngeal and throat swabs and provide antibiotics to high-risk contacts and consider for medium risk contacts. Vaccinate eligible contacts. Provide information to all identified contacts.

Revision history				
Version	**Date**	**Revised by**	**Changes**	**Approval**
1.0	01/01/2017			
1.1	23/01/2024	Communicable Diseases Branch	Reformatting. Extensive detail on case and contact management added as per latest evidence. Appendix A added.	Chief Health Officer

Contents

1. The disease

Infectious agent

Diphtheria is an infection caused primarily by toxin producing *Corynebacterium diphtheriae* bacteria, a gram-positive bacillus. A lysogenic ß-phage is required for the production of a potent exotoxin that inhibits protein synthesis in mammalian cells and is the major virulence mechanism leading to human disease. Nontoxigenic strains occasionally cause less severe disease. These do not meet the definition of diphtheria.

Corynebacterium ulcerans bacteria can also carry the phage and cause diphtheria. They are predominantly animal pathogens but cause human disease as zoonotic infections.

Reservoir

C. diphtheriae: Humans. The disease has rarely been isolated from horses, cattle and domestic cats.

C. ulcerans: A range of domestic and wild animals

Mode of transmission

C. diphtheriae: Transmission occurs person to person via respiratory droplets or direct contact with respiratory secretions or cutaneous exudate of an infected person. Due to prolonged bacterial shedding, cutaneous diphtheria plays an important role in transmission to susceptible persons, via contact with the wound or contaminated fomites. Transmission from cutaneous lesions can cause respiratory disease in cases and contacts.

C. ulcerans: Transmission of *C. ulcerans* between humans has never been confirmed. Historically *C. ulcerans* has been associated with drinking raw or unpasteurised milk products. It has also been linked to direct contact with domestic and farm animals. In the international literature four reports of detection of asymptomatic *C. ulcerans* nasopharyngeal carriage among contacts of confirmed cases have raised the possibility of human-to-human transmission, although these cases were also exposed to a common animal source.

Clinical presentation and outcome

The disease diphtheria refers to infection with toxigenic strains of *C. diphtheriae* or *C. ulcerans*, which are phenotypically indistinguishable. There are two main forms – respiratory and cutaneous.

Non-toxigenic strains of *C. diphtheriae* can also cause infections in mucous membranes, and invasive infections including septicaemia, endocarditis and septic arthritis.

Respiratory diphtheria

Classic respiratory diphtheria is an upper respiratory tract illness typically associated with a toxin mediated pseudomembrane at the back of the throat and can be associated with severe systemic manifestations. Onset is often gradual, with symptoms of fever, sore throat and weakness. Primary infection most often involves the tonsils and pharynx, but may also involve the larynx, nose, trachea and bronchi. Dysphagia, headache and altered voice occur in fewer than half of patients. Significant neck oedema (“bull neck”) and difficulty breathing occur in <10% of patients and are associated with an increased risk of death. Isolated spots of grey or white exudate appear on the pharynx, which extend and coalesce over 24 hours to form a confluent, sharply demarcated pseudomembrane. It progressively thickens, becomes tightly adherent to the underlying tissue, and darkens in colour. This pseudomembrane is caused by liberation of a specific cytotoxin. Dislodging the pseudomembrane, mechanically or as the disease progresses, may cause profuse bleeding, asphyxiation and death.

Systemic manifestations are primarily due to effects of diphtheria toxin. Myocarditis and polyneuropathy are the prominent toxic manifestations. Cardiac effects usually begin about one week after onset of illness and may include dysrhythmias, conduction disturbances and dilated cardiomyopathy. Neuropathy typically begins weeks to months after onset of diphtheria in 20%–25% of untreated cases and is the cause of 15% of deaths. Neuropathy can present as cranial nerve paresis, respiratory and abdominal muscle weakness, quadriparesis or quadriplegia, peripheral sensory disturbances, and a variety of autonomic disturbances.

The case fatality rate of classic respiratory diphtheria is 5-10%, even with appropriate treatment.

Cutaneous diphtheria and other sites of infection

Cutaneous diphtheria usually appears on exposed limbs, particularly the legs and presents either as:

- secondary infection of existing skin lesions commonly associated with *Staphylococcus aureus* and group A streptococci growth **or**
- primary punched out ulcers with well-demarcated edges and a cover of bluish-grey necrotic slough or membrane.

Cutaneous diphtheria is only rarely associated with systemic toxic effects in the individual.

Incubation period

Median incubation period from exposure to onset of symptoms is 1.4 days. The range is generally 2 to 5 days but may be longer, with duration up to 10 days reported. Chronic carriage of toxigenic strains can occur without clinical disease.

Infectious period

C. diphtheriae: The period of communicability is variable. Untreated cases are colonised for 18.5 days on average and 95% of cases clear *C. diphtheriae* within 48 days. Asymptomatic cases cause 76% fewer secondary cases than symptomatic cases and appropriate vaccination with diphtheria toxoid vaccine reduces transmission by 60%. Effective antimicrobial therapy reduces communicability by up to 2 weeks and terminates bacterial shedding from respiratory colonisation on average within 5.2 days.

For the purposes of contact tracing, follow up, and recommendations around isolation and restriction, the symptoms of the case, closeness, and duration of contact are important considerations in the likelihood of spread of the disease. Prolonged contact is usually required for spread, particularly from an asymptomatic person.

As asymptomatic carriage and transmission can occur prior to onset of symptoms, consider the **infectious period** as:

- 7 days prior to onset of respiratory symptoms or
- 7 days prior to positive nasopharyngeal and/or throat swab (if asymptomatic) or
- The date of skin infection began

whichever is earlier.

UNTIL

- Demonstrated clearance of infection by nasopharyngeal and throat swabs, for respiratory diphtheria or
- 72 hours of appropriate antibiotics have been received for cutaneous diphtheria AND wound can be appropriately covered (see ‘isolation and restriction’).

C. ulcerans: Transmission of *C. ulcerans* between humans has never been confirmed. Asymptomatic, nasopharyngeal carriage of toxigenic, genetically related strains in close contacts of cases has been

reported, indicating this route of transmission is theoretically possible.

Persons at increased risk of disease

- Unvaccinated or under-vaccinated people
- People living in crowded or unsanitary conditions
- Travellers to countries with higher rates of diphtheria or lower vaccination coverage: parts of the South Pacific, South and South-East Asia, the Middle East, Eastern Europe, South and Central America.

Cutaneous diphtheria is more common in tropical countries and is associated with contact with animals.

Immunity

Infection can occur in vaccinated as well as unvaccinated people. Lifelong immunity is generally (but not always) acquired following disease or subclinical infection. Vaccination reduces the frequency and severity of disease and provides prolonged, but not lifelong, immunity. Post-vaccination antibody levels wane by 0.6% per year since vaccination. Immunity is antibody modulated and primarily against the toxin rather than the bacteria; therefore, vaccinated persons can still harbour the organism.

Infants born to immune mothers have passive protection, which is usually lost before six months of age. Serosurveys in Australia indicate decreasing levels of adult immunity.

Disease occurrence and public health significance

Diphtheria was a common cause of death among children in the pre-vaccine era. Diphtheria has been well controlled in Australia since the introduction and widespread use of the diphtheria-containing vaccine.

In Australia, most cases of diphtheria are reported from Queensland. From 1 January 2011 to 31 December 2021, Queensland recorded six cases of respiratory diphtheria (0.01 per 100,000 population per year) and 39 cases of cutaneous diphtheria (0.07 per 100,000 population per year). Cases had largely been observed in overseas travellers and their contacts. Two unvaccinated adults died from respiratory diphtheria in 2011 and 2018. In 2022, notifications of locally acquired diphtheria cases increased in Queensland, with four (0.1 per 100,000 population) respiratory cases and twenty (0.4 per 100,000 population) cutaneous cases, related to an outbreak on in Northern Queensland.

In NSW there was one case of locally acquired respiratory diphtheria and three cases of overseas acquired cutaneous diphtheria in 2018 (no notifications were received between 2000-2017). Cases have continued in NSW, with four cases reported in 2022, three of which were locally acquired.

The public health management of these infections can be complex, including managing the emergence of antibiotic resistance.

2. Routine prevention activities

Apart from direct case and contact management of diphtheria, the following activities are routine prevention activities at the population level.

Vaccination

The most effective preventive measure is widespread vaccination with diphtheria-containing vaccines, both routine vaccination of infants and children and routine booster vaccination in adolescents and adults. Special efforts should be made to ensure that people at higher risk of exposure, e.g., healthcare workers, are fully vaccinated. Vaccine-induced immunity wanes over time and, without booster immunisations, the proportion of the population who are susceptible increases.

Increased awareness

Amongst general practitioners and clinicians, it is important to promote ongoing education on diphtheria that outlines clinical features, diagnosis, treatment and timely referral to public health units (PHU).

Communicating to the public when cases occur in specific communities or locations likely improves public awareness and recognition of disease.

3. Surveillance objective

- To identify cases and prevent further transmission
- To monitor the epidemiology to inform improved prevention strategies

4. Data management

Within 1 working day of notification the PHU should enter probable and confirmed cases onto NCIMS.

5. Communications

The laboratory or clinician should notify the PHU of any clinically suspected case, culture positive diphtheria case (prior to obtaining toxin testing result) or confirmed case. The clinician should notify the PHU of the case's age, sex, date of onset, clinical status, laboratory findings and vaccination history. PHUs should notify CDB immediately of a probable or confirmed case and or any death from diphtheria.

6. Case definition

Both **confirmed cases** and **probable cases** should be notified.

Confirmed case

A confirmed case requires laboratory definitive evidence **and** clinical evidence (for a confirmed case).

Laboratory definitive evidence

Isolation of toxigenic* *Corynebacterium diphtheriae* or toxigenic* *C. ulcerans* from site of clinical evidence.

*As indicated by detection of toxin gene by nucleic acid testing

Clinical evidence (for a confirmed case)

1. Upper respiratory tract infection **or**
2. Skin lesion

Probable case

A probable case requires:

1. laboratory suggestive evidence **and** clinical evidence (for a probable case) **or**
2. clinical evidence (for a probable case) and epidemiological evidence.

Laboratory suggestive evidence

Isolation of *C. diphtheriae* or *C. ulcerans* from a respiratory tract specimen (toxin production unknown).

Clinical evidence (for a probable case)

Upper respiratory tract infection with an adherent membrane of the nose, pharynx, tonsils, or larynx.

Epidemiological evidence

An epidemiological link is established when there is contact between two people involving a plausible mode of transmission at a time when:

1. one of them is likely to be infectious (usually 2 weeks or less and seldom more than 4 weeks after onset of symptoms) **and**
2. the other has an illness which starts approximately 2-5 days after this contact **and**
3. at least one case in the chain of epidemiologically linked cases (which may involve many cases) is laboratory confirmed.

Possible case

A possible case requires:

A skin lesion **and** either

1. isolation of *C. diphtheriae* or *C. ulcerans* from a wound swab (toxin production unknown) **or**
2. epidemiological evidence.

This should be recorded on NCIMS as a “possible case” until either confirmed or excluded.

Notification procedure

Diphtheria is to notified by:

- Attending clinicians on clinical diagnosis (ideal reporting by telephone within 1 hour of diagnosis)
- Laboratories on microbiological confirmation (ideal reporting by telephone within 1 hour of diagnosis)

Confirmed, probable and possible cases should be entered onto the jurisdictional notifiable diseases database.

Clinical notification (for possible cases)

Cases may be suspected as described above and laboratory confirmation is awaited. Possible cases should be notified to the local PHU.

7. Laboratory testing

Corynebacterium species are commensal organisms of the skin and throat. They generally do not cause disease. *C. diphtheriae* or *C. ulcerans* may not be identified from a skin, nasopharyngeal or throat swab unless there is a specific request noting clinical suspicion conveyed to the laboratory via the request form e.g., “culture for suspected diphtheria”. Swabs should be collected using Amies transport medium swabs.

Laboratory confirmation is typically by a combination of culture, bacterial isolation and preliminary identification of *C. diphtheriae* or *C. ulcerans* in a clinical laboratory followed by confirmation and toxigenicity testing at a reference laboratory.

Culture

In NSW, most laboratories will identify C. diphtheriae or C. ulcerans by microbiological culture on standard blood agar or preferably on tellurite-containing media, such as Hoyle's agar. Diphtheria culture should be specified on the request form to ensure the appropriate selective media is used. Some laboratories do not routinely carry appropriate media and will send specimens on for culture to an appropriate laboratory. PHUs should anticipate a delay in result and work with the relevant laboratories to expedite transport as required.

Nucleic acid testing (NAT) for tox gene

In NSW, isolates from clinical specimens identified as *C. diphtheriae* or *C. ulcerans* are routinely referred to the Centre for Infectious Diseases and Microbiology Laboratory Services (CIMDLS), Institute of Clinical Pathology and Medical Research (ICPMR), Westmead Hospital for diphtheria toxin testing by NAT. This test is designed to detect the phage encoded diphtheria toxin gene, "tox". Detection of the tox gene indicates that the strain is toxin-gene positive not necessarily toxigenic.

For the practical response purposes of this guideline, and for consistency with the national case definition, detection of tox gene by NAT is evidence of and equivalent to isolation of toxigenic *C. diphtheriae* or toxigenic *C. ulcerans*.

Diphtheria toxin testing at ICPMR is done during normal business hours Monday to Friday, with specimens labelled urgent being prioritised, with an approximate turnaround time of 3 days from receipt of C. diphtheriae or C. ulcerans isolate to NAT result. Receipt of the primary clinical specimen rather than an isolate at ICPMR will increase turnaround times. Urgent after-hours testing should be requested by senior PHU staff directly (e.g., PHU director, staff specialist, or appropriate delegate) to the clinical microbiologist on-call via the Westmead Hospital switchboard (02 8890 5555) if the result will have clinical or public health implications.

Strain differentiation

Whole genome sequencing of isolates or multi-locus sequence typing (MLST) can be performed for surveillance purposes or investigation of epidemiological links. The clinical microbiologist on-call via Westmead Hospital switchboard can facilitate this if required.

8. Case management

Response times

On the same day of notification of a confirmed case, begin follow-up investigation.

Investigation of cases pending toxin result (probable and possible)

On the same day of notification, begin follow up investigation for a probable case. The treating clinician should have an urgent direct conversation with an infectious disease specialist to assess the likelihood of diphtheria, if necessary facilitated by the PHU. If local infectious disease services are not available, the NSW specialist service for High Consequence Infectious Disease on-call clinician should be contacted for advice.

The below steps outlined in 'case investigation', including preliminary contact tracing should be considered in:

- probable cases
- clinically suspicious cases - this may be the circumstance where diphtheria is a possibility, but the person does not meet the current case definitions e.g., a person with a known epidemiological link and acute respiratory symptoms without a pseudomembrane

- situations with public health implications (e.g., homelessness, large potential number of contacts, large exposure event, priority populations).

The below steps should be considered, particularly if there is likely to be significant delays in obtaining definitive testing results. Apply appropriate transmission-based precautions while awaiting toxin test results (see 'isolation and restriction' below). If speaking with the case, urge household members ensure they are up to date with their vaccinations.

On the same day of notification, possible cases should have a preliminary risk assessment conducted by the PHU (director or appropriately senior staff) in conjunction with specialist infectious disease advice. This risk assessment should guide the extent of initial investigation whilst awaiting toxin testing results. If there are minimal potential public health impacts (e.g., wound can be covered, low number of potential contacts), it may be appropriate to obtain clinical history, including vaccination status, and ensure the isolate is sent initially only for toxin testing at ICPMR and the appropriate isolation and restriction protocols are in place (see 'isolation and restriction; Cutaneous Diphtheria' below). Nasopharyngeal and throat swabs of the possible case or contact tracing of the possible case could be delayed until toxin testing results are available.

Response procedure

Case investigation

Classical respiratory diphtheria is a medical emergency due to the possible need for airway protection. Urgent referral for medical assessment is warranted with consideration of diphtheria antitoxin.

The response to a notification will usually be carried out in collaboration with the case's medical team. Ensure that action has been taken to:

- discuss with the treating doctor the need to interview the case or the relevant caregiver in order to provide information and seek a contact history.
- establish what the case or the relevant caregiver has already been told about the diagnosis before beginning the interview.
- obtain clinical history including any history of travel and vaccination status.
- ensure nasopharyngeal, throat and wound swabs have been taken (including nasopharyngeal and throat swabs for confirmed cutaneous cases). Amies transport medium swabs (for bacterial culture) should be used. Specify "culture for suspected diphtheria" on request form.
- if *C. diphtheriae* or *C. ulcerans* is isolated, ensure the isolate is sent to ICPMR for toxin testing. The PHU should assess how urgently this result is needed, based on the risk to contacts and ability to restrict and isolate probable and possible cases, or any other relevant factors, as toxin testing is conducted during business hours Monday to Friday. Urgent testing requested out of hours should be discussed by senior PHU staff directly with the clinical microbiologist on call at ICPMR.
- if the initial nasopharyngeal and/or throat swabs of a case with confirmed cutaneous diphtheria are positive (indicating nasopharyngeal carriage), then manage as per a confirmed respiratory case.
- apply isolation and restriction measures.
- carry out contact tracing.
- inform CDB and the adjacent PHUs (if relevant) of the notification.
- Discuss a media release with CDB to help alert community members of the risk and promote vaccination.

If a non-toxigenic strain of *C. diphtheria* or *C. ulcerans* is identified, public health interventions can cease.

Exposure investigation

Investigate the possible source of exposure; contact with a confirmed, probable, or possible case and/or travel history.

Due to the zoonotic nature of *C. ulcerans* infection, it is important to identify any potential animal source. Enquire about consumption of raw milk and contact with animals, including livestock and domestic animals. Where the case's infection has been acquired in Australia and the case has had contact with animals during the incubation period, call the One Health Branch in Health Protection NSW to discuss screening of potential animal sources.

Case treatment

Antibiotics

The treating clinician with specialist infectious disease advice as required will determine appropriate therapy for confirmed, probable and possible cases of diphtheria.

Choice of antibiotic therapy should consider the likelihood of penicillin resistance, and the presence of other bacteria (especially in wounds).

Antibiotics should be given immediately but AFTER appropriate swabs are taken wherever possible.

Generally, treatment should continue for 14 days. Elimination of respiratory diphtheria should be confirmed by nasopharyngeal swab culture (see "isolation and restriction"). If microbiological clearance by negative nasopharyngeal and throat culture is not achieved, an additional 10-day course of antibiotics is recommended.

Diphtheria antitoxin (DAT)

DAT is considered the mainstay of treatment for respiratory diphtheria. Antibiotics are required to eradicate the organism, stop further toxin production and help prevent transmission. DAT is not usually required for asymptomatic carriage, cutaneous infection or prophylaxis. Post infection administration of DAT reduces mortality by 76%.

NSW has access to a limited supply of DAT. DAT can be requested after consultation with the on-call physician for the NSW specialist service for High Consequence Infectious Disease (HCID), located at Westmead Hospital. The treating clinician of any suspected, probable, or confirmed case should liaise with the HCID on-call physician to discuss clinical indications of DAT use and recommended dosage. The HCID on-call physician will use the HCID Standard Operating Procedure and DAT protocol to coordinate the transfer of DAT when indicated.

Ask the treating clinician or HCID on-call physician to provide an update of any patient requiring DAT and if so the PHU should notify CD on-call. If the local PHU is notified in the first instance of any case that potentially requires DAT, the PHU should direct the treating clinician to the HCID on-call physician.

The NSW specialist service for HCID on-call physician can be contacted via 1800 HCID 00 (1800 424 300).

When indicated, DAT should be given promptly. DAT is most effective against circulating diphtheria toxin and less effective once the toxin is bound to tissue, meaning DAT does not reverse symptoms caused by bound toxin. Rather, it limits disease progression making early administration critical. Mortality is most significantly reduced if given within 24 hours, with reduced efficacy if administered after this. Clinicians should not await laboratory confirmation of toxin testing to administer DAT if there is strong clinical suspicion for diphtheria and should discuss with the HCID on-call physician.

DAT is only to be used in a hospital setting with oversight by the infectious diseases or treating physician. DAT is derived from equine serum. There is the potential risk of a hypersensitivity reaction. Sensitivity testing should be considered before giving antitoxin and should be carried out by the treating team in conjunction with the HCID on-call physician.

Immunisation

Ascertain the case's diphtheria vaccination status.

Cases of both cutaneous and respiratory diphtheria should be vaccinated in the convalescent phase of their disease as clinical infection may not induce adequate immunity. Children and adult cases who have completed their primary course of diphtheria-containing vaccines should receive one booster dose of a diphtheria-containing vaccine if it is more than 12 months since their last dose. Unvaccinated or incompletely vaccinated cases should commence a primary or catch-up course of diphtheria vaccination as per the Australian Immunisation Handbook. If a case received DAT, diphtheria vaccination should be delayed for four weeks.

Education

The case should be advised of the nature of the infection and its mode of transmission. Provide the NSW Health factsheet to cases and contacts.

Isolation and restriction

Respiratory diphtheria

Cases with respiratory diphtheria should be managed with standard, contact and droplet precautions. Further detail can be found in the Infection Prevention and Control Practice handbook.

Droplet and contact precautions should remain until two negative nasopharyngeal and throat cultures taken at least 24 hours apart and more than 24 hours after the cessation of appropriate antimicrobial therapy are obtained.

Confirmed and probably cases of respiratory diphtheria should be excluded from work, school or childcare until clearance nasopharyngeal and throat cultures are obtained.

Contact and droplet precautions can be ceased if probable respiratory cases are excluded with negative diphtheria toxin testing result.

Cutaneous diphtheria

Cases with confirmed or possible cutaneous diphtheria should be managed with standard and contact precautions. Wounds should be covered. In addition, droplet precautions should be used until:

- The initial nasopharyngeal and throat swabs are culture negative; **or**
- 72 hours of appropriate antimicrobial therapy has been completed, whichever is shorter.

Contact precautions should continue until:

- All wounds are clinically improving and can be covered by an occlusive waterproof dressing or have healed; **and**
- 72 hours of appropriate antimicrobial therapy has been completed.

Contact and droplet precautions can be ceased if possible cutaneous cases are excluded with negative diphtheria toxin testing result.

Confirmed, and possible cases of cutaneous diphtheria should be excluded from group settings including e.g., childcare, school, aged care, or visiting a healthcare facility until the above criteria for precautions and antibiotics are met or the possible case is excluded (non-toxigenic test result obtained).

9. Environmental evaluation

If there is a possible local animal source for a *C. ulcerans* case, the PHU should contact the One Health Branch.

10. Contact management

Identification of contacts

Contacts are tested and treated to avert incubating disease, prevent further spread and eliminate asymptomatic carriage.

Contact tracing is required for confirmed cases of toxigenic *C. diphtheria* or *C. ulcerans*.

Initiate contact tracing (focusing on education and vaccination) for high risk contacts of probable cases (and consider possible cases) where there is high clinical suspicion of diphtheria or likely to be a delay in receiving results of toxin testing.

Contact definition

Contacts are individuals who were in contact with the case during their infectious period without appropriate protection.

Contacts can be classified as high, medium, or low risk according to the level of exposure to a case, see Table 1. Further examples of high, medium and low risk contacts can be found in Appendix A.

Table 1: Contacts classification based on exposure risk

		Respiratory	**Cutaneous**
Exposure	High	Household and household-like contacts (overnight, intimate partner, co-traveller) Direct oral droplet exposure without appropriate PPE e.g., mouth to mouth resuscitation	Household and household-like contacts (overnight, intimate partner) Direct exposure to infected wound without appropriate PPE
	Medium	Close exposure ≥ 8 hours in shared space e.g., residential institution, childcare, classmate, visitor to household, plane travel adjacent to case* Indirect prolonged exposure to unmasked case e.g., shared space at school >20 hours cumulative	Indirect prolonged exposure ≥20 hours cumulative when wound uncovered e.g., residential accommodation sharing living space, childcare
	Low	All other exposures e.g., event attendance, public area, casual visitors to home of case, people working in same room as case, healthcare workers with brief exposures, or people with < 20 hours in a shared space without direct interaction	

***** *Aircraft: The risk of transmission on an aircraft is low, especially for flights of less than 8 hours duration. Should a case of respiratory diphtheria travel on a long-distance flight (> 8 hours) while infectious, the passengers seated immediately adjacent to them (generally this is 2 rows in front, 2 rows behind and 2 adjacent seats) should be considered household-like contacts unless there are mitigating circumstances. Consideration could be given to contact tracing 2x2 adjacent seats of a long-distance flight (> 8 hours) in the instance that someone with cutaneous diphtheria travelled with an uncovered infected wound or returns positive initial nasopharyngeal or throat swab. In these instances, it is recommended to call CDB to discuss further and an expert panel may be required.*

For health care workers treating a cutaneous case, ask the infection control staff to identify the procedures used to treat the case's wound/s and assess if appropriate precautions were used while undertaking wound care. Importantly, identify if any potential exposure to droplets was likely to have occurred and assess if droplet precautions were used. For example, droplets may be generated when vigorously washing the wound or irrigating the wound under pressure. Healthcare workers who have

used appropriate transmission-based precautions do not need to be considered contacts and can be provided with information only.

If the initial nasopharyngeal and/or throat swabs of a case with cutaneous diphtheria are toxin positive (indicating nasopharyngeal carriage), then manage contact tracing as per a confirmed respiratory case.

Further guidance on contact risk assessment and management in complex settings may require an expert advisory group (EAG). Contact CDB for advice.

Investigation

All contacts should have their immunisation history checked if feasible. It may be practically difficult to check immunisation status of low-risk contacts, although public communications should direct low risk contacts to check their own vaccination records.

Regardless of their vaccination status, high risk contacts of either respiratory or cutaneous diphtheria cases should have nasopharyngeal and throat, and any wound swabs taken for culture (ideally before the commencement of antibiotics).

For medium risk contacts, a risk assessment should be conducted as to if nasopharyngeal and throat swabs (or wound swabs if appropriate) are required. Consideration should be given to:

- Infectiousness of case during exposure event
    - Symptomatic
    - PPE use by the case and contact e.g., mask / coverage of wound
- Type and duration of interaction
    - Significant interaction e.g., well known to case / close friend
    - Prolonged single interaction rather than multiple short interactions
- Potential co-exposure to upstream cases / multiple case exposures
- Evidence of carriage in the cohort, or presence of other cases

If there are a large number of contacts to be swabbed, notify the relevant laboratory to ensure laboratory staff capacity and to expedite results.

Symptom surveillance for evidence of disease is needed for 7 days from direct exposure to the case. In some situations where persons or their carer/s are unable to adequately self-monitor, this may require daily clinical examination for symptoms of diphtheria.

If a contact returns a positive toxigenic diphtheria result from a wound swab, they will fulfill the case definition for a confirmed case and should be managed as such.

If contacts return a positive toxigenic diphtheria nasopharyngeal or throat swab (contact may be asymptomatic), then the contact should be clinically managed as per a confirmed case, however, they do not meet the case definition of a confirmed or probable case. Assessment if further contact tracing of the asymptomatic carrier is required. In this instance, an expert panel may be convened, please contact CD-On-call in CDB. In this circumstance, these contacts should be recorded as ‘contact’ in NCIMS.

DAT has no proven role in the prophylaxis of contacts or the treatment of carriers.

Antibiotic prophylaxis

Antibiotics should be provided to all high-risk contacts and considered in medium risk contacts, using the same principles described above in assessing requirement for nasopharyngeal and throat swabs. Antibiotics are generally not required for low-risk contacts. See Table 2 for choice of antibiotic.

Penicillin resistant isolates are increasingly being documented in Queensland. Choice of antibiotics and dosing regimen should consider antibiotic sensitivities, clinical tolerance, and nature of contact with the case. Check sensitivities of isolate before recommending antibiotic prophylaxis and seek the advice of

an infectious diseases physician if sensitivities are awaited or conflict with recommended antibiotics. If contacts are commenced on antibiotics prior to isolate sensitivities being available, ensure to follow up once they are reported. If the case's isolate is resistant to the antibiotics commenced by the contact, the contact will need to restart with a course of appropriate antibiotics.

Table 2: First line antibiotics for use in contacts

Age	Agent		Dose	Route	Duration
Infant or child < 6 years old	For penicillin susceptible isolates[1]	Benzathine benzylpenicillin	600,000 Units = 450 mg	IM	Single dose
	OR	Azithromycin[2]	12 mg/kg up to 500 mg daily	PO	5 days
Child ≥6 years or adult	For penicillin susceptible isolates[1]	Benzathine benzylpenicillin	1.2 million Units = 900 mg	IM	Single dose
	OR	Azithromycin[2]	500mg (child 12 mg/kg up to 500 mg daily) daily	PO	5 days

[1]Amoxicillin may be an appropriate option for isolates reported as having "intermediate" susceptibility to penicillin (equates to susceptible increased exposure); discuss with infectious diseases physician and/or clinical microbiologist. Isolates reported as resistant to penicillin are considered resistant to amoxicillin unless testing indicates otherwise.
[2]Where a macrolide antibiotic is recommended, discuss with clinical microbiologist to ensure sensitivity testing is undertaken

Table 3: Alternative antibiotics for use in adults ≥12 years based on available sensitivities

Antibiotic	Dose	Route	Duration
Clindamycin	150-300 mg QID	PO	7 days
Doxycycline[1, 2]	Initially 200 mg on day 1 (100 mg BD) followed by 100 mg daily	PO	7 days

[1]Use in adult contacts ≥50 kg in weight. Doxycycline is contraindicated in pregnancy and breast feeding
[2]Where penicillin and macrolide antibiotics are contraindicated, not tolerated or impractical, doxycycline may be considered for children aged 8-11 years who weigh ≥50 kg

Contacts with initially positive toxigenic nasopharyngeal or throat swabs should have clearance testing with nasopharyngeal and throat swabs after completion of treatment. If positive, a further 10-day course of antibiotic therapy is indicated.

Immunisation

Previously vaccinated high and medium risk contacts should receive a booster dose of diphtheria containing vaccine if more than 12 months has elapsed since their last dose. Unvaccinated or incompletely vaccinated contacts should commence a primary or catch-up course of diphtheria vaccination. Pregnant contacts requiring immunisation, are recommended to receive dTpa vaccination. If the diphtheria exposure and subsequent dTpa vaccination occurs at less than 20 weeks gestation, the contact should discuss with their healthcare provider regarding the risks and benefits of a further second dose of dTpa at 32 weeks or greater gestation for pertussis protection.

Low risk contacts should be advised to receive a vaccination if unvaccinated or incompletely vaccinated or if not up to date with booster vaccination. In practice, it may not be possible to directly advise low risk contacts of their potential risk, e.g., in the circumstance where a case attended a large event. Consideration of a letter or media release may be needed in this situation, which should include both general education on symptom monitoring and vaccination advice. If this is a broader event likely affecting contacts across jurisdictions, discuss with CDB.

Education

Advise all high, medium and low risk contacts of the nature of the infection and its mode of transmission and to monitor for symptoms for 7 days from last exposure and seek medical advice promptly should symptoms appear.

Isolation and restriction

Advise all contacts requiring antibiotics to avoid contact with people who are vulnerable to diphtheria and not to visit vulnerable settings until 72 hours of an appropriate course of antibiotics have been completed OR until negative cultures from nasopharyngeal, throat and any wound swabs are obtained, whichever is shorter.

Vulnerable settings include those which involve:

- Contact with infants aged 6 months and under
- Care of the sick, elderly, and those requiring dependent care
- Contact with immunosuppressed individuals.

This requires exclusion from the workplace if in a vulnerable setting.

Healthcare workers who have cared for a case of either respiratory or cutaneous diphtheria without appropriate precautions should be excluded from work until negative nasopharyngeal and throat swabs are returned. If the healthcare worker is unable to remain excluded from the workplace, additional precautions may be needed according to local infection control policies (such as wearing a surgical mask).

11. Special situations

Outbreaks

An outbreak is defined as two or more cases who share a plausible epidemiological link e.g., clustered in time and place. An outbreak management team may need to be established. CDB and all relevant public health units should be notified and involved. Key issues include nomination of roles to ensure efficient reporting and communication of issues within the response framework. Early communication of risk to affected institutions is essential.

Communication to external stakeholders and the media will involve discussion of often complex medical concepts e.g., ‘carriage’ of the organism in vaccinated populations. It is imperative that early discussion take place with agreement on the key public health messages. In the event of a local outbreak, the local PHU should lead the media and communication response.

An outbreak should prompt an urgent review of vaccination status in that group and consideration of urgent catch-up immunisation or a pop-up vaccination clinic as required.

An expert advisory group may be called at the discretion of the public health unit managing the case(s) or CDB. Particularly, an expert group may be appropriate for situations that are extraneous to these guidelines.

Public health response for toxigenic diphtheria cases in Aboriginal communities

Early consultation and partnership with community leaders and representatives is important when managing diphtheria cases and contacts in an Aboriginal community. If an outbreak control team is convened, include appropriate Aboriginal stakeholders. This member could be the health service Aboriginal Health director or delegate, Aboriginal Community Controlled Health Service member or council nominee.

In addition to case and contact investigation and management as outlined above, consider the following public health actions in partnership with the Aboriginal community:

- Alert all local health services, Aboriginal Community Controlled Health Services, and the community of the risk of toxigenic respiratory diphtheria (even if the case has cutaneous diphtheria) and the need for primary and booster vaccinations
- Ensure referral hospitals are aware of the protocol to access DAT
- Health services to opportunistically check vaccination status and offer catch-up and booster doses to whole community
- Consider an active outreach vaccination campaign in the community. Factors supporting an active campaign include:
    - Low vaccination rates and/or booster coverage indicated from existing data
    - New or increasing incidence of toxigenic diphtheria cases
    - One or more respiratory diphtheria cases
    - Community concerns and support raised in community consultation
    - Surge staffing and feasibility.

Appendix A: Contact risk classification and management

Settings based contact risk category matrix

Setting	Case type	Contact definition	Contact risk category
Household	Resp and skin	All household members and those who have spent the majority of a day and/or overnight in the same house as the case after onset of symptoms (and in 7 days prior to symptoms for resp)	High
Residential institutions including prisons, hospital wards (patients), homeless facilities and boarding schools	Resp and skin	Direct wound contact, sleeping in same room overnight	High
		Sleeping in same connected space and sharing living facilities (apart from sharing open recreational spaces)	Medium
		All other (including sharing open recreational spaces only)	Low
Air Travel*	Resp	Passengers seated immediately adjacent (2x2) to case on flight of ≥8hrs	High
	Skin	Passengers seated immediately adjacent (2x2) to case on flight of ≥8hrs	Low/Medium
Schools (not school boarding facilities)	Resp	Very close / prolonged contact	Medium/High
		Other classroom contact	Low
	Skin	Classroom contacts	Low (Unless direct wound contact)
Childcare	Resp	Staff and children who are known to have had close contact with the symptomatic case for ≥20 hours cumulative	Medium/High
		Indirect prolonged exposure to unmasked case e.g., shared space ≥20 hours cumulative	Medium
		All other children and staff at the centre	Low
	Skin	Staff and children who are known to have had close contact for ≥20 hours if the case's wound was uncovered and/or staff or children in direct contact with the case's wound	High
		Indirect prolonged exposure ≥20 hours	Medium

		cumulative when wound uncovered e.g., shared space	
		All other children and staff at the centre or all children and staff if the case's wound was covered	Low
Health care workers	Resp	Cared for the case without a mask Direct oral droplet exposure without appropriate PPE	High
	Skin	Had contact with the wound without wearing a mask and had likely exposure to droplets (gloves worn)	High
		Had contact with the wound wearing gloves. No / unlikely exposure to droplets	Low

**Aircraft:*
There is usually no requirement to contact trace those in adjacent seats in the following circumstances:

- *Someone with appropriately covered cutaneous diphtheria and negative initial nasopharyngeal and throat swabs travelled on a long-distance flight.*

Management

High Risk Contact: Likely/definite exposure to respiratory droplets, or direct contact with respiratory secretions or wound exudate (e.g., prolonged, close exposure to uncovered wound or respiratory droplets without PPE)

- Provide information and advice to monitor for symptoms for at least 7 days after contact
- Swab# nasopharynx and throat, and any skin lesions
- Provide antibiotics
- Avoid contact with vulnerable populations (infants aged ≤6 months, sick, elderly and those requiring dependent care, and immunosuppressed individuals) until swabs returned negative result or 72 hours of antibiotics completed, whichever is shorter. In the household this requires avoidance and work situations this requires exclusion from the workplace.
- Recommend a booster dose of vaccine if greater than 12 months since last dose received
- Primary or catch-up course of vaccination if unvaccinated or incomplete.

Medium Risk Contact: Uncertain exposure requiring further risk assessment

At a minimum:

- Provide information and advice to monitor for symptoms for at least 7 days after contact
- Consider swab# of nasopharynx and throat, and any skin lesions
- Consider antibiotics
- Recommend a booster dose of vaccine if greater than 12 months since last dose received
- Primary or catch-up course of vaccination if unvaccinated or incomplete.

Additional measures will depend on consideration of risk factors.

Low risk Contact: Very unlikely/no exposure to respiratory droplets, nor direct contact with respiratory secretions or wound (e.g., appropriate PPE, distant contact only, covered wound).

Where appropriate and feasible:

- Provide information about symptoms
- Recommend opportunistic booster dose of vaccine if >10 years since last dose
- Primary or catch-up course of vaccination if unvaccinated or incompletely vaccinated.

Additional measures will depend on consideration of risk factors.

[#] *Swabs should ideally be combined nasopharyngeal and throat swabs, however, in institutional settings where there may be requirement to swab large numbers of contacts, combined nasal/deep nasal and throat swabs may be substituted to improve timeliness.*

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