



CENTRE FOR DISEASE CONTROL

NORTHERN TERRITORY

**Guidelines for the
Control of Diphtheria
in the
Northern Territory**

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Northern Territory Government

Department of Health and Community Services

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Section 1 Background and Clinical Features

1.1 Background

Diphtheria is caused by toxigenic strains of *Corynebacterium diphtheriae*, a Gram positive, non-sporing, non-capsulate bacillus.

Corynebacterium diphtheriae is endemic in the Northern Territory (NT), and is regularly cultured from wound and nasopharyngeal swabs, particularly in Aboriginal people. Strains of *C. diphtheriae* can be divided into those that produce toxin ('toxigenic strains') and those that do not ('non-toxigenic strains'). The usual cause of life-threatening disease is toxin production from toxigenic strains, but cases of invasive endocarditis and septicaemia by non-toxigenic strains have also been reported. Rarely, other *Corynebacterium* species, such as *Corynebacterium ulcerans* may produce diphtheria toxin and lead to classic respiratory diphtheria. In 1992 there was an adult death from toxigenic diphtheria recorded in the NT. Since that time there has only been one other toxigenic isolate recorded in the NT which was from a skin lesion in a worker returned from East Timor.

Universal childhood vaccination with diphtheria toxoid and maintenance of adult boosters with adult diphtheria tetanus (ADT) vaccine at age 15 and 50 years is the only effective control measure. Although vaccination against diphtheria does not prevent or reduce carriage of *C. diphtheriae*, it boosts antibody levels against the diphtheria toxin and hence protects against development of the toxigenic disease, should infection occur with a toxigenic strain.

1.2 Clinical features

Toxigenic disease can result from infection by toxigenic strains of Corynebacterium species anywhere on the body.

Infection with *C. diphtheriae* can cause a spectrum of illness ranging from subclinical to severe life-threatening disease. Inapparent infections outnumber clinical cases. Two forms of disease can occur:

1.2.1 Cutaneous diphtheria

Cutaneous diphtheria is quite common in tropical areas and may be caused by either toxigenic or nontoxigenic strains: it is usually mild; typically consisting of non-distinctive sores or shallow ulcers and only rarely involves toxic complications.¹

1.2.2 Respiratory diphtheria

Respiratory diphtheria is typically caused by toxigenic strains of *C. diphtheriae*. Mortality from toxigenic disease is 5-10%.^{2,3} Initial signs of illness include a sore throat and low-grade fever; swelling of the neck from inflammation can develop and is a sign of severe disease that is usually associated with systemic absorption of toxin.⁴ The most important manifestation is the production of a membrane across the back of the throat causing respiratory obstruction. This characteristic lesion is an asymmetrical adherent greyish white membrane with surrounding inflammation. Other complications of the toxin are myocarditis and nerve paralysis. Late neurological effects of the toxin include cranial and peripheral motor and sensory nerve palsies that may appear 2-6 weeks after the absorption of the toxin.

1.3 Mode of transmission

Transmission is by droplet spread, usually by person-to-person contact, but occasionally through food or articles soiled with discharges from infected lesions (e.g. clothes, bed linen or table surfaces). Raw milk has also served as a vehicle.

1.4 Incubation period

Incubation is usually 2 to 5 days, but may be longer.

1.5 Period of communicability

Cases are infectious until virulent bacilli have disappeared from discharges and lesions (usually less than 2 weeks, seldom more than 4 weeks). Rarely, chronic carriers may shed organisms for 6 months or more; however appropriate antibiotic treatment rapidly stops shedding.⁴

1.6 Susceptibility and resistance

Infants born of immune mothers are relatively immune; protection is passive and usually lost by 6 months. Clinical disease does not always lead to lasting immunity;^{4,5} conversely, immunity is often acquired through inapparent infection.

Vaccination against diphtheria with a primary course of 3 doses is recommended at 2, 4 and 6 months with boosting doses given at 4 years and 15 years. A complete course of immunisation induces protective levels of anti-toxin lasting throughout childhood but immunity wanes by middle age therefore a booster dose is recommended at 50 years of age.³

1.7 Method of diagnosis

Culture of *C. diphtheriae* from the infected site. Direct microscopy is of no value.

Section 2 Clinical Management

CDC must be urgently notified by telephone if disease is suspected on clinical grounds (while waiting for laboratory confirmation)

2.1 Collection of specimens from a suspected case

- The preferred specimen is a cotton tipped swab of the eroded epithelium underneath the membrane and the membrane itself.
- Nasopharyngeal cultures are indicated in children who do not have an obvious membrane and should be obtained with a flexible alginate (wire) swab that reaches deep into the back of the nose.
- Any chronic, crusting, cutaneous lesion should also be swabbed. Before cultures of wounds are taken, lesions should be cleansed with sterile normal saline and crusted material removed. A cotton-tipped applicator should then be firmly applied to the base of the wound.
- Transport in ordinary semi-solid transport medium, such as Amies or Stuarts.
- Specimens should be collected prior to administration of antibiotics.

2.2 Case management

Management of cases is based on the clinical condition and the toxigenicity of the infection, if known.

2.2.1 Clinical systemic diphtheria / results of toxigenicity pending

Confirm with the local laboratory that the specimen has been sent to the reference laboratory for urgent PCR toxigenicity testing. A result should be available in 24-48 hours.

Since clinical systemic diphtheria is usually caused by a toxigenic strain it is a **medical emergency**. Management involves seeking advice from an experienced physician, and includes the administration of antibiotics (to eliminate infection and prevent spread) and equine diphtheria antitoxin on the basis of clinical diagnosis alone. Administration of antitoxin is the most important aspect of treatment in this situation and must not be delayed until bacteriological/toxigenicity confirmation. Life support measures, including endotracheal intubation or emergency tracheotomy may be necessary to overcome respiratory obstruction.

Cases should remain in strict respiratory isolation until 2 cultures from both the nose and throat taken not less than 24 hours apart, and not less than 24 hours after ceasing antibiotic therapy, are negative for diphtheria bacilli. If culture is impractical, isolation may be ended after 14 days of appropriate antibiotic treatment.

2.2.2 Toxigenic infection

The same isolation criteria apply as for systemic disease above. The management of toxigenic infections in the absence of systemic disease involves seeking advice from an experienced physician, as it may involve the administration of equine diphtheria antitoxin. Vigorous cleansing of wounds, if present, and the administration of antibiotics is recommended.

Diphtheria infection does not necessarily confer immunity⁴ so during the convalescent stage of their illness, fully immunised individuals should receive a booster dose of diphtheria containing vaccine (unless they have received a dose within the last 12 months).⁵ Unimmunised or incompletely immunised individuals should commence ‘catch-up’ vaccination and receive/complete the primary course and boosters in accordance with the *Australian Immunisation Handbook* recommendations.

2.2.3 Non-toxigenic infection

Treatment of non-toxigenic infection will depend on the local manifestations of the infection, and a decision on whether to treat will need to be made on individual circumstances. Unimmunised or incompletely immunised individuals should commence “catch-up’ vaccination and receive/complete the primary course and boosters in accordance with the *Australian Immunisation Handbook* recommendations.

Section 3 Public Health Management

3.1 Case Definition and Notification

NT case definitions are the same as the National Notifiable Diseases Surveillance System (NNDSS) definitions. Both confirmed and probable cases should be reported.

3.1.1 Confirmed case

A confirmed case requires laboratory definitive evidence only.

- **Laboratory definitive evidence** – isolation of **toxigenic** *C. diphtheriae* or **toxigenic** *C. ulcerans*

3.1.2 Probable case

A probable case of diphtheria disease requires either:
laboratory suggestive evidence **AND** clinical evidence

OR

Clinical evidence **AND** epidemiological evidence

- **Laboratory suggestive evidence** – isolation of *C diphtheria* or *C ulcerans* (toxin production unknown)
- **Clinical evidence** – at least one of the following :
pharyngitis and/or laryngitis (with or without a membrane);
OR
toxic (cardiac or neurological) symptoms
- **Epidemiological evidence** – an epidemiological link is established when there is:
contact between 2 people involving a plausible mode of transmission at a time when :
 - one of them is likely to be infectious (usually 2 weeks or less and seldom more than 4 weeks after onset of symptoms)**AND**
 - the other has an illness which starts within approximately 2-5 days after the contact**AND**
 - at least 1 case in the chain of epidemiologically linked cases (which may involve many cases) is laboratory confirmed

3.2 Active Surveillance

Active surveillance includes follow-up of contacts, as detailed below. In addition, community members with symptoms compatible with diphtheria up to 2 weeks after diagnosis of the index case should be investigated. This includes anyone presenting with a sore throat or runny nose, particularly if the nasal discharge is blood stained or only apparent on one side.

3.3 Definition of a contact

- All household members and other persons with history of habitual, close contact with the index case.
- Anyone who has had significant contact with nasopharyngeal secretions of the index case during the previous week (i.e. mouth kissing or mouth to mouth resuscitation).
- Anyone who has spent 4 hours or more a day for 5 consecutive days, or more than 24 hours with the index case in the week preceding the onset of illness (e.g. contacts in child care centres, schools etc).

3.4 Management of asymptomatic contacts

Management of contacts is based on the clinical condition of the index case and the toxigenicity of the infection, if known.

3.4.1 Contact management when the index case has:

- ***clinical systemic diphtheria OR***
- ***confirmed toxigenic strain (with or without systemic disease)***
- Take nasopharyngeal swabs (or nose and throat swabs) for culture and place in ordinary semi-solid transport medium.
- Fully immunised contacts should be given a booster dose of a diphtheria containing vaccine. (NB a booster dose is not required if the last dose was given less than 5 years earlier).⁴
- Unimmunised or incompletely immunised contacts should commence ‘catch-up’ immunisation following the recommendations in the *Australian Immunisation Handbook*.

- Antibiotic prophylaxis (see section 3.5).
- Adult contacts whose occupations involve handling food/milk products or close association with children should be excluded from work until swabs prove them not to be carriers or 48 hours post commencement of antibiotic prophylaxis.
- Child contacts should be excluded from school, day care etc until swabs prove them not to be carriers or 48 hours post commencement of antibiotic prophylaxis.
- Observe all asymptomatic contacts closely for 7 days.

3.4.2 Contact tracing is NOT required when the index case has:

- ***no evidence of systemic disease with a confirmed non-toxigenic organism^{4,5} OR***
- ***no evidence of systemic disease with toxigenicity pending****

*If the laboratory result comes back as a toxigenic strain, refer to section 3.4.1.

3.5 Antibiotic prophylaxis for contacts of systemic diphtheria and/or toxigenic infection

Antibiotic prophylaxis should be given regardless of the immunisation status of the contact.

Weight < 30 kg: Benzathine penicillin (Bicillin LA), 600,000 units (450mg/1ml)
1ml as a single intramuscular dose.

Weight ≥ 30 kg: Benzathine penicillin (Bicillin LA), 1,200,000 units (900mg/2ml)
2ml as a single intramuscular dose.

If penicillin allergy present or compliance assured:

Erythromycin orally for 7 days in 4 daily divided doses

Children 40mg / kg / day

Adults 1gm / day

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