

DIPHTHERIA

INTERIM GUIDELINES* - KERALA

Public Health Division, Directorate of Health Services,

Thiruvananthapuram, Kerala

(As updated on 24 April 2017)

Diphtheria is a toxic infection caused by Coryne bacterium species, ie., *C. diphtheriae*, an exclusive human pathogen, with affinity to mucous membranes and skin, and occasionally by *C. ulcerans*.

It is spread by airborne droplets, or direct contact with respiratory/skin exudates. After an average incubation of 3-4 days it produces signs and symptoms. These are due to the strong toxin it produces, which has far reaching effects on the heart, nervous system or renal, in addition to severe local inflammation and necrosis.

Commonest sites of infection are pharynx and tonsils, nose and nasopharynx, larynx, and occasionally mucosa of the eye, ear and genitalia.

Commonest manifestations

- The formation of an extending grey/brown/black colored thick adherent pseudo-membrane at these sites is the most characteristic finding. Attempted removal is difficult, and causes bleeding.
- Local toxicity and the oedema it produces, along with regional lymphadenopathy cause a brawny thickening /swelling all round the neck, giving a 'bullneck' appearance.
- A striking lack of generalised symptoms like fever even with severe local effects is often noted, and even considered a diagnostic point.

Affected age ranges

In an endemic situation, diphtheria generally affects children below 15 years. As more and more children have become protected with Diphtheria toxoid vaccination, the affected segment has shifted up into adolescents and young people mostly. Declining rates of immunisation can cause the infection to shift down again into the pediatric age groups also increasingly.

Case fatality ranges from 3-23%.

- Causes of death are mainly the toxic cardiomyopathy, /myocarditis, (which occurs in 10 to 25 % patients, and is solely responsible for up to 50-60% deaths along with mechanical obstruction of the respiratory tract. The cardiomyopathy occurs mostly from the 2nd to 3rd week, while neuropathy can occur between 10-90 days of onset. The neuropathy manifests as poly neuritis.

or as ocular/palatal palsies resulting in accommodation defects, nasal twang of voice
/regurgitation of feeds

Diagnosis

Diagnosis is based on the clinical features, (pseudo-membrane, 'bullneck', paucity of general symptoms,) immunization history, culture results, and toxin production studies

Lab Investigations

- Culture of Throat swabs -- Two dry swabs (double swabs) together in one tube (for culture and staining) are to be taken, and sent to the nearest Govt. Medical College Microbiology lab, or the Regional Public Health Lab, whichever is nearer.
- If delay anticipated in transit is >6 hrs, use tubes with a transport medium,(contact the nearest RPHL/ GMCH Microbiology)
- Culture tubes with Silica gel transport medium do not need cold chain, but those with Amies medium will need standard cold chain transport /2-8 deg C storage
- Throat Swabs can be taken locally at DH/GH level instead of referring to MCHs for this purpose
- 'SUSPECT/PROBABLE DIPHTHERIA ' should be superscribed on the request forms specially

Public Health /Epidemiological Case Definition for clinical respiratory diphtheria:

- *A General case is defined as an upper respiratory tract illness characterized by sore throat, a low grade fever, and an adherent membrane of the tonsil(s), pharynx, larynx, and/or nose.*
- **A confirmed case** is either a clinical case from which *C. diphtheriae* is isolated from respiratory specimens (nasal or throat swab, membrane tissue) or a clinical case that is epidemiologically linked to a laboratory- confirmed diphtheria case.
- **A probable case** is a clinically compatible case that is not yet laboratory confirmed and is also not epidemiologically linked to any laboratory confirmed case

Differential Diagnosis

- Other diseases that can occasionally produce a similar membranous pharyngitis-
 - Streptococcal pharyngitis
 - Adenoviral/streptococcal tonsillitis
 - Infectious mononucleosis.
 - Patients who have been treated with immunosuppressive drugs can present with a membrane that mimics diphtheria.
 - Agranulocytosis
 - Candidiasis
- Isolated diphtherial laryngitis (can usually be differentiated from *H. influenzae*- type b epiglottitis, spasmodic croup, or the presence of a foreign body by the gradual onset in case of diphtherial disease.)

- Viral laryngo-tracheitis or bacterial tracheitis (Differentiation from isolated diphtherial laryngitis difficult on the basis of symptoms alone.)

Treatment

Diphtheria antitoxin

- It is used in a single intravenous empirical dosage is the mainstay of treatment.
- Diphtheria antitoxin is given as i.v infusion ***after test dose*** as per vial instructions. Dose is dependent on degree of general toxicity of the patient, site and size of membrane, and duration of illness as shown below.-

Pharyngeal/laryngeal disease < 2 days duration	20000-40000 Units
Nasopharyngeal disease	40000-60000 Units
Extensive disease / >3 days duration/ 'bullneck' +	80000-120000 Units

Antibiotics

Crystalline penicillin (for cases) and erythromycin (for contacts/less severe cases etc) halts the bacterial growth, but cannot alter the toxic systemic impacts of the toxin. These two remain the drugs of choice .

The efficacy of azithromycin is not documented, and is uncertain

Antibiotic dosages for patients

- Crystalline penicillin i.v. 1.5 Lakh U/Kg/Day , divided 6 hrly or in adults 20 Lakh Units x 6 hrly, ATD, x14 days. Doses as high as 40 L Units 6 hrly have been used in exceptional circumstances
- Erythromycin 40 mg/Kg/day divided 6 hrly, or in adults 500 mg 6 hrly orally after food x 14 days

Antibiotic dosages for contacts

- Erythromycin 40 mg/Kg/day divided 6 hrly, or 250 mg 6 hrly orally after food x 10 days

Supportive care

Good nutritional support, and bed rest for at least 2 weeks, (or longer, depending on presence of complications)

Actively watch/ monitor for any late onset manifestations of cardiomyopathy/neuropathy in convalescents too.

A list of red flag signs should be informed/ counselled to discharged patients families, for reporting back in case of need

The management of a patient with suspected diphtheria shall follow the general sequence below

- (i) Administration of diphtheria antitoxin as soon as possible after testing for hypersensitivity to horse serum; early administration of appropriate antitoxin is critical for survival (5).
- (ii) Establishing the diagnosis through appropriate bacterial cultures
- (iii) Administration of antibiotics
- (iv) Appropriate supportive care including special attention to maintaining an adequate airway in the presence of laryngeal or extensive pharyngeal membranes and to careful monitoring for cardiac rhythm disturbances or other manifestations of myocarditis.
- (v) Contact tracing, and assessment/chemoprophylaxis should also be considered, in linkage with the IDSP District Surveillance Officer

Immunisation

- Immunity to Diphtheria declines over time. Adults and adolescents may thus become susceptible later on in life. Absence of immunity in unvaccinated/incompletely vaccinated individuals or reduced immunity in persons at risk (eg healthcare workers who are constantly exposed as part of their job) makes them prime targets for immunisation, Such categories deserve prioritization for immunisation if vaccine availability is slow or phased in nature
- Vaccine used is - **Td vaccine at a dose of 0.5 ml i.m.** Td vaccine, being a toxoid should never be frozen in storage.
- Td vaccine being a toxoid vaccine is safe for use in pregnant women also.
- **Schedules** are as follows --
 1. **Infants and children 0 -7 years:-** to immunize as per National immunization Schedule using DPT/(catch-up with DPT one dose in missed vaccination cases)
 2. **Children 7-10 years:-** in immunized, only one dose of Td at 10 years; in unimmunized and partially immunized (eg 5 yr booster missed) ,three doses at 0, 1 and 6th months recommended.
 3. **Children 10-16 years:** 1 dose if documented as immunised with 5th yr booster, or three doses at 0, 1 and 6th month if previous immunisation status unknown/uncertain. The above is recommended initially in contacts of the known diphtheria cases.
 4. **Adults:** for general public, at present only for contacts of cases at 0, 1 and 6th months.
 5. **All health care workers** as per defined risk,. at 0, 1 and 6th months

*Directorate of Health Services Thiruvananthapuram, Dated 24 April 2017

*These guidelines , issued by the Directorate of Health Service in the context of the surges of diphtheria in some parts of the State, may be considered as interim guidelines, and will be valid till any new orders/modifications in this regard are issued at any later stage. Medical Officers are requested to refer to the most recently updated versions which will be put up on the DHS and Arogyakeralam websites