The Republic of the Union of Myanmar

Ministry of Health

Clinical Management Guidelines of Diphtheria

(Version 1)

Date : 31st July 2023

Place : Nay Pyi Taw

Ministry of Health

Department of Medical Services

Clinical Management Guidelines of Diphtheria (Version 1)(31-7-2023)

1. Background

Diphtheria is a clinical syndrome caused by an exotoxin produced by the bacterium of *Corynebacterium diphtheriae*; non-toxigenic strain of *Corynebacterium diphtheriae* are not associated with the syndrome but can cause localized inflammation. Most commonly, toxigenic infection results in respiratory or cutaneous disease. It leads to the clinical syndromes of pharyngitis, naso-pharyngitis, tonsillitis, laryngitis (or any combination of these) associated with a firmly adherent pseudo-membrane over the tonsils, pharynx, larynx and/or nares. In severe cases, infection can spread into trachea causing tracheitis and/or severe cervical adenopathy leading to life-threatening airway obstruction. Death can occur from asphyxiation or aspiration of sloughed pseudo-membrane. *C.diphtheriae* can also cause skin and wound infections. Diphtheria is most commonly spread from person to person, usually through respiratory droplets, like from coughing or sneezing or by direct contact with either respiratory secretions or infected skin lesions.

The onset of disease is insidious. Following an incubation period of 2-5 days (with a range of 1-10 days), low-grade fever begins and a pharyngeal pseudomembrane develops over 2-3 days, along with lymphadenopathy and diffuse systemic toxicity, resulting in a rapid, thready pulse, weakness, and irritability. Although the systemic effects of diphtheria can occur in the first week of illness, they usually occur later (1-2 weeks after onset for myocarditis, 2-8 weeks for neuritis). *C. ulcerans* can produce a diphtheria toxin that is immunologically similar to that produced by *C. diphtheriae*. *C. pseudotuberculosis* and other Corynebacterium species are similar to *C. diphtheriae* and *C. ulcerans* in that it can harbour the phage-borne diphtheria toxin gene.

2. Case Definition

Clinical case definition for diphtheria (Probable case): an upper respiratory tract illness with an adherent membrane of the tonsil(s), pharynx, larynx, and/or nose; or, infection of a non-respiratory anatomical site (e.g., skin, wound, conjunctiva, ear, genital mucosa)

Laboratory criteria for diagnosis: Isolation of *C. diphtheriae* from a clinical specimen from any site and confirmation of toxin-production by Elek test or by another validated test capable of confirming toxin-production.

Case classification: For reporting purposes, cases are classified as suspect or confirmed:

Suspect: an upper respiratory tract illness with an adherent membrane of the tonsil(s), pharynx, larynx or nose that is not laboratory confirmed and is not epidemiologically linked to a laboratory-confirmed case

Confirmed: an upper respiratory tract illness with an adherent membrane of the tonsil(s), pharynx, larynx or nose, and isolation of toxin-producing *C. diphtheriae* from the nose or throat, or epidemiologic linkage to a laboratory-confirmed case of diphtheria

OR

An infection at a non-respiratory anatomical site (e.g., skin, wound, conjunctiva, ear, genital mucosa) with isolation of toxin-producing *C. diphtheriae* from that site

Close contacts

Household members (all persons who sleep in the same house/tent during the last 5 nights before onset of disease of the case) and any persons with close contact (less than one metre) for a prolonged time (over 1 hour) during the 5 days prior to onset of disease of the case (e.g. caretakers, relatives, or friends who regularly visit the home) as well as medical staff exposed to oral or respiratory secretions of a case-patient.

3. **Clinical presentation**

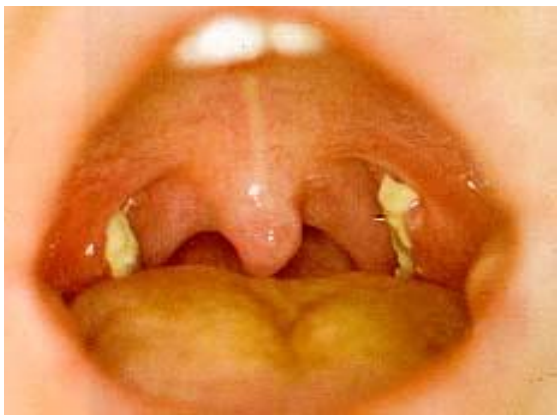
   Symptoms: Initial symptoms include malaise, sore throat and nasal discharge resembling viral upper respiratory illness (URTI). Symptoms can then progress to bloody nasal discharge, hoarse voice, cough, and/or pain with swallowing. In children, this may cause drooling or pooling of secretions. In severe cases, patients may develop noisy breathing (inspiratory stridor) and shortness of breath. Fever may or may not be present. Skin can become infected with the diphtheria bacteria (cutaneous diphtheria); clinically wounds have a grey covering over it.

   Throat and nares examination: Conduct a careful examination. Be careful not to cause distress in children as this may worsen the clinical situation.

   (In private clinics, throat inspection only is recommended.)

   On inspection, child may also have an obviously swollen neck, referred to as **"bull neck"** due to swollen cervical lymph nodes, soft tissue edema and mucosal edema.

   Look at the nares and throat to visualize the typical gray-white adherent membrane overlying the inflamed, edematous mucosa. The grey membrane may be localized asymmetrically (i.e. affecting nares, tonsils, pharynx) or may extend to affect the larynx and trachea. When this membrane is agitated with a swab it does not "come off" and may cause profuse bleeding if dislodged.



Look for presence danger signs (impending airway or circulatory failure): **If any present, call for help for urgent supportive treatment.**

Any sign of respiratory distress such as inspiratory stridor, fast breathing, chest indrawing, accessory muscle use, or restlessness are warning signs of impending airway obstruction and the need to secure the airway.

The presence of lethargy, cyanosis or SpO_2 < 90% is ominous in child with upper airway obstruction (implies overt airway obstruction) and emergent need to secure airway.

Any sign of shock such as capillary refill > 3 seconds, presence of cold extremities, fast pulse rate, or low blood pressure, is also an emergency that needs urgent attention.

Look for other serious complications: Within 1-12 weeks, after the initial pharyngeal phase, some patients may develop myocarditis (congestive heart failure, conduction abnormalities, and arrhythmias), debilitating neurologic dysfunction (neuropathy of cranial and peripheral nerves, and/or motor weakness/paralysis), or renal failure.

4. **Differential diagnosis**

Differential diagnosis of pharyngitis	
Group A streptococcus	Fever, no coughing, tonsillar exudate and follicles, tender jugulodigastric nodes
EBV	Fever pharyngitis, adenitis, hepatomegaly, splenomegaly
Vincent's Angina	Acute onset of painful bleeding gums, ulcers and sluffing of the gingiva
Oral candida	White/ yellow patches on the inner cheeks, tongue, roof of the mouth, and throat, gelatinous mass can be removed Cracking and redness at the corners of the mouth
Differential diagnosis of stridor	
Viral croup	Barking cough, respiratory distress, hoarse voice,
Retropharyngeal abscess	Soft tissue swelling in back of the throat, difficulty in swallowing, fever
Epiglottis	Soft stridor, Septic' child, Little or no cough, Drooling of saliva, Inability to drink
Anaphylaxis	History of allergen exposure, Wheeze, Shock, Urticaria and oedema of lips and face

5. **Investigation**

During outbreak, routine sampling of throat samples is not recommended. However, collection of samples should be considered in the following situations:

- When diagnosis is unclear (i.e. swollen neck without adherent pseudomembrane);
- or if suspect antimicrobial resistance.

Specimen of choice is a throat swab that should be collected as early as possible during the course of illness of the suspected cases. Nasopharyngeal swab is also considered as a good specimen for diphtheria diagnostics especially in infants or small children.

See **Appendix A** for sample collection protocols.

Investigations for complications should be done according to the condition of patient.

6. Clinical management

Summary of initial clinical management of all clinically suspected diphtheria cases
1. Place patient immediately in isolation room (or area) and apply standard, droplet and contact precautions when caring for the patient.
2. Administer diphtheria antitoxin (DAT) as soon as possible.
3. Administer antibiotics (penicillin, erythromycin or azithromycin) as soon as possible.
4. Monitor closely and provide supportive therapy for severe complications (i.e. airway management, cardiac, neurologic and renal failure)
5. Vaccinate with an age-appropriate diphtheria toxoid-containing vaccine.

The disease is usually not contagious after completing 48 hours of effective antibiotic therapy.

6.1.Admission criteria

Patients with a diagnosis of probable or confirmed Diphtheria and with severe symptoms will require admission to a facility capable of dealing with the respiratory and systemic complications as well as isolation for first 48 hours.

This includes tertiary and secondary level hospitals, and specialist private hospitals (facilities with inpatient and surgical capacity, and the ability to provide high level nursing care, experienced medical and/or infectious disease doctors, along with anaesthetic and surgical specialists).

Patients with probable diphtheria but mild symptoms require at least 48 hours isolation but can be discharged within 48 hours of treatment commencing if clinically well enough.

6.2.Antitoxin therapy (DAT): Administer as soon as possible.

DAT is an equine serum product that is highly effective and the gold standard for treatment of diphtheria.

DAT should be administered **immediately** to probable cases with respiratory diphtheria (sore throat, low grade fever and presence of adherent membrane on tonsils, pharynx or nose) based on clinical diagnosis. Do not wait for laboratory diagnosis.

Diphtheria toxin that has already entered the host cells is unaffected by DAT. Therefore, to reduce complications and mortality DAT should be administered as soon as possible after disease onset.

Due to small risk for a serious allergic reaction to the horse serum (0.6 % anaphylaxis), perform a **sensitization test** for all candidate patients.

DAT should be administered in a closely monitored setting with appropriate medical interventions available, if needed.

Pregnant women should not receive DAT.

The amount of antitoxin recommended varies with larger amounts recommended for persons with extensive pseudomembrane, neck swelling, systemic signs and with longer interval since onset. The dose is the same for children and adults. Do not repeat dosing.

If limited availability, then use lower dose range. Severity of diphtheria	**Dosage for adults and children**
Laryngeal or pharyngeal of 2 days duration	20,000-40,000 IU
Nasopharyngeal disease	40,000-60,000 IU
Extensive disease of 3 or more days of duration or any patient with diffuse swelling of the neck (respiratory distress, hemodynamic instability)	80,000-100,000IU

How to deliver diphtheria antitoxin

General information for family/patient: DAT is an equine serum product that is highly effective and the gold standard for treatment of diphtheria. Antitoxin is used to stop the damaging effect of the toxin and prevent the life-threatening manifestations of diphtheria infection. However, there is small risk of serious allergic reaction: < 0.6 % anaphylaxis, 4% fever, and 8.8% serum sickness.

Dose: The amount of antitoxin recommended varies with larger amounts recommended for persons with extensive local lesions and with longer interval since onset. The dose is the same for children and adults.

Route: The IV route is the preferred route of administration of DAT, especially in severe cases. The antitoxin dose should be mixed in 250 –500 mL of normal saline and administered slowly over 2 – 4 hours, closely monitoring for anaphylaxis. The antitoxin may be given IM in mild or moderate cases.

Temperature: Antitoxin should be warmed to 32 – 34°C (90 – 95°F) before injection.

Environment: Ensure appropriate monitoring and medical interventions are available for adult and paediatric patients in case serious allergic reaction ensues.

Monitoring devices: pulse oximeter, BP cuff, thermometer

Emergency medicines: adrenaline (1:1000), salbutamol, antihistamine, hydrocortisone, crystalloid fluid, oxygen supply and delivery devices

Emergency equipment: bag valve mask, IV giving devices, airway management

Procedure:

1. Health care worker uses contact and droplet precautions: gloves, long-sleeved gown, surgical mask and eye protection.
2. Monitor patient vital signs: BP, HR, RR, SpO2, mental status, before and after administration.
3. Perform sensitization testing

Sensitization testing

Inject 0.1 ml SC and wait 15 minutes. If there is no reaction then inject further 0.25 ml SC. If no reaction after 15 minutes, then inject remainder IM or IV.

6.3.Antibiotic therapy

Antibiotics should be given when diphtheria is suspected clinically and it is not a replacement for antitoxin.

Antibiotics	***Doses***	***Duration***
Erythromycin (oral or IV)	40–50 mg/kg/day, maximum 2 g/day	14 days
Aqueous penicillin G (IV)	100,000–150,000 units/kg/day divided into four doses	14 days
Penicillin G procaine (IM)	25,000–50,000 units/kg/day divided into two doses	14 days

Ref-CDC (Protocol CDC IRB # 4167 ,Version Number 12.0 ,February 9, 2023) and Indian Academy of Pediatrics (IAP) (STANDARD TREATMENT GUIDELINES 2022
Diphtheria

or

Antibiotic treatment for probable and confirmed cases: Antibiotics should be administered as soon as possible.

1. For patients who cannot swallow or are critically ill, use IV or IM preparations.
2. For severely ill patients unable to take oral therapy, use IV/IM formulation at the onset. Once patient improves clinically, step down to oral antimicrobials
3. For less sick patients, oral therapy can be used at the onset.
4. Check for penicillin allergy (risk of anaphylaxis from penicillin is very rare).

For severely ill patients, choose one of the following: Procaine benzyl penicillin (penicillin G): administer IM All persons: 50 mg/kg once daily (maximum 1.2 grams a day). Treat for total 14 days. * Powder for injection: 1 g (=1 million IU); 3 g (=3 million IU) in vial.
Aqueous benzyl penicillin (penicillin G): administer IM or slow IV All persons: 100,000 units/kg/day administer in divided dose of 25 000 IU/kg every 6 hours. Maximum dose is 4 MIU or 2.4 grams per day.

*Powder for injection: 600 mg (= 1 million IU); 3 g (= 5 million IU) (sodium or potassium salt) in vial
IV Erythromycin All persons: 40-50 mg/kg/day (maximum, 2 gm/day). Administer in divided dose, 10-15 mg/kg every 6 hour, maximum 500 mg per dose. Treat for total 14 days.

For patients who can swallow and are less ill, use oral preparation. Choose one: Oral phenoxymethylpenicillin V All persons: 50 mg/kg/day, administer in divided dose 10-15 mg/kg/dose administered every 6 hours. Maximum is 500 mg per dose. Treat for 14 days.
Oral erythromycin All persons: 40-50 mg/kg/day (maximum, 2 gm/day). Administer in divided dose, 10-15 mg/kg every 6 hour, maximum 500 mg per dose. Treat for total 14 days.
Oral azithromycin For children: 10-12 mg/kg once daily (max. 500 mg/day). Treat for total of 14 days. For adults: 500 mg once daily. Treat for total of 14 days. Note: There is no data to support the exact duration required for azithromycin

Ref- Operational protocol for clinical management of Diphtheria Bangladesh, Cox's Bazar (Version 10th Dec 2017) WHO

6.4.Supportive therapy for patients with complications

Monitor the patient closely

1. The patient's condition, especially respiratory status, should be assessed often, at least every 2-4 hours, for any signs of respiratory distress from the development of airway obstruction or aspiration. This includes vital signs and pulse oximetry.

2. Also monitor cardiac function with ECG for conduction abnormalities and arrhythmias (if possible).

If patient shows any sign of inspiratory stridor, fast respiratory rate, chest indrawing, restlessness, lethargy, or cyanosis, then call for help and proceed with airway management.	

Oxygen therapy

Avoid using oxygen routinely as oxygen can mask airway obstruction, use with caution**:**

Desaturation in isolated upper airway obstruction is a sensitive sign for impending airway compromise and deterioration. If there is desaturation ($SpO_2 < 90\%$), this is a sign that the airway is obstructing and you need to act to secure the airway. Use oxygen while you are in the process of securing the airway.

If signs of airway compromise, proceed to secure airway. Securing airway is a life-saving intervention. Call for help immediately.

1. Securing airway is life-saving intervention. Consult senior doctor, with extensive experience with difficult airway management immediately. This includes an anesthetist, intensivist, surgeon (preferably, an ears, nose, throat (ENT) surgeon). Tracheostomy in infants carries significant risks, so should be done with great caution by skilled surgeons.
2. If there are signs of incipient (impending) complete airway obstruction (signs of respiratory distress such as inspiratory stridor, fast respiratory rate, restlessness, chest wall in-drawing, accessory muscle use, desaturation), then secure airway immediately. If skilled personnel are available, take patient to operating theatre. A graded approach is recommended, with orotracheal approach preferred (when possible). If airway not secured with orotracheal approach, then proceed to tracheostomy (if experienced surgeon available) or needle cricoithyroidotomy (see Appendix B)(as a temporalizing emergency procedure until tracheostomy can be performed emergency procedure).
3. If patient develops complete airway obstruction (cyanosis, SpO2 < 90-94, lethargy), then perform an emergent tracheostomy (if experienced surgeon is available) or needle cricoidthyroidotomy (temporizing emergency procedure).
4. Administration of nebulized adrenaline is used in many causes of upper airway obstruction as a temporizing measure. Though specific data on efficacy in acute respiratory diphtheria is not available, can consider its use for upper airway obstruction. As a trial administer nebulized adrenaline (2 ml of 1:1000 solution). If effective can repeat hourly.

Manage shock

1. A child with all 3 signs of shock (delayed CR > 3 seconds + weak and fast pulse + cold extremities or frank hypotension) needs careful resuscitation. Because shock can be due to sepsis or cardiac failure, it is imperative to look for signs of cardiac failure. If there are no signs of cardiac failure and/or fluid overload (absence of crackles, hepatomegaly and edema), then give gentle fluid bolus. If suspect shock is due to heart failure, then use inotropes (such as dopamine or adrenaline) and do not administer fluids.

Other supportive treatments

1. If the patient has fever (>38 °C) or pain - give paracetamol.
2. Encourage the child to eat and drink. If the child has difficulty in swallowing, nasogastric feeding may be required. The nasogastric tube should be placed with extreme caution by an experienced clinician or, if available, an anesthetist.
3. Avoid frequent examinations and invasive procedures when possible or disturbing the child unnecessarily.

Myocarditis (may occur 2–7 weeks after the onset of illness) can present with a weak, irregular pulse and evidence of heart failure. Treat with supportive therapies according to national standards.

Neurologic paralysis (may occur 1 to 3 months after the onset of the disease) and can lead to difficulty with swallowing (paralysis of the soft palate), vision (ocular motor paralysis), breathing (paralysis of respiratory muscles) and ambulation (limb paralysis). Treat with supportive therapies according to national standards.

6.5.Vaccination

Active immunization against diphtheria should be undertaken during convalescence from diphtheria, because disease does not necessarily confer immunity**.**

6.6.Care of all close contacts

For close contacts, regardless of their immunization status, administer antibiotics for prophylaxis.

Choose one of the following antibiotics for prevention: IM benzathine penicillin: a single dose For children aged ≤ 5 years: administer 600 000 units For those > 5 years: administer 1 200 000 units
Oral erythromycin For children: 40 mg/kg/day, administered in divided dose, 10 mg per dose, every 6 hours For adults: 1 g/day for adults, administered in divided dose, 250 mg per dose every 6 hours Treat for total 7 days
Oral Azithromycin Children: 10-12 mg/kg once daily, to a max of 500mg/day. Treat for total 7 days Adults: 500mg once daily. Treat for total 7 days.

Asymptomatic, previously immunized close contacts healthcare workers should receive a booster dose of an age-appropriate diphtheria toxoid-containing vaccine [Td] if they have not received a booster dose of a diphtheria toxoid-containing vaccine within 5 years.

If not fully immunized or if immunization status is not known, they should be immunized with Td vaccine, Three doses: at least 4 weeks interval between each dose.

Contacts who cannot be kept under surveillance should receive penicillin G benzathine rather than erythromycin.

<table>
<tr><th colspan="3">Recommended diphtheria toxoid vaccination for contacts, by previous vaccination history</th></tr>
<tr><td><3 dose or unknown</td><td colspan="2">≥3 Dose</td></tr>
<tr><td rowspan="2">Immediate dose complete primary series according to schedule</td><td>Last dose > 5 years previously</td><td>Last dose < 5 years previously</td></tr>
<tr><td>Immediate booster dose</td><td>Children in need of their 4th primary dose or booster dose should be vaccinated;
Otherwise, vaccination not required.</td></tr>
</table>

7. **Prevention and Vaccination**

The current immunization schedule of Myanmar is three primary doses of Pentavalent vaccine at 2, 4 and 6 months of age and booster dose at 18 months.

ပုံမှန်ကာကွယ်ဆေးထိုး၊ ဆေးတိုက်ခြင်း အစီအစဉ်

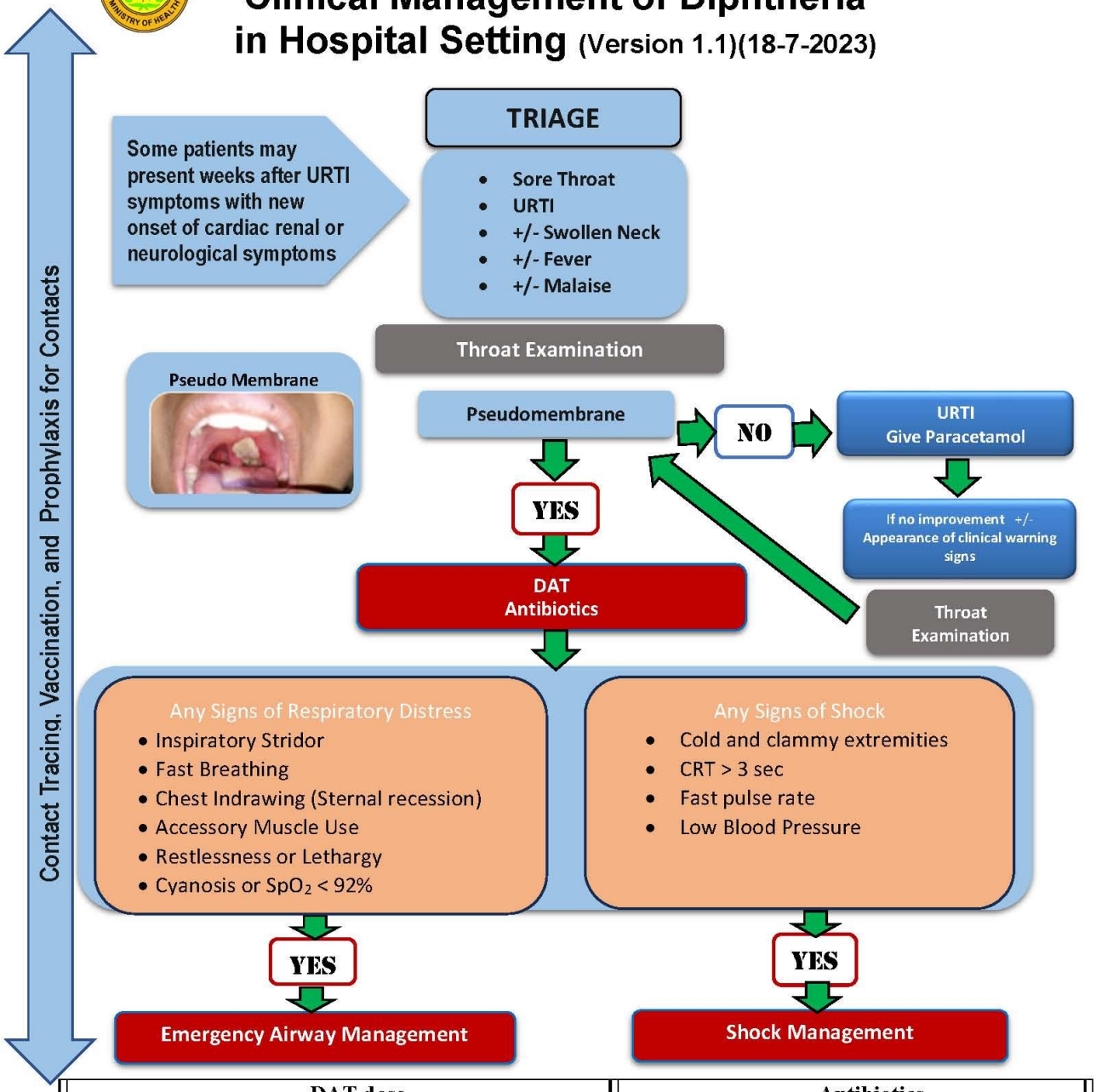
အသက်		ကာကွယ်ဆေးများ	ကာကွယ်ပေးသည့်ရောဂါများ
မွေးပြီးပြီးချင်း		ဘီစီဂျီ*	ပြင်းထန်တီဘီရောဂါ
		အသည်းရောင်အသားဝါ (ဘီ)	အသည်းရောင်အသားဝါ(ဘီ)
(၂) လ		ဘီစီဂျီ*	ပြင်းထန်တီဘီရောဂါ
		ပိုလီယို (ပထမ)	ပိုလီယိုအကြောသေရောဂါ
		ပြင်းထန်ဝမ်းပျက်ဝမ်းလျှောရောဂါ (ရိုတာ) (ပထမ)	ပြင်းထန်ဝမ်းပျက်ဝမ်းလျှောရောဂါ
		ပြင်းထန်အဆုတ်ရောင် (ပီစီဗီ) (ပထမ)	ပြင်းထန်အဆုတ်ရောင်ရောဂါ
		ဆုံဆို့-ကြက်ညှာ-မေးခိုင်-အသည်းရောင်အသားဝါ (ဘီ)-ဦးနှောက်အမြှေးရောင် (ငါးမျိုးစပ်ကာကွယ်ဆေး) (ပထမ)	ဆုံဆို့နာ၊ ကြက်ညှာ၊ မေးခိုင်၊ အသည်းရောင်အသားဝါ (ဘီ)၊ ဦးနှောက်အမြှေးရောင်ရောဂါ/အဆုတ်ရောင်ရောဂါ
(၄) လ		ပိုလီယို (ဒုတိယ)	ပိုလီယိုအကြောသေရောဂါ
		ပြင်းထန်ဝမ်းပျက်ဝမ်းလျှောရောဂါ (ရိုတာ) (ဒုတိယ)	ပြင်းထန်ဝမ်းပျက်ဝမ်းလျှောရောဂါ
		ပြင်းထန်အဆုတ်ရောင် (ပီစီဗီ) (ဒုတိယ)	ပြင်းထန်အဆုတ်ရောင်ရောဂါ
		ပိုလီယိုထိုးဆေး	ပိုလီယိုအကြောသေရောဂါ
		ဆုံဆို့-ကြက်ညှာ-မေးခိုင်-အသည်းရောင်အသားဝါ (ဘီ)-ဦးနှောက်အမြှေးရောင် (ငါးမျိုးစပ်ကာကွယ်ဆေး) (ဒုတိယ)	ဆုံဆို့နာ၊ ကြက်ညှာ၊ မေးခိုင်၊ အသည်းရောင်အသားဝါ (ဘီ)၊ ဦးနှောက်အမြှေးရောင်ရောဂါ/အဆုတ်ရောင်ရောဂါ
(၆) လ		ပိုလီယို (တတိယ)	ပိုလီယိုအကြောသေရောဂါ
		ပြင်းထန်အဆုတ်ရောင် (ပီစီဗီ) (တတိယ)	ပြင်းထန်အဆုတ်ရောင်ရောဂါ
		ဆုံဆို့-ကြက်ညှာ-မေးခိုင်-အသည်းရောင်အသားဝါ (ဘီ)-ဦးနှောက်အမြှေးရောင် (ငါးမျိုးစပ်ကာကွယ်ဆေး) (တတိယ)	ဆုံဆို့နာ၊ ကြက်ညှာ၊ မေးခိုင်၊ အသည်းရောင်အသားဝါ (ဘီ)၊ ဦးနှောက်အမြှေးရောင်ရောဂါ/အဆုတ်ရောင်ရောဂါ
(၉) လ		စက်သက် - ကျိုက်သိုး (ပထမ)	စက်သက်ရောဂါ၊ ကျိုက်သိုးရောဂါ
		ဂျပန်ဦးနှောက်ရောင်	ဂျပန်ဦးနှောက်ရောင်ရောဂါ
(၁) နှစ်ခွဲ		စက်သက် - ကျိုက်သိုး (ဒုတိယ)	စက်သက်ရောဂါ၊ ကျိုက်သိုးရောဂါ
		ဆုံဆို့-ကြက်ညှာ-မေးခိုင်-အသည်းရောင်အသားဝါ (ဘီ)-ဦးနှောက်အမြှေးရောင် (ငါးမျိုးစပ်ကာကွယ်ဆေး) (စတုတ္ထ)	ဆုံဆို့နာ၊ ကြက်ညှာ၊ မေးခိုင်၊ အသည်းရောင်အသားဝါ (ဘီ)၊ ဦးနှောက်အမြှေးရောင်ရောဂါ/အဆုတ်ရောင်ရောဂါ
(၉) နှစ်		သားအိမ်ခေါင်းကင်ဆာ (ပထမ)	သားအိမ်ခေါင်းကင်ဆာရောဂါ
(၁၀) နှစ်		သားအိမ်ခေါင်းကင်ဆာ (ဒုတိယ)	သားအိမ်ခေါင်းကင်ဆာရောဂါ

ဆေးရုံဆေးခန်းတွင် မွေးဖွားသောကလေးများကို မွေးဖွားပြီးပြီးချင်း ၂၄ နာရီအတွင်းအသည်းရောင်အသားဝါ(ဘီ)ကာကွယ်ဆေးထိုးပေးနေပါသည်။

*ဘီစီဂျီကာကွယ်ဆေးကို မွေးဖွားပြီးနှစ်ပါက အသက်(၂)လမတိုင်မီတွင်လည်းကောင်း၊ အသက် (၂)လတွင် အပြေးကာကွယ်ဆေးများနှင့်အတူလည်းကောင်း ထိုးနှံနုပါသည်။

Gavi The Vaccine Alliance | World Health Organization | unicef

Clinical Management of Diphtheria in Hospital Setting (Version 1.1)(18-7-2023)



DAT dose		Antibiotics
Laryngeal or pharyngeal of 2 days duration	20,000-40,000 IU	14 days course of antibiotics. Antibiotic of choice is Penicillin
Nasopharyngeal disease	40,000-60,000 IU	Alternatives are Erythromycin or Azithromycin
Extensive disease of 3 or more days or diffuse swelling of the neck	80,000-100,000IU	**Aqueous penicillin G (IV/IM)** 100,000–150,000 units/kg/day divided into four doses **Penicillin G procaine (IM)** 25,000–50,000 units/kg/day divided into two doses

World Health Organization

APPENDIX A: Specimen collection, storage and transportation

Laboratory confirmation of diphtheria is useful for diagnosis of clinically suspected cases in the early phases of a response, or when diagnosis is equivocal.

During outbreak, routine sampling of throat samples is not recommended. However, collection of samples should be considered in the following situations:

- When diagnosis is unclear (i.e. swollen neck without adherent pseudomembrane);
- or if suspect antimicrobial resistance.

Specimen of choice is a throat swab that should be collected as early as possible during the course of illness of the suspected cases if indicated. Nasopharyngeal swab is also considered as a good specimen for diphtheria diagnostics especially in infants or small children. The chances of positivity fall rapidly after 2-3 weeks of onset or by use of appropriate antibiotics.

Window period from onset: 2 days-4 weeks

Type of specimens: Throat swab
Nasopharyngeal swab
Pieces of Pseudomembrane
Specimen from cutaneous lesion

Ideally, two samples should be collected from each suspected case; a nasopharyngeal and oropharyngeal swab and placed into Stuart/ Amies transport media with or without charcoal.

Material required for specimen collection

- Strong light source for illuminating the pharynx
- Wooden sticks (disposable tongue depressors)
- Throat swab: cotton, dacron
- Amies transport medium or other suitable transport medium
- Saline solution in sterile container (for Pseudomembrane)
- Skin punch or scalpel (for cutaneous diphtheria)
- Gloves
- Face masks
- Goggles
- Zip lock bag
- Disposable bag
- Labels
- Laboratory request form/ Case investigation form

Oropharyngeal/throat swabs

1. Pharynx should be clearly visible and well illuminated.
2. Depress the tongue with a tongue depressor; swab the throat without touching the tongue, uvula or inside of the cheeks.
3. Rub vigorously over any membrane, white spots or inflamed areas; slight pressure with a rotating movement must be applied to the swab.
4. Place into the Amies/ Stuart transport medium.

Nasopharyngeal swabs

1. Insert the swab into one nostril, beyond the anterior nares.
2. Gently introduce the swab along the floor of the nasal cavity, under the middle turbinate until the pharyngeal wall is reached, rotating swab 2-3 times. Force must not be used to overcome any obstruction.
3. Place into the Amies/ Stuart transport medium.

Pseudomembrane

1. To be undertaken preferably by an infectious disease specialist as there is a considerable risk of severe bleeding. If a membrane is present, lift the edge of the pseudomembrane and swab beneath it.
2. Using sterile forceps gently lift the pseudomembrane where possible and aseptically remove pieces of the membrane.
3. Place the membrane into Amies/ Stuart transport medium or a small volume (2 ml) of sterile broth or saline.

Specimen for cutaneous lesions

1. Lesions should be moistened with sterile normal saline and crusted material removed.
2. Press the swab firmly into the lesion.
3. Place into the Amies/ Stuart transport medium.

Storage and transportation: 2-8°C

Dispatch: The specimens are labeled and sent to National Health Laboratory with completely filled case investigation form.

APPENDIX B

How to perform percutaneous needle cricothyroidotomy or "needle cric"

Needle cricothyroidotomy is indicated as a life-saving, last-resort procedure in children younger than 10 years who have upper airway obstruction

This procedure can be performed by a paediatrician, intensivist, anaesthetist, emergency physician, general surgeon or family physician.

After inserting the needle cric, then need to arrange child to be transported quickly to hospital with surgeon that can perform tracheostomy within 60 minutes.

Preparation: Pre-assemble the "needle cric kit" and have available in the resuscitation area. The simplest equipment, appropriate for use in infants, consists of the following:

14G over-the-needle catheter

To connect to BVM(Bag valve mask): a 3.0-mm ETT adapter coupled with an IV extension set

(Or)

To connect directly to oxygen: 3- or 5-mL syringe with side port "hole" to allow exhalation, with oxygen tubing inserted inside with a "tight fit"

It is good practice to preassemble the kit, place it in a clear bag, seal the bag, and tape it in an accessible place in the resuscitation area.

How to preform procedure

1. Prepare your adapter: The catheter can be attached either to a 3.0 mm ETT adaptor to provide bag ventilation (if available). Or, can be attached directly to oxygen supply using a 3-way stopcock or 2-5 ml syringe as adaptor.

If you have three-way stopcock, then attached to oxygen tubing. The three-way stopcock will allow for inspiration of oxygen and exhalation.

Alternatively, use a 2-5 ml syringe with plunger removed as the "adapter". Use scalpel to make a "hole" to serve as exhalation side port, either in the syringe or in the tubing itself. Insert oxygen tubing inside the syringe. Make sure the exhalation side-port is patent and below the oxygen tubing.

_Humidified oxygen source

2. Position: Place the child in the supine position with the head extended over a towel under the shoulder. This forces the trachea anteriorly such that it is easily palpable and can be stabilized with two fingers of one hand. The key to success is strict immobilization of the trachea throughout the procedure.

3. Anatomy: “Carefully palpate the cricothyroid membrane.” In smaller children, it may be impossible to precisely locate the cricothyroid membrane, so the proximal trachea is utilized for access . The priority is an airway and provision of oxygen. Complications from inserting the catheter elsewhere into the trachea besides the cricothyroid membrane are addressed later.

4. Sterile technique: Clean skin and wear sterile gloves.

5. Needle insertion: Consider the trachea as one would a large vein, and cannulate it with the catheter-over-needle device directed caudally at a 30° angle. Aspirate air to ensure tracheal entry and then slide the catheter gently forward while retracting the needle.

6. Connect adaptor: The catheter can be attached either to a 3.0 mm ETT adaptor to provide bag ventilation (if available). Or, can be attached directly to oxygen supply. Both are described below: Attach to BVM(Bag valve mask): Attach 3.0-mm ETT adapter and commence bag ventilation. The provider will note exaggerated resistance to bagging. This is normal and is related to the small diameter of the catheter and the turbulence created by ventilating through it. It is not generally the result of a misplaced catheter or poor lung compliance secondary to pneumothorax. It is helpful to practice BMV(Bag mask ventilation) through a catheter to experience the feel of this increased resistance. **The operator must allow for full expiration** through the patient’s glottis (if not completely obstructed) and not through the catheter in order to prevent breath-stacking and barotrauma. This can be accomplished by watching for the chest to fall after inspiration. A secondary source of oxygen can be put over the mouth.

Attach to oxygen source directly (no BVM): If you have three-way stopcock, then attached to end of catheter that should already be connected to oxygen tubing. The three-way stopcock will allow for inspiration of oxygen and exhalation. Alternatively, attach the 2-5 ml syringe with exhalation side port, already connected to oxygen tubing. For inhalation, occlude exhalation side-port for one second, then allow exhalation for 3-4 seconds (look at chest wall rise and fall to determine ventilation. Always make sure the exhalation side-port is not blocked by oxygen tubing.

7. Transport: Transfer patient to a hospital with experienced surgeon that will be readily available to secure surgical airway. Ventilation through the small-bore catheter is limited, and after 40-60 minutes, hypercapnia may develop. Some report reasonable ventilation for up to 40-60 minutes (and in some cases, up to 2 hours.) Transfer should be done expediently, with patient on monitor, while careful bag ventilation and/or oxygen therapy.

8. Communication: Communicate clearly with receiving doctor so that there is not delay in securing airway promptly once child arrives.

References:

CDC, Expanded Access Investigational New Drug (IND) Application Protocol:

Use of Diphtheria Antitoxin (DAT) for Possible Diphtheria Cases, BB-IND 11184, Protocol CDC IRB # 4167, Version Number 12.0, February 9, 2023

WHO, Operational protocol for clinical management of Diphtheria Bangladesh, Cox's Bazar (Version 10th Dec 2017)

Indian Academy of Pediatrics (IAP), Standard Treatment Guidelines 2022 Diphtheria