Diphtheria

Srinivas Murthy, MD CM, MHSc
University of British Columbia
Diphtheria facts

- **Causative agent:** toxigenic strains of *Corynebacterium diphtheria* (*C. diphtheria*)

- **Presentation:** pharyngitis, nasopharyngitis, tonsillitis, laryngitis (or any combination) associated with a firmly adherent pseudo-membrane over the tonsils, pharynx, larynx and/or nares

- **Transmission:** respiratory droplets or close contact with either respiratory secretions or infected skin lesions. Incubation period is 2-5 days.
Diphtheria Pathogenesis

3. Pharyngeal diphtheria
   - pharyngitis, hypoxia
   - pseudomembrane obstruction
   - fever, lymphadenitis

4. Cutaneous diphtheria

5. Toxic peripheral neuropathy

6. Myocarditis & heart failure

(Uthman et al, 2012)
‘The strangling angel of children’

*Corynebacterium Diphtheriae*
- Common respiratory pathogen, disease in toxigenic strains
- Causes upper-respiratory symptoms, leading to pharyngitis and a firmly-adherent pseudomembrane over tonsils
- Pseudomembrane expansion leads to airway obstruction and death
- Person-to-person spread
# Long-term complications

<table>
<thead>
<tr>
<th>Complication</th>
<th>Incidence Rate (n=6350)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuropathy</td>
<td>5%</td>
</tr>
<tr>
<td>Renal dysfunction</td>
<td>1-2%</td>
</tr>
<tr>
<td>Cardiac symptoms</td>
<td>8%</td>
</tr>
<tr>
<td>Generalized weakness/weight loss</td>
<td>25%</td>
</tr>
<tr>
<td>Sudden Cardiac death</td>
<td>0.3%</td>
</tr>
</tbody>
</table>
Cutaneous Diphtheria
Presenting symptoms

<table>
<thead>
<tr>
<th>Sign</th>
<th>Incidence (n=6350)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>84.7%</td>
</tr>
<tr>
<td>Difficulty swallowing</td>
<td>31%</td>
</tr>
<tr>
<td>Pseudomembrane</td>
<td>37%</td>
</tr>
<tr>
<td>Gross lymphadenopathy</td>
<td>31.1%</td>
</tr>
</tbody>
</table>
Diphtheria cases – 2018:2019, CXB
Diphtheria Management - Principles

- Antibiotics
- DAT
- Supportive care
- Tracing of contacts for vaccination/post-exposure prophylaxis
IMMEDIATELY REFER TO NEAREST DIPHTHERIA TREATMENT CENTRE

Are there Clinical Warning Signs?

- Pseudo-Membrane
  - Stridor
  - Fast Respiratory Rate
  - Chest in-drawing
  - Restlessness or lethargy
  - Bull neck
  - Delayed capillary refill
  - Fast Heart rate and cold extremities
  - Central Cyanosis

- Bull Neck

Yes

DAT (give as soon as possible)
Antibiotics (give as soon as possible)

No

Antibiotics (give as soon as possible)
DAT (20-40,000IU) if pseudomembrane
**A needle cric will reliably provide oxygen, but ventilation usually reliable up to 40-60 minutes, perhaps up to 2 hours.**

**Emergent scenario**

*Patients with emergency signs: lethargy, cyanosis, SpO2 < 90-94%*

- Are surgeon (preferably ENT), anesthetist, intensivist, emergency physician available?
  - Yes, present
    - Most experienced doctor takes one attempt at orotracheal intubation using difficult airway algorithm.
    - If unsuccessful, then tracheostomy* (caution).
    - If above not possible, then perform needle cric.
    - Call for help and arrange transfer to hospital with more experienced surgeon (i.e. ENT) to secure airway.
  - Not present
    - Preform needle cric
    - Call for help.
    - Arrange transfer to hospital with more experienced surgeon (i.e. ENT) to secure definitive airway.

**40-60 minutes**

- Transfer patient.
- Perform tracheostomy.

*Tracheostomy in infants can be difficult, surgeon should be well experienced in this procedure, preferable ENT. If not available, then proceed with needle cric, call for help.*
Clinical management of diphtheria
Guideline
2 February 2024
Diphtheria Management - Principles

- Antibiotics
- DAT
- Supportive care
- Tracing of contacts for vaccination/post-exposure prophylaxis
Recommendation: Antibiotics

In patients with suspected or confirmed diphtheria, WHO recommends using macrolide antibiotics (azithromycin, erythromycin) in preference to penicillin antibiotics [Strong recommendation, low certainty evidence].

Remarks:

• Antibiotics should be administered alongside DAT and should not be delayed.
• Recent evidence suggests that there is increasing resistance to penicillins and less resistance to macrolide antibiotics. Local antimicrobial susceptibility testing is vital to ensure the ongoing appropriate use of antibiotics. Advice on laboratory testing in outbreaks is available here.
• The choice of macrolide will depend on availability and feasibility.
Diphtheria Management - Principles

• Antibiotics
• DAT
• Supportive care
• Tracing of contacts for vaccination/post-exposure prophylaxis
Recommendation: DAT sensitivity testing

Strong recommendation against

In patients with suspected or confirmed diphtheria, WHO recommends not to perform routine sensitivity testing prior to administration of diphtheria antitoxin [Strong recommendation, moderate certainty evidence].

Remarks:

• Due to the risk of allergic reaction, ensure sufficient trained staff and equipment are available and the patient is cared for in an area where they can be monitored closely.
Recommendation: DAT sensitivity testing

Figure: Outcome probabilities based on alternative strategies

Patients with suspected or confirmed diphtheria for whom diphtheria antitoxin is indicated:
- Perform allergy testing, and (if necessary) desensitization before DAT is given.
- Give DAT and manage subsequent allergy and reactions as they arise.

* Ehrlich et al. data used to produce these estimates were from patients in whom D. pneumoniae was isolated from blood cultures before antibiotic administration.

Red boxes (left side of diagram) represent the probability tree where allergy testing and (where necessary) desensitisation is performed before DAT is administered.

Blue boxes (right side of diagram) represent the probability tree where DAT is given, and allergies are treated as they arise (with no allergy testing, and no desensitisation).
Recommendation: DAT dosing

Conditional recommendation for

In patients with suspected or confirmed symptomatic diphtheria, WHO suggests administration of a single dose of diphtheria antitoxin with choice of dose based on disease severity and time since symptom onset, in comparison with a fixed dose for all patients [Conditional recommendation, very low certainty evidence].

Remarks:

- DAT must be administered as soon as possible as early administration of DAT is associated with improved clinical outcomes. Early treatment may reduce overall DAT usage by avoiding the higher doses required once disease has progressed.
**Recommendation: DAT dosing**

<table>
<thead>
<tr>
<th>Characteristic of diphtheria disease</th>
<th>Dose of diphtheria antitoxin (IU)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Laryngitis or pharyngitis and • Duration &lt; 48 hours</td>
<td>20 000</td>
</tr>
<tr>
<td>• Nasopharyngeal disease (extensive pseudomembrane) and • Duration &lt; 48 hours</td>
<td>40 000</td>
</tr>
<tr>
<td>One or more of: • Diffuse swelling of the neck • Any disease ≥ 48 hours • Severe disease (respiratory distress, shock)</td>
<td>80 000</td>
</tr>
</tbody>
</table>
Diphtheria Management - Principles

- Antibiotics
- DAT
- Supportive care
- Tracing of contacts for vaccination/post-exposure prophylaxis
Upcoming recommendations

• Should close contacts receive prophylaxis?
• How long do contacts receive prophylaxis?
• How long should infected be isolated?
• What is the optimal early airway management strategy?
Thank you