

This is a notifiable acute upper respiratory tract infection, but sometimes it infects the skin. Hippocrates first described the disease in the 4th century BC and major epidemics swept through Europe in the 17th century. It was known as "*the strangling angel of children.*"



### Pathogenesis

- *Corynebacterium diphtheriae* is a Gram-positive, aerobic, non-motile, rod-shaped bacterium, pathogenic only in humans.
- The bacterium is classified as gravis, mitis or intermedius.
- Pharyngeal or cutaneous diphtheria is caused by toxigenic strains of *C. diphtheriae* and occasionally by *C. ulcerans*. The latter is usually an infection of cattle.
- Only bacteria infected by a Corynebacteriophage can produce the disease-causing exotoxin that can affect heart, peripheral nerves, and kidneys.
- A fibrinous pseudomembrane is produced usually on the respiratory mucosa.

### Epidemiology

- Infection now a rarity in developed countries where majority vaccinated
- But prevalent in some parts of Africa, Asia & Indonesia
- Mortality has remained at 10%
- Mainly affects children <15y

### Risk factors

- Transmission is by droplet, milk, food handlers, fomites, or contact with skin lesions.
- Once recovered some patients become carriers for weeks, months or even a lifetime.
- Poor living conditions and lack of immunisation
- Adults are at risk as they lose protection from childhood vaccines unless they have boosters. 70% of older adults are at risk.

### Presentation

*Incubation period:* It is usually 2 to 5 days, but may be up to 10 days.

#### *Presentation*

- Early URTI symptoms: nasal discharge that is initially watery and then purulent and blood-stained. The nostril may be sore or crusted with pseudomembrane visible within nose.
- In diphtheria of the upper respiratory tract, there is a pseudomembranous pharyngitis with fever, enlarged anterior cervical lymph nodes and oedema of soft tissues giving a "bull neck" appearance.
- The pseudo-membrane may cause respiratory obstruction.
- Swallowing may be difficult if unilateral or bilateral paralysis of the palatal muscles
- Asymptomatic carriage is possible and an important source of transmission.
- Cutaneous infection is usually mild, but chronic:
  - Typical findings are vesicles or pustules that form a "punched-out" ulcer
  - It often appears on the lower legs, feet and hands.
  - Initially painful with a dark pseudomembrane which separates to show a haemorrhagic base ± exudate. Usually heals in 2-3mo to leave a depressed scar.
- Infections at other mucocutaneous sites include OM, conjunctivitis and vulvovaginitis.
- Sporadic cases of septic arthritis occur.



## Effects of toxin

- Cardiomyopathy and myocarditis is usually evident by 2 weeks. There may be arrhythmias early or late in the illness. Myocardial involvement accounts for around half of all deaths.
- Neuritis affects motor nerves, firstly with paralysis of the soft palate, causing dysphagia and nasal regurgitation, then ocular nerves, peripheral nerves and diaphragm with resulting infection and respiratory failure.
- Nephritis and proteinuria may be features.
- Thrombocytopenia may be seen in the full blood count.

## Differential diagnosis

- Infection with *C. ulcerans* also causes membranous tonsillitis, but is rarely toxic.
- *C. pseudodiphtheriticum* does not produce a toxin, but can cause exudative pharyngitis with a pseudomembrane.
- The disease may also resemble infectious mononucleosis, streptococcal or viral tonsillitis, peritonsillar abscess, oral thrush, epiglottitis, herpes simplex and impetigo.
- If there are neurological symptoms and a lumbar puncture is performed, elevated protein in the CSF may lead to a false diagnosis of Guillain-Barré syndrome.

## Investigations

- Bacterial culture (Loeffler's medium) from patient and close contacts
- ELISA or PCR detection
- Toxigenicity tests by specialist laboratories
- Serum AST and ECG in cardiac cases

## Management

### Non-drug

- Antitoxin should be given within 48 hours of onset:
  - Myocarditis and palsies do not respond to steroids or delayed dose of antitoxin.
  - The antitoxin is derived from horse serum and so reactions are common.
  - Dosage is determined by the site of infection, and severity (20,000-150,000u IV).
- Barrier nursing is required.
- Cutaneous lesions should be thoroughly cleaned with soap. Antitoxin is of no value.
- Patients should be immunised in the convalescent stage
- Drugs: Benzylpenicillin IV is followed by oral penicillin V for 10 to 14 days. Erythromycin is used with penicillin allergy.

### Surgical

Urgent tracheostomy may be required for respiratory obstruction.

### Contact testing:

Swab close contacts, treat with a single dose IM benzylpenicillin or a week of PO erythromycin.

## Prognosis

- Overall 5 to 10% mortality, but it is up to 20% in those <5 and >40 years.
- Recovery is slow and particular caution should be advised after myocarditis.
- Complete recovery from neurological damage is usual in those who survive.

## Prevention

- The Schick test was historically used to test for immunity.
- Vaccination is standard for children.
- 10yr boosters suggested for adults (as ADT)