

Corynebacteria

Introduction

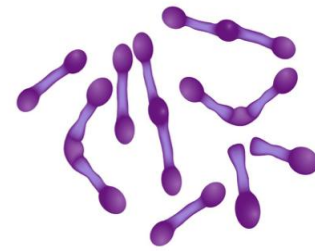
- Corynebacterium belongs to family Corynebacteriaceae
- The genus *Corynebacterium* presently consists of **66 species**, **38** of which are medically relevant.
- Some medically important species includes: *C. diphtheriae*, *C. ulcerans*, *C. pseudotuberculosis*, *C. pseudodiphtheriticum*, *C. xerosis*
- Many species of the medically relevant corynebacteria are part of the normal flora of the skin and mucous membranes in humans.
- Non-diphtheritic *Corynebacterium* can even be found in the mucosa and normal skin flora of humans and animals(**diphtheroids**) and are widely distributed in nature and are mostly harmless

Diphtheria

- Acute infectious disease caused by toxigenic strains of *Corynebacterium diphtheriae*
- Ancient disease known since the time of Hippocrates
- Derived from Greek word diphtheros-meaning leather like
- Also known as Klebs-Loeffler bacillus
- Characteristic leathery pseudomembrane formation over tonsil

Characteristics of causative agent

- Gram-positive
- Noncapsulated, non motile
- Facultative anaerobe
- non sporulating club-shaped
- aerobic bacillus
- Subdivided into four biovars: *belfanti*, *gravis*, *intermedius*, and *mitis*
- “Chinese character” arrangement on Gram stain
- Metachromatic granules (Polar bodies)



Corynebacterium diphtheriae

Virulence factor

- Diphtheria toxin is the major virulence factor
- ❖ The 'virulence' of diphtheria bacilli is due to their capacity to:
 - Establish infection and growing rapidly
 - Quickly elaborate an exotoxin

Epidemiology

- Leading cause of childhood death in the prevaccine era
- Various studies showed resurgence of the disease or a shift to older populations
- Collectively, India, Nepal, and Indonesia have reported 96%–99% of the cases in the South-East Asia region since 2000
- ❖ Generally, gravis infections tend to be more severe than mitis infections
- ❖ Humans are the only reservoir
- ❖ Source of infection : may be a case or carrier
- ❖ Carrier:
 - Nasal carriers are particularly dangerous than throat carriers
 - Estimated ratio to be 95 carriers for 5 clinical cases

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- Immunization does not prevent the carrier state
- Particularly affects children aged 1 to 5
- In countries where widespread immunization is practiced, a shift in age incidence has been observed from preschool to school age
- Both sexes are affected
- Herd immunity of over 70% is considered necessary to prevent epidemic spread, but some believe that the critical level may be as high as 90%
- Winter months favour its spread

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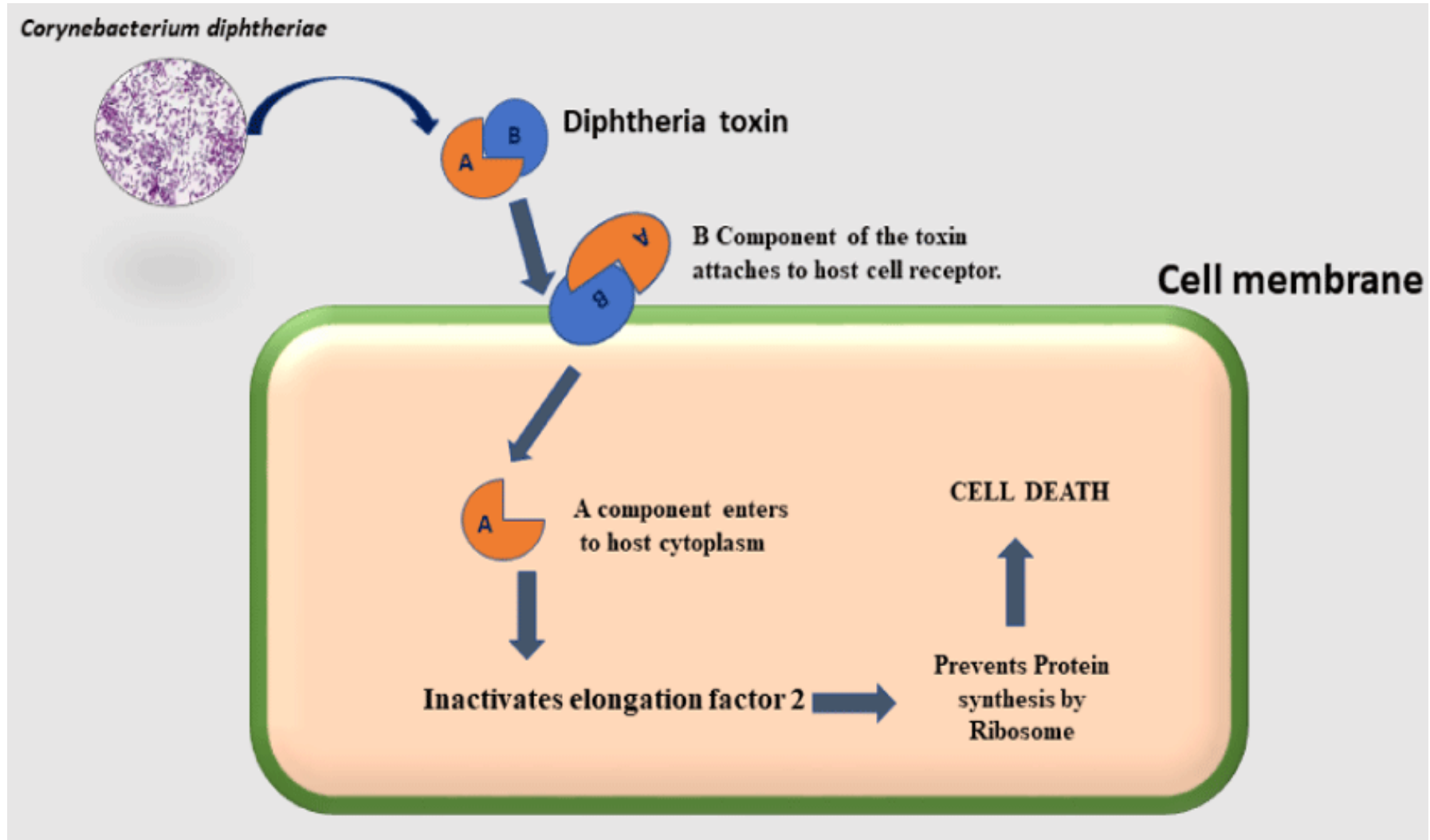
❖ Mode of transmission:

- Spread mainly by droplet infection
- Directly to susceptible persons from infected cutaneous lesions
- Transmission by contaminated objects is also possible, but for only short periods

❖ Portal of entry:

- Common portal of entry is the respiratory tract
- Sometimes portal of entry may be the skin cuts, wounds and ulcers not properly attended to and also umbilicus in the newborn

Pathogenesis



Clinical manifestation

❖ Respiratory diphtheria:

- Most common form of diphtheria
- Tonsil and pharynx (faucial diphtheria) are most common sites followed by nose and larynx
- Incubation period is about 3-4 days

➤ **Faucial diphtheria:**

- ✓ sore throat, malaise, and low-grade fever
 - ✓ Formation of mucosal ulcers, lined by a rough leathery greyish white pseudomembrane coat
 - ✓ Pseudomembrane is composed of inner band of fibrin surrounded by neutrophils, RBC, bacteria
 - ✓ In severe cases, it may extend to larynx and bronchial airways
- ## ❖ Bull neck appearance: tonsillar swelling and neck edema, foul breath, thick speech, and stridor

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❖ Cutaneous Diphtheria:

- Due to organism itself
 - Presents as punched-out ulcerative lesions with necrosis
 - Rarely pseudomembrane formation
 - Most commonly occur on the extremities
 - Increasing trend especially in vaccinated children
- ❖ Complications of diphtheria include polyneuropathy, myocarditis, pneumonia, renal failure, encephalitis, pulmonary embolism

Treatment

- ❖ Respiratory diphtheria:

- Equine serum containing diphtheria antitoxin (DAT)

- ❖ Antibiotic therapy : Penicillin and erythromycin

Minor role once the toxin is released, but they are useful in following terms;

- ❖ If given early (<6 hrs of infection)

- ❖ Prevents further release of toxin

- ❖ Cutaneous diphtheria

- ❖ Treatment of carriers

Laboratory Diagnosis

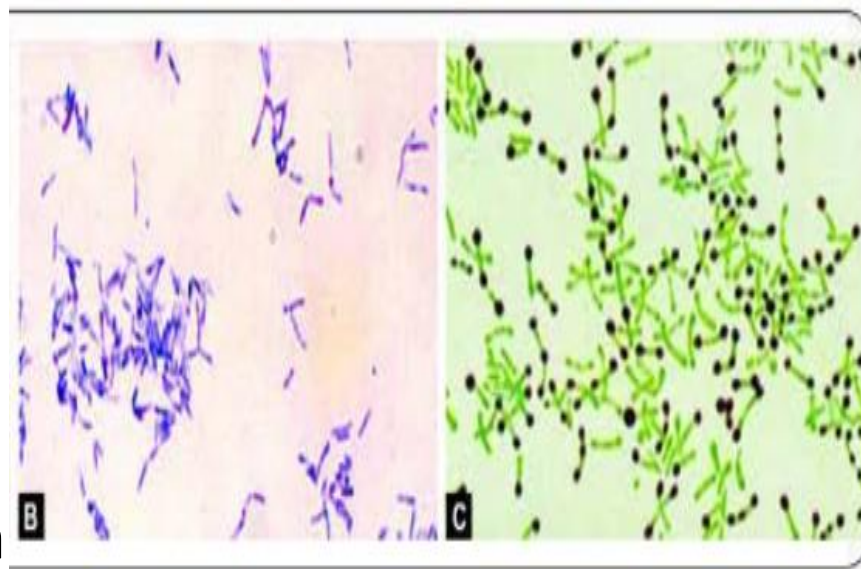
- Specimen:

- Swabs of throat, tonsils, nasopharynx, any skin lesions and a portion of pseudomembrane

- Direct smear:

- Gram stain-club shaped
gram positive chinese letter
arrangement

- Albert's stain- Green bacilli with
bluish black metachromatic granules.



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- Culture media:

- Enriched media-Blood agar, chocolate agar and Loeffler's serum slope
- Selective media-Pottassium tellurite agar and Tinsdale medium (produce black colonies)

- ❖ Biochemical Identification:

- Hiss's serum sugar media: Ferments glucose, maltose and/or starch
- Urease test negative
- Pyrazinamidase test is positive for *C. diphtheriae*

Prevention and control

- ❖ Early detection of case and carrier:

- Active search for cases and carriers should start immediately amongst family and school contacts
- Carriers can be detected only by culture method

- ❖ Isolation:

- ❖ All cases, suspected cases and carriers should be promptly isolated, preferably in a hospital, for at least 14 days or until proved free of infection
- ❖ Carriers should be treated with 10 day course of oral erythromycin
- ❖ When diphtheria is suspected, treatment should be started immediately without delay

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❖ Contacts

- If primary immunization or booster dose was received within the previous 2 years, no further action would be needed
- If primary course or booster dose of diphtheria toxoid was received more than 2 years before, only a booster dose of diphtheria toxoid need be given

❖ Vaccination: most important measure

- Single vaccine : diphtheria toxoid
- Combined vaccine: DPT contains diphtheria toxoid, Pertussis (whole cell), and (tetanus toxoid)
- Pentavalent vaccine : DPT, hep B, HI type b
- Adminstration of DPT: Three doses of pentavalent vaccine at 6, 10, 14 weeks of birth intramuscularly

Infections resembling diphtheria

- **Clinically resembling diphtheria:** *C. ulcerans* and *C. pseudotuberculosis* produce diphtheria toxin and cause localized ulcerations in throat, clinically resembling diphtheria. They also produce black colored colony with brown halo on Tinsdale medium similar to *C. diphtheriae*. However, both give a positive urease test, thus can be differentiated from *C. diphtheriae* which is urease negative.
 - *C. ulcerans* causes infections in cows and human infections may occur through cow's milk.
 - *C. pseudotuberculosis* (Preisz-Nocard bacillus) causes pseudotuberculosis in sheep and suppurative lymphadenitis in horses. Human infection is very rare.

Infections by other species

***C. jeikeium*:** It is lipophilic species, colonizes skin of hospitalized patients. It can cause bacteremia, endocarditis and meningitis, especially in immunocompromized hosts. It is usually multidrug resistant, responds only to vancomycin.

***C. urealyticum*:** It is skin commensal, rarely causes urinary tract infection (pyelonephritis) and alkaline encrusted cystitis (struvite stones in alkaline urine) in immunocompromized and renal transplanted patients.

***C. pseudodiphtheriticum*:** It is a known commensal in throat. However, in immunocompromized patients, it can cause exudative pharyngitis (may mimic respiratory diphtheria) and endocarditis. It can be easily differentiated biochemically as it is pyrazinamidase test positive, urease positive and does not ferment glucose.