Corynebacterium

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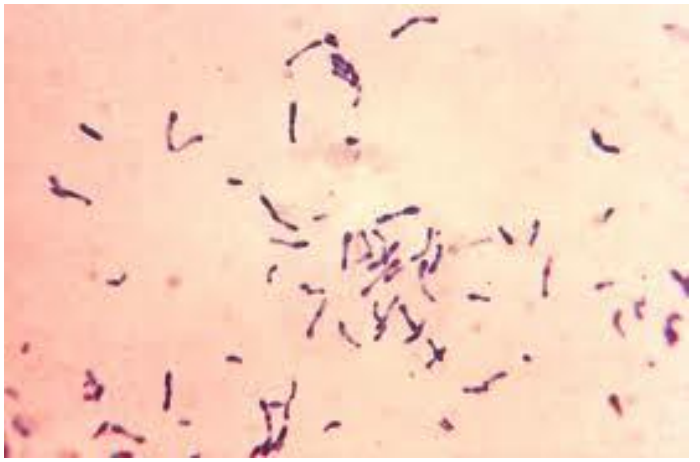
Corynebacterium

- Gram positive, aerobic, asporogenous, non-motile, rods with wider ends (clube shape) arranged in palisades or clusters with V-shaped forms
- Name (ancient greek)
  - coryne - „curved object = club“
  - Bacterion „little rod“
  - Diphtheria „leather“
    - infection is characteristic by tough leathery membrane



Corynebacterium - description

- Widely distributed (pathogenic and non-pathogenic species)
- More than **100 species** – about half (56) documented in human infection
- Closely related to *Mycobaterium*, *Nocardia*, *Streptomyces*
- **Short-chain mycolic acids** are present in all medical relevant species

Epidemiology

- Commensal of skin, mucous membrane in humans and mammals

- ***C. diphtheriae*** – pathogenic – reservoir nasopharynx, skin lesions

- *C. tuberculosis* – source – infected animals

- non-pathogenic species (more than 50)
- distributed in environment – soil, plants, foodstuff

Clinical significance

- Difficult to establish the clinical significance due to natural habitat of coryneform bacteria on skin **contaminants or opportunistic pathogens**?
- Main clinical disease - **diphtheria**
  - (*C. diphtheriae*, *C. ulcerans*)
- **Decline** in incidence due to **immunisation**, HOWEVER
  - still endemic in some sub- or tropical countries (individuals or ethnic group)
  - In 1990s reemerged in the states of former Soviet Union

Clinical presentation of diphtheria

- **Pharyngeal diphtheria** – sore throat, dysphagia, grey pseudomembranes on throat (could lead to abstruction), low-grade fever, cervical lymphadenopathy, malaise, headache
- **Cutaneous diphtheria** – ulcers on skin without systemic infection (homeless, poor hygienic status)
- **Endocarditis** (toxin positive or negative strains)

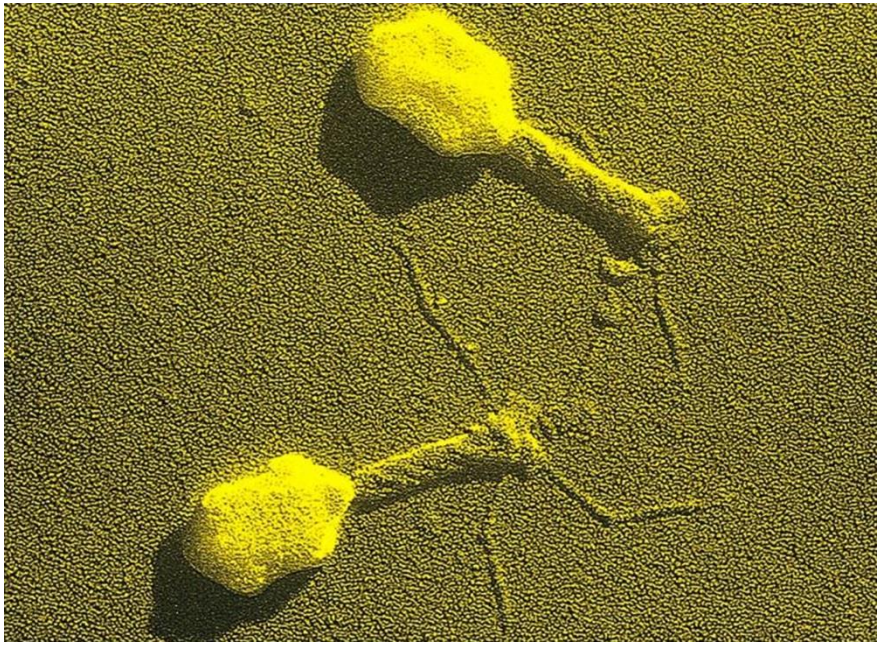
- Systemic effects (due to effect of exotoxin):
  - Myocarditis, arrythmias
  - Neuritis (laryngeal nerve)
  - Kidney dammage

Corynebacterium diphtheriae

- Divided to **4 distinct subspecies** which differ in morphology and certain biochemical properties
  - *C. diphtheriae* **gravis, mitis, intermedius, belfanti**
- Cause of diphtheria
- Produce exotoxin
- Bacterium must be infected (lysogenized) by bacteriophage (β phage) carrying ***tox* gene**

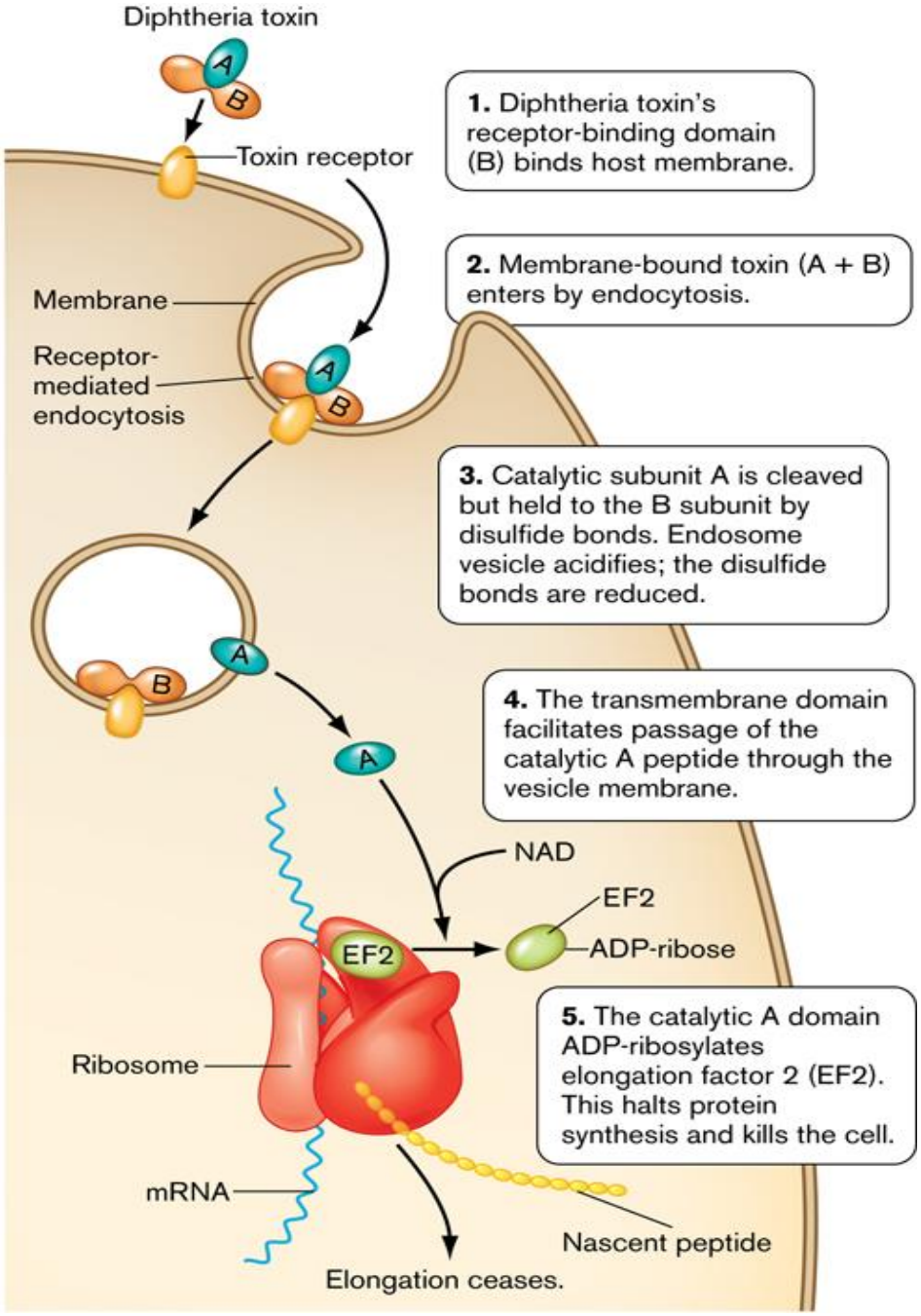
Bacteriophages

- Bacteriophages are viruses that transfect bacteria with genomic material.
- They introduce genes into bacterial cells by transduction (transfer of genes from one bacteria to another).



Exotoxin

- Classic A-B exotoxin
- It has two subunits
  - **A – catalytic region**
    - Terminates protein synthesis by inactivating elongation factor-2
  - **B – receptor-binding and translocation region**
    - to mediate binding of toxin to cell membrane receptors of host cell
- Toxin receptor – heparin-binding epidermal growth factor (present especially on nerve and heart cells)
- Toxin effect – inhibition of protheosynthesis, cell death


Diphtheria toxin
A
B
Toxin receptor
1. Diphtheria toxin's receptor-binding domain (B) binds host membrane.
Membrane
Receptor-mediated endocytosis
2. Membrane-bound toxin (A + B) enters by endocytosis.
3. Catalytic subunit A is cleaved but held to the B subunit by disulfide bonds. Endosome vesicle acidifies; the disulfide bonds are reduced.
4. The transmembrane domain facilitates passage of the catalytic A peptide through the vesicle membrane.
NAD
EF2
ADP-ribose
Ribosome
5. The catalytic A domain ADP-ribosylates elongation factor 2 (EF2). This halts protein synthesis and kills the cell.
mRNA
Nascent peptide
Elongation ceases.

Host response

- Local inflammation in throat (skin in case of cutaneous diphtheria
- Production of exudates and pseudomembranes
- Production of antibodies to netralise the exotoxin

The pseudomembrane consists of fibrin, necrotic tissue, blood cells and bacterial colonies. The name *Diphtheria* is derived from the Greek word for *leather*, referring to this tough pseudomembrane.

Epidemiology

- Diphtheria occurs worldwide (low income countries, low-vaccine uptake)
- **Humans are the only reservoirs** (nasopharynx, skin)
- Transmition by airborne droplets
- Poor skin hygiene (cutaneous form)

Clinical diseases - respiratory diphtheria

- Infection usually begins in the throat (pharynx) within two to four days after contact.
- Inflammation and patches of exudate appear in the epithelial cells of the throat and tonsils.
- Myocarditis can be detected after 1 to 2 weeks (heart failure, arrhytmias, death)

Clinical diseases - respiratory diphtheria

- Localized swelling may result in the classic 'bull neck, appearance

Clinical diseases - cutaneous diphtheria

- After skin contact
- Chronic, non-healing ulcer

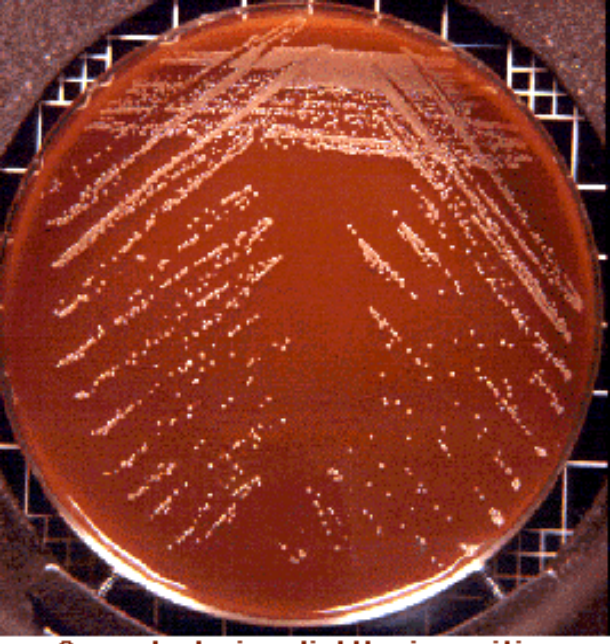
Clinical diseases - diphtheria

- Mortality from diphtheria can range from 30 to 50%, frequently occurring in children.

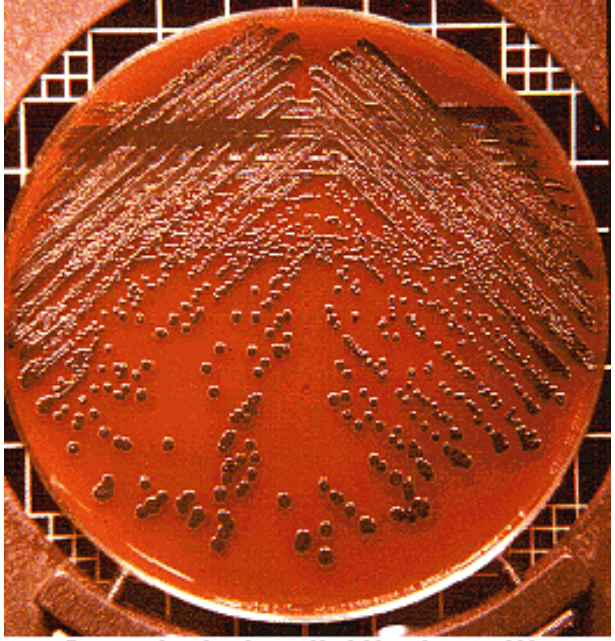
- Suffocation is the primary cause of death, followed by myocarditis and polyneuritis due to the toxicity of the diphtheria exotoxin.

Laboratory diagnosis

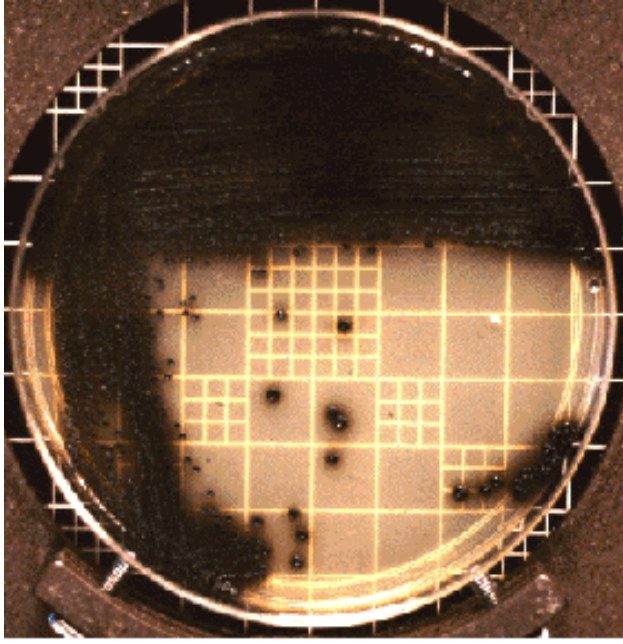
- **Specimen** – throat swabs (skin swabs)
- **Microscopy**
  - Gram positive, club shape, cells are arranged in V or L shapes, or in a palisade (fence) shape
- **Culture**
  - enriched blood agar
  - tellurite blood agar (Clauberg agar)
    - Tellurite inhibits growth of upper respiratory tract bacteria
    - It is reduced by corynebacteria – black colored colonies
  - Tinsdale medium (dark halo around colonies is due to the production of H_2S from cystine – cysteinase)
- **Toxin production**
  - Eleck plate – precipitation test (toxin vs antitoxin)
  - Cell cultures
  - PCR of *tox* gene



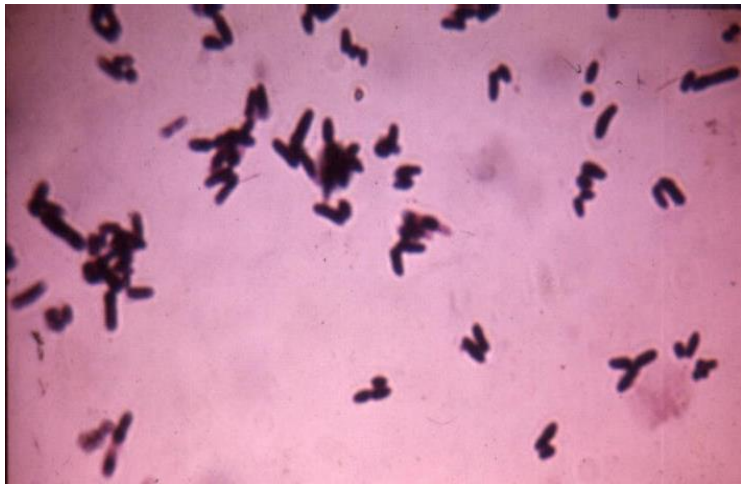
Corynebacterium diphtheriae, mitis
Chocolate agar



Corynebacterium diphtheriae, mitis
Chocolate tellurite agar



Corynebacterium diphtheriae, mitis
Tinsdale agar



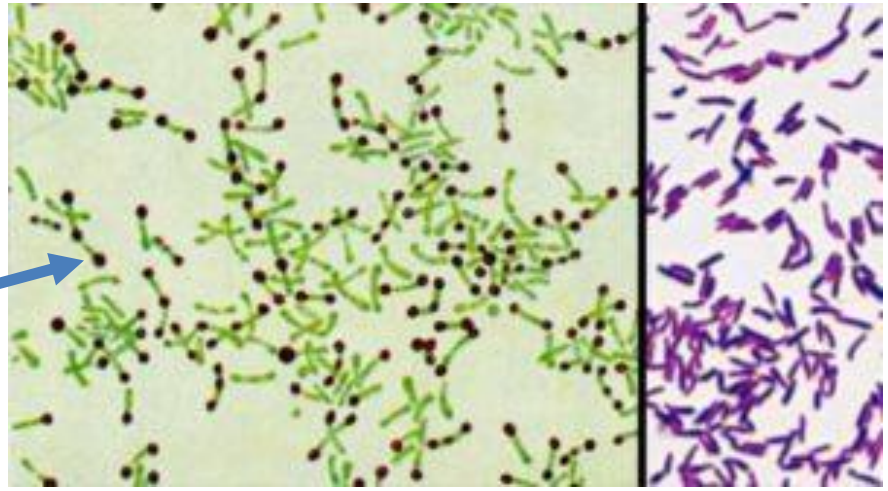
Corynebacterium – gram staining

Corynebacterium diphtheriae

- Contain metachromatic granules (inclusion bodies) composed of inorganic polyphosphates – serving as energy reserves

Albert staining

Gram staining



Metachromatic granula

Prevention

- A toxoid vaccine is the best strategy for the diphtheria vaccine.
- the diphtheria toxoid is one of the most effective vaccines
- It has been administered to children in the trivalent (DPT) (Diphtheria, pertussis, and tetanus) vaccine since 1955.

Therapy

- Diphtheria antitoxin
- Antibiotic
  - Penicillin G
  - Alternatively in patients with allergy to penicillin - erythromycin