Corynebacterium diphtheriae

Friday, September 19, 2025 7:08 PM

 Introduction

📌 Disease

- Primary disease → Diphtheria
- Other Corynebacteria (diphtheroids) → Opportunistic infections

🔬 Important Properties

- Gram-positive rods → Club-shaped (wider at one end)
- Arrangement → Palisades or V-/L-shaped formations
- Beaded appearance → Due to polyphosphate granules (energy storage)
- Metachromatic staining → Cell = blue; Granules = red

📖 Exam tip: Always mention "club-shaped + metachromatic granules" in MCQs and viva.

Transmission

- Natural host → Humans only
- Reservoir → Upper respiratory tract
- Mode → Airborne droplets
- Other route → Skin infection (via preexisting lesion, esp. tropics or poor hygiene)

Pathogenesis

Mechanism of Diphtheria Toxin

1. Organism must invade & colonize throat
2. Exotoxin production → Essential for disease
    - Action: Inhibits protein synthesis by ADP-ribosylation of EF-2
    - Effect: Halts elongation during protein translation
    - Target: All eukaryotic cells (prokaryotic EF is

unaffected)

Structure of Toxin

- B (Binding) domain → Attaches to glycoprotein receptors on host cell membrane
- A (Active) domain →
    - Cleaves nicotinamide from NAD
    - Transfers ADP-ribose to EF-2
    - → EF-2 inactivated → protein synthesis blocked

📌 Other ADP-ribosylating exotoxins: Cholera toxin, Pertussis toxin, E. coli LT toxin

🧬 Genetic Basis

- Toxin gene is carried by Beta bacteriophage (lysogenic phage)
- Only lysogenized strains produce exotoxin → Pathogenic
- Non-lysogenized strains → Nonpathogenic

🛡️ Host Response

1. Local response → Inflammation + fibrinous exudate → Tough, gray pseudomembrane (hallmark lesion)

2. Systemic response → Antitoxin (neutralizing antibodies) block binding domain → Prevent cell entry

📄 Diagnostic Test – Schick Test

- Principle → Tests immunity to diphtheria toxin
- Method → Intradermal injection of 0.1 mL purified standardized toxin
- Interpretation:
    - Inflammation (4–7 days) → No antitoxin → Susceptible
    - No reaction → Antitoxin present → Immune
- Rarely used today (historical/epidemiological importance)

📝 Flowchart: Pathogenesis of Diphtheria

C. diphtheriae infection → Colonization of throat

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Production of diphtheria toxin (only if lysogenized by Beta phage)

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B domain binds to cell receptor

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A domain enters cell → ADP-ribosylation of EF-2

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Protein synthesis inhibited

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Cell death → Local pseudomembrane formation + systemic toxicity

 Corynebacterium diphtheriae – Clinical Findings, Diagnosis & Management

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📌 Clinical Findings

- Hallmark sign → Thick, gray, adherent pseudomembrane over tonsils & throat

- Other symptoms (nonspecific): Fever, sore throat, cervical adenopathy

⚠ Major Complications

1. Airway obstruction → Extension of pseudomembrane into larynx/trachea

2. Cervical lymphadenopathy → *"Bull neck" appearance*

3. Myocarditis → Arrhythmias, circulatory collapse

4. Neurologic complications →

    - Cranial nerve paralysis (soft palate & pharynx → nasal regurgitation)
    - Peripheral neuritis (extremity weakness/paralysis)

🩺 Cutaneous Diphtheria

- Ulcerating skin lesions with gray membrane

- Usually indolent, non-invasive
- Systemic symptoms rare
- Seen mostly in indigent persons in developed countries

📜 Laboratory Diagnosis

Steps in Diagnosis

- Clinical suspicion is paramount → Treatment should not wait for lab results
- Culture methods:
    - Loeffler's medium
    - Tellurite plate → C. diphtheriae reduces tellurium → gray-black colonies (diagnostic)
    - Blood agar plate
- Toxin demonstration:
    - Animal inoculation test

- Elek's gel diffusion precipitin test (antibody-based)
- PCR assay for toxin gene

- Smear examination:

  - Gram stain → Pleomorphic, club-shaped gram-positive rods
  - Methylene blue stain → Shows metachromatic granules

💊 Treatment

Principles

- Immediate administration of antitoxin (based on clinical suspicion)

  - Neutralizes unbound toxin only (cannot reverse toxin already bound to cells)
  - Derived from horse serum → Risk of hypersensitivity & serum sickness

- Antibiotics (adjunct therapy)

- Penicillin G or Erythromycin
- Stop bacterial growth → reduce toxin production → decrease chronic carriers
- ❌ Not a substitute for antitoxin

🛡️ Prevention

Vaccine: Diphtheria Toxoid (DTaP)

- Prepared by → Treating exotoxin with formaldehyde (detoxifies but preserves antigenicity)

- Schedule:

  - Primary: 3 doses at 2, 4, 6 months
  - Boosters: at 1 year & 6 years
  - Adult booster: Every 10 years (Tdap/Td)

- Limitation: Prevents disease but does not prevent nasopharyngeal carriage

📊 Quick Table: Clinical Features & Complications

Feature	Description

Local lesion	Gray pseudomembrane over throat/tonsils
Airway	Obstruction due to membrane extension
Cardiac	Myocarditis → Arrhythmias, collapse
Nervous System	Cranial nerve paralysis, peripheral neuritis
Skin form	Ulcer with gray membrane, indolent, rare systemic signs

📝 Flowchart: Clinical Course of Diphtheria

C. diphtheriae infection → Colonization of throat

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Exotoxin release → Local pseudomembrane formation

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Local effects: Sore throat, fever, cervical nodes

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Complications:

Airway obstruction

Myocarditis
Nerve paralysis