Respiratory System Module 2025-2026

Corynebacterium diphtheriae

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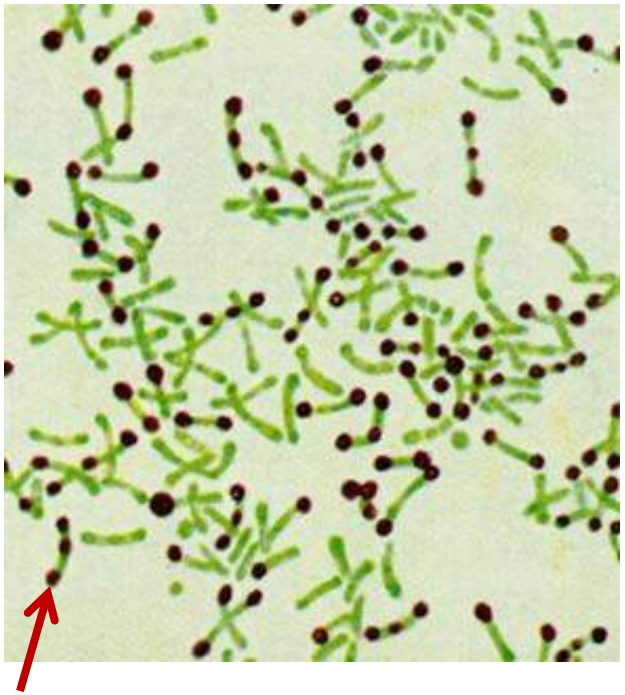
age	vaccination
1 month	BCG
2 months	DTP, Hib, HBV, IPV ,rota
3 months	DTP, Hib, HBV, IPV /OPV,rota
4 months	DTP, Hib, HBV, IPV ,rota
9 months	Measles
12 months	MMR
18 months	Booster DTP, polio OPV.MMR
4-6yr - school entry	MMR, OPV.Td
15-16 yr - 10th grade	Td.chek MMR

INTRODUCTION

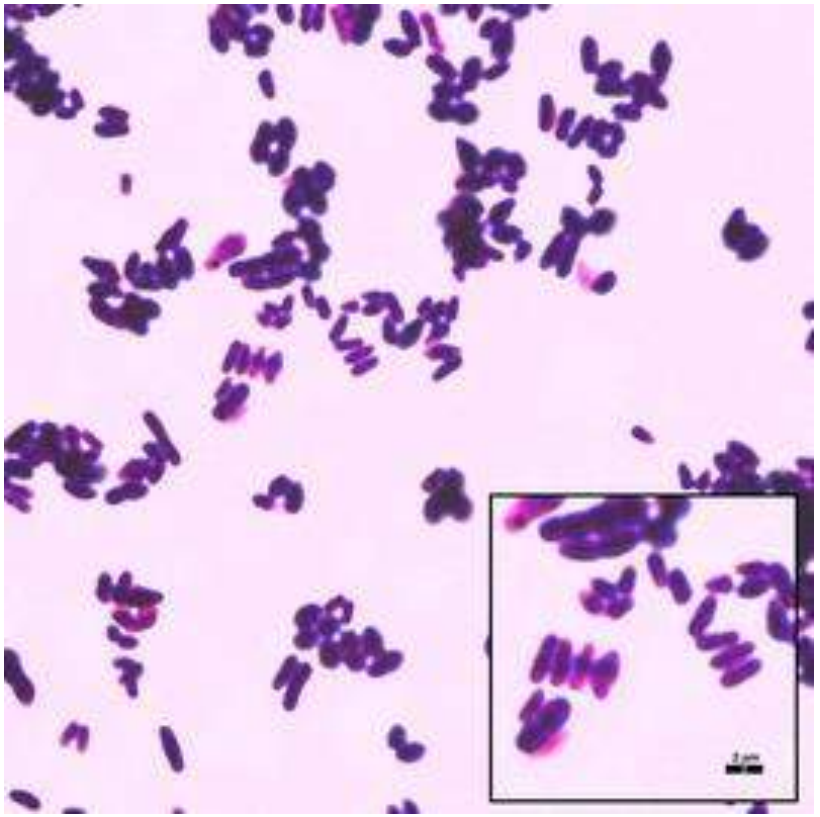
- Corynebacteria (from the Greek koryne, club)
- They are small pleomorphic Nonencapsulated & nonspore-forming bacteria.
- Gram-positive rods.
- Typically form clusters of parallel rays (palisades) that are referred to as *Chinese characters* .

Corynebacteria

Clubbed end



Chinese characters



Volutin granules: a storage form of complexed inorganic polyphosphate granules which serves as food reserves

Palisade

EPIDEMIOLOGY

1. Worldwide, there is declining trend of diphtheria cases due to vaccination coverage.
2. **Source of infection**: Carriers (95%), cases (5%).
3. **Carriers**: Nasal carreiers are more dangerous due to frequent shedding than thraot carriers . Incedence of carreier rate varies from 0.1 to 5%.
4. **Transmission**:
   - Via respiratory droplets
   - Rarely by contact with infected skin lasions.

- **Reservoir**: There are no significant reservoirs other than humans.

5. **Commonly infected**: Children aged 1-5 yrs.
6. Before immunization programs, it was a primarily infection of children younger than 12 years, but now, shifted into the adult population due to incomplete immune status or total inhibition of it (alcohol or immunocompromised drugs).

PATHOGENESIS

Diphtheria toxin

1. Is an A-B toxin expressed after a bacterial infection by a bacteriophage.
2. It can induce protective antibodies (antitoxin).
3. LD50 of ~100 ng/kg of body weight.

The DT mechanism of action

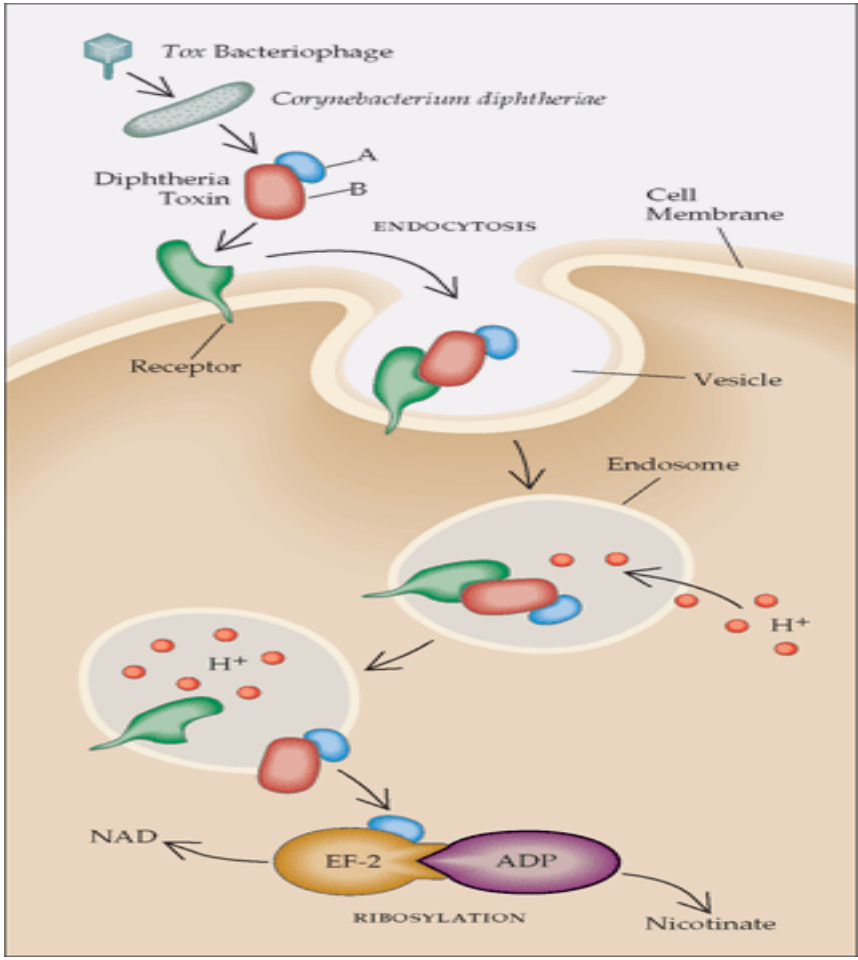
1. DT binds to receptors on the surface of eukaryotic cells
2. The A-subunite results in inhibition of polypeptide chain elongation by the elongation factor EF-2.
3. EF-2 is an essential factor for protein synthesis. It promotes the GTP-dependent translocation of the nascent protein chain from the A-site to the P-site of the ribosome.

PATHOGENESIS

The DT mechanism of action

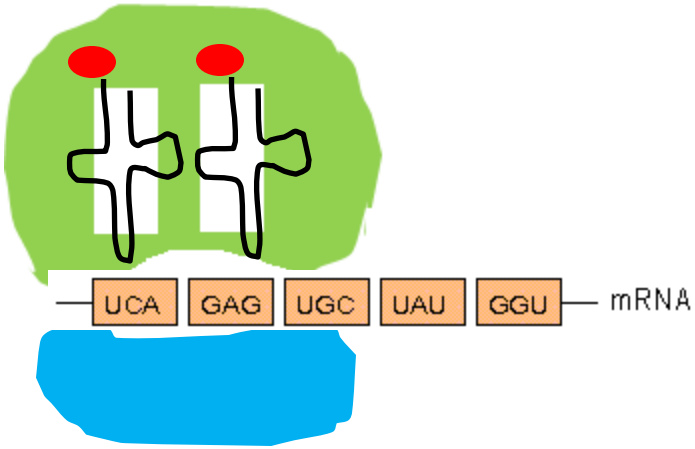
DT has two submits

- Subunit B
  - receptor-binding domain and translocation domain
- Subunit A
  - catalytic domain

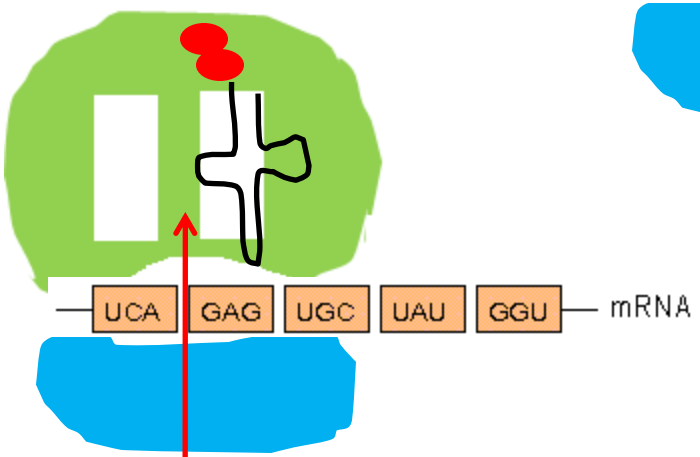


Inhibition of protein synthesis

mRNA translation



The inhibition of protein Synthesis will cause cellular death and necrosis



DT

The DT results in inhibition of polypeptide chain elongation by the EF-2.

EF-2 is an essential factor for protein synthesis. It promotes the GTP-dependent translocation of the nascent protein chain from the A-site to the P-site of the ribosome

Manifestations

Types of diphtheria

- Respiratory diphtheria
- Cutaneous diphtheria
- Systemic diphtheria (Toxin absorption)

Manifestations

Respiratory diptheria

1. The most common form of diptheria
2. Incubation period of 3 to 4 days
3. Stages
   - **A. Faucial diphtheria (fauces, the cavity at the back of the mouth leading into the pharynx).**
     - I. In place of the penetration (mucous membranes or skin) bacteria intensively multiplies and produces exotoxin that is accompanied by hyperemia, edema and vascular congestion with increased permeability of small blood vessels and epithelial necrosis;

This leads to local damage

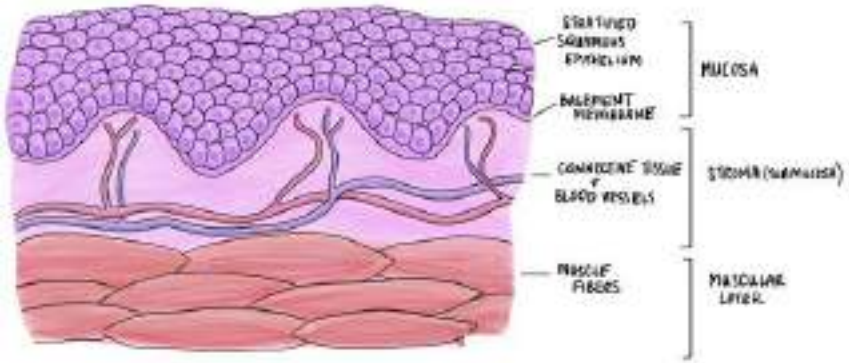
Manifestations

Respiratory diptheria

II. Fibrinogen of serum leaves the capillaries, reacts with thromboplastin of the necrotic epithelium) transforms into the insoluble fibrin (Diphtheritic membrane);

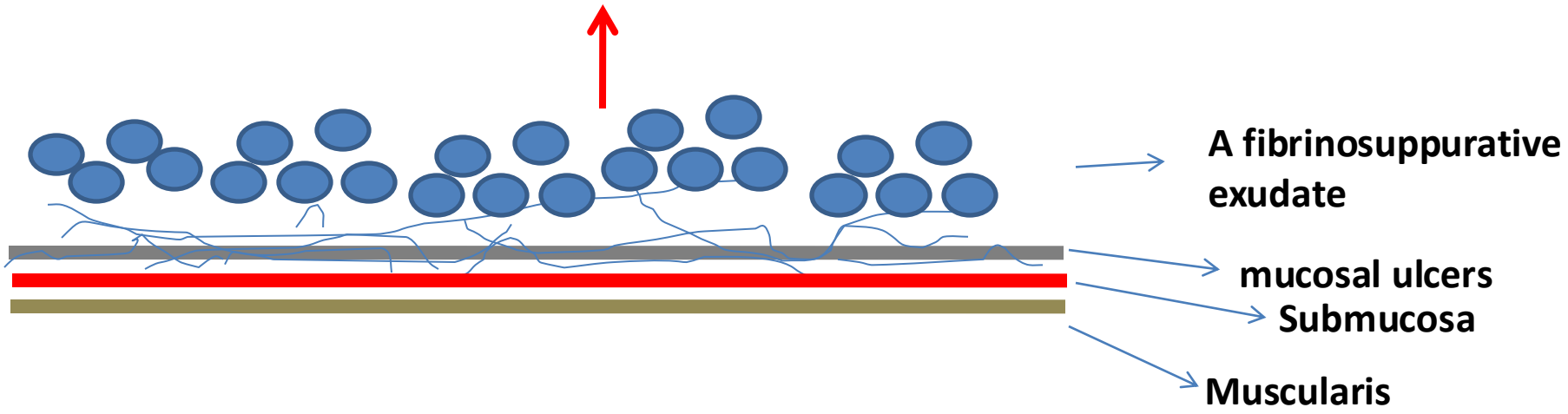
- Fibrin tightly holding a fibrinous film on the surface of the mucosa.
- Membranes increase and thicken up to 5 – 6 days of illness.
- Membrane is thick, leathery, grey-white and composed of bacteria, necrotic epithelium, phagocytes and fibrin;
- It is firmly adherent to the underlying tissues, bleeding follows its forcible removing.
- Has tendency to extend to another organs.
- Can detach in 5 -10 days.

Manifestations



The Compostion of the Pseudomembranes

Membrane is thick, leathery, grey-white and composed of bacteria, necrotic epithelium, phagocytes and fibrin



Manifestations

Respiratory diptheria

-The clinical diagnosis are based on the initial manifestations including:

- ✓ Headache
- ✓ Weakness
- ✓ Sore throat
- ✓ Voice change
- ✓ Dysphagia
- ✓ Low-grade fever
- ✓Diagnosis requires the isolation of C. diphtheriae or the histopathologic isolation of compatible gram-positive organisms

Manifestations

Respiratory diptheria

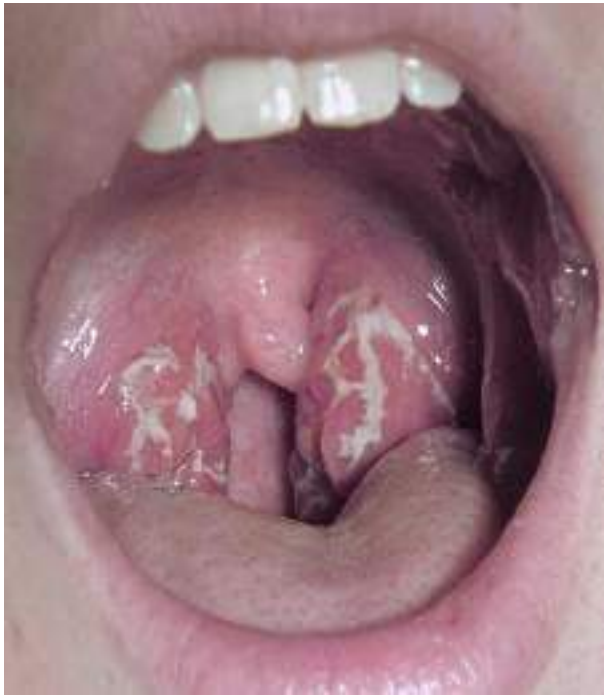
B. Extension of the membrane: in sever cases, it may extend into the larynx and the bronchial airways, which may lead to fatal airway obstruction leading to asphyxia. This mandates immedites tracheostomy.

C. **Bull-neck apperance:** A few patients develop massive swelling of the tonsils and present with "bull-neck" diphtheria, which results from lymphadenopathy, massive edema of the submandibular and paratracheal region which is characterized by foul breath, thick speech, and stridor breathing.

- The infection gradually resolves, and the membrane is coughed up after 5 to 10 days.

The Diphtheritic vs. Streptococcal Pharyngitis

Diphtheritic

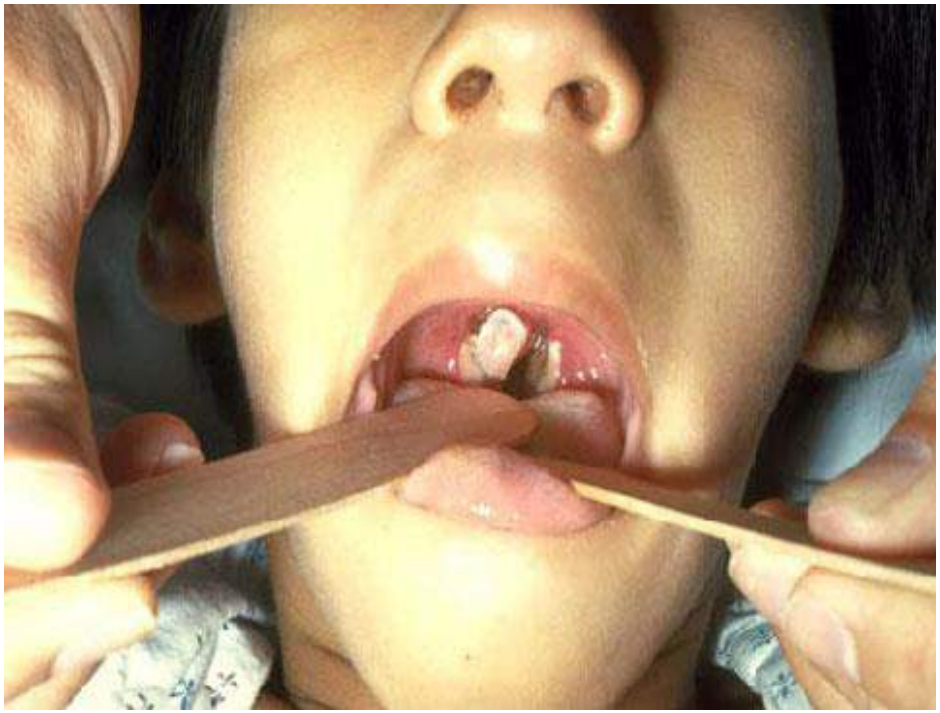


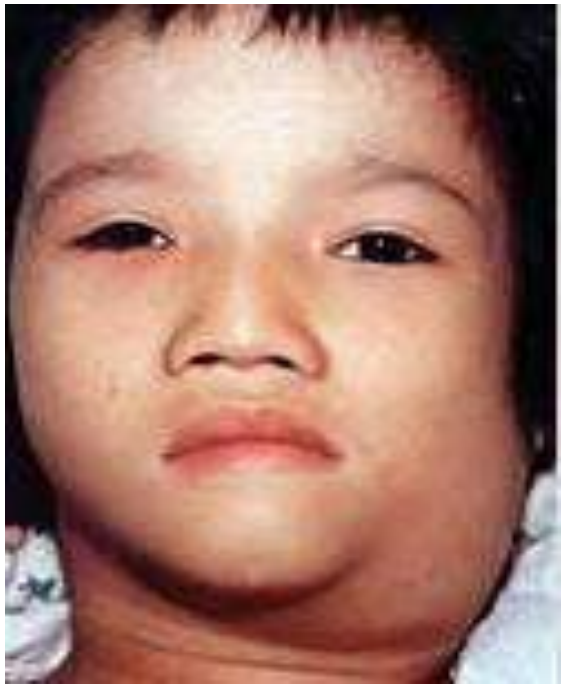
Streptococcal

The diphtheritic pseudomembrane is gray or whitish and sharply demarcated. Unlike the exudative lesion associated with streptococcal pharyngitis, the pseudomembrane in diphtheria is tightly adherent to the underlying tissues. Attempts to dislodge the membrane may cause bleeding. Laryngoscopy may be diagnostically helpful.

Manifestations

Respiratory diphtheria





Manifestations

Systemic diphtheria (Toxin absorption)

The exotoxin invades the regional lymph nodes and subcutaneous tissue (lymphadenitis and edema of the subcutaneous layer) and bloodstream, fixes on the target cells with their subsequent toxic lesions:

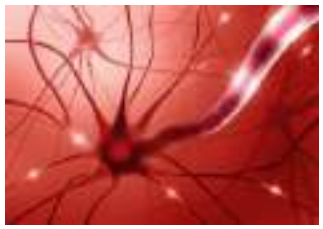
1. Diphtheritic myocarditis:

- ✓ Appears during the 2-3 week in severe cases of respiratory diphtheria.
- ✓ It is manifested by cardiac enlargement, weakness, arrhythmia, and congestive heart failure with dyspnea.

Manifestations

Systemic diphtheria (Toxin absorption)

2. Nervous system involvement



- ✓ Appears later in the course of disease
- ✓Toixn mediated noninflammatory demyelinating disorder
- ✓ Most often involving paralysis of the soft palate, oculomotor (eye) muscles, or selective muscle groups.
- ✓ The paralysis is reversible and is generally not serious unless the diaphragm is involved

3. Adrenal glands - hemorrhage, tissue necrosis.

4. kidneys – symptoms of nephrosis

Recovery after the toxic damage is in 4 - 5 weeks to 6 months if the patient survives

Manifestations

Diphtheria of other localization

1. Ear (otitis externa)
2. The eye: purulent and ulcerative conjunctivitis
3. The genital tract : purulent and ulcerative vulvovaginitis
4. Sporadic cases of pyogenic arthritis

Laboratory Diagnostics

Diagnosis should be considered in patients who have

- Severe pharyngitis, particularly with difficulty swallowing, respiratory compromise, or signs of systemic disease including myocarditis or generalized weakness.

Specific diagnosis: -

- Microscopy of the smears and its bacteriologic investigation (swabs should be taken from nose and tonsils beneath the membrane and before antibiotic therapy);
- Bacteriologic culture is essential for confirmation,
- Serologic test – quantity of antibody titer to diphtherical exotoxin;
- Toxigenicity test (PCR, ELISA);
- **Nonspecific diagnosis** - CBC – moderate leucocytosis, increased ESR; - ECG, medical consultations of neurologist, cardiologist and ENT.

Laboratory Diagnostics

In the differential diagnosis, the leading causes of pharyngitis that should be considered are

- Respiratory viruses (rhinoviruses, influenza viruses, parainfluenza viruses, coronaviruses, and adenoviruses; ~25% of cases),
- Group A streptococci (15–30%),
- Group C streptococci (~5%),
- Atypical bacteria such as *Mycoplasma pneumoniae and Chlamydia pneumoniae* (15–20% in some series),
- Other viruses such as herpes simplex virus (~4%) and Epstein-Barr virus
- Others

Treatment

Teatment should be started immediatley on clinical suscpesion of dihphthia which includes:

1. Antidiphtheric serum or ADS (antitoxin): the treatment of choice as it neutralizes the toxin.

Stage of infection	Dose of ADS
Mild, early pharyngeal cases	20,000-40,000 units
Moderately sever cases	40,000-60,000 units
Sever, extensive or late cases	80,000-1,00,000 units

2. Maintenance of an open airway.

3. Antimicrobial therapy:

- Penicillin or Erythromycin is the drug of choice.
- Elimination of the organism should be documented by negative results of at least 2 successive cultures of specimens from the nose and throat (or skin) obtained 24 hr apart after completion of therapy.

Vaccination

Types of vaccine:

1. Single vaccine: Diphtheria toxoid
2. Combined vaccine: various vaccine available are
   - DPT: Contains DT (diphtheria toxoid), P (pertussis whole cell), and TT (tetanus toxoid). It is the vaccine of choice for infants.**(why).**
     - Pertussis in this vaccine which is used as a whole cell acts as an adjuvant whih increases the immunogenecity of DT and TT.
   - Td

Protective titer:

Following vaccination, an antitoxin titer of ≥0.1 unit/ml is said to protective

Management Patients in whom diphtheria is suspected

- Should be hospitalized in respiratory isolation rooms, with close monitoring of cardiac and respiratory function.
- A cardiac workup is recommended to assess the possibility of myocarditis.
- In patients with extensive pseudomembranes, possibility a tracheostomy or intubation will be required.
- In some settings, pseudomembranes can be removed surgically.

Communicability

- Transmission may occur as long as virulent bacilli are present in discharges and lesions.
- The time is variable, but without antibiotics, organisms usually persist 2 weeks or less and seldom more than 4 weeks.
- Chronic carriers may shed organisms for 6 months or more.
- Effective antibiotic therapy promptly terminates shedding.

Case study

- A 2 year old child experienced an upper respiratory infection.
- He had anorexia and fatigue.
- The patient was seen in the emergency room. He had a fever of 39.9°C.
- Physical examination revealed a clear chest, exudative pharyngitis, and bilaterally enlarged cervical lymph nodes.
- A throat culture was taken and the child given a course of penicillin.

It was noted that the throat culture had not grown any group A streptococci

On day 10 of the infection, the child's condition worsened. He became increasingly lethargic; developed respiratory distress on the day of admission. On examination, 38.9^{o}C, had an exudate in the posterior pharynx that was described as yellowish, and thick membrane which bled when scraped and removed. The patient's medical history revealed that he had received no immunizations. The patient was admitted to hospital. Diagnosis and treated for diphtheria.

Thank You