

Diphtheria

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Essentials of diagnosis & typical features:

- A gray, adherent pseudomembrane, most often in the pharynx but also in the nasopharynx or trachea.
- Sore throat, serosanguineous nasal discharge, hoarseness, and fever in a nonimmunized child.
- Peripheral neuritis or myocarditis.
- Positive culture.
- Treatment should not be withheld pending culture results.

General Considerations:

Diphtheria is an acute infection of the upper respiratory tract or skin caused by toxin-producing *Corynebacterium diphtheriae*. Significant numbers of elderly adults and unimmunized children are susceptible to infection. Diphtheria still occurs in epidemics in countries where immunization is not universal. Travelers to these areas may acquire the disease. *Corynebacteria* are gram-positive club-shaped rods with a beaded appearance on Gram stain.

Diphtheria toxin kills susceptible cells by irreversible inhibition of protein synthesis.

The toxin is absorbed into the mucous membranes and causes destruction of epithelium and a superficial inflammatory response. The necrotic epithelium becomes embedded in exuding fibrin and red and white blood cells, forming a grayish pseudomembrane over the tonsils, pharynx, or larynx. Any attempt to remove the membrane exposes and tears the capillaries, resulting in bleeding. The diphtheria bacilli within the membrane continue to produce toxin, which is absorbed and may result in toxic injury to heart muscle, liver, kidneys, and adrenals, and is sometimes accompanied by hemorrhage. The toxin also produces

neuritis, resulting in paralysis of the soft palate, eye muscles, or extremities. Death may occur as a result of respiratory obstruction or toxemia and circulatory collapse. The patient may succumb after a somewhat longer time as a result of cardiac damage. The incubation period is 1–6 days.

A. Symptoms and signs:

1. **Pharyngeal diphtheria**—Early manifestations of diphtheritic pharyngitis are mild sore throat, moderate fever, and malaise, followed fairly rapidly by prostration and circulatory collapse. The "pulse is more rapid than the fever would seem to justify". A pharyngeal membrane forms and may spread into the nasopharynx or the trachea, producing respiratory obstruction. The membrane is tenacious and gray and is surrounded by a narrow zone of erythema and a broader zone of edema. The cervical lymph nodes become swollen, and swelling is associated with brawny edema of the neck (so-called **bull neck**). Laryngeal diphtheria presents with stridor, which can progress to obstruction of the airway.

2. **Other forms**—Cutaneous, vaginal, and wound diphtheria account for up to one third of cases and are characterized by ulcerative lesions with membrane formation.

B. Laboratory findings:

Diagnosis is clinical. Direct smears are unreliable. Material is obtained from the nose, throat, or skin lesions, if present, for culture on Loeffler and tellurite agar. Between 16 and 48 hours are required before identification of the organism. A toxigenicity test is then performed. Cultures may be negative in individuals who have received antibiotics. The white blood cell

count is usually normal, but hemolytic anemia and thrombocytopenia are frequent.

Complications:

A. **Myocarditis:** Diphtheritic myocarditis is characterized by a rapid, thready pulse; indistinct heart sounds, ST-T wave changes, conduction abnormalities, dysrhythmias, or cardiac failure; hepatomegaly; and fluid retention. Myocardial dysfunction may occur from 2 to 40 days after the onset of pharyngitis.

B. **Polyneuritis:** Neuritis of the palatal and pharyngeal nerves occurs during the first or second week. Nasal speech and regurgitation of food through the nose are seen. Diplopia and strabismus occur during the third week or later. Neuritis may also involve peripheral nerves supplying the intercostal muscles, diaphragm, and other muscle groups. Generalized paresis usually occurs after the fourth week.

C. **Bronchopneumonia:** Secondary pneumonia is common in fatal cases.

Prevention:

A. Immunization: Immunization with diphtheria toxoid combined with pertussis and tetanus toxoids (DTP) should be used routinely for infants and children.

B. Care of exposed susceptibles: Children exposed to diphtheria should be examined, and nose and throat cultures obtained. If signs and symptoms of early diphtheria are found, antibiotic treatment should be instituted. Immunized asymptomatic individuals should receive diphtheria toxoid if a booster has not been received within 5 years. Unimmunized close contacts should receive either erythromycin orally (40 mg/kg/d in four divided doses) for 7 days or benzathine penicillin G intramuscularly (25,000 units/ kg), active immunization with diphtheria toxoid, and observation daily.

Treatment:

A. Specific measures:

1. **Antitoxin**—To be effective, diphtheria antitoxin should be administered within 48 hours.

2. **Antibiotics**—Penicillin G (150,000 units/ kg/d intravenously) should be given for 10 days. For penicillin-allergic patients, erythromycin (40 mg/ kg/d) is given orally for 10 days.

B. General measures:

Bed rest in the hospital for 10–14 days is usually required. All patients must be strictly isolated for 1–7 days until respiratory secretions are noncontagious. Isolation may be discontinued when three successive nose and throat cultures at 24-hour intervals are negative. These cultures should not be taken until at least 24 hours have elapsed since the cessation of antibiotic treatment.

C. Treatment of carriers:

All carriers should receive treatment. Erythromycin (40 mg/kg/d orally in three or four divided doses), penicillin V potassium (50 mg/kg/d for 10 days), or benzathine penicillin G (600,000–1,200,000 units intramuscularly) should be given. All carriers must be quarantined. Before they can be released, carriers must have three negative cultures of both the nose and the throat taken 24 hours apart and obtained at least 24 hours after the cessation of antibiotic therapy.

Prognosis:

Mortality varies from 3% to 25% and is particularly high in the presence of early myocarditis. Neuritis is reversible; it is fatal only if an intact airway and adequate respiration cannot be maintained. Permanent damage due to myocarditis occurs rarely.

Review questions:

Question 1: All of the following are essentials of diagnosis and typical features of diphtheria except:

1. A gray, adherent pseudomembrane, most often in the pharynx but also in the nasopharynx or trachea.
2. Sore throat, serosanguineous nasal discharge, hoarseness, and fever in a nonimmunized child.
3. Peripheral neuritis or myocarditis.
4. Positive culture.
5. Treatment should be withheld pending culture results.

*Key answer: 5. Treatment should **not** be withheld pending culture results.*

Question 2: Which of the followings is **true** regarding diphtheria infection:

1. Corynebacteria are "gram-negative club-shaped rods" with a beaded appearance on Gram stain.
2. The pulse is more rapid than the fever would seem to justify.
3. **Bull neck** is due to swelling of the cervical nodes with brawny edema. It is regarded as pathognomonic.
4. Direct smears are reliable and material is obtained (from the nose, throat, or skin lesions) for culture on Loeffler and tellurite agar is essential.
5. Penicillin G (150,000 units/ kg/d intravenously) should be given for 10 days and antitoxin should be given regardless of time since the initial presentation.

Key answer: all are false except 2 is true.

Question 3-4: 4-yr-old male presented with mild sore throat, moderate fever, and malaise, followed few days later by prostration and circulatory collapse. On examination: the pulse is more rapid than the fever would seem to justify. A pharyngeal membrane found which is tenacious and gray and is surrounded by a narrow zone of erythema and edema. The cervical lymph nodes are swollen with an edema of the neck. Which of the following is the most likely diagnosis?

1. *Corynebacterium diphtheriae* infection.
2. *Candida* infection of the oropharynx.
3. Infectious mononucleosis due *Epstein barr* virus infection.
4. Follicular tonsillitis by *streptococcus pyogenes*
5. Tuberculosis of the oral mucosa.

Key answer: 1

For the child in the previous clinical scenario, which of the followings is **incorrect** next step?

1. Antitoxin to that peculiar pathogen should be given within 2 days of diagnosis.
2. Effective antimicrobial should be given for 10 days.
3. All patients must be strictly isolated for 1–7 days until respiratory secretions are noncontagious. Isolation may be discontinued when three successive cultures at 24-hour intervals are negative.
4. All carriers should receive treatment, antitoxin and must be quarantined.
5. Mortality may reach up to 25% particularly in the presence of early myocarditis.

Key answer: 4 no need of antitoxin.