**Corynebacterium**

The genus Corynebacterium includes Corynebacterium diphtheriae, the cause of the prototypic toxin-mediated disease diphtheria

* **Corynebacteria**

Corynebacteria are small, slender, pleomorphic, gram-positive rods of distinctive morphology They are nonmotile and unencapsulated, and they do not form spores.

* **Corynebacterium diphtheriae**

Diphtheria, caused by C. diphtheriae, is an acute respiratory or cutaneous disease and may be life threatening. The development of effective vaccination protocols and widespread immunization beginning in early childhood has made the disease rare in developed countries. However, diphtheria is a serious disease throughout the world, particularly in those countries where the population has not been immunized.

* **Epidemiology:** C. diphtheriae is found in the throat and naso - pharynx of carriers and in patients with diphtheria. This disease is a local infection, usually of the throat, and the organism is primary spread by respiratory droplets, usually by convalescent or asymptomatic carriers. It is less frequently spread by direct contact with an infected individual or a contaminated fomite
* **Pathogenesis:** Diphtheria is caused by the local and systemic effects of a single exotoxin that inhibits eukaryotic protein synthesis. The toxin molecule is a heat-labile polypeptide that is composed of two fragments, A and B. Fragment B binds to susceptible cell membranes and mediates the delivery of fragment A to its target. Inside the cell, fragment A separates from fragment B and catalyzes a reaction between nicotine adenine dinucleotide (NAD+) and the eukaryotic polypeptide chain elongation factor, EF-21. Toxin gene expression is also regulated by environmental conditions. Low iron conditions induce toxin expression, whereas high iron condition repress toxin production.
* **Clinical significance:** Infection may result in one of two forms of clinical disease, respiratory or cutaneous, or in an asymptomatic carrier state
* **a. Upper respiratory tract infection:** Diphtheria is a strictly localized infection, usually of the throat. The infection produces a distinctive thick, grayish, adherent exudate (pseudomembrane) that is composed of cell debris from the mucosa and inflammatory products . It coats the throat and may extend into the nasal passages or downward in the respiratory tract, where the exudate sometimes obstructs the airways, even leading to suffocation.
* As the disease progresses, generalized symptoms occur caused by production and absorption of toxin .Although all human cells are sensitive to diphtheria toxin, the major clinical effects involve the heart and peripheral nerves. Cardiac conduction defects and myocarditis may lead to congestive heart failure and permanent heart damage. Neuritis of cranial nerves and paralysis of muscle groups, such as those that control movement of the palate or the eye .
* **b. Cutaneous diphtheria:** A puncture wound or cut in the skin can result in introduction of C. diphtheriae into the subcutaneous tissue, leading to a chronic, nonhealing ulcer with a gray membrane. Rarely, exotoxin production leads to tissue degeneration and death
* **Immunity:** Diphtheria toxin is antigenic and stimulates the production of antibodies that neutralize the toxin’s activity
* **Laboratory identification:** The presumptive diagnosis and decision to treat for diphtheria must be based on initial clinical observation, low-grade fever, and cervical adenopathy (swelling of the neck). Erythema of the pharynx progressing to adherent gray pseudomembranes increases suspicion of diphtheria. However, a definitive diagnosis requires isolation of the organism, which must then be tested for virulence using an immunologic precipitin reaction to demonstrate toxin production. C. diphtheriae can be isolated most easily from a selective medium, such as Tinsdale agar which contains potassium tellurite, an inhibitor of other respiratory flora, and on which the organism produces several distinctive black colonies with halos.
* C. diphtheriae from clinical material or culture has a distinctive morphology when stained, for example, with methylene blue. This morphology includes characteristic bands and reddish (polychromatic) granules that are often seen in thin, sometimes club-shaped rods that appear in clumps, suggestive of Chinese characters. This presentation is often referred to as a “palisade arrangement” of cells. Initial decision to treat for diphtheria must be based on clinical observation. Culture and assay for toxin production are required for confirmation of the diagnosis. Such tests are performed only in reference public health laboratories. There are several methods, as follows:
* A filter paper disk containing antitoxin (10 IU/disk) is placed on an agar plate. The cultures to be tested for toxigenicity are spot innoculated 7–9 mm away from the disk. After 48 hours of incubation, the antitoxin diffusing from the paper disk has precipitated the toxin diffusing from toxigenic cultures and has resulted in precipitin bands between the disk and the bacterial growth. This is the modified Elek method described by the WHO Diphtheria Reference Unit.
* Polymerase chain reaction-based methods have been described for detection of the diphtheria toxin gene *(tox).* The two assays are not widely available.
* Enzyme-linked immunosorbent assays can be used to detect diphtheria toxin from clinical *C diphtheriae* isolates.
* An immunochromographic strip assay allows detection of diphtheria toxin in a matter of hours. This assay is highly sensitive.

**Treatment:** Treatment of diphtheria requires prompt neutralization of toxin, followed by eradication of the organism. C. diphtheriae is sensitive to several antibiotics, and passive immunization with preformed diphtheria toxin antibodies is a mandatory part of treatment of diphtheria. Because diphtheria is highly contagious, suspected diphtheria patients must be isolated. Antibiotic treatment, such as **erythromycin or penicillin .**

**Prevention:** The cornerstone of diphtheria prevention is immu - nization with toxoid, usually administered in the DTaP triple vaccine, together with tetanus toxoid and pertussis antigens .