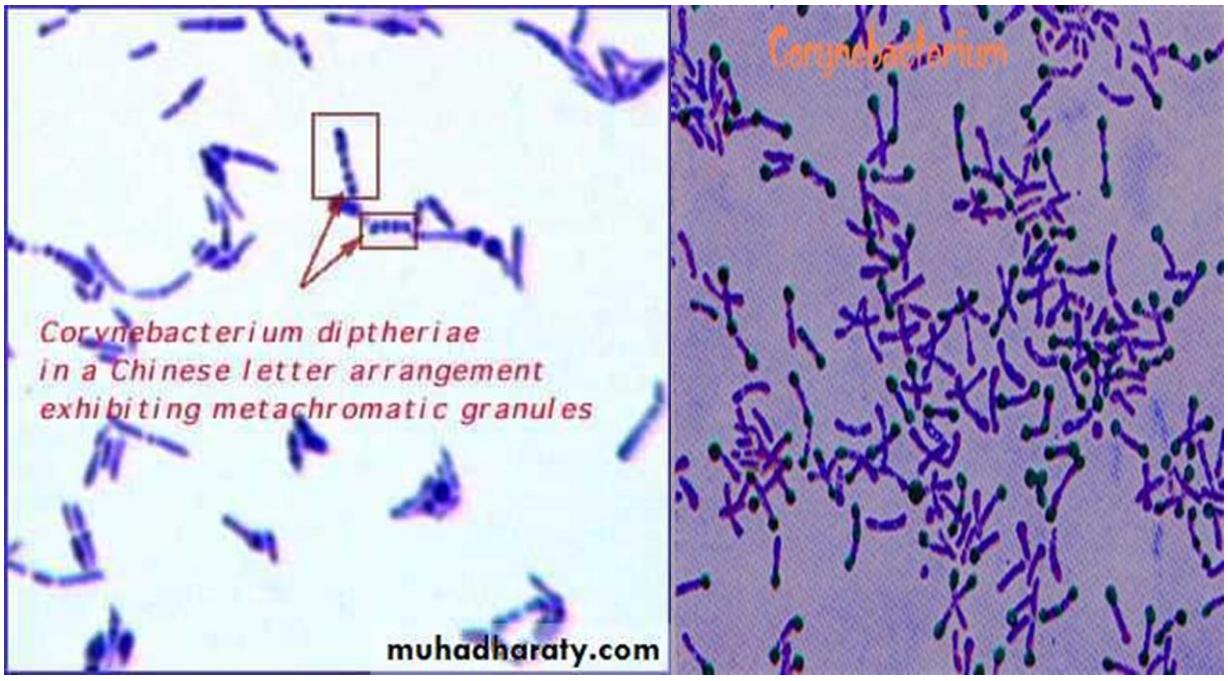
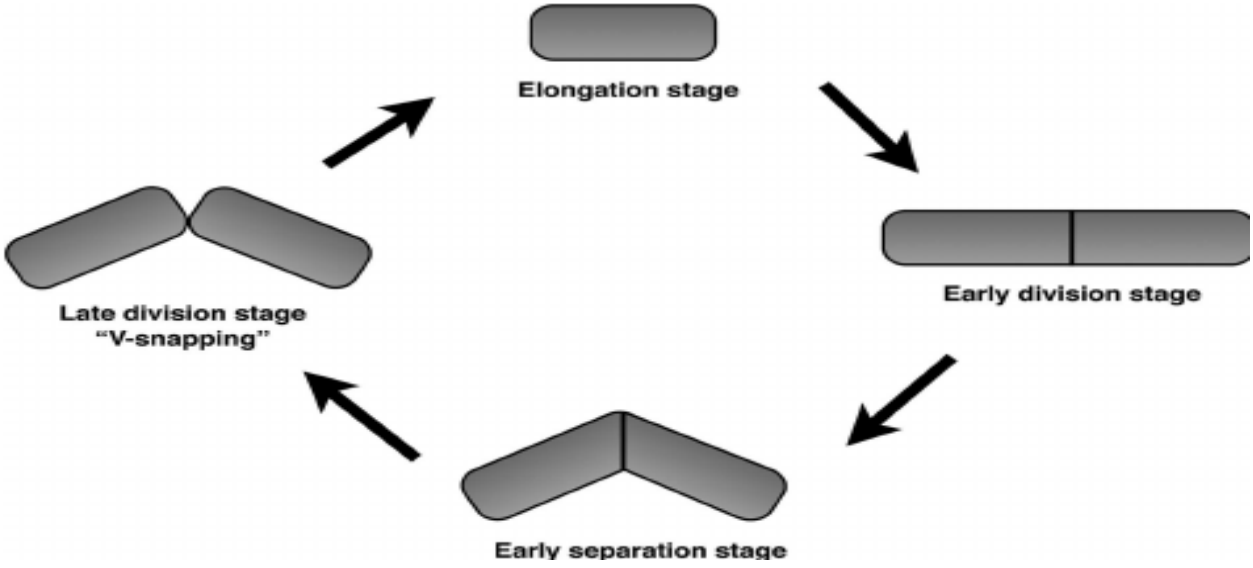
Corynebacterium diphtheriae

It is also known as the Kleb's Loeffler bacterium, according to discovery by Kleb's and Loeffler. Gram-positive rod bacterium with club-shaped at one or both ends. Aerobic or facultative anaerobic, non-motile, non-capsulated, non-spore forming and saprophytes.

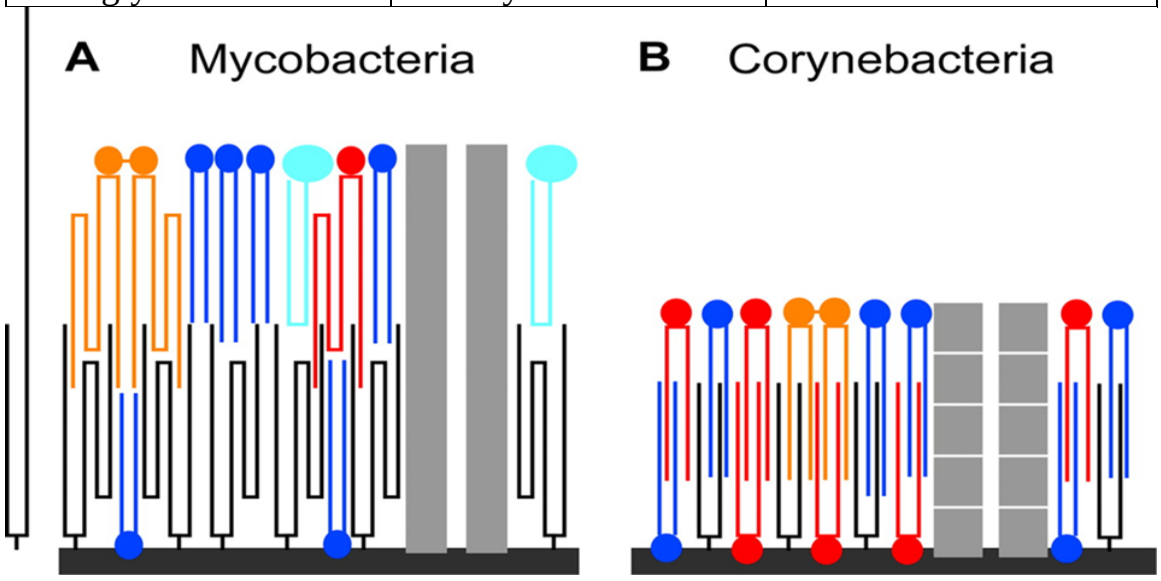
Their cytoplasm frequently contains metachromatic granules or volutin granules as a storage form of energy), that give it a beaded shape. Due to their snapping division (A distinctive type of binary fission resulting in an angular arrangement of cells (hinge), cells often lie in clusters resembling Chinese letters.





The cell wall is distinctive with mycolic acids or corynemycolic acids. It is related to the Actinomycetes and CMN group (*Corynebacterium*, *Mycobacterium* and *Nocardia*.). Mycolic acids are unique long chain fatty acids essential for viability and virulence.

Mycobacterium	Nocardia	Corynebacterium
Longest long chain	Intermediate long chain	Shortest long chain
Strongly acid fast	Weakly acid fast	No acid fast



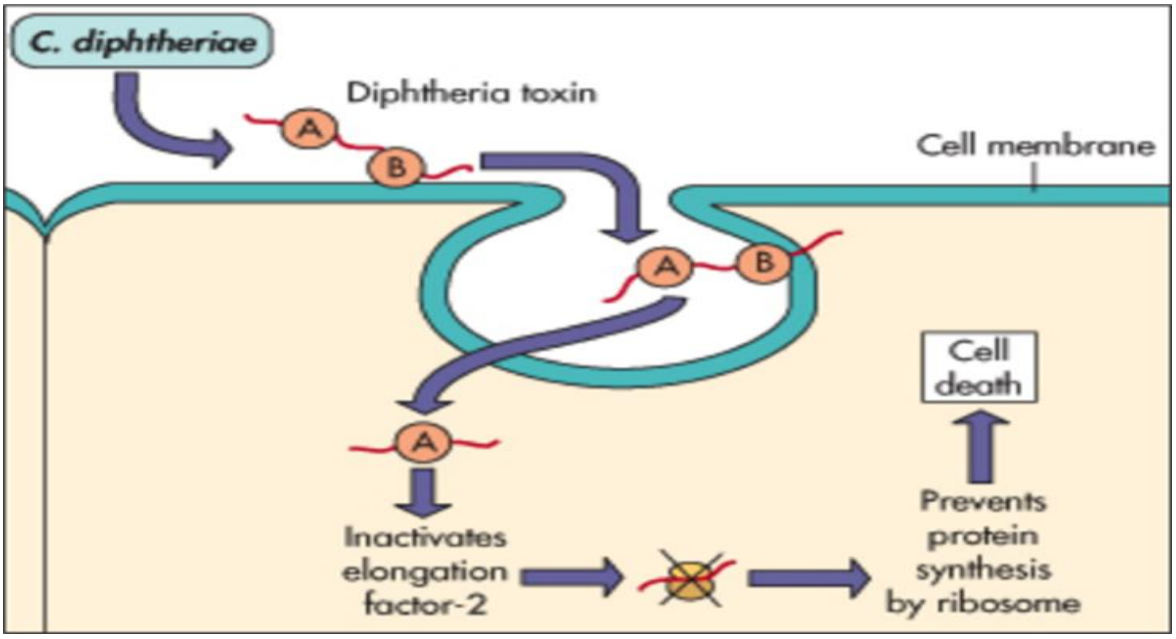
Pathogenicity

Corynebacterium diphtheriae is non- pathogenic by itself, but it can acquire a particular virulence tox gene by a bacteriophage (also known as phage, is virus that infect and replicate only in bacterial cells) to allow it to manufacture the powerful diphtheria exotoxin that can cause people to get very sick. The tox gene is incorporated into the genome of non-toxigenic bacteria, transcribed and translated causing a buildup of diphtheria toxin.

Corynebacterium diphtheriae possessing the tox gene are said to be pathogenic bacteria which cause diphtheria as an acute, communicable and deadly toxin-mediated disease. In contrast *C. diphtheriae* lacking the tox gene are said to be non-pathogenic bacteria.

Diphtheria toxin

Diphtheria toxin is a single polypeptide chain consisting of two subunits known as an A-B toxin. Binding to the host cell surface of the B subunit by specific receptor (heparin-binding epidermal growth factor), that is present on many human cells allows the A subunit to penetrate the host cell by endocytosis. After that, the A fragment separates from the B fragment and becomes an active enzyme. The B fragment is released from the host cell. This enzyme catalyzes a chemical reaction that inactivates substance required for movement of the ribosome on mRNA (inactivate elongation factor 2). It halts protein synthesis by blocking the transfer of amino acids from tRNA to the growing polypeptide chain on the ribosome and the cell dies. Cells that lack the appropriate receptor do not take up the toxin and are unaffected by it. This receptor specify explains why some tissues of the body are not affected in diphtheria, while others such as heart, spleen, muscles, liver, kidney and nerves are severely damaged.



Clinical presentations

- Site of infection (respiratory or cutaneous)
- Immune status of the patient
- Virulence of the organism

Transmission

Diphtheria spread from person to person, usually through

- Respiratory droplets, like from coughing, sneezing or laughing.
- Nasopharyngeal secretions
- Direct contact with cutaneous infection (open sores or ulcers).
- Fomites such as dust and clothes, the organism can survive for up to 6 months.

Source of infection

- People carry the bacteria without having symptoms.
- Carriers who have recovered from an infection.

Those at increased risk of getting sick include:

- People in the same household
- People with a history of frequent, close contact with the patient

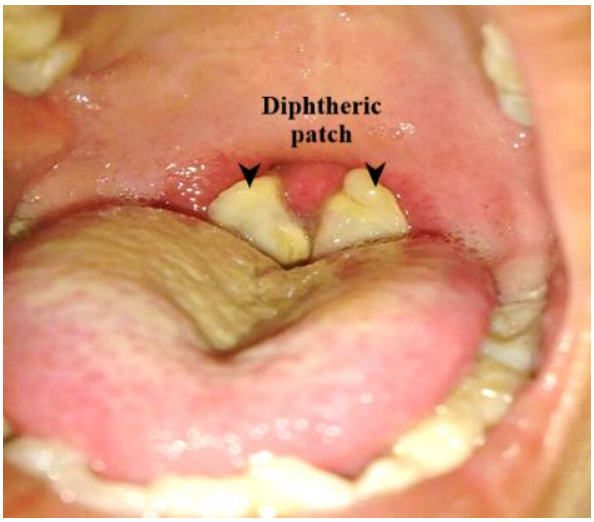
- People living in areas with high populations and unsanitary environments, accompanied by malnutrition and unvaccinated will have a greater chance to be attacked by diphtheria

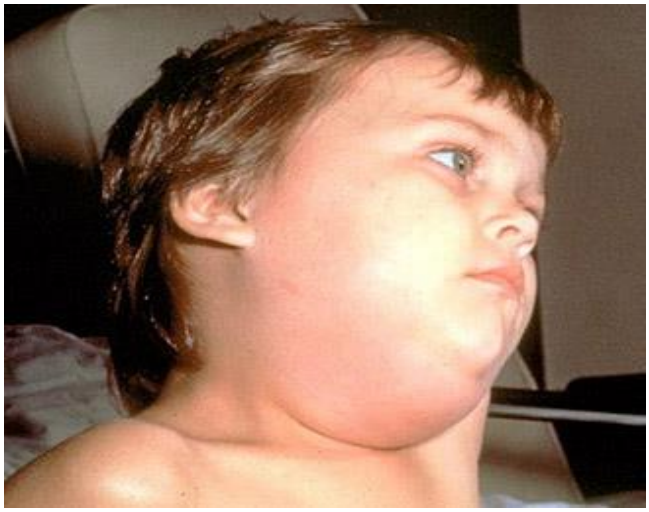
Respiratory diphtheria

The bacteria most commonly infect the respiratory system (most often in the nose and throat). When the bacteria get into and attach to the lining of the respiratory system, it can cause mild to severe infection depending on the body part that is affected. The main symptoms of this type are weakness, sore throat, mild fever, swollen glands in the neck, malaise, pharyngitis and fatigue.

The bacteria make a toxin that kills healthy tissues in the respiratory system. Within 2-3days, the dead tissue forms a thick, gray to white coating a pseudo membrane. It can cover tissues in the nose, tonsils, voice box, and throat, making it very hard to breathe and swallow, causing the patient to suffocate. If the toxin gets into the blood stream, it can cause heart, nerve, and kidney damage.

This disease mostly occurs in children under 5 years of age, but currently occurs in children over 5 years (5-19 years) and in adults over the age of 40 years.





Cutaneous diphtheria

Cutaneous diphtheria is acquired by skin contact with other infected persons. The organism which colonizes the skin surface (mouth and nose) gains entry into the subcutaneous tissue through breaks in the skin. A papule will develop and evolve into a chronic no healing ulcer (open sores), sometimes covered with a grayish membrane. The ulcer may also be infected with *Staphylococcus aureus* or group A *Streptococcus*. Endemic in poor parts of the world that lack adequate immunization.

- Cutaneous diphtheria.

Complications

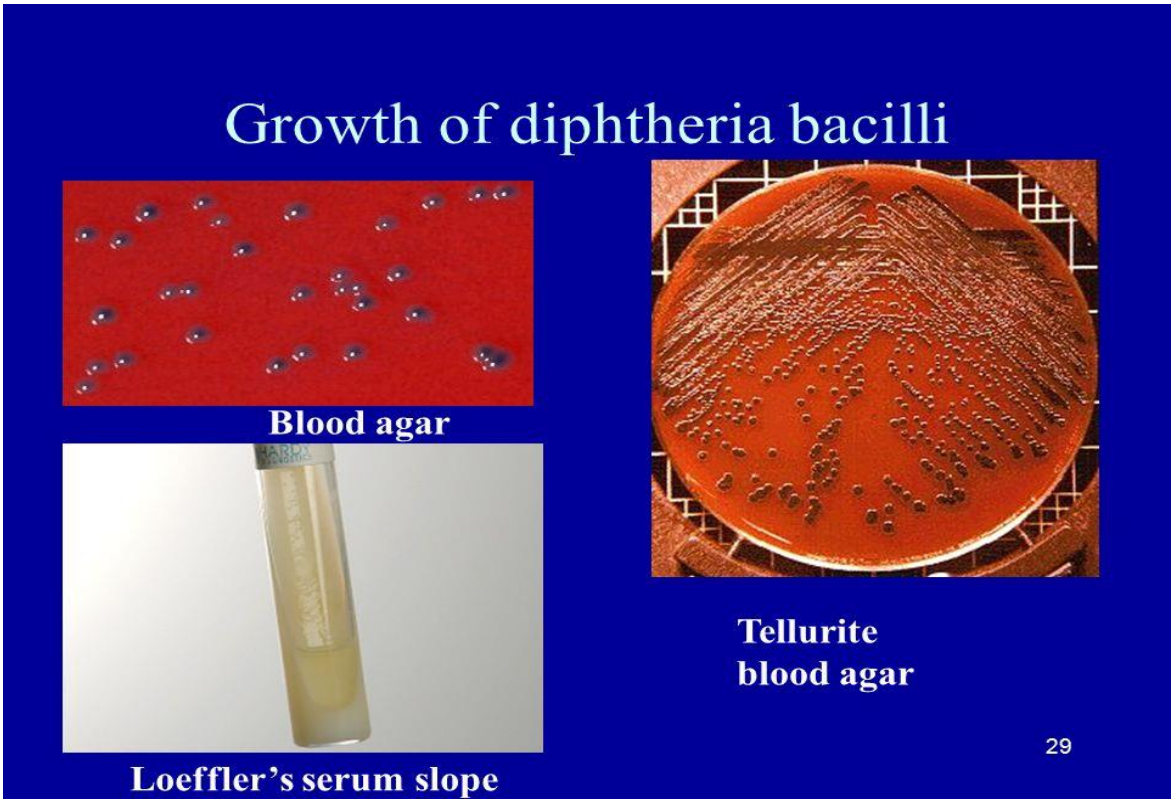
Breathing obstruction, acute circulatory failure, neuropathy, pneumonia and otitis media, conjunctivitis, vulvovaginitis and kidney failure.

For some people, respiratory diphtheria can lead to death. Even with treatment, about 1 in 10 patients die. Without treatment, up to half of patients can die from the disease.

Diagnosis of diphtheria

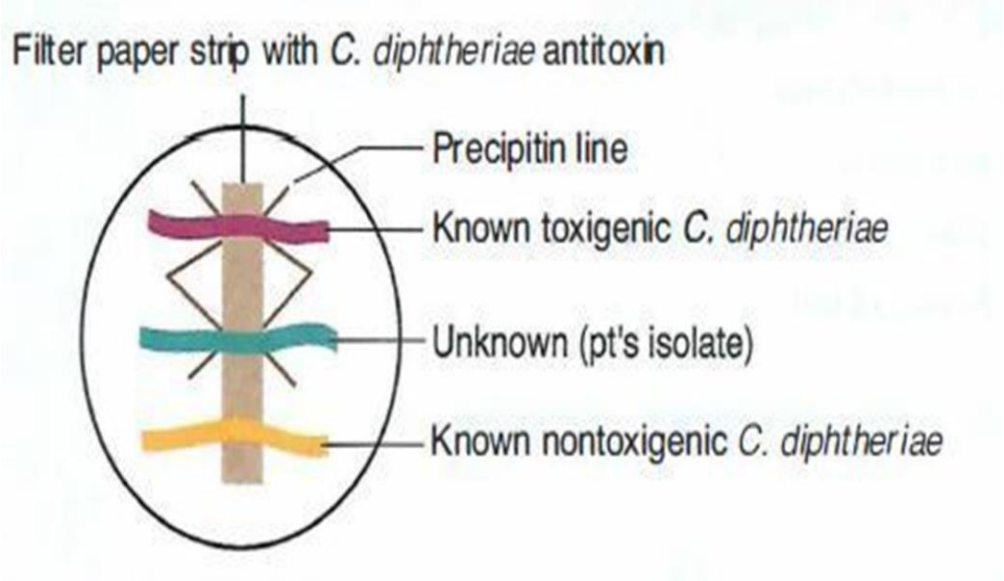
1. Culture testing

- Swabs from nose, back of the throat or ulcer before antimicrobial drugs are used.
- Culturing on laboratory enrichment media
- Smears stained with Loffler's methylene blue or gram stain.



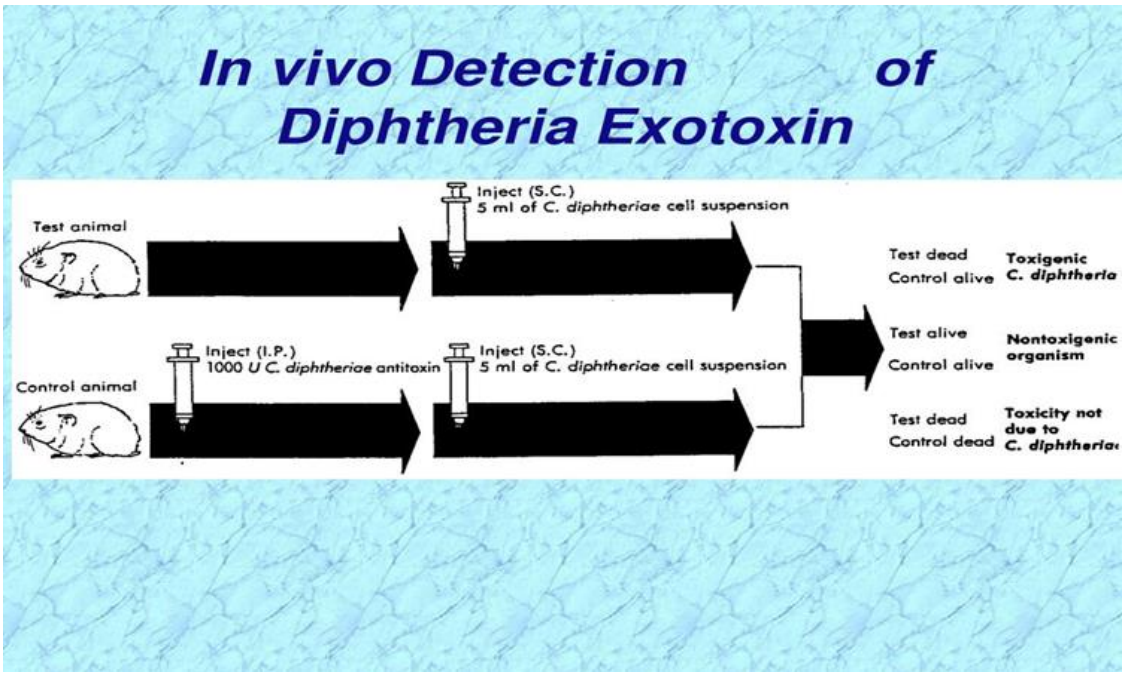
2. Toxigenicity testing

1. **Modified Elek test** is performed by filter paper disc antitoxin is placed on agar plate. The cultures to be tested for toxigenicity streaked across with the disk. Antitoxin will precipitate toxin and formed bands between the disk and bacterial growth.



2. Animal inoculation

Test animal (mice) inject with C. *diphtheriae* cell suspension and control animal (mice) inject with *C. diphtheriae* cell suspension and diphtheria antitoxin. If the test mice dead and control mice alive means *C. diphtheriae* is toxigenic. If the test mice and control mice alive means *C. diphtheriae* is nontoxigenic. If the test mice and control mice dead mean toxicity not due to *C. diphtheria.*



3. **Polymer Chain Reaction (PCR)** based methods have been described for detection of the diphtheria toxin gene (tox).
4. **Enzyme -linked immunosorbent assays (ELISA)** can be used to detect diphtheria toxin.

Treatment

Rapid suppression of toxin-producing bacteria with antimicrobial drugs (penicillin and erythromycin) and arrest toxin production. Early administration of specific antitoxin against diphtheria toxin to inhibit the progression of toxin. To limit contact with diphtheria bacilli to a minimum, patients with diphtheria should be isolated.

Prevention

The best and most successful way to prevent diphtheria is by vaccination. Vaccination DPT (diphtheria, pertussis and tetanus) all three given together take at the first months and booster immunizations every 10 years throughout life.