1. Introduction

_Corynebacterium diphtheriae_ is a thin, club-shaped Gram-positive aerobic bacillus that exists in 4 biotypes (_gravis, mitis, belfanti_ and _intermedius_). The most severe disease is caused by the exotoxin of the gravis type. Toxin production occurs only when the bacillus itself is infected by a specific virus, carrying the genetic information for the toxin (toxigenic _C. diphtheriae_). In addition to the bacterial exotoxin, also cell-wall components such as O and K antigens are important for the development of disease. Diphtheria exotoxin causes local and systemic cell destruction.

Diphtheria spreads from person to person, either from acute cases or from asymptomatic carriers, by respiratory droplets or direct contact with secretions from the respiratory tract or from infected skin. It is highly contagious.

Children under the age of 15 years are most at risk.

Diphtheria is perfectly preventable by vaccination and is no longer endemic, thanks to high vaccination coverage rates in most countries. In countries with low (< 50%) routine immunisation coverage, the risk of epidemics still exists.

Before the Expanded Programme on Immunisation of the WHO (EPI, started in 1974), around 1 million cases occurred every year, with 50 000-60 000 deaths annually. Thanks to vaccination, the incidence decreased enormously. In 2000, 30 000 cases were reported with 3000 deaths. In 2009, only 857 cases were reported.

2. Disease

Diphtheria is a disease of the upper respiratory tract, caused by the exotoxin. The incubation period is 2-5 days. Most cases are mild with sore throat and fever or no symptoms at all. But the toxin can cause inflammation of the pharynx, the larynx and trachea. When the toxin arrives in the blood or lymph system, it can attack any organ, including heart (myocarditis) and nervous system (polyneuritis). The case-fatality rate is more than 10%. Characteristic is a grey-white membrane (pseudo membrane) that forms in the throat caused by the destructive effects of the toxin on epithelial cells, composed of leucocytes, bacteria, cellular debris and fibrin. It is fixed to underlying tissues and bleeds if pulled away. When it spreads to the larynx, it can cause death by suffocation.

Also skin infections can occur, mainly in adults, whose antibody levels are not longer high enough to offer protection. This can be a further source of transmission.
Diphtheria disease might not cause immunity. Persons recovering from diphtheria should begin or complete active immunization with diphtheria vaccine.

Urgent treatment is needed to reduce complications and mortality. Intramuscular or intravenous antitoxin is administered on clinical suspicion without waiting for laboratory confirmation. Antibiotics (penicillin or erythromycin) have no effect on established exotoxic lesions but limit further bacterial growth and the duration of corynebacterial carriage that often occurs after clinical recovery.

Emergency tracheotomy should be done to prevent or relieve respiratory obstruction in laryngeal diphtheria.

3. Vaccines

Diphtheria vaccine is manufactured in a large number of countries. The manufacturing process is relatively simple and the vaccine can be purchased at low cost. The productions steps include growth of toxin producing C. diphtheriae in liquid media, sterilization of the exotoxin-containing supernatant, addition of formalin to convert toxin into toxoid, adsorption to aluminium salt and adding of thiomersal as preservative (for multi-dose vials that do not contain aP). A low dose diphtheria toxoid (adult doses, indicated as d) is also available to use from the age of 7 years, to avoid local reactions at the injection site with booster doses.

- Presentation, administration and conservation of the vaccine

It is almost exclusively available in combination with tetanus toxoid (T) as DT or with tetanus and pertussis vaccine as DTP. It may also be combined with hepatitis B and Haemophilus influenzae type b (Hib) in a tetravalent or pentavalent vaccine.

Administration is by intramuscular injection only.

Vaccines should be stored between +2°C and +8°C. Vaccines that have been frozen should not be used.

- Vaccination schedule

For childhood vaccination DTP is generally used. Three doses of vaccine are recommended from 6 weeks of age and given at least 4 weeks apart. Boosting is possible at the age of 12 months, at school entry and just before the end of primary school.

People who live in low or non endemic areas may require boosters at about 10-years interval. The combination of an adult-dose diphtheria toxoid with tetanus toxoid (dT) is the best choice for this.

For previously un-immunized children aged 1-6 years, a recommended schedule is 2 doses, 2 months apart and a third dose after 6-12 months (DTP). The schedule for primary immunization of children older than 7 and adolescents using the dT combination is 2 doses 2 months apart and a third dose after 6-12 months.
• **Vaccine Efficacy and safety**

It is one of the oldest and safest vaccines currently available. Severe reactions are rare. No anaphylactic reactions have been reported. However, local reactions at the site of injection are common but in general they are mild. Pregnancy and immunosuppression are not contraindications.

4. **WHO recommendations**

Thanks to introduction in the EPI programme and high coverage, reported cases of diphtheria decreased dramatically. The global coverage of 3 doses DTP reached 82% in 2009.

Local diphtheria outbreaks in several developed countries have demonstrated the importance of sustained high coverage of childhood immunization programs.

5. **References**


