

The Seven Most Frequently Asked Questions about Diphtheria

	QUESTION	ANSWER											
1.	What is diphtheria?	<p>Diphtheria is an acute disease of bacterial origin that can affect the nasopharynx and may lead to obstruction of the airways and potentially, death.⁵</p> <p>The most frequent symptoms are sore throat, fever (generally mild, rarely exceeding 38.5°C), difficulty when swallowing and breathing. The severity of the signs and symptoms is usually proportional to the extent of the local disorder since it is related to production of the toxin in the diphtheria membrane. When a sufficient amount of the toxin is absorbed, the patient may be pale, have a rapid pulse, and present extreme weakness.^{5,6}</p> <p>Symptoms appear in 2 to 5 days (ranging from 1 to 10) after exposure to the agent.⁶</p>											
2.	What is the causative agent?	<p>The causative agent is <i>Corynebacterium diphtheriae</i>, a gram-positive bacillus, which has four biotypes: <i>mitis</i>, <i>intermedius</i>, <i>gravis</i>, and <i>belfanti</i>. The most significant virulence factor of <i>C. diphtheriae</i> is the exotoxin that produces local and systemic cellular necrosis.⁶</p> <p><i>C. diphtheriae</i> is transmitted from one person to another through direct contact with the mucous membranes of the airways of a sick individual or carrier. Transmission rarely occurs through contact with skin lesions or fomites.⁵</p>											
3.	What is the definition of a suspected case of diphtheria recommended by the WHO?	<p>Upper respiratory tract illness characterized by nasopharyngitis, pharyngitis, tonsillitis or laryngitis, and presence of adherent pseudo membrane of the tonsils, pharynx, larynx and/or nose.</p> <p>Note: Some countries may consider expanding the definition of a suspected case to include mild cases with no pseudo membrane or non-scarring ulcers in a person with a history of travel to endemic countries or countries with diphtheria outbreaks.</p>											
4.	How is the diagnosis of diphtheria confirmed?	<p>Through a <i>C. diphtheriae</i> culture and demonstration of secretion of the exotoxin using an immunoprecipitation reaction (e.g. modified Elek Test).⁵</p> <p>Polymerase chain reaction (PCR) is useful for detection of the diphtheria toxin gene, which provides a rapid diagnosis when the culture is not positive. In these cases, the epidemiological context should be considered and each case evaluated.⁵</p>											
5.	How should the sample be obtained for laboratory diagnosis?	<p>Two samples should be collected after initial contact with the suspected case: a pharyngeal swab and nasal swab. Both samples should be obtained using cotton-tip swabs. These samples should ideally be obtained before initiating antibiotic treatment.</p> <p>The pharyngeal swab should be obtained under direct visualization, preferably from the edge or directly beneath the pseudo membrane, twirling the swab, then removing and placing it in the transport medium.</p> <p>To take the nasal swab, gently insert the swab into the nostril until the anterior wall of the pharynx is reached and rub gently. The swabs should be appropriately labeled with a unique identifier and the source of the sample and placed in the appropriate transport media (Amies or Stuart transport media). If possible, a sample of the pseudo membrane should also be obtained and placed in saline solution (not formalin).</p>											
6.	What is the recommended management of diphtheria cases?	<p>Diphtheria antitoxin (DAT): Should be administered as soon as the disease is suspected. The antitoxin neutralizes the circulating (unbound) toxin, but not the toxin fixed to the tissues.⁷</p> <p>Antibiotics: Antibiotics eliminate the bacteria and thus reduce the duration of communicability and carriage. The recommended antibiotics are penicillin and erythromycin for 14 days.⁷</p> <p>Other measures: Healthcare-associated infection prevention and control (HAIPC), monitoring (respiratory, cardiac, renal), support measures, strict rest (two weeks), and vaccination during the convalescence period.</p>											
7.	What is the recommended DAT dose and how is it administered?	<p>The recommended dose is the same for children and adults, and ranges between 20,000 and 100,000 units depending on the location and extent of the pseudo membrane, the interval since the time of onset of symptoms, and the severity of the infection (Table 1).⁷</p> <p>Table 1. Suggested dose ranges for use of DAT</p> <table border="1"> <thead> <tr> <th>Indication</th> <th>Dose (units)</th> <th>Form of administration</th> </tr> </thead> <tbody> <tr> <td>Pharyngeal or laryngeal (48 hours or less)</td> <td>20,000 to 40,000 IU</td> <td rowspan="2">Intramuscular (IM)</td> </tr> <tr> <td>Nasopharyngeal lesions</td> <td>40,000 to 60,000 IU</td> </tr> <tr> <td>Extensive disease (three days or longer) or diffuse swelling of the neck</td> <td>80,000 to 100,000 IU</td> <td>Intravenous (IV)</td> </tr> </tbody> </table> <p>Source: PAHO/WHO. <i>Tratamiento de las enfermedades infecciosas</i>. Seventh Edition. 2017-2018 pp 38, 61.</p> <p>Once the dose and form of administration are determined, a single dose of antitoxin should be administered. The DAT is mixed with 250-500 ml of normal saline solution and is slowly administered over 2-4 hours, closely monitoring the patient for anaphylaxis. The dose should not be repeated. IV is the preferred form in severe cases, with IM used in mild to moderate cases.⁸</p> <p>Staff who administer DAT should be trained and should have the experience, equipment and drugs required to treat the patient in the event of anaphylaxis symptoms. Use of DAT in pregnant women should be based on a risk-benefit analysis.⁸</p> <p>It is important to always read the brochure on the available product to confirm doses and the manufacturer's recommendations regarding susceptibility testing, administration, adverse events, etc.⁸</p>	Indication	Dose (units)	Form of administration	Pharyngeal or laryngeal (48 hours or less)	20,000 to 40,000 IU	Intramuscular (IM)	Nasopharyngeal lesions	40,000 to 60,000 IU	Extensive disease (three days or longer) or diffuse swelling of the neck	80,000 to 100,000 IU	Intravenous (IV)
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⁵ Stanley A Plotkin, et al. Plotkin's Vaccines. Seventh edition, pp 261-275

⁶ WHO position paper on diphtheria vaccine. Available at: <http://apps.who.int/iris/bitstream/handle/10665/258681/WER9231.pdf?sequence=1>

⁷ Pan American Health Organization/World Health Organization. Treatment of infectious diseases. Seventh Edition. 2017-2018 pp 38, 61.

⁸ Centers for Disease Control and Prevention. Diphtheria Antitoxin (DAT) Protocol. Version 7.0. September 21, 2016. Available at: <https://www.cdc.gov/diphtheria/downloads/protocol.pdf>