



Epidemiological Update

Diphtheria

28 February 2018

Diphtheria in the Americas - Summary of the situation

In 2017, there were four countries in the Region of the Americas—Brazil, the Dominican Republic, Haiti, and the Bolivarian Republic of Venezuela—that reported confirmed diphtheria cases. As of epidemiological week (EW) 8 of 2018, four countries in the Region—Brazil, Colombia, Haiti, and Venezuela—have reported suspected and confirmed diphtheria cases.

Following is a summary of the situation in each country with reported suspected and confirmed cases in 2018.

In **Brazil**, in 2017 there were 40 suspected cases reported in 14 states, of which 35 were discarded and 5 have been confirmed in four states: Acre (1), Minas Gerais (2), Roraima (1 fatal case, imported from Venezuela), and São Paulo (1). Three of the 5 confirmed cases (2 in Minas Gerais and 1 in São Paulo) had received the full doses schedule. The confirmed cases range from 4 to 66 years of age (median 19 years); four are male and one female. Additionally, in EW 2 of 2018 a suspected case was reported in the state of Bahia and is currently under investigation.

In **Colombia**, in EW 7 of 2018 a fatal confirmed case of diphtheria was reported in the Department of La Guajira, imported from Venezuela. The case is a 3-year-old child from Venezuela, with unknown vaccination history and onset of symptoms on 2 January. The case died on 8 January and was laboratory confirmed by culture and by RT-PCR technique as positive for *Corynebacterium diphtheriae* without identifying biotype and positive toxin. To date, there are no secondary cases reported.

In **Haiti**, since the beginning of the outbreak at the end of 2014 up to EW 6 of 2018, there have been 410 probable cases of diphtheria reported, including 75 deaths.¹ Reported case-fatality rates were 22.3% in 2015, 27% in 2016 and 10.7% in 2017 and 2018. During the first four epidemiological weeks of 2018, 2 to 5 probable cases per EW were reported similar to that observed during the last four weeks of 2017.

Females accounted for 57% of the total probable cases in 2015, 50% in 2016, 60% in 2017, and 47% in 2018 (up to EW 6). With respect to vaccination coverage, between 2015 and 2018 the unvaccinated cases accounted for 17% (2018) to 38% (2015) of the total cases. Children less than 10 years of age accounted for 64% of the probable cases reported between 2017 to EW 4 of 2018.

¹ Per the Haiti Ministry of Public Health and Population, a probable case is defined as any person, of any age, that presents laryngitis, pharyngitis or tonsillitis with false adherent membranes in the tonsils, pharynx and / or nasal pits, associated with edema of the neck.

Suggested citation: Pan American Health Organization / World Health Organization. Epidemiological Update: Diphtheria. 28 February 2018, Washington, D.C.: PAHO/WHO; 2018

Since the beginning of the outbreak the departments reporting the highest number of probable cases are Artibonite, Centre, and Ouest.

In **Venezuela**, since the beginning of the outbreak in July 2016 up to EW 5 of 2018 a total of 969 probable diphtheria cases were reported (324 cases in 2016, 609 in 2017, and 36 in 2018) 726 of which were confirmed by laboratory or clinically, and 113 died (17 in 2016 and 96 in 2017); with a case fatality rate of 15.5%.

In 2016 cases were reported in five states (Anzoátegui, Bolívar, Delta Amacuro, Monagas, and Sucre), and in 2017 there were 22 states and the Capital District reporting confirmed cases. In 2018, 9 federal entities reported confirmed cases. Cases were reported in all age groups, however, the majority of cases occurred in the 5 to 39 age group, with the highest incidence rate in the group of 5 to 19 years of age.

The health authorities are intensifying epidemiological surveillance, case detection, medical care and vaccination, in addition to maintaining constant training of health personnel (based on the updated manual of standards, guidelines and procedures for the management of the disease) and health education.

Advice for Member States

The Pan American Health Organization / World Health Organization (PAHO/WHO) advises Member States to continue their efforts to maintain high vaccination coverage in all territorial entities with the full 3-dose primary series and booster doses.

PAHO/WHO stresses that the populations at greatest risk are unvaccinated children under 5 years of age, schoolchildren, healthcare workers, military service personnel, prisoner community, and people who, due to the nature of their occupation are in contact with high numbers of people on a daily basis.

Although travelers are not at special risk of diphtheria, PAHO/WHO recommends that national authorities remind travelers heading to endemic countries or outbreak settings that before travel they need to be up to date with their diphtheria vaccination, according to the national vaccination schedule established in each country.

PAHO/WHO recommends Member States strengthen their surveillance systems for early detection of suspected cases to initiate timely and adequate treatment of cases, including the provision of diphtheria antitoxin and contact follow up.

Adequate clinical management is key to reduce complications and mortality. Following is advice for health authorities on case management.

Clinical management

Initial clinical management

The clinical management of patients with suspected diphtheria includes administration of antibiotic, diphtheria antitoxin (DAT), and implementation of infection prevention and control measures. The following is recommended:

- Place patient immediately in an isolation room (or area) and apply standard, droplet and contact precautions when caring for the patient.
- Administer diphtheria antitoxin (DAT) as soon as possible.
- Administer antibiotics (penicillin, erythromycin, or azithromycin) as soon as possible.
- Monitor closely and provide supportive therapy for severe complications (i.e., airway management, cardiac, neurological, and renal failure).

Antibiotic treatment

Antibiotics should be given as soon as possible after suspected disease onset, without waiting for laboratory confirmation.

- For patients who cannot swallow or are critically ill, intravenous (IV) or intramuscular (IM) administration should be used. Once the patient improves clinically, oral administration can be carried out.
- Oral therapy can be used in patients with mild or moderate symptoms.
- Before initiating treatment, penicillin allergy should be checked.

Antibiotic treatment
<ul style="list-style-type: none"> • Procaine benzyl penicillin (penicillin G): administer IM All persons: 50mg/kg once daily (maximum 1.2 grams a day). Treat for a total of 14 days.
<ul style="list-style-type: none"> • Aqueous benzyl penicillin (penicillin G): administer IM or slow IV All persons: 100,000 units/kg/day administer in divided does of 25,000 IU/kg every 6 hours. Maximum does is 4 MIU or 2.4 grams per day.
<ul style="list-style-type: none"> • IV Erythromycin All persons: 40-50 mg/kg/day (máximum, 2gm/day). Administer in divided dose, 10-15 mg/kg every 6 hours, maximum 500 mg per dose. Treat for a total of 14 days.

Antibiotic treatment (oral preparation), for patients who can swallow or are less ill.
<ul style="list-style-type: none"> • Oral phenoxymethyl penicillin V All persons: 50 mg/kg/day, administer in divided dose 10-15 mg/kg/dose administered every 6 hours. Maximum is 500 mg per dose. Treat for 14 days.
<ul style="list-style-type: none"> • Oral erythromycin All persons: 40-50 mg/kg/day (maximum, 2gm/day). Administer in divided dose, 10-15 mg/kg every 6 hours. Maximum 500 mg per dose. Treat for total 14 days.
<ul style="list-style-type: none"> • Oral azithromycin <u>For children:</u> 10-12 mg/kg once daily (maximum 500 mg/day). Treat for 14 days. <u>For adults:</u> 500 mg once daily. Treat for 14 days. Note: There is no data to support the exact duration required for azithromycin.

Diphtheria antitoxin (DAT) therapy

DAT is highly effective and the gold standard for diphtheria treatment.

- Diphtheria toxin that has already entered the host cells is unaffected by DAT. Therefore, to reduce complications and mortality DAT should be administered as soon as possible after disease onset.
- Due to small risk for a serious allergic reaction, perform a sensitization test (i.e., Besredka test) for all candidate patients.
- DAT should be administered in a closely monitored setting with appropriate medical interventions available, if needed.
- The amount of antitoxin recommended varies with larger amounts recommended for persons with extensive pseudomembrane, neck swelling, systemic signs and with longer interval since onset. The dose is the same for children and adults. Do not repeat dosing.

Clinical presentation	Dosage for adults and children
Laryngeal or pharyngeal of 2 days duration	20,000 - 40,000 UI
Nasopharyngeal disease	40,000 - 60,000 UI
Extensive disease of 3 or more days of duration or any patient with diffuse swelling of the neck (respiratory distress, hemodynamic instability).	80,000 - 100,000 UI

- Pregnant women should not receive DAT.

Infection prevention and control measures

- Vaccinate with an age appropriate diphtheria toxoid-containing vaccine.
- Apply standard precautions, droplet and contact precautions, at all times.
- Keep the isolation area segregated from other patient-care areas.
- Maintain one meter between patients, when possible.
- After discharge, restrict contact with others until completion of antibiotic therapy (i.e., remain at home, do not attend school or work until treatment course is complete).

Care of close contacts

Close contacts include (irrespective of age): household members (all persons who sleep in the same house/tent during the **last 5 nights** before onset of disease of the case) and any persons with a history of direct close contact (**less than one meter**) for a prolonged time (**over 1 hour**) during the **5 days prior to onset of disease** of the case (e.g. caretakers, relatives, or friends who

regularly visit the home) as well as health care staff exposed to oral or respiratory secretions of a case-patient.

All close contacts should be assessed for signs and symptoms of diphtheria and kept under daily surveillance for 7 days from the last contact. Adult contacts must avoid contact with children and must not be allowed to handle food until proven not to be carriers.

All the contacts must receive a single dose of benzathine benzylpenicillin intramuscularly (600,000 units for children under 6 years, 1.2 million units for those 6 years or older). If the culture is positive, antimicrobial should be given as outlined above.

Laboratory diagnosis

Material for bacteriological culture should be obtained by swabbing the edge of the mucosal lesions or directly under the membrane. Gram staining is not recommended, as other *Corynebacterium* can normally colonize the throat.

Once *C. diphtheriae* is isolated, biotype can be determined. Suspected colonies may be tested for toxin production using the toxin production test or Elek immunodiffusion test.

Additionally, diphtheria toxin gene (*tox*) can be detected directly in *C. diphtheriae* isolates using polymerase chain reaction (PCR) which allow results to be obtained in a few hours. However, detection of the *tox* gene does not confirm the production of toxin, therefore, the application of PCR techniques should be considered as a complementary test and not a substitute for bacteriological culture.

References

1. Diphtheria vaccine: WHO position paper – August 2017. Available at: <http://bit.ly/2CCN7UW>
2. World Health Organization. Operational protocol for clinical management of Diphtheria Bangladesh, Cox's Bazar. 10th Ed., December 2017. Available at: <http://bit.ly/2CL4XE7>
3. Faulkner A, Acosta A, Tejpratap S.P, Tiwari. Manual for the Surveillance of Vaccine-Preventable Diseases, 5th Edition, 2011. Diphtheria: Chapter 1. Available at: <http://bit.ly/2oFCA5j>