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Epidemiological Update Diphtheria in Hispaniola

2 March 2021

In the context of the COVID-19 pandemic, the Pan American Health Organization / World Health Organization (PAHO / WHO) reiterates to Member States that vaccination and epidemiological surveillance of vaccine-preventable diseases should be considered an essential health service that should not be interrupted. PAHO/WHO also reminds Member States that a single laboratory-confirmed case of diphtheria should trigger a public health response and that two cases with an epidemiological link, of which at least one has been laboratory-confirmed, is considered an outbreak.

Summary of the situation in the Americas

In 2021, between epidemiological week (EW) 1 and EW 7, two countries have reported confirmed cases of diphtheria: the Dominican Republic with 5 fatal cases and Haiti with 6 cases, including 1 death.

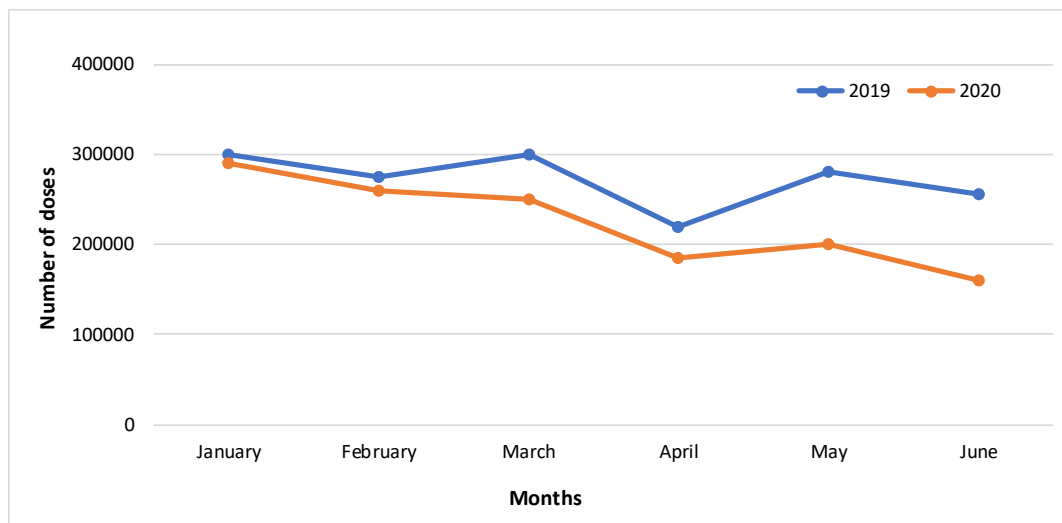
In 2020, a total of 5 countries reported a total of 80 confirmed cases of diphtheria, including 21 deaths in the Region of the Americas: Brazil (2 cases), the Dominican Republic (3 cases, including 2 deaths), Haiti (66 cases, including 16 deaths), Peru (4 cases, including one death) and the Bolivarian Republic of Venezuela (5 cases, including 2 deaths).

In recent years, Latin America has experienced a decline in coverage of the third dose of the diphtheria, tetanus, and pertussis vaccine (DTP3) among infants less than 1-year-old. Between 2010 to 2019, coverage for the Region decreased by 10 percentage points, from 95% to 85%. This results in more than 2.1 million unvaccinated children in 2019. During recent years, countries with the largest cohorts of children, such as Brazil which accounts for 20% of the cohort under 1-year-old, and Mexico which accounts for 15% of the cohort, have reported a decrease in their DTP3 vaccination coverage, which has had an impact on the overall DTP3 coverage for the Region. However, countries with smaller cohorts of children, such as Haiti and Suriname, have also reported declines in the last decade.

Since WHO declared COVID-19 a Public Health Emergency of International Concern (PHEIC) on 11 March 2020, PAHO/WHO has closely monitored the impact of the pandemic on vaccination coverage. Comparing vaccination coverage in 2020 with 2019, there was a decrease in the number of DTP3 doses administered between March and June 2020 compared to the same time period in 2019 (**Figure 1**).

Suggested citation: Pan American Health Organization / World Health Organization. Epidemiological Update: Diphtheria. 2 March 2021, Washington, D.C.: PAHO/WHO; 2021

Figure 1. Total number of DTP3 doses administered in 25 countries of Latin America and the Caribbean. 2019-2020 (January-June).



Source: PAHO/WHO. Sixth ad hoc Meeting of PAHO's Technical Advisory Group (TAG) on Vaccine-preventable Diseases. United States of America (virtual meeting). 16 November 2020. Available at: <https://bit.ly/2OftrRj>

Diphtheria in Hispaniola

Hispaniola is the second largest island in the Caribbean¹ (after Cuba) and is comprised of two countries: Haiti and the Dominican Republic. The population on the island exceeds 20 million inhabitants^{1,2}; Haiti accounts for 11,402,533 inhabitants^{1,2} (414 inhabitants per km²) and the Dominican Republic accounts for 10,847,904 inhabitants^{1,2} (224 inhabitants per km²). In 2019, in Haiti, only 35% of the population had access to basic sanitation and 65% had access to safe drinking water. In the Dominican Republic, 84% of the population had access to basic sanitation and 97% had access to drinking water³.

According to the World Migration Report published in 2020⁴ by the International Organization for Migration (IOM), in 2018, Haiti had the third largest refugee population among Latin American and Caribbean countries. The same report indicates that in 2019, the population of Haiti that migrated to South America increased. Additionally, in 2019, more than 65% of the immigrant population in the United States came from five Caribbean countries, including Haiti and the Dominican Republic. The report also mentions that, in the Caribbean, the most important intra-regional migratory corridor includes the Haitian population that migrates to the Dominican Republic.

¹ UN Country Profiles 2020. Available at: <https://data.un.org/en/index.html>

² UN Population Prospects 2020. Available at: <https://population.un.org/wpp/>

³ The Sustainable Development Goals Report 2020. Available at: <https://bit.ly/2NTLRI>

⁴ International Organization for Migration (IOM). World Migration Report 2020. Available at: <https://bit.ly/3bDvixK>

Several events have affected and weakened the Haitian health system in the last decade. In 2010, the earthquake in Haiti had unprecedented effects in this country, affecting its long-term capacity to respond to various events of public health risk that have occurred concomitantly since then, including one of the most important, the cholera epidemic, which affected the entire island. Cholera was introduced in Haiti in October 2010⁵. Only a month later, in November, the first case of cholera was confirmed in the Dominican Republic, imported from Haiti, after which an epidemic broke out in the Dominican Republic, with household and community outbreaks occurring in rural and border areas⁶. Both countries reported cholera cases through 2019.

In 2019, DTP3 vaccination coverage in Haiti was 79% and only 15% of the communes had DTP3 coverage greater than or equal to 95%. In 2019, in the Dominican Republic, DTP3 coverage was 94% and in 2020, 80% of municipalities had coverage below 95%. During 2020, vaccination coverage with DTP3 has decreased in both countries due to the impact of the COVID-19 pandemic on health services.

Since 2014, there has been an uninterrupted transmission of diphtheria in Haiti and, since 2015, sporadic cases of diphtheria have been reported in several provinces of the Dominican Republic.

Given the following factors, conditions exist for the occurrence of a diphtheria outbreak of greater magnitude on the island of Hispaniola and for the potential spread of the disease to other countries in the Region of the Americas: 1) the decrease in vaccination coverage; 2) waning immunity over time with only a 3-dose primary vaccination schedule (among children less than 1-year-old) in the absence of naturally acquired immunity or booster doses; 3) lack of a vaccination policy for adolescents and adults in various countries; and 4) active migration, amongst other factors.

The following is the epidemiological situation for diphtheria in Haiti and the Dominican Republic, both have reported new confirmed cases since the Epidemiological Update for measles and diphtheria published on 1 February 2021⁷.

In the **Dominican Republic**, between EW 1 and EW 7 of 2021, a total of 5 confirmed cases of diphtheria⁸ were reported, all fatal. No epidemiological link was identified between these cases.

The following is a description of the 5 confirmed cases:

Case 1 corresponds to a 9-year-old Haitian female resident of Peravia Province who had symptom onset on 13 January 2021. The case had no travel history and no vaccination history. The case died on 1 February.

⁵ PAHO/WHO. Haiti reaches one-year free of Cholera. Available at: <https://bit.ly/2NPA4dr>

⁶ National Plan for the Elimination of cholera in the Dominican Republic. Available at: <https://bit.ly/2ZZFDs6>

⁷ Pan American Health Organization / World Health Organization. Epidemiological Update: Measles and Diphtheria. 1 February 2021, Washington, D.C.: PAHO/WHO; 2021. Available at: <https://bit.ly/3q4hLOQ>

⁸ All of the cases have been confirmed by culture, including four which were confirmed by the US CDC as toxigenic *Corynebacterium diphtheriae* biovar mitis (diphtheria toxin production confirmed by the Elek test).

Case 2 corresponds to a 14-year-old Dominican male resident of Baoruco Province who had symptom onset on 18 January 2021. The case had no travel history and no vaccination history. The case died on 20 January.

Case 3 corresponds to a 3-year-old Dominican male resident of San Cristobal Province who had symptom onset on 28 January 2021. The case had no travel history and no vaccination history. The case died on 4 February.

Case 4 corresponds to a 5-year-old Dominican male resident of Monte Plata Province who had symptom onset on 1 February 2021. The case had no travel history and no vaccination history. The case died on 7 February.

Case 5 corresponds to a 3-year-old Dominican male resident of Monte Plata Province who had symptom onset on 14 February 2021. The case had no travel history and no vaccination history. The case died on 21 February.

Corynebacterium diphtheriae was isolated by culture from samples for each of the 5 cases. Four of the samples were confirmed by the United States Centers for Disease Control and Prevention (US CDC) as toxigenic *Corynebacterium diphtheriae* biovar mitis (diphtheria toxin production confirmed by the Elek test).

In 2020, a total of 3 confirmed cases of diphtheria, including 2 deaths, were reported. No epidemiological link was identified between these cases. Information regarding these cases has been shared in the Epidemiological Update of 22 September 2020⁹ and 17 November 2020¹⁰.

Corynebacterium diphtheriae was isolated from samples for each of the 3 confirmed cases. All were laboratory-confirmed by US CDC as toxigenic *Corynebacterium diphtheriae* biovar mitis (diphtheria toxin production confirmed by the Elek test).

The diphtheria vaccination schedule in Dominican Republic includes 3 doses for children under 1 year of age, and 2 boosters, which are administered at 18 months and 4 years of age.

The country has a national vaccination policy for health personnel.

The country does not meet the 95% target established in the regional immunization action plan.

In **Haiti**, between EW 32 of 2014 and EW 6 of 2021, there were 1,211 suspected cases¹¹ of diphtheria reported, including 145 deaths. Of the total cases, 394 were confirmed (380 laboratory-confirmed and 14 by epidemiological link), including 79 confirmed deaths (**Table 1, Figure 2**).

⁹ PAHO/WHO. Epidemiological Update: Diphtheria. 22 September 2020, Washington, D.C.: PAHO/WHO; 2020. Available at: <https://bit.ly/3r7H042>

¹⁰ PAHO/WHO. Epidemiological Update: Measles and Diphtheria. 17 November 2020, Washington, D.C.: PAHO/WHO; 2020. Available at: <https://bit.ly/3sFjJ9X>

¹¹ According to the Haiti Ministère de la Santé Publique et de la Population (MSPP), a suspected case is defined as any person, of any age, that presents with laryngitis, pharyngitis, or tonsillitis with adherent pseudo-membranes in the tonsils, pharynx and / or nasal pits, associated with edema of the neck.

Table 1. Suspected and confirmed cases of diphtheria reported in Haiti, 2014-2021 (until epidemiological week 6 of 2021)¹².

Year	Suspected cases	Confirmed cases*	Confirmed Deaths**	Case-fatality rate** (%)
2014	18	4	2	50%
2015	77	31	7	23%
2016	118	54	21	39%
2017	194	73	6	8%
2018	375	105	14	13%
2019	195	55	12	22%
2020	194	66	16	24%
2021	40	6	1	17%
Total	1,211	394	79	20%

*Confirmed by laboratory criteria or epidemiological link

**Among confirmed cases

Source: Haiti Ministère de la Santé Publique et de la Population (MSPP)

In 2020, the number of suspected cases reported (194 cases) is lower than the number reported during the same period in both 2018 (375 cases) and 2019 (195 cases) (**Table 1**). Of the 194 cases reported, 66 were confirmed, including 16 deaths (62 cases were laboratory-confirmed and 4 by epidemiological link). Considering the long duration that the disease has been transmitted within the country, diphtheria is considered endemic in Haiti.

The case-fatality rates among cases confirmed by laboratory or epidemiological link were 23% in 2015, 39% in 2016, 8% in 2017, 13% in 2018, 22% in 2019, and 24% in 2020.

In 2020, among the 66 confirmed cases, 56% were among 6 to 14-year-olds and 23% among 1 to 5-year-olds. Regarding deaths, 9 were among 6 to 14-year-olds, 4 were among 1 to 5-year-olds, and 3 were among 15-year-olds and older.

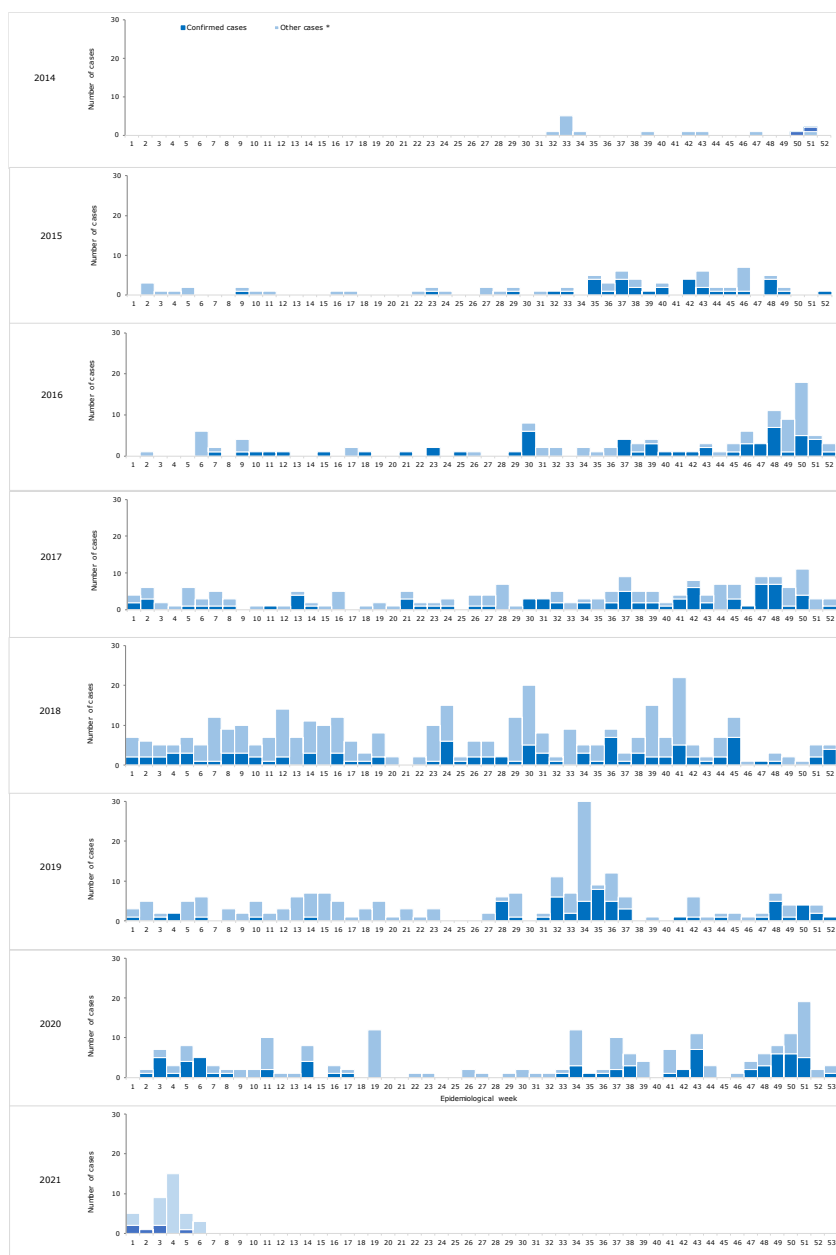
In 2020, the highest cumulative incidence rates of suspected cases have been reported in the communes of Mont-Organisé (70 cases per 100,000 population), Terrier-Rouge (23 cases per 100,000 population), and Trou du Nord (18 cases per 100,000 population) in the Nord Est Department; and Pignon (58 cases per 100,000 population) and Port-Margot (14 cases per 100,000 population) in the Nord Department.

Between EW 1 and EW 6 of 2021, a total of 40 suspected cases were reported, of which 6 were confirmed by laboratory, including one death. Of the 6 confirmed cases, 3 were reported among 6 to 14-year-olds, 2 among 1 to 5-year-olds, and one among 15-year-olds and older. The death occurred in the 1 to 5-year-old age group.

¹² Preliminary data subject to change based on retrospective investigation.

Between EW 1 and EW 6 of 2021, the case-fatality rates among confirmed cases was 17%. During the same period, the highest cumulative incidence rates of suspected cases have been reported in the communes of Thiotte (8 cases per 100,000 population) and Anse à Pitre (6 cases per 100,000 population) in the Sud Est Department; and Terrier-Rouge (6 cases per 100,000 population) in the Nord Est Department.

Figure 2. Distribution of reported diphtheria cases by epidemiological week (EW) of symptom onset and year. Haiti, EW 32 of 2014 to EW 6 of 2021.



*'Other cases' refers to all cases with negative laboratory results, those for which test results are pending, or those for which viable samples were not available.

Source: Haiti Ministère de la Santé Publique et de la Population (MSPP). Data reproduced by PAHO/WHO.

The diphtheria vaccination schedule in Haiti includes 3 doses in under 1-year-olds, and 1 booster, which is administered between 12 and 23 months of age.

The country does not meet the 95% target established in the regional immunization action plan.

The country does not have a national vaccination policy for health personnel.

Advice for Member States

The Pan American Health Organization / World Health Organization (PAHO/WHO) has issued guidelines for immunization programs in the context of the COVID-19 pandemic, updated on 24 April 2020, available at <https://bit.ly/2YK9SIV>, in consultation with members of the PAHO/WHO Technical Advisory Group (TAG) for vaccine preventable diseases (VPD). These guidelines are aligned with the recommendations from the WHO's Strategic Advisory Group of Experts on Immunization (SAGE).

PAHO/WHO reiterates the recommendations to Member States to continue their efforts in ensuring vaccination coverage of more than 95% with the primary series (3 doses) and booster doses (3 doses). This vaccination schedule will provide protection throughout adolescence and adulthood (up to 39 years and possibly beyond). Booster doses of the diphtheria vaccine should be given in combination with tetanus toxoid, using the same schedule and age-appropriate vaccine formulations; namely diphtheria, tetanus, and pertussis (DPT), for children aged 1 to 7 years old, and diphtheria toxoid (Td) for children over 7 years old, adolescents, and adults.

PAHO/WHO reiterates that toxigenic strains of *Corynebacterium diphtheriae* continue to circulate in all parts of the world and the disease can reappear if the protection of the population decreases; however, it can be prevented through vaccination.

PAHO/WHO emphasizes that the unvaccinated population or those persons with an incomplete vaccination scheme (less than 6 doses) are at risk.

PAHO/WHO urges countries with ongoing diphtheria outbreaks to implement vaccination strategies based on the epidemiology of the disease, focused on the affected geographic areas. It may be necessary to include adult vaccination. It is important to comply with the guidelines established in the WHO Framework for Decision-Making: Implementation of Mass Vaccination Campaigns During COVID-19.

Vaccination of healthcare workers and underserved groups living in densely populated areas is also recommended.

Although travelers do not have a special risk for diphtheria infection, it is recommended that national authorities remind travelers going to areas with diphtheria outbreaks to be properly vaccinated prior to travel in accordance with the national vaccination scheme established in each country. If more than five years have passed since their last dose, a booster dose is recommended.

PAHO/WHO recommends that Member States strengthen their surveillance systems and laboratory diagnostic capacity for diphtheria. Laboratory diagnosis is made by culture of the microorganism on selective media, biochemical tests, and the Elek test that confirms the production of diphtheria toxin. Polymerase chain reaction (PCR) detects the presence of the diphtheria toxin gene (*tox*) and is useful to detect the presence of the bacteria, especially in samples that have had difficulties in obtaining, handling, or transporting or in cases that have started antimicrobial treatment prior to obtaining the sample.

PAHO/WHO recommends performing the Elek test to confirm toxin production, mainly in sporadic cases and in countries with active outbreaks that report cases in new locations or that present cases with no direct epidemiological link to a confirmed case.

PAHO/WHO recommends maintaining a supply of diphtheria antitoxin for its timely use and reduction of fatality rates, and training hospital personnel on its use and administration.

Vaccination is key to preventing cases and outbreaks, and proper clinical management reduces complications and mortality.

PAHO/WHO recommends conducting training courses on the epidemiology of diphtheria, clinical picture, laboratory diagnosis, management, epidemiological investigation, and response to outbreaks.

References and useful links

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4. Sixth ad hoc Meeting of the PAHO Technical Advisory Group on Vaccine-Preventable Diseases. United States of America (virtual meeting), November 16, 2020. Available at: <https://bit.ly/2NK2Ps8>
5. Fifth ad hoc Meeting of the Technical Advisory Group (TAG) on Vaccine-Preventable Diseases. USA, August 4, 2020 (virtual meeting). Available at: <https://bit.ly/3q6vpRA>
6. Diphtheria vaccine: WHO position paper – August 2017. Available at: <http://bit.ly/2CCN7UW>
7. Final report of the 3rd ad hoc Meeting of the Technical Advisory Group (TAG). Ad-hoc Virtual Meeting, March 19, 2018. Available at: <https://bit.ly/3bVj39w>

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