



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 for vaccine-preventable diseases should be considered essential health services and should not be interrupted. Given the decline in diphtheria vaccine coverage, PAHO/WHO also reminds Member States that it is important to have a plan to vaccinate the most vulnerable populations and to maintain a permanent supply of diphtheria antitoxin to control potential outbreaks.

### Situation Summary in the Americas

In 2021, between epidemiological week (EW) 1 and EW 42, four countries reported confirmed cases of diphtheria: Brazil with one case, Colombia with one fatal case, Haiti with 18 cases including 3 deaths, and the Dominican Republic with 18 cases including 12 deaths.

The Region of the Americas has reported a steady decline in vaccination coverage since 2010. Vaccination coverage for the third dose of diphtheria, tetanus, and pertussis (DTP3) vaccine in the Region of the Americas declined from 94% to 84% between 2010 and 2020<sup>1</sup>. Between January 2019 and January 2020, DTP3 coverage decreased by 33%. The decline in coverage was observed in most countries in the Region, thereby increasing the population of individuals susceptible to vaccine-preventable diseases. Furthermore, the COVID-19 pandemic has also affected the epidemiological and laboratory surveillance systems for vaccine-preventable diseases.<sup>2</sup>

The following is the epidemiological situation for diphtheria in Colombia, Haiti, and the Dominican Republic, countries that have reported new confirmed cases since the Epidemiological Update on Diphtheria published on 25 June 2021<sup>3</sup>.

In **Colombia**, between EW 1 and EW 41 of 2021, 7 probable cases of diphtheria were reported, of which one was laboratory-confirmed, 5 were discarded, and one remains under investigation.

During EW 41 of 2021, a confirmed fatal case of diphtheria was reported in Sucre Department in a 10-year-old Venezuelan female who had resided in Santiago de Tolú Municipality, Sucre

<sup>1</sup> Pan-American Health Organization/World Health Organization. Immunization in the Americas 2020 Summary - Comprehensive Family Immunization Family, Health Promotion, and Life Course. Available at: <https://bit.ly/3CkF7q5>.

<sup>2</sup> Pan American Health Organization, XXVI Meeting of PAHO's Technical Advisory Group (TAG) on Vaccine-Preventable Diseases. Vaccines bring us closer, 14– 16 July 2021 (virtual). Available at: <https://bit.ly/3n7oeZV>

<sup>3</sup> Pan American Health Organization / World Health Organization. Epidemiological Update: Diphtheria. 25 June 2021, Washington, D.C. PAHO/WHO. 2021. Available at: <https://bit.ly/3EJlZf>

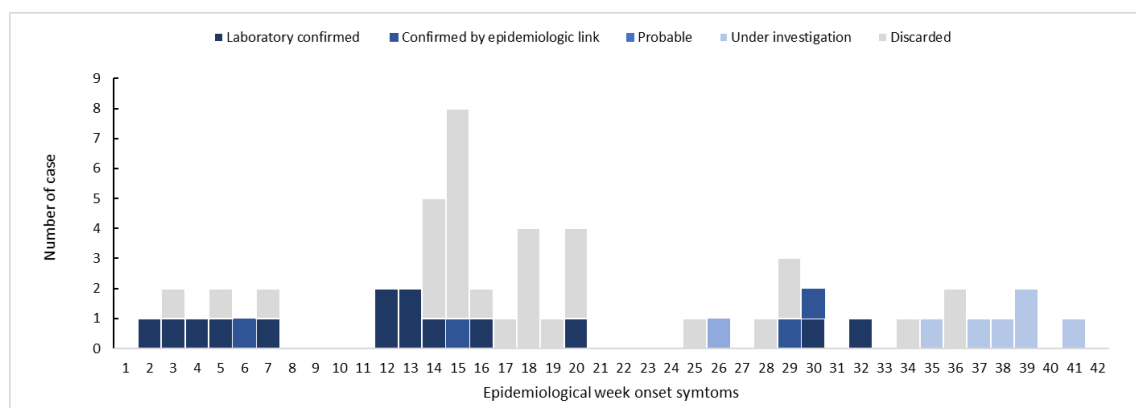
Department, for the past 5 years. The case had onset of symptoms on 27 September 2021 and died on 5 October; the case had no history of travel and had an unknown vaccination history. The case was laboratory-confirmed (positive for *Corynebacterium diphtheriae* by RT-PCR and with the identification of the diphtheria toxin gene).

In the **Dominican Republic**, between EW 1 and EW 42 of 2021, a total of 56 probable cases of diphtheria were reported, of which 18 were confirmed (14 by laboratory and 4 by epidemiological link) including 12 confirmed deaths (11 by laboratory and one by epidemiological link). Of the total cases reported in 2021, 31 were discarded, one was classified as probable, and 6 remain under investigation. (**Figure 1**) Information regarding the first 13 confirmed cases reported in 2021 was previously published in the Epidemiological Update on Diphtheria published on 23 April<sup>4</sup> and 25 June<sup>5</sup> 2021.

Among the 18 confirmed cases between EW 1 and EW 42 of 2021, all were of Dominican nationality, 11 were male, ages ranged from 1 to 14 years (median 8 years), all had an incomplete vaccination history, and none reported a recent travel history. Confirmed cases were reported in the provinces of Monte Plata (7 cases including 5 deaths), Santo Domingo (3 cases including 2 deaths), Elías Piña (3 cases including 2 deaths), San Cristobal (2 cases including 1 death), Peravia (1 fatal case), Bahoruco (1 fatal case), and Hato Mayor (1 case). The most recent confirmed case had symptom onset on 9 August 2021 and was reported from Monte Plata Province.

Between EW 1 and EW 42 of 2021, a total of 11 laboratory-confirmed deaths were reported, of which 7 were male and ages ranged from 1 to 14 years old (median 5 years). The most recent fatal case had symptom onset on 27 July 2021 and was reported from Elías Piña Province.

**Figure 1.** Distribution of reported diphtheria cases by epidemiological week (EW) of symptom onset. EW 1 to EW 42 of 2021, the Dominican Republic.



**Source:** Data from the Dominican Republic Ministry of Health and reproduced by PAHO/WHO.

Among the 14 cases for which *Corynebacterium diphtheriae* was isolated by culture, the results were confirmed by the United States Centers for Disease Control and Prevention (US CDC) as *Corynebacterium diphtheriae* biovar mitis, toxigenic (diphtheria toxin producer by Elek test).

<sup>4</sup> Pan American Health Organization / World Health Organization. Epidemiological Update: Diphtheria on the island of Hispaniola. 23 April 2021, Washington, D.C. OPS/WHO. 2021. Available: <https://bit.ly/3BozPnu>

<sup>5</sup> Pan American Health Organization / World Health Organization. Epidemiological Update on Diphtheria. 25 June 2021, Washington, D.C. PAHO/WHO. 2021. Available in: <https://bit.ly/3jMWyZb>

The diphtheria vaccination schedule in the 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. Vaccination with the third diphtheria booster is not routinely carried out.

The country has a national vaccination policy for health personnel.

The country does not meet the minimum target of 95% vaccination coverage established in the regional immunization action plan for DTP3 for children under 1 year of age. DTP4 coverage is less than 90%.

In **Haiti**, between EW 32 of 2014 and EW 38 of 2021, a total of 1,334 suspected diphtheria cases<sup>6</sup> were reported, including 147 deaths; of these, 406 cases were confirmed (391 by laboratory and 15 by epidemiological link) including 80 confirmed deaths (**Table 1, Figure 2**).

**Table 1.** Suspected and confirmed diphtheria cases reported in Haiti, 2014-2021 (through EW 38 of 2021).<sup>7</sup>

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	193	66	15	23%
2021	164	18	3	17%
<b>Total</b>	<b>1,334</b>	<b>406</b>	<b>80</b>	<b>20%</b>

\*Confirmed by laboratory criteria (PCR-positive) or epidemiological link

\*\*Among confirmed cases

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

Between EW 1 and EW 38 of 2021, the number of suspected cases reported (164 cases) is similar to the number of cases reported during the same period in 2019 (165 cases) but higher than the number of suspected cases reported during the same period in 2020 (110 cases). Among the 164 cases reported, 17 were laboratory-confirmed and one case was confirmed by epidemiological link; there were 3 deaths among the confirmed cases. Considering the prolonged transmission of the disease, diphtheria is considered endemic in Haiti.

Between 2015 and 2021, case-fatality rates among confirmed cases were 23% in 2015, 39% in 2016, 8% in 2017, 13% in 2018, 22% in 2019, 23% in 2020, and 17% in 2021.

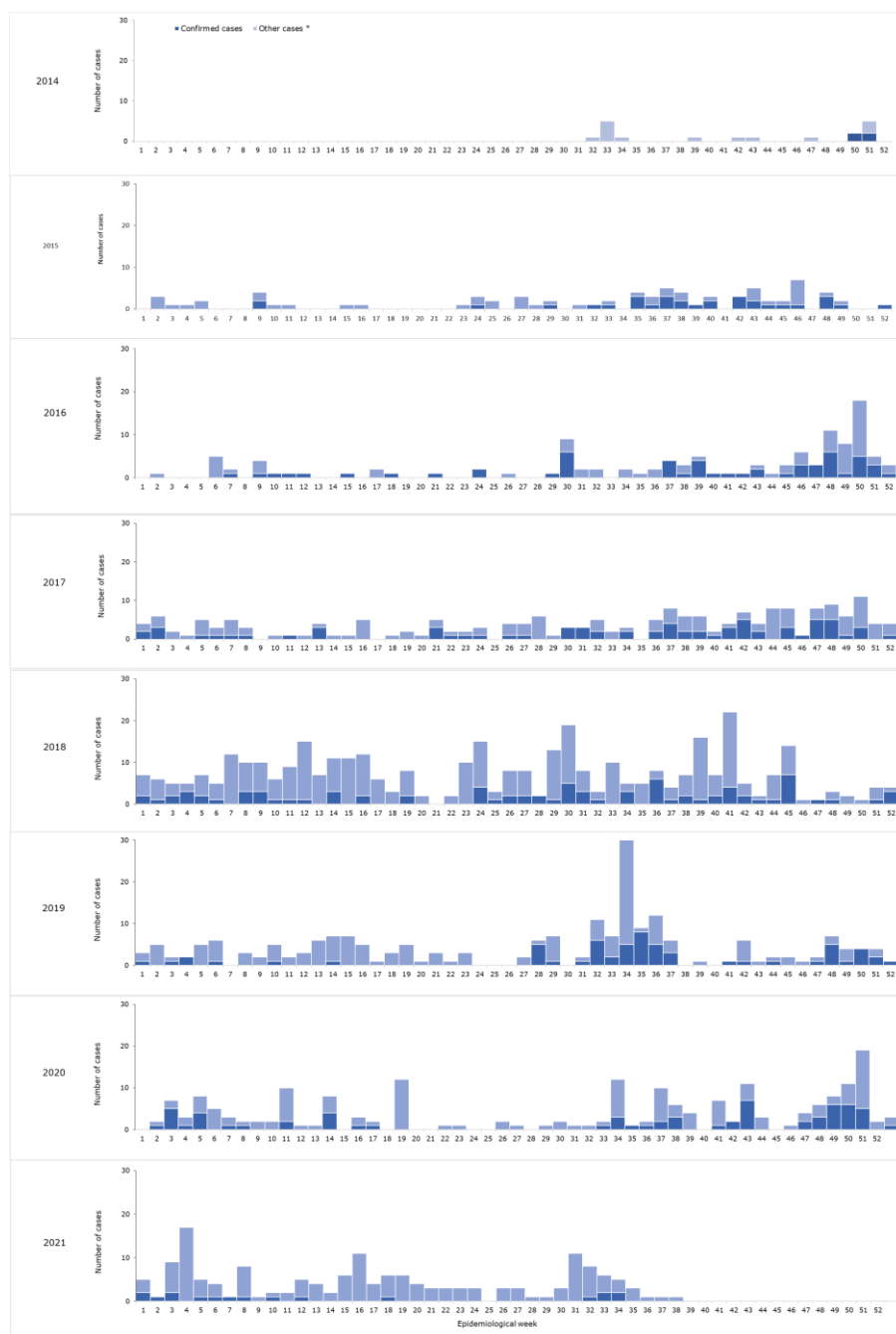
Between EW 1 and EW 38 of 2021, among the 18 confirmed cases, 55.5% occurred in the 6 to 14 years age group and 27.7% occurred in the 1 to 5 years age group. Regarding deaths, one occurred in the 6 to 14 years age group and two occurred in the 1 to 5 years age group.

<sup>6</sup> 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 pseudomembranes in the tonsils, pharynx and / or nasal pits, associated with edema of the neck.

<sup>7</sup> Preliminary data subject to change based on retrospective investigation.

Between EW 1 and EW 38 of 2021, the highest cumulative incidence rates of suspected cases were recorded in the communes of Thiotte (32 cases per 100,000 population) in the South-East Department; Terrier Rouge (20.1 cases per 100,000 population), and Carice (19.2 cases per 100,000 population) in the North-East Department; and Plaine du Nord (19.0 cases per 100,000 population) in the North Department.

**Figure 2.** Distribution of reported diphtheria cases by epidemiological week (EW) of symptom onset and year. Haiti, EW 32 of 2014 to EW 38 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 one booster, which is administered between 12 and 23 months of age. Vaccination with the diphtheria component after childhood is only carried out for pregnant women.

The country does not meet the minimum target of 95% vaccination coverage established in the regional immunization action plan for DTP3 among children under 1 year. Vaccination coverage with DTP4 is under 50%.

The country does not have a national vaccination policy for health personnel, and the vaccination of contacts of suspected cases is not systematically carried out.

## 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 and 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 to Member States the recommendation to continue efforts in ensuring vaccination coverage of more than 95% with the primary series (3 doses) and boosters (3 doses) in a uniform manner in all municipalities of the country. This vaccination schedule will provide protection throughout adolescence and adulthood (up to 39 years and possibly longer). Booster doses of the diphtheria vaccine should be administered in combination with the tetanus toxoid, using the same vaccination schedule and age-appropriate vaccine formulations: specifically, the diphtheria, tetanus, and pertussis (DPT) vaccine for children aged 1 to 7 years old, and the diphtheria toxoid (Td) vaccine for children over 7 years old, adolescents, and adults.

PAHO/WHO reiterates and urges Member States to take the necessary measures to implement the WHO recommendation to replace the tetanus toxoid (TT) vaccine with the combined diphtheria toxoid (Td) vaccine, in order to ensure sustained protection against diphtheria and tetanus. This is in accordance with the TAG recommendation in 1997<sup>8</sup> and the 2018<sup>9</sup> joint statement from WHO and UNICEF for the replacement of TT by Td.

PAHO/WHO reminds Member States that diphtheria has been controlled due to vaccinations, but that the etiological agent associated with the disease has not been eliminated nor is it the subject of an elimination program. Therefore, given the reduction in vaccination coverage among children, the decline in immunity induced by vaccines over time, and the lack of (3) booster doses in adolescents/adults, it is highly probable that diphtheria cases will occur. If vaccination coverage is not increased using the primary schedule (3 doses) and the (3) recommended boosters, the disease may once again become endemic in the Region.

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

PAHO/WHO reiterates to Member States that every opportunity should be taken to 1) complete vaccination schedules for those who are unvaccinated, or who are partially vaccinated, especially

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<sup>8</sup> Conclusions and Recommendations of the XII TAG Meeting, held in Guatemala, Guatemala, 8-12 September 1997. Available at: <https://bit.ly/2QO9LW8>.

<sup>9</sup> WHO/UNICEF joint communique. Replacement of TT with Td vaccine for dual protection. 28 June 2018. Available at: <https://bit.ly/32tbm6h>.

in densely populated areas; 2) complete the vaccination schedule when entering into military services or other institutions with similar requirements; 3) assess the vaccination status upon entering school; and 4) further promote the use of Td instead of TT for the vaccination of pregnant women as part of prenatal care, and for when tetanus prophylaxis is needed following injuries.

PAHO/WHO emphasizes that vaccination during pregnancy is recommended since transplacental maternal antibodies provide passive immunity to the newborn during the first months of life.

PAHO/WHO urges countries with ongoing diphtheria outbreaks to implement vaccination strategies based on the epidemiology of the disease, with a focus on the affected geographical areas, which may include vaccination of adults. It is important to comply with the guidelines established in the WHO Framework for Decision-Making: Implementation of Mass Vaccination Campaigns during COVID-19.

Although travelers are not particularly at-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.

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 been difficult to obtain, handle, or transport, or among cases that have started antimicrobial treatment prior to obtaining the sample.

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

PAHO/WHO urges Member States to maintain a supply of diphtheria antitoxin for its timely use and reduction of fatality rates, and to train hospital personnel on its use and administration. It should be considered that there is a very limited market for this product and that there are difficulties in transporting this product due to the COVID-19 pandemic.

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

1. **Colombia** International Health Regulations (IHR) National Focal Point (NFP) report received by PAHO/WHO via email communication.
2. **Haiti** Ministère de la Santé Publique et de la Population (MSPP) report received by PAHO/WHO via email communication.
3. **Dominican Republic** International Health Regulations (IHR) National Focal Point (NFP) report received by PAHO/WHO via email communication.
4. WHO. Diphtheria. Surveillance standards for vaccine-preventable diseases. September 2018. Available at: <https://bit.ly/3qPWosc>.
5. Sixth ad hoc Meeting of the PAHO Technical Advisory Group on Vaccine-Preventable Diseases. United States of America (virtual meeting), 16 November 2020. Available at: <https://bit.ly/2NK2Ps8>
6. Fifth ad hoc Meeting of the Technical Advisory Group (TAG) on Vaccine-Preventable Diseases. USA, 4 August 2020 (virtual meeting). Available at: <https://bit.ly/3a6vpRA>.
7. Diphtheria vaccine: WHO position paper – August 2017. Available at: <http://bit.ly/2CCN7UW>
8. WHO/UNICEF Joint Communication. Replacement of TT with Td vaccine for dual protection. 28 June 2018. Available at: <https://bit.ly/32fbm6h>
9. Final report of the 3rd ad hoc Meeting of the Technical Advisory Group (TAG). Ad-hoc Virtual Meeting, 19 March 2018. Available at: <https://bit.ly/3bVj39w>.
10. Pan American Health Organization/ World Health Organization. The Immunization Program in the Context of the COVID-19 Pandemic. Version 2 (24 April 2020). Available at: <https://bit.ly/35lZwgQ>.
11. World Health Organization. Framework for decision-making: implementation of mass vaccination campaigns in the context of COVID-19. 22 May 2020. Available at: <https://bit.ly/2Zkha0K>
12. Pan American Health Organization/ World Health Organization. Immunization throughout the Life Course at the Primary Care Level in the Context of the COVID-19 Pandemic. 17 June 2020. Available at: <https://bit.ly/3m50K6j>.
13. Pan American Health Organization/ World Health Organization. Summary of the Status of National Immunization Programs during the COVID-19 Pandemic, 19 July 2020. Available at: <https://bit.ly/2GHpO2V>.
14. Pan American Health Organization/World Health Organization. Immunization in the Americas 2020 Summary - Comprehensive Family Immunization Family, Health Promotion, and Life Course. Available at: <https://bit.ly/3CkF7a5>.
15. Pan American Health Organization, XXVI Meeting of PAHO's Technical Advisory Group (TAG) on Vaccine-Preventable Diseases. Vaccines bring us closer, 14–16 July 2021 (virtual). Available at: <https://bit.ly/3n7oeZV>