

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. Considering the decline in coverage of the diphtheria vaccine, PAHO / WHO also reminds Member States that it is important that they have a plan to maintain a permanent supply of diphtheria antitoxin to control possible outbreaks.

Summary of the situation in the Americas

In 2021, between epidemiological week (EW) 1 and EW 24, three countries have reported confirmed cases of diphtheria: Brazil with one (1) confirmed case, the Dominican Republic with 13 confirmed cases including 10 deaths, and Haiti with 12 confirmed cases including 2 deaths.

In recent years and mainly during the pandemic due to COVID-19, 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. Additionally, vaccination among the younger population and adults, especially men, continues to be very low. Therefore, the occurrence of confirmed cases is considered a risk for the rest of the countries and territories in the Region of the Americas.

The following is the epidemiological situation for diphtheria in Brazil, the Dominican Republic, and Haiti, the three countries that have reported new confirmed cases of diphtheria since the previous Epidemiological Update for Diphtheria published on 23 April 2021¹.

In **Brazil**, between EW 1 and EW 24 of 2021, 11 suspected cases of diphtheria were reported, of which one was laboratory-confirmed, 8 were discarded and 2 remain under investigation.

In 2021, as of EW 24, one confirmed case has been reported. The case is a 26-year-old male who had symptom onset on 24 April 2021. The case had an incomplete vaccination schedule of a single dose received on 26 July 2011, had no travel history, and is a resident of Alta Floresta Municipality in the state of Mato Grosso. The case was culture-confirmed. During the field investigation and contact follow-up, no other cases were identified among the contacts.

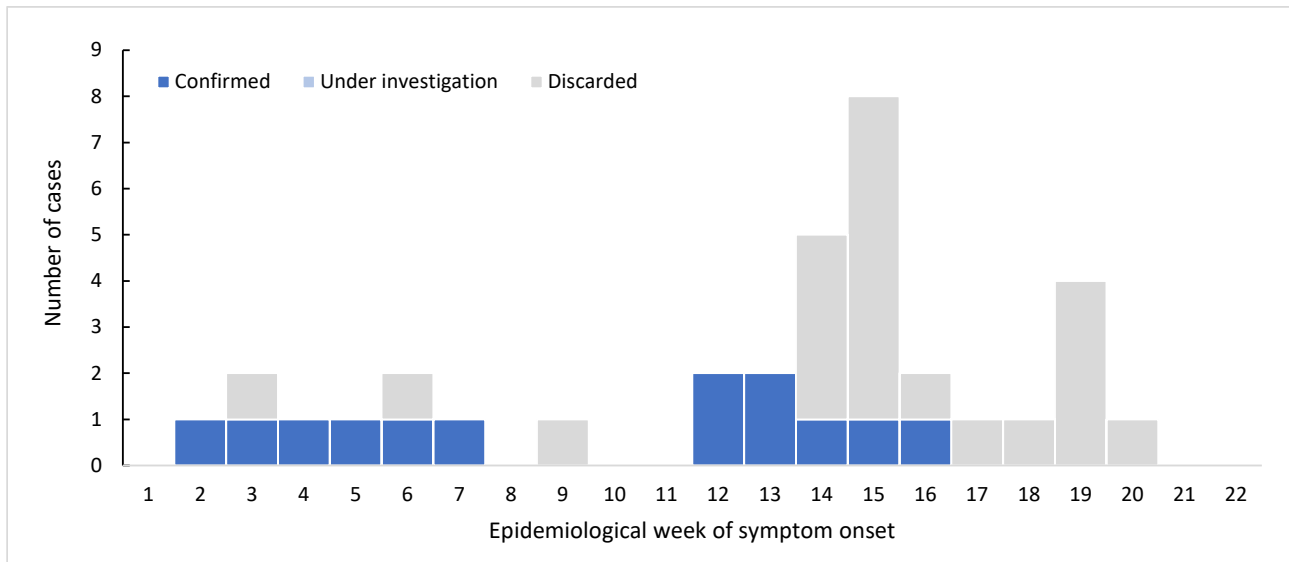
In *Brazil*, between 2019 and 2020, 59 suspected cases of diphtheria were reported, of which 5 (8.4%) were confirmed, with no deaths reported. The federal units that reported the confirmed cases were Pernambuco (1 case), Rondônia (1 case), Minas Gerais (1 case), Rio Grande do Sul (1 case), and Mato Grosso (1 case).

¹ Pan American Health Organization / World Health Organization. Epidemiological Update: Diphtheria in Hispaniola. 23 April 2021, Washington, D.C.: PAHO/WHO; 2021. Available at: <https://bit.ly/3xEg4Md>

In the **Dominican Republic**, between EW 1 and EW 22 of 2021, a total of 35 probable cases of diphtheria were reported, of which 13 were confirmed, including 10 deaths (11 by Elek test and 2 by epidemiological link), and 22 were discarded (**Figure 1**). Information regarding the first 12 cases was shared in the 23 April 2021 Epidemiological Update¹.

In 2021, the most recent confirmed fatal case reported is a 1-year-old Dominican female who had symptom onset on 21 April 2021. The case had no travel history nor vaccination history, and was a resident of Monte Plata Province. This case was confirmed by laboratory criteria.

Figure 1. Distribution of reported cases of diphtheria by epidemiological week (EW) of symptom onset. EW 1 to EW 22 of 2021, the Dominican Republic.



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

Corynebacterium diphtheriae was isolated by culture from samples for 11 of the cases. All of these 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).

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 is not done routinely with the third diphtheria booster.

The country has a national vaccination policy for health personnel.

The country does not meet the 95% vaccination coverage target 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 22 of 2021, there were 1,281 suspected cases² of diphtheria reported, including 146 deaths. Of the total cases, 400 were confirmed (386 laboratory-confirmed and 14 by epidemiological link), including 79 confirmed deaths (**Table 1, Figure 2**).

Table 1. Suspected and confirmed cases of diphtheria reported in Haiti, 2014-2021 (until epidemiological week 22 of 2021)³.

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	111	12	2	17%
Total	1,281	400	79	20%

*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 22 of 2021, the number of suspected cases reported (111 cases) is higher than the number reported during the same period in both 2019 (71 cases) and 2020 (69 cases). Of the 111 cases reported, 12 were laboratory-confirmed, including 2 deaths. Considering the long duration that the disease has been transmitted within the country, 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.

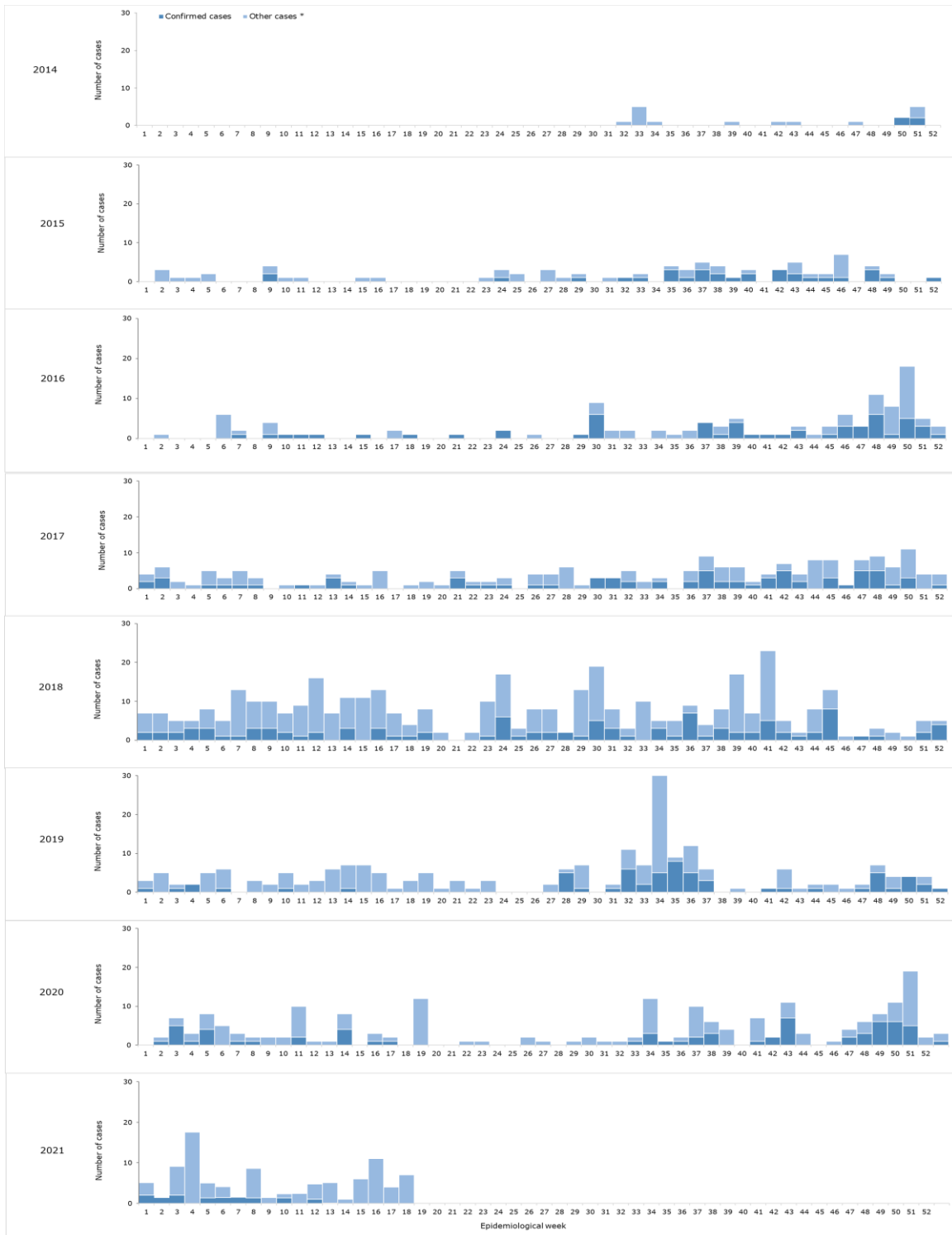
Between EW 1 and EW 22 of 2021, among the 12 confirmed cases, 58% were among 6 to 14-year-olds and 25% among 1 to 5-year-olds. Regarding deaths, one (1) among 1 to 5-year-olds and one (1) was among 6 to 14-year-olds.

Between EW 1 and EW 22 of 2021, the highest cumulative incidence rates of suspected cases have been reported in the communes of Thiotte (16 cases per 100,000 population) and Cayes Jacmel (9 cases per 100,000 population) in the Sud-Est Department; and Terrier Rouge (9 cases per 100,000 population) in the Nord-Est Department.

² 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.

³ Preliminary data subject to change based on retrospective investigation.

Figure 2. Distribution of reported diphtheria cases by epidemiological week (EW) of symptom onset and year. EW 32 of 2014 to EW 22 of 2021, Haiti.



*'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 95% vaccination coverage target 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, 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) in a homogeneous manner in all municipalities of the country. 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 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, to ensure sustained protection against diphtheria and tetanus. This is in accordance with the TAG recommendation in 1997⁴ and the 2018⁵ 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 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 following 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.

⁴ Conclusions and Recommendations of the XII TAG Meeting, held in Guatemala, Guatemala, 8-12 September 1997. Available at: <https://bit.ly/2QO9LW8>

⁵ WHO/UNICEF joint communique. Replacement of TT with Td vaccine for dual protection. 28 June 2018. Available at: <https://bit.ly/32t6m6h>

PAHO/WHO reiterates to the Member States that opportunities should be taken to 1) complete vaccine schedules for those who were not vaccinated, or are partially vaccinated, especially in densely populated areas or; 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 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, focused 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 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 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, as well as the difficulties in transporting them due to the pandemic of COVID-19.

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. **Brazil** International Health Regulations (IHR) National Focal Point (NFP) report received by PAHO/WHO via email communication.
2. **Dominican Republic** International Health Regulations (IHR) National Focal Point (NFP) report received by PAHO/WHO via email communication.
3. **Haiti** Ministère de la Santé Publique et de la Population (MSPP) 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), November 16, 2020. Available at: <https://bit.ly/2NK2Ps8>
6. 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>
7. Diphtheria vaccine: WHO position paper – August 2017. Available at: <http://bit.ly/2CCN7UW>
8. WHO/UNICEF joint communique. Replacement of TT with Td vaccine for dual protection. 28 June 2018. Available at: <https://bit.ly/32tbm6h>
9. 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>
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/3m50K6i>
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>