Epidemiological Alert
Risk of dengue outbreaks due to increased circulation of DENV-3 in the Americas Region

Corrigendum[1] - 10 February 2025

The occurrence and magnitude of dengue outbreaks are usually associated with the introduction or increase in circulation of a serotype other than the one that previously predominated in an affected region. Given the risk of an increase in the circulation of DENV-3 in the southern hemisphere of the Americas Region during the peak dengue season, the Pan American Health Organization / World Health Organization (PAHO/WHO) urges Member States to prepare for a possible increase in cases and ensure early diagnosis and timely care dengue and other arbovirus cases, in order to prevent severe cases and deaths associated with these diseases.

Summary of the situation in the Americas Region

In 2024, there was a historic increase in dengue cases in the Americas Region with 13,027,747 cases reported by 50 countries and territories. Of this total, 6,906,396 were laboratory-confirmed, 22,684 were characterized as severe dengue (0.17%) and 8,186 were fatal cases (case fatality rate 0.063%). The countries that reported the highest proportion of cases were Brazil with 10,232,872 cases, Argentina with 581,559 cases, Mexico with 558,846 cases, Colombia with 320,982 cases, and Paraguay with 295,785 cases *(1)*.

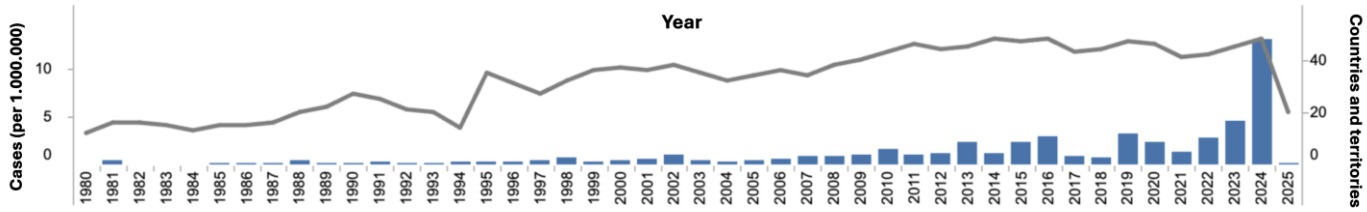
Between epidemiological week (EW) 1 and EW 4 of 2025, 23 countries and territories in the Americas Region have reported 238,659 suspected cases of dengue (**Figure 1**) *(1)*. The six countries that concentrate 98% of these cases in the Region are Brazil, with 194,564 cases (87%), Colombia with 12,740 cases (5.6%), Nicaragua with 5,702 cases (2.5%), Peru with 5,735 cases (2.5%), and Mexico with 5,649 cases (2.5%) *(1)*. Between EW 1 to EW 4 of 2025, of the total suspected cases reported, 57,899 (24%) were laboratory-confirmed. Of this total, 263 were characterized as severe dengue (0.11%) and 23 fatal cases were registered (case fatality rate 0.010%) *(1)*.

Up to EW 4 of 2025, all four serotypes of the dengue virus are circulating in the Americas Region. Brazil, Costa Rica, El Salvador, Mexico, and Panama report simultaneous circulation of the four serotypes (DENV-1, DENV-2, DENV-3, and DENV-4) *(1)*.

[1] This corrigendum to the epidemiological alert originally published on 7 February 2025, includes the clarification that the dengue cases described in 2025 in the Americas Region are suspected cases; this corrigendum has been made on page 1.

Suggested citation: Pan American Health Organization/World Health Organization. Epidemiological Alert: Risk of dengue outbreaks due to the increased circulation of DENV-3 in the Americas Region. 7 February 2025. Washington, D.C.: PAHO/WHO; 2025.

Figure 1. Total number of reported dengue cases and number of countries and territories, 1980 – 2025 (up to EW 4) in the Americas Region.



Source: Adapted from the Pan American Health Organization. PLISA Health Information Platform for the Americas, Dengue Indicators Portal. Washington, D.C.: PAHO; 2025 [cited 3 February 2025]. Available from: https://www3.paho.org/data/index.php/en/dengue.html.

Figure 2. Dengue cases in 2024 - 2025 (up to EW 4) and last 5-year average, Americas Region.

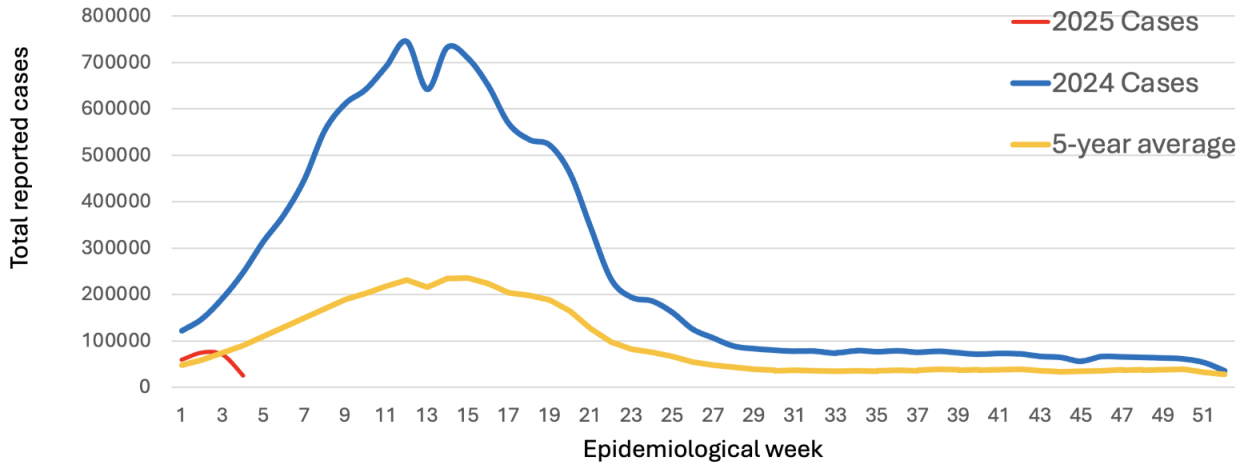


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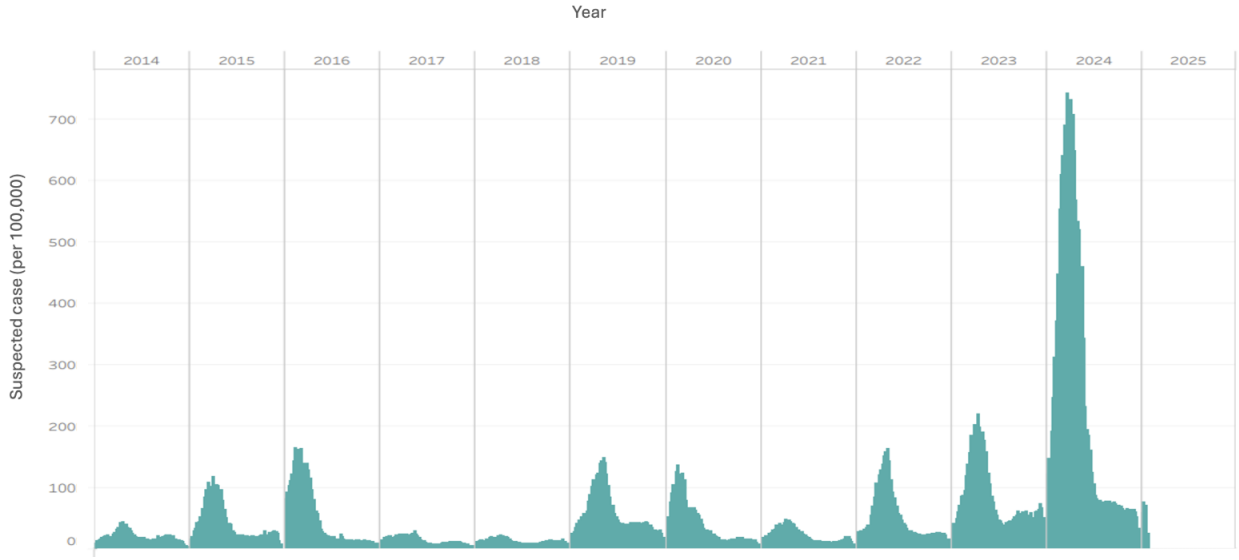
Figure 3. Dengue cases in 2014 - 2025 (up to EW 4), Americas Region.



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Circulation of Dengue Serotype 3 in the Americas Region

The dengue virus has four different serotypes: DENV-1, DENV-2, DENV-3, and DENV-4, which circulate in the Americas *(1)*. The available evidence suggests that infection with one serotype confers lifelong immunity to that serotype. However, subsequent infections with other serotypes have also been shown to increase the risk of severe disease. The interaction between these serotypes and the population has significant implications for the occurrence and magnitude of outbreaks, which are usually associated with the introduction or increase in circulation of a serotype different from the one that previously predominated in a region due to the susceptibility of the population.

The following report will analyze epidemiological data regarding the risk of increased circulation of DENV-3 in the southern hemisphere of the Americas Region and a possible increase in dengue cases with greater severity, due to the susceptibility of infection by this serotype in the population.

Status of DENV-3 in the Americas Region

A study conducted in 2010 *(2)* analyzed the epidemic behavior of dengue from 1980 to 2007, pointing to a significant increase in reported cases, from approximately one million cases in the 1980s to 4.7 million during the 2000-2007 period. The most frequently isolated serotypes during the 1990s were DENV-1 and DENV-2, while in the period 2000-2007, the most frequent were DENV-2 and DENV-3.

In 1994, the DENV-3 serotype was reintroduced to the Americas after a 16-year absence. Colombia and Puerto Rico reported this serotype in 1977 and 1978 *(3)*, but it was not detected

again until 1994, in Nicaragua and Panama. Initially, DENV-3 spread throughout the Central American Isthmus and Mexico subregion, and then reached Puerto Rico, other Caribbean islands, and South America. In 2000, DENV-3 was detected in Rio de Janeiro, Brazil causing a large-scale outbreak that lasted three years. Although DENV-3 was the predominant serotype and the only one linked to fatal cases, DENV-1 and DENV-2 s were also detected. Subsequently, DENV-3 spread to more cities in Brazil *(4)*. The circulation of DENV-3 increased throughout the Americas Region after its introduction in the Andean and Southern Cone subregions[2] in the year 2000 *(1)*.

In 2024, **Argentina** reported the circulation of DENV-3, marking the introduction of a new genotype for this serotype in the country and the Region. The cases were identified in the province of Entre Ríos. While the circulation of DENV-3 was limited, representing 0.19% of the cases serotyped, this finding represents a risk of introduction and spread of this serotype *(5)*.

In 2023, **Brazil** again documented the circulation of DENV-3 *(6)*. Prior to 2023, the last outbreaks associated with DENV-3 occurred in the period from 2003 to 2008, when this serotype was the most prevalent. This serotype, introduced from South Asia, had not previously been detected in the Americas Region *(7, 8)*. The prolonged absence and lack of recent circulation of the DENV-3 serotype in Brazil could increase the susceptibility of the population (especially in persons under 15 years of age), underscoring the importance of early detection and continuous monitoring of its spread. The Brazil Ministry of Health alerted about the risks of the new circulation of this serotype *(9),* informing the population that DENV-3 is one of the most virulent, associated with more severe clinical manifestations together with DENV-2 *(10)*.

In 2024, **Colombia** documented the expansion of the areas of DENV-3 circulation, to areas where serotypes DENV-1 and DENV-2 had been the most prevalent. The first isolations of DENV-3 were reported in the Casanare region and were associated with cases of severe dengue and deaths in children *(11)*.

In **Costa Rica**, between 2019 and 2021, the circulation of DENV-3 was not reported in the country, however, in 2022 this serotype represented 0.18% of the total serotyped samples, a percentage that increased to 25% during 2023. During 2024, DENV-3 was the predominant serotype in the country, with 56% of the total serotyped samples *(12)*.

In **Guatemala**, in August 2024, the results of the surveillance of the dengue virus in Guatemala showed that 77% of the samples analyzed corresponded to DENV-3. By the end of 2024, 83% of serotype determinations corresponded to DENV-3, 12% to DENV-2, 4% to DENV-1 and less than 1% to DENV-4. The highest number of deaths occurred in pediatric patients (under 15 years of age, 66% of cases) *(13, 14)*.

In **Mexico**, between 1995 and 2008, constant circulation of DENV-3 was recorded, reaching its maximum level in 1997, with 88% of samples positive for this serotype of the total serotyped samples. Between 2009 and 2021, the circulation of DENV-3 was low, with annual values ranging

[2] Note: Subregions and corresponding countries and territories follow the divisions described in PLISA Health Information Platform for the Americas, Dengue Indicators Portal. Washington, D.C.: PAHO; 2025 [cited 3 February 2025]. Available from: https://www3.paho.org/data/index.php/en/dengue.html

from 0.1% to 6% of the total. However, a notable increase in circulation was observed in 2022 (25%), 2023 (59%), and 2024 (86%) *(15)*.

In **Nicaragua**, a pediatric dengue cohort study started in 2004/2005 showed that DENV-2 and DENV-3 have been the most common serotypes over the past 20 years, with secondary infections predominant for DENV-2 and similar numbers of primary and secondary infections for DENV-3. DENV-3 was associated with greater severity in both primary and secondary infections under the 1997 and 2009 World Health Organization (WHO) classifications, whereas DENV-2 was more associated with greater severity under the 1997 classification in secondary cases. The analysis did not include DENV-4 due to the limited number of cases caused by this serotype in these studies *(16)*.

In 2024, in **Peru** the circulation of DENV-3 was identified in the regions of Lima, Loreto, San Martín, Piura, Cajamarca, Amazonas, Ancash, Ica, Callao, Ayacucho, Huánuco, and Ucayali regions where previously only the presence of DENV-1 and DENV-2 had been reported *(17)*.

In **Puerto Rico**, after more than ten years of DENV-1 predominance, the proportions of DENV-2 and DENV-3 serotypes increased significantly during 2023-2024, with DENV-3 replacing DENV-1 as the predominant serotype *(18)*.

Public health impact

The reappearance of a serotype that did not circulate in the last decade, such as DENV-3, combined with the increase in the susceptible population, not only increases the probability of severe cases of dengue, but could also cause epidemics that overload health services, exceeding their capacity to respond. The risk of DENV-3 circulation in the Americas Region is high due to the widespread distribution of mosquito vectors, human mobility, and partial (and in many areas absent) immunity in the populations. Recent data indicate an increase in the circulation of DENV-3, highlighting the urgent need to implement integrated and effective strategies to control the spread of the virus. On the other hand, one studied showed that the dengue vaccine TAK-003 from the producer Takeda demonstrated lower protection against DENV-3 compared to serotypes DENV-1 and DENV-2, especially in seronegative children (without a history of dengue), in whom protection was not demonstrated against symptomatic disease or hospitalization caused by DENV-3 *(19)*.

PAHO/WHO stresses the importance of strengthening epidemiological surveillance, clinical management, and laboratory confirmation, as well as improving monitoring systems and promoting prevention campaigns to reduce the incidence of dengue. Likewise, in countries that have introduced the vaccine, it is very important to strengthen safe vaccination procedures and surveillance of events supposedly attributable to vaccination or immunization (ESAVI).

Guidance for national authorities

The following are key recommendations related to surveillance, case management, adequacy of health care services, diagnosis, prevention measures, communication, and community participation.

Surveillance

PAHO/WHO encourages continued epidemiological surveillance and the reporting of suspected and confirmed cases of dengue, chikungunya, Zika, and Oropouche.

Since clustering of cases is common in these diseases (dengue, chikungunya, Zika, and more recently, Oropouche), efforts should be made to analyze the spatial distribution of cases to allow for a rapid response at the local level from the most affected areas. Information on the hotspots of these diseases should be directed for intensive vector control.

Sentinel entomological surveillance contributes to assessing changes in the risk of vector-borne diseases and the impact of vector control measures.

In countries that have implemented vaccination, there is a need to harmonize dengue surveillance activities with ESAVI surveillance in the detection, case reporting, and investigation processes, in accordance with PAHO's ESAVI surveillance guidelines *(20)*.

All cases of severe dengue in vaccinated people should be immediately reported to the national ESAVI surveillance teams and follow the appropriate operating procedures.

Case management

Measures to ensure adequate clinical management of suspected cases of dengue should be a priority. Capacities must be strengthened at the primary health care level and from this level prevent progression to severe forms and deaths from dengue. For this, it is necessary for healthcare workers to make an early clinical diagnosis and recognize warning signs in dengue (such as intense and sustained abdominal pain or tenderness of the abdomen, persistent vomiting, clinical accumulation of fluid, bleeding of the mucosa, lethargy, restlessness, enlargement of the liver> 2 cm below the rib rim, and progressive increase in hematocrit) in order to initiate appropriate management in accordance with the recommendations published in PAHO clinical guidelines *(21, 22)*. In cases where dengue is suspected, healthcare workers should provide clear guidance to patients and/or families to monitor for warning signs and seek immediate medical attention should at least one of these signs occur. These measures will also help to reduce the number of patients who must be referred to hospitals, thus avoiding the saturation of these facilities and intensive care units (ICU). At the same time, all second- and third-level hospitals must be prepared to handle cases of dengue with warning signs and cases of severe dengue.

It is important that prior to the season of increased transmission of dengue (and other arboviruses), the healthcare workers in charge of the clinical care of these cases are properly trained. PAHO has a free virtual course on dengue for this purpose, currently available in Spanish through its Virtual Campus of Public Health *(23)*. More information on the clinical management of dengue cases is available in the PAHO published Guidelines for the clinical diagnosis and treatment of dengue, chikungunya, and Zika *(21)* and the Tool for the diagnosis and care of patients with suspected arboviral diseases *(22)*.

PAHO reiterates the recommendations for technical teams in charge of malaria control, which also apply to personnel involved in arbovirus care, available from: https://iris.paho.org/handle/10665.2/52080 *(24)*.

Adequacy of healthcare services

In view of a possible increase in the incidence of dengue in the Region, Member States are urged to prepare their healthcare services to provide a timely and correct response to the population at all levels of care.

- Organize screening, patient flow, and clinical surveillance and hospitalization areas in each institution, at different levels of care.
- Reorganize health services in outbreak/epidemic situations at different levels of patient care, to avoid overcrowding of hospitals.
- Strengthening of patient care networks in the clinical diagnosis, management, follow-up, as well as referral and counter-referral of patients with suspected dengue, chikungunya, or Zika.

Laboratory diagnosis

It is important to keep in mind that the initial diagnosis of dengue virus (DENV) infection is clinical, and adequate suspicion can guide the confirmation protocol. Laboratory results should be analyzed with clinical information and according to epidemiological context, for surveillance purposes and not for clinical decision-making.

Laboratory confirmation of dengue infection is based on virological tests (RT-PCR, detection of NS1 antigen by ELISA, and in some cases viral isolation in culture for further characterization) and serological tests (detection of IgM). However, for the confirmation of cases, virological assays that demonstrate the presence of the whole virus, its genetic material or its proteins should be prioritized. Virological assays for dengue are performed on serum samples taken during the first 5 days after the onset of symptoms (acute phase) (**Figure 4**) *(25)*.

On the other hand, serological assays based on the detection of IgM should be analyzed carefully, taking into account the time that antibodies circulate in the blood after an infection, as well as the possibility of cross-reaction with other flaviviruses (including Zika, yellow fever, and others) and non-specific detection. Thus, a single IgM result in a patient only indicates contact with the virus, these cases being defined as a probable case of dengue. A second sample taken at least one week apart, processed in parallel with the first and with a quantitative serological assay (PRNT, for example) that allows to demonstrate seroconversion or increase in the antibody titer, may be useful to clarify the diagnosis (**Figure 5**) *(25)*.

It is important to have a clear laboratory algorithm that allows for early detection. Although multiple molecular methodologies (*multiplex* PCR) are useful when there is no clear clinical suspicion, in the case of dengue that meets the established definitions and where the clinical symptoms are compatible, it is suggested to prioritize protocols for specific detection (*singleplex*) of the virus *(25)*.

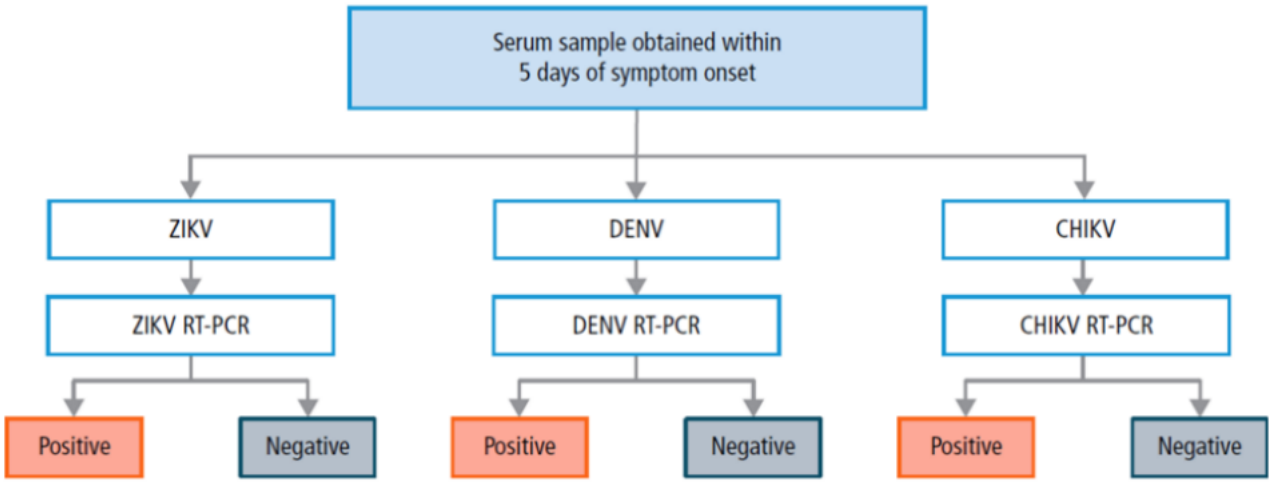
In suspected cases of dengue in vaccinated people, the algorithm established in the technical note published specifically for that population should be followed, which is available from: https://www.paho.org/en/documents/technical-note-detection-and-differentiation-dengue-virus-context-dengue-vaccine *(26)*.

In fatal cases, tissue samples (liver, spleen, kidney) must be analyzed both for the detection of genetic material (RT-PCR) and for histopathological and immunohistochemical study. Biopsies in a patient with suspected dengue fever are completely contraindicated. In cases of death of people vaccinated against dengue, they should be immediately notified to the ESAVI surveillance system and a thorough investigation should be carried out in accordance with the national protocol and the corresponding regional recommendations.

On the other hand, the use of immunochromatographic tests, also known as rapid tests (NS1 and/or antibodies) is not recommended since due to their low sensitivity false negative results can be obtained; Its use should be limited to community studies under established protocols, but in no case to rule out infection or to implement medical conduct.

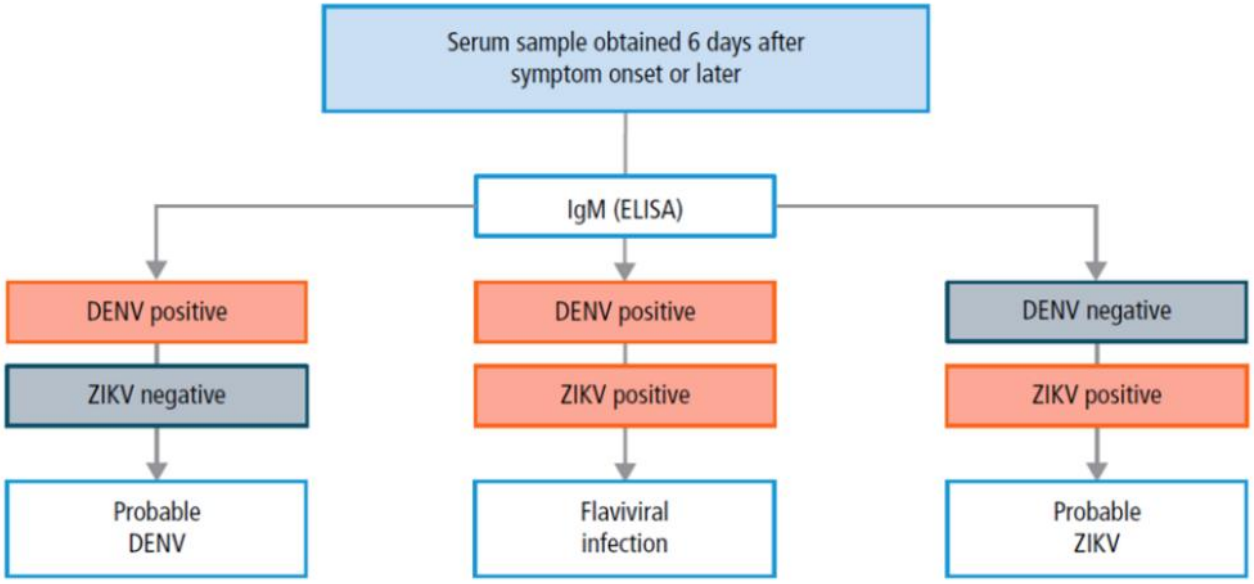
Since laboratory services are a key component of dengue epidemiological and virologic surveillance, timely detection and characterization of appropriate specimens should be maintained. As far as possible and depending on the capacities of each laboratory, it is recommended to take samples from 100% of those cases characterized as **severe and fatal cases** of dengue, while only a proportion of those cases with or without warning signs will be necessary for surveillance (10-30% or a maximum number of samples depending on the installed capacity).

Figure 4. Algorithm for virological testing in suspected cases of dengue, chikungunya, and Zika



Source: Pan American Health Organization. Recommendations for Laboratory Detection and Diagnosis of Arbovirus Infections in the Region of the Americas. Washington, D.C., PAHO; 2022. Available from: https://iris.paho.org/handle/10665.2/57555.

Figure 5. Algorithm for serological testing in suspected cases of dengue and Zika



Source: Pan American Health Organization. Recommendations for Laboratory Detection and Diagnosis of Arbovirus Infections in the Region of the Americas. Washington, D.C.: PAHO; 2022. Available from: https://iris.paho.org/handle/10665.2/57555.

Genomic surveillance and characterization of DENV-3 *(6-8)*

Dengue genomic surveillance in the Americas plays a crucial role in monitoring the evolution, transmission, and spread of different serotypes and genotypes of DENV. With the increasing frequency and severity of outbreaks in the region, genomic sequencing has become a useful tool for public health authorities to identify emerging variants, monitor viral diversity, and detect potential changes in transmission dynamics early.

DENV-3 consists of five distinct genotypes (I–V), with genotype III (GIII) being the most widespread and detected in major outbreaks in Asia, Africa, and the Americas. Originating in South Asia in the mid-1970s, GIII was introduced to the Americas in the 1990s, where it established an endemic lineage, GIII-American-I, which evolved separately from its Asian counterpart. This lineage was widely transmitted across the continent for more than two decades, with the most recent sequences reported in Mexico in 2021. In Brazil, the first autochthonous case of the GIII-American-I lineage was detected in 2000 in Rio de Janeiro. Multiple introductions from the Lesser Antilles contributed to its rapid spread, particularly in the southeastern and northern regions. However, since 2010, DENV-3 has accounted for less than 1% of serotyped dengue cases in Brazil, with little confirmed transmission in recent years.

In 2023, a new introduction of DENV-3 GIII was detected in northern Brazil, also native to South Asia. The phylogeographic analysis showed that the circulating DENV-3 corresponds to the American-II lineage, different from the one previously detected. Analyses conducted so far point to the Caribbean as the most likely introduction site, although the results may be skewed due to the lack of representative DENV-3 genomes from most Caribbean countries. The

introduction and establishment of this lineage coincides with an epidemic of DENV-3 in Jamaica during 2018-2019, the largest in 40 years, and subsequently the rapid expansion in Central America, where the circulation of the new lineage has been demonstrated. The findings so far support the hypothesis that DENV-3 GIII-American-II was introduced from India to the Caribbean around 2018-2019 and subsequently spread to Central America, South America, Brazil, Suriname, and Florida during 2022-2023, highlighting the importance of continuous genomic surveillance to monitor its transmission dynamics.

As dengue continues to pose a major public health threat in the Americas, integrating genomic surveillance into routine monitoring of the disease contributes to improving early warning systems and mitigating future outbreaks.

Prevention and control measures for *Aedes*

PAHO/WHO urges Member States to make effective use of available resources to prevent and/or control vector infestation in affected areas and in health services. This can be achieved through the implementation of integrated entomological surveillance and vector control strategies, which include the following processes:

- Identify and mobilize material, human and financial resources to promote the execution of strategic vector surveillance and control actions in areas at risk.
- Selection of surveillance and control methods based on knowledge of vector biology and disease transmission dynamics at the local level.
- Use of multiple surveillance, prevention and control interventions, often in combination and synergistically.
- Collaboration of the health sector with public and private sectors linked to environmental management whose work impacts the reduction of vector populations.
- Integration of individuals, families and other key partners (education, finance, tourism, water and sanitation, and others) into prevention and control activities.

Strengthening of the legal framework that allows for an integrated and intersectoral approach. Given the high infestation by *Aedes aegypti* and the presence of *Ae. albopictus* in the Region, it is recommended that prevention and control measures be aimed at reducing the density of the vector and have the acceptance and collaboration of the local population. The prevention and control measures to be implemented by national and/or local authorities must include the following:

- Strengthen environmental management actions, mainly the elimination of breeding sites of the vector in homes and common areas (health centers, parks, schools, cemeteries, etc.).
- Reorganize solid waste collection services to support breeding site elimination actions, prioritizing areas of greatest transmission and, if necessary, plan intensive actions in specific areas where regular garbage collection has been interrupted.
- Apply measures for the control *(27)* of breeding sites through the use of physical, biological and/or chemical methods, which actively involve individuals, the family and the community.

- Define areas of high risk of transmission (risk stratification) *(28)* and prioritize those where there are concentrations of people (schools, terminals, hospitals, health centers, etc.). In these facilities, the presence of the mosquito must be eliminated in a diameter of at least 400 meters around. It is important to pay special attention to healthcare units, so that they are free of the presence of the vector and its breeding sites and do not become points of radiation of the virus.
- In areas where active transmission is detected, it is suggested to implement measures aimed at eliminating infected adult mosquitoes (mainly through the use of insecticides) in order to stop and cut transmission. This action is of an exceptional nature and is only effective when it is carried out with duly trained personnel under internationally accepted technical guidelines; and when it is carried out concomitantly with the other proposed actions. The main action to interrupt transmission when it occurs intensively is the elimination of adult mosquitoes infected with the Dengue virus (active transmission) through indoor fumigation, using individual equipment or spatial fumigation using heavy equipment mounted on vehicles, in addition to the destruction and/or control of vector breeding sites within homes and their surroundings *(29)*.
- An effective adult control modality that can be used, considering the operational capabilities available, is indoor residual spraying, which should be applied selectively to *Ae. aegypti* resting places, taking care not to contaminate food, drinking water storage containers or those used for cooking. This intervention in treated areas is effective for a period of up to four months and can be used in shelters, homes, health services, schools, and others. For more information, see the PAHO Manual for indoor residual spraying in urban areas for *Aedes aegypti* control *(30)* and the guidance on Control *of Ae. aegypti* in the scenario of simultaneous transmission of COVID-19 *(31)*.
- Appropriately choose the insecticide to be used (following PAHO/WHO recommendations), its formulation, and to be aware of the susceptibility of *Aedes* populations to this insecticide *(32)*.
- Guarantee the proper functioning of fumigation equipment and its maintenance and ensure insecticide reserves.
- Intensify supervision actions (quality control and coverage) of the field work of operators, both indoor fumigation actions with individual equipment, and spatial fumigation tasks with heavy equipment mounted on vehicles, ensuring compliance with personal protection measures.

PAHO also reiterates the recommendations for technical teams in charge of vector control *(28, 29)*.

Personal prevention measures

Patients infected with dengue, chikungunya, and/or Zika viruses are the reservoir of infection for others both in their homes and in the community. It is necessary to communicate to patients, their families and the affected community about the risk of transmission and ways to prevent contagion by reducing the vector population and contact between the vector and people.

To minimize vector-patient contact, it is recommended to:

- A patient should rest under mosquito nets, impregnated, or not, with insecticide.
- Sick people, as well as other members of the household, should wear long sleeves to cover the limbs.
- Repellents containing DEET, IR3535 or Icaridin, can be applied to exposed skin or clothing, and their use must be in strict accordance with the instructions on the product label.
- Use wire-mesh/mosquito nets on doors and windows.

Communication and community engagement

PAHO recommends establishing and implementing a rapid communication action plan focused on:

- Measures to prevent the formation of breeding sites of the vector and elimination of such sites to prevent transmission, and
- Information on symptoms and warning signs of dengue when the epidemiological situation of the country requires it, such as in the face of the increase in cases or cases of deaths due to dengue.

PAHO recommends taking into account as main audiences: individuals, pregnant women, parents and caregivers, communities, neighborhood councils, educational centers, municipalities, public and private sectors: messages on measures to prevent the formation of vector breeding sites and their elimination to avoid the transmission of arboviruses.

Audiences:

- Individuals, communities, neighborhood committees, municipalities, public and private sectors: messages on measures to prevent the formation of vector breeding sites and elimination of these to avoid the transmission of dengue and other arboviruses. Also, information about the warning signs of dengue to seek immediate medical attention.
- Health workers (including nurses, doctors, and first level care personnel and hospitals) and technicians of the vector control program: information on symptoms and warning signs of dengue that are present or increasing in the country.

Every effort should be made to obtain community support for dengue prevention and control.

Simple Information, Education, and Communication (IEC) materials can be disseminated through various media outlets (including social media or closed-circuit television (CCTV) in primary care health units).

The population and household members should be encouraged to eliminate mosquito breeding sources, both domestic and peri domiciliary. This is a task for everyone: the family, the community, the public and private sectors.

Highly productive mosquito breeding sites, such as water storage containers (drums, elevated tanks, clay pots, etc.) should be subject to prevention measures against vector breeding. Other breeding sites, such as roof gutters and other water-holding containers, should also be cleaned periodically.

Both health care personnel and affected communities should be encouraged to know the symptoms of dengue, as well as its warning signs and how to act in the event of such manifestations.

Working with local teams is encouraged, as they know how to make this information more effective, and in many cases national campaigns and messages are not as effective as local initiatives *(27)*.

Vaccination

General aspects:

- The currently authorized dengue vaccine is not expected to have a major impact on the epidemiological behavior of the disease in the short or medium term.
- Should any Member State decide to introduce the TAK-003 dengue vaccine, PAHO's Strategic Advisory Group (SAG) on Vaccine-Preventable Diseases (VPD) (formerly Technical Advisory Group/TAG) recommends that a pilot project be implemented initially, as part of a robust post-marketing phase 4 study *(33)*.
- Brazil and Argentina have identified a safety signal[3] consisting of a risk of post-vaccination anaphylaxis between 8 and 28 times higher compared to other vaccines (Brazil: 44 cases per million doses administered as of March 2024; Argentina: 14 cases per million doses administered as of September 2024) *(33- 36)*. It is necessary for countries to incorporate measures for timely identification and treatment of adverse events, prioritizing intramural vaccination.

Vaccination recommendations (37, 38):

The WHO Strategic Advisory Group of Experts on Immunization (SAGE), the PAHO Strategic Advisory Group on Immunizations (SAG), and the PAHO Special Program on Comprehensive Immunization (CIM) technical team recommend:

- **Scenario of use**: Introduction of the vaccine in settings with a high burden of disease and high transmission intensity can be considered. The SAG recommends that any introduction of the TAK-003 vaccine be conducted with a pilot project and be accompanied by a robust post-marketing Phase 4 study.
- **Age**: Children from 6 to 16 years old. Countries wishing to introduce this vaccine should have an adequate vaccination service for adolescents.
- **Special groups**: WHO recommends vaccination of people aged 6 to 60 years with comorbidities residing in endemic areas. Comorbidities include sickle cell anemia, diabetes, hypertension, or underlying conditions that predispose to hemorrhagic diathesis.

[3] **Signal**: Information from one or multiple sources (including observations and experiments) that suggests a potential new causal association or a new aspect of a known association between an intervention and a related, adverse, or beneficial event or set of events that is judged to be sufficiently likely to warrant verification action. When the effect is deleterious, it is a sign of safety. In this particular case of the anaphylaxis signal, the association under study is the relationship between the TAK-003 vaccine and this adverse event *(33)*.

- **Travelers**: WHO recommends vaccination of people aged 6 to 60 years from non-endemic countries traveling to endemic countries.
- **Contraindications**: It is contraindicated in pregnant women, breastfeeding women, people with congenital or acquired immunodeficiencies (including those receiving immunosuppressive therapies such as chemotherapy or high doses of systemic corticosteroids (e.g., 20 mg/day or 2 mg/kg body weight/day of prednisone for 2 weeks or more) within 4 weeks prior to vaccination). It is also contraindicated in people with symptomatic HIV infection or those with asymptomatic infection, but with evidence of immunological impairment.
- **Precautions**: In view of the safety signal of anaphylaxis and until more data is available, all vaccinated people should be observed for at least 15 minutes after receiving the vaccine. People with a history of anaphylaxis, either from another vaccine or from different causes, should be observed for 30 minutes. In addition, it is recommended that vaccination activities be carried out in environments that facilitate the timely and adequate diagnosis and treatment of anaphylaxis, prioritizing intramural vaccination or in health facilities.
- **Knowledge gaps**: According to SAGE recommendations, the risk of vaccine-enhanced disease (EPAV) by serotypes 3 and 4 in vaccinated seronegative people cannot be ruled out, which is a factor of uncertainty. That is, in individuals without a history of dengue at the time of vaccination, there could be an increased risk of severe disease in subsequent infections caused by serotypes 3 and 4.
- **Surveillance of Events Supposedly Attributable to Vaccination or Immunization (ESAVI) and Adverse Events of Special Interest (AESI).**
    - Ensuring proper reporting, investigation, causation assessment, and classification of reported cases, especially those suspected of vaccine-associated dengue-enhanced disease, is critical.
    - Given the expected increase in DENV-3 cases in the Region, it is essential that surveillance systems, especially those for severe cases, collect data on vaccination history, including the date and number of doses.
    - Due to the difficulty of differentiating between HIV-positive and seronegative people at the time of vaccination, the frequency of presentation of severe cases by age cohort should be evaluated, also considering the history of vaccination, in order to identify possible excess risks in the presentation of severe cases between the vaccinated and unvaccinated. If possible, a cohort analysis is recommended, using individual electronic vaccination records.
    - It is crucial to follow the ESAVI surveillance procedures established in the PAHO regional manual, promoting harmonization with dengue surveillance, to ensure that complete information is available on the safety of the vaccine in the different epidemiological contexts of transmission of the virus.
    - Both dengue surveillance teams and ESAVI surveillance teams need to be aware of the guidelines for dengue vaccine safety surveillance published by PAHO.

Note: The TAK-003 vaccine is currently available for procurement through PAHO's Revolving Fund. Limited availability of the vaccine is expected in the short and medium term.

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