RESPONSE TO DENGUE CASES

in Non-Endemic Areas of the United States

Contents

Summary	3
1. Investigating Suspected Dengue Cases	4
Algorithm A. Investigating suspected dengue casesTable. DENV Risk Categories for Mosquito-borne DENV transmission and Action Items	
2. DENV transmission risk levels and recommended actions for travel associated dengue ca	
Box 1. Additional factors that may increase or decrease the probability of vector-borne transmission	
2.1.1 No probability of vector-borne transmission	
Box 2. Recommendations for all areas regardless of vector-borne transmission risk	
States, 2017*	
2.1.3 Moderate probability of vector-borne transmission:	13 ad
dengue casesdengue cases	
3. Recommended Actions for Ongoing Local Transmission	16
3.1 In the setting of locally acquired cases in one geographic area	
are higher than expected compared to the median for previous years	
Algorithm C. Recommended actions for locally acquired dengue cases	19
Appendices	20
Appendix A. Dengue Case Report Form	20
Appendix B. Strategies to control Aedes aegypti or albopictus mosquitoes	21
Appendix C. Recommendations for Entomological Surveillance	23
Appendix D. CDC Dengue Resources	25
Appendix E. Enhanced dengue surveillance for ongoing local transmission	27
Active case finding around travel associated dengue cases	27
Implementation of syndromic surveillance for dengue	27
Expanded diagnostic testing for DENV in areas with locally acquired dengue cases	27

Summary

This document was developed by the Centers for Disease Control and Prevention (CDC) to assist state, Tribal, local, and territorial (STLT) health departments in areas where dengue is not endemic to investigate and respond to importation and potential transmission of dengue virus (DENV). This includes algorithms to guide the investigation of suspected dengue cases (Algorithm A), DENV transmission risk levels and recommended actions for travel associated dengue cases (Algorithm B), and recommended actions for locally acquired dengue cases (Algorithm C). This document provides guidance on how to use the algorithms and additional considerations when implementing recommended actions. The CDC is available to support STLT partners and healthcare providers for any inquiries, consultations, or assistance with investigations. Please contact the Dengue Branch at dengue@cdc.gov.

1. Investigating Suspected Dengue Cases

STLT jurisdictions should investigate and report all dengue virus (DENV) infections. People with suspected dengue based on clinical criteria or exposures should be offered confirmatory testing whenever possible based on CDC <u>guidance for dengue testing</u>. STLT partners should use a standardized form to investigate all suspected cases, and report confirmed and probable cases to ArboNET. CDC has provided an example of a dengue <u>case investigation form</u> (Appendix A. **Dengue Case Report Form**) to assist STLT partners with case investigation and data collection. The goal of the investigation is to confirm that a case represents a recent DENV infection and to determine its origin (travel associated or locally acquired) to guide public health action (Algorithm A. Investigating suspected dengue cases).

A suspected DENV infection is defined as a clinically compatible case of <u>dengue</u>, <u>dengue-like</u> <u>illness</u>, <u>or severe dengue</u> with one of the following:

 Travel to a dengue endemic country or location with an ongoing outbreak or known risk of dengue transmission in the two weeks before onset of an acute febrile illness (i.e., travel associated).

Note: Local transmission has been documented in parts of the continental United States; any returning traveler from a jurisdiction with ongoing local DENV transmission and compatible symptoms should be tested. If results are positive and travel was to a location in the United States, state health officials should notify the jurisdiction where infection was acquired. CDC can facilitate notifications to other jurisdictions if needed. Travel to an area with DENV transmission does not necessarily rule out the possibility of locally acquired DENV. Taking a good travel history, including determining the duration and location of travel, is crucial for correct classification of cases.

 Association in time and place (e.g., household member, family member, classmate, or neighbor) with a confirmed or probable dengue case (i.e., locally acquired).

All suspected DENV infections should undergo laboratory testing when possible. Suspected DENV infections can be further classified using the laboratory criteria:

Confirmed:

- Positive nucleic acid amplification test (NAAT) (e.g., RT-PCR) or non-structural protein 1 (NS1) antigen test. NAAT testing is available at most public health labs and NS1 testing is available at some commercial laboratories.
- Change from negative to positive IgM or IgG antibody result (e.g., seroconversion) in paired acute and convalescent samples.

Probable

 Positive IgM antibodies in a single sample with unknown or negative NAAT or NS1 antigen test results

Suspect

- Absence of positive IgM anti-DENV by validated immunoassay in a serum or CSF specimen collected <5 days after illness onset and in which molecular diagnostic testing was not performed in a patient with an epidemiologic linkage
- Do not report cases as suspect who have a clear alternative explanation for symptoms or whose test results are conclusive to rule out acute dengue infection

Health departments often become aware of cases through laboratory reports rather than clinical reports and work to determine if clinical compatible symptoms were present or if there was travel or an epidemiological link. When reviewing suspected cases with laboratory testing, please ensure that the correct test was ordered and performed. If incorrect testing was ordered (i.e., IgG or IgM testing without NAAT or NS1 antigen on a sample collected 0-7 days from symptom onset), repeat testing of original specimens with NAAT. Negative RT-PCR (or NS1 antigen) and IgM results in a specimen collected within 7 days of symptom onset, and negative IgM results in specimens collected 7 days to 3 months after symptom onset provide strong evidence of lack of DENV infection. If further testing of acute specimens is not possible, consider classifying for local purposes as a suspect case or following up to request convalescent serum to identify IgM and/or IgG seroconversion if those tests were initially negative or equivocal.

CSTE dengue case definition

For a comprehensive list of laboratory criteria, clinical descriptions, case classifications, and epidemiological linkages, please refer to the <u>2015 CSTE dengue case definition</u>. Of note, there are minor differences in the interpretation of IgM and plaque reduction neutralization test (PRNT) results in this document as compared to the 2015 CSTE dengue case definition for classifying confirmed and probable cases. In the 2015 case definition, positive IgM results were considered evidence of confirmed dengue if the person lived in or traveled to an area without ongoing transmission of another flavivirus (e.g., WNV, JEV, YFV), clinical evidence of coinfection with one of these flaviviruses, or recent vaccination against a flavivirus (e.g., YFV, JEV). However, given the possibility of flavivirus cross-reactivity from Zika in many areas where dengue is endemic, as well as WNV in many parts of the United States, in this document single IgM positive results are considered probable. A revision of the CSTE dengue case definition is planned for 2025. Jurisdictions may choose to follow the 2015 case definition if preferred.

Confirmed and probable DENV cases

Once a DENV confirmed or probable case has been identified, investigators should inquire about other symptomatic persons in the same place of residence (i.e. household, shelter, etc.) as the DENV infection and recommend DENV testing. During case investigations, persons with DENV infection and their household members should be provided directions to prevent the spread of dengue, identify and eliminate possible vector habitats around the household, and instructions on when to seek additional care or testing if symptomatic. Investigators should determine whether the case traveled to an area with active DENV transmission, including any U.S. states or territories with ongoing local transmission. For travel associated cases, STLT partners should follow Algorithm B. DENV transmission risk levels and recommended actions for travel associated dengue cases.

If a confirmed or probable case is thought to be locally acquired in a non-endemic area, the transmission route should be thoroughly investigated. Investigators should determine if mosquito vectors that transmit DENV (e.g., *Aedes aegypti* and *Aedes albopictus*) have been documented in the area and inquire about other less common modes of non-vector-borne transmission such as DENV infection related to transmission through recent receipt of blood, organ, or tissues or through occupational exposure (e.g., needlestick or mucosal exposure to DENV in a hospital or laboratory). Sexual transmission can also be considered but is extremely rare. Compared to *Aedes aegypti*, which is the most important vector of DENV, *Aedes albopictus* is a competent DENV vector but is less frequently associated with large outbreaks.

If a locally acquired case meets the *probable* case definition (i.e., positive IgM antibodies in a single sample), additional testing should be attempted. This may be done by conducting NAAT testing on any available acute specimens, repeating commercial laboratory tests at a public health laboratory to strengthen the overall interpretation, or by collecting additional specimens to evaluate seroconversion or the presence of neutralizing antibodies by plaque reduction neutralization testing (PRNT).

If a confirmed locally acquired case is reported in a jurisdiction where local transmission of dengue has never been reported STLT partners may require assistance with testing of samples or results validation. For assistance with locally acquired suspect, probable or confirmed cases, please consult with CDC Dengue Branch for additional support.

Once a locally acquired case is confirmed, follow recommendations for local DENV transmission shown in <u>Algorithm C recommended actions for locally acquired dengue cases</u>. A jurisdiction may decide to implement the recommendations in Algorithm C when a probable case is identified and no further testing is possible, and the clinical presentation and available test results, other exposures, and local epidemiology indicate there is the possibility of local transmission.

RESPONSE TO DENGUE

in Non-Endemic Areas of the U.S.

Algorithm A. Investigating suspected dengue cases

Does the case meet laboratory criteria for recent DENV infection? Yes No • Follow case report form for investigation. If you suspect dengue based on clinical and · Identify other symptomatic or ill people in the exposure criteria, perform dengue testing. household and recommend dengue testing. If testing has been performed and is negative, rule • Tell everyone in the household how to prevent the out as not a case. spread of dengue. If no specimen is available for testing, classify as · Advise patients to seek care in the presence a suspect case. of warning signs of severe dengue. Has the person been to an area with active DENV transmission (including within the continental United **→** No States) in the 2 weeks before symptom onset? Locally acquired dengue If a locally acquired case is suspected in a nonendemic area, investigate all possible routes of infection, including: Known presence of and exposure to Aedes mosquitoes Yes Receipt of blood, organs, or tissue products Travel-associated dengue Possible laboratory or occupational exposure. Follow recommendations for travel-associated dengue cases (Algorithm B). Does the case meet laboratory criteria for a confirmed case? Yes Follow recommendations for local dengue No transmission (Algorithm C). For *probable* (*IgM*+) locally acquired cases in areas without documented DENV transmission, attempt confirmatory testing. Retest original specimens by RT-PCR. Collect additional specimens to evaluate seroconversion or presence of neutralizing antibodies by PRNT. If a probable case is confirmed (e.g., NAAT+) follow recommendations in Algorithm C. A jurisdiction may decide to implement the **Additional Considerations** recommendations in Algorithm C when a probable For case confirmation in areas where local case is identified and no further testing is possible if transmission of DENV has never been the clinical presentation, available test results, other reported, including re-testing of specimens exposures, and local epidemiology indicate there is and result validation, contact the CDC the possibility of local transmission. Dengue Branch for assistance Consider pursuing additional mosquito or human (dengue@cdc.gov). surveillance in the area.

Table. DENV Risk Categories for Mosquito-borne DENV transmission and Action Items

Risk categories	Are Aedes aegypti or Ae. albopictus present?	Has local DENV transmission occurred in the past?	Summary of recommended actions
None	No	N/A	Recommendations for all areas: Increase public awareness of protection against mosquito bites during travel to endemic areas. Healthcare provider outreach to consider and test for DENV infection.
Low	Yes	No	Recommendations for all areas, plus:
Moderate	Yes	Yes	Source reduction, larvicide and insecticide spraying around reported cases. Mosquito surveillance in areas with historically high numbers of travelassociated or locally acquired cases. Active case finding around reported case(s). Enhanced healthcare provider outreach to offer dengue testing to patients with signs and symptoms highly compatible with dengue.
Local DENV transmission identified	Yes	Yes	Recommendations for moderate transmission areas plus:

2. DENV transmission risk levels and recommended actions for travel associated dengue cases

Once a travel associated dengue case has been identified in your jurisdiction, Algorithm B. DENV transmission risk levels and recommended actions for travel associated dengue cases provides considerations around the risk of local vector-borne transmission, which depends on two principal factors:

- The presence of mosquito vectors that transmit DENV, Aedes aegypti and Aedes albopictus. Local vector control agency surveillance data can be used to confirm the presence and density of mosquito vectors. In the absence of local vector control data, jurisdictions can use CDC's estimated potential range of Aedes aegypti and Aedes albopictus in the United States to inform potential presence (Figure 1. Estimated potential range of Aedes aegypti and Aedes albopictus in the United States, 2017*.).
- Whether local DENV transmission has been documented before.

Box 1. Additional factors that may increase or decrease the probability of vector-borne transmission.

Increased probability of transmission:

- High number of travel associated cases (>10 cases per year)
 - o If more travel associated cases are identified in a jurisdiction, there is a higher probability of spread of DENV infection if *Aedes* mosquito vectors are present.
- Presence of Aedes aegypti
 - Although Ae. albopictus has also proven to be a competent vector for dengue, Ae. aegypti
 is more frequently associated with large outbreaks in endemic areas.
- High human population density
 - Because the average flight range of Aedes spp. is approximately 100–200 meters (a few blocks), urban areas with high density are at higher risk of ongoing DENV transmission.
- Higher numbers of *Aedes* vector breeding sites (e.g., small backyard containers, yard drains, neglected swimming pools, discarded tires, drainage ditches with standing water)
 - Aedes mosquitoes only need a small amount of water to lay eggs. Bowls, cups, fountains, tires, barrels, vases, and any other container storing water make a great "nursery" for mosquitoes.
- High precipitation
 - Increased rainfall increases suitable breeding sites for Aedes aegypti and albopictus, increasing their populations in an area.
- Average daytime temperatures between 68–95°F
 - Higher risk of transmission in warmer months (spring and summer) than winter.
 - The highest levels of dengue transmission have been <u>observed in these temperature</u> ranges.

Decreased probability of transmission:

- Elevation ≥6.000 feet
 - Higher elevation climates are less suitable for proliferation of Aedes aegypti and albopictus.

Algorithm B. DENV transmission risk levels and recommended actions for travel associated dengue cases also provides considerations for public health action in each scenario. Risk categories include no probability of transmission, low probability of transmission, and moderate probability of transmission. Additional factors that can be considered when informing risk levels are also provided (**Box 1**). Depending on the risk category for transmission of DENV, additional actions can be taken as described below (**Table**).

2.1 DENV vector-borne transmission risk categories, definitions, and recommended actions

2.1.1 No probability of vector-borne transmission

<u>Definition:</u> areas where *Aedes aegypti* or *albopictus* mosquitoes are not known to be present.

- Public health actions:
 - Follow recommendations for all areas (<u>Box 2</u>).

2.1.2 Low probability of vector-borne transmission

<u>Definition:</u> areas where *Aedes aegypti* or *albopictus* are present but where local transmission of DENV has not been documented.

- Public health actions:
 - Follow recommendations for all areas (<u>Box 2</u>).
 - Establish communication channels between public health and vector control agencies to coordinate surveillance and vector control efforts.
 - Consider implementing source reduction, larviciding, and outdoor residual insecticide spraying targeting mosquito resting places and containers that cannot be eliminated guided by the presence of *Aedes spp*. mosquitoes and insecticide resistance patterns to reduce mosquito abundance.
 - Implementation will depend on the availability of resources and expertise in implementing vector control.
 - More detailed information on vector control methods and surveillance are available in Appendix B. Strategies to *control* Aedes aegypti *or* albopictus.
 - Appendix C. Recommendations for Entomological Surveillance and at https://www.cdc.gov/mosquitoes/mosquito-control/index.html and Surveillance and Control of Aedes aegypti and Aedes albopictus in the United States (cdc.gov).

Box 2. Recommendations for all areas regardless of vector-borne transmission risk.

All jurisdictions should work to inform the public and healthcare providers on how to prevent, diagnose, manage, and report dengue cases. Specific recommendations include:

Public

- Increase traveler awareness about how to protect themselves against mosquito bites during and after travel and to seek care if they develop symptoms.
- O When Aedes mosquito vectors are present:
 - Encourage the public to use screens in windows and doors, repair screens that have tears or holes in them, and keep doors to the outside closed to prevent mosquito bites.
 - Promote the use of <u>EPA-registered repellents</u> and protective clothing while in areas where mosquito bites are possible.

• Healthcare providers

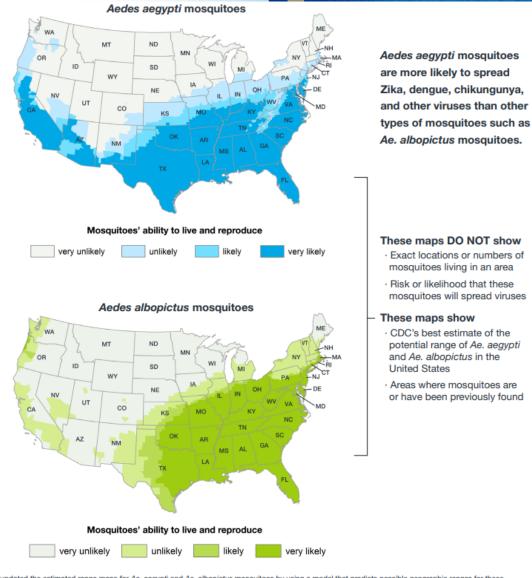
- <u>Educate healthcare providers</u> to consider and test for DENV infection in febrile travelers returning from areas with ongoing dengue transmission within the last 14 days
- Familiarize healthcare providers with DENV testing, including the <u>recommended test types</u> <u>and interpretation</u> (ensuring the appropriate test is chosen according to time after symptoms onset).

Suspected dengue cases

Advise patients to seek care in the presence of warning signs of severe dengue.

RESPONSE TO DENGUE

in Non-Endemic Areas of the U.S.



* CDC has updated the estimated range maps for Ae. aegypti and Ae. albopictus mosquitoes by using a model that predicts possible geographic ranges for these mosquitoes in the contiguous United States. The model used county-level records, historical records, and suitable climate variables to predict the likelihood (very low, low, moderate, or high) that these mosquitoes could survive and reproduce if introduced to an area during the months when mosquitoes are locally active. Maps are not meant to represent risk for spread of any specific disease. (See Johnson TL et al. Modeling the environmental suitability for Aedes (Stegomyia) aegypti and Aedes (Stegomyia) albopictus (Diptera: Culicidae) in the contiguous United States. Jrl Med Entomol. Sept. 2017;[ahead of print].)

U.S. Department of Health and Human Services

CS264451-F February 16, 2018

Figure 1. Estimated potential range of *Aedes aegypti* and *Aedes albopictus* in the United States, 2017*.

Control and Prevention

2.1.3 Moderate probability of vector-borne transmission:

<u>Definition:</u> areas where *Aedes aegypti* or *Ae. albopictus* are present and where local transmission of DENV has been confirmed. *Aedes albopictus* is a less efficient vector, but it has been associated with DENV outbreaks in some areas.

- Public health actions:
 - Follow recommendations for low probability areas.
 - Vector control:
 - Implement vector control around reported case(s).
 - Engage in community outreach and educational campaigns on effective mosquito control, the importance of clean-up campaigns to remove or reduce aquatic habitats and reporting possible mosquito sources to authorities.
 - If resources are available, jurisdictions can consider conducting enhanced mosquito surveillance tasks in areas or communities with historically high numbers of travel associated cases, including immature (larvae/pupae) surveys to identify the most productive aquatic habitats of Aedes aegypti and Ae. albopictus and target control measures towards these habitats. Where feasible, annual insecticide resistance assays (CDC Bottle Bioassays) are useful to determine levels of resistance and which chemicals will be most effective in killing mosquitoes.
 - More detailed information on vector control methods and surveillance are available in Appendix B. Strategies to *control* Aedes aegypti *or* albopictus.
 - Appendix C. Recommendations for Entomological Surveillance and at https://www.cdc.gov/mosquitoes/mosquito-control/index.html and Surveillance and Control of Aedes aegypti and Aedes albopictus in the United States (cdc.gov).
 - The intensity of vector control efforts should take into consideration the presence of <u>risk factors</u> that may increase the probability of transmission including the presence of *Aedes aegypti* that is a more efficient mosquito vector. For example, if multiple travel associated cases have been reported in New York City during the months of January–March, given average temperatures and precipitation transmission is unlikely. In contrast, the risk of transmission is higher if travel associated cases are reported in California during the months of June–October. The latter scenario may require more intensive vector control measures than the former.

Enhanced surveillance:

- Consider enhanced surveillance in areas with increased risk, such as higherthan-expected numbers of travel associated cases in a small geographic area. This can be done through:
 - Active case finding in the household or place of residence of travel associated cases, including anyone with symptoms compatible with dengue.

• Healthcare provider outreach

- Inform healthcare providers to consider testing for dengue in patients exhibiting signs and symptoms that are highly compatible with dengue (e.g., fever and at least one of the following: thrombocytopenia, leukopenia, body aches, joint pain, or rash), regardless of recent travel history, and in the absence of another diagnosis, and provide them with <u>dengue clinical management resources</u> (<u>Appendix D. CDC Dengue Resources</u>).
- Jurisdictions can provide guidance based on the local risk assessment and available resources. Determining which patients to test for dengue in the absence of a travel history to an area with known dengue transmission can be challenging due to the non-specific clinical presentation. Factors that would increase suspicion for dengue include signs or symptoms of fever and thrombocytopenia, leukopenia, body aches, joint pain, or rash, as well as reported travel among household members or patient residence in an area where travel associated dengue cases are frequently reported.

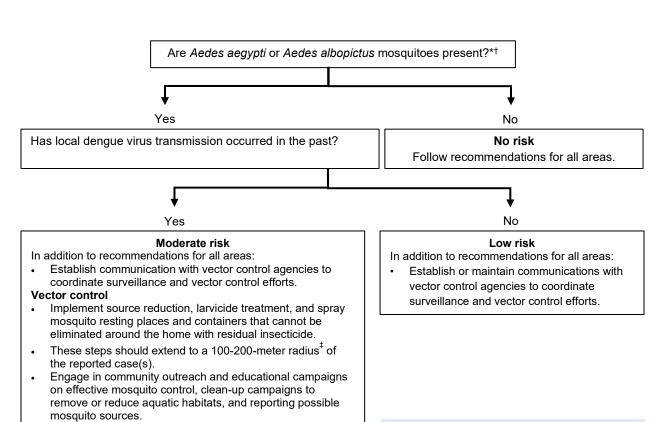
RESPONSE TO DENGUE

in Non-Endemic Areas of the U.S.

Algorithm B. DENV transmission risk levels and recommended actions for travel associated dengue cases

Recommendations for all areas:

- Increase traveler awareness about <u>how to protect themselves against mosquito bites</u> during and after travel and to seek care if they develop symptoms.
- · Encourage people to use and repair screens in windows and doors to prevent mosquito bites.
- Promote the use of EPA-registered repellents and protective clothing while in areas where mosquito bites are
 possible.
- Educate healthcare providers to consider and test for dengue virus (DENV) infection in febrile returning travelers from an area with ongoing DENV transmission within the last 14 days.
- Familiarize healthcare providers with DENV testing, including the recommended test types and interpretation.
- Advise patients to seek care in the presence of warning signs of severe dengue.
- If travel was to a location in the United States, state health officials should notify the jurisdiction where infection
 was acquired.



Enhanced surveillance

- Consider enhanced surveillance in areas with increased risk, such as higher-than-expected numbers of travel-associated cases in a small geographic area or historical locally acquired cases. Use larvae/pupae surveys to identify and target the most productive aquatic habitats.
- Active case finding around travel-associated cases, including anyone symptomatic or with recent travel to an area with dengue transmission.

Healthcare provider outreach

- Inform healthcare providers to consider testing for dengue in patients with symptoms highly compatible with dengue regardless of recent travel history, and in the absence of another diagnosis.
- Provide them with <u>clinical management resources</u>.

- * As confirmed by local vector surveillance or based on best estimates of the <u>potential range of Aedes</u>.
- † Other factors that may affect dengue transmission include:

Increase:

- High numbers of travel-associated cases
- High human population density
- Elevated *Aedes* abundance and increased frequency of breeding sites
- High precipitation
- Average daytime temperatures between 68–95°F.
- Decrease:
- Elevation ≥6,000 feet
- ‡ Average flight range of a newly emerged *Aedes* mosquito

3. Recommended Actions for Ongoing Local Transmission

When evaluating the extent of local transmission, a focus should be placed on the epidemiological links between cases and the geographic areas where local transmission is suspected. In general, local transmission risk is highest within the household of a travel associated case. However, DENV infections in patients with no history of travel in the last two weeks and no clear epidemiological link with a confirmed or probable case indicate that local transmission may be occurring more broadly.

When ongoing local transmission is suspected, the intensity of public health action will depend on whether locally acquired DENV infections are reported in multiple geographic areas. Locally acquired cases are in distinct geographic areas if case residences (or other suspected location of acquisition) are >500 meters from each other. A summary of actions in response to a confirmed case of locally acquired DENV infection is provided in Algorithm C. Recommended actions for locally acquired dengue cases.

3.1 In the setting of locally acquired cases in one geographic area, the following actions are recommended:

Coordination:

- Coordinate with CDC, other agencies, and authorities regarding local the DENV transmission event and response.
- Develop or strengthen communication channels between epidemiology and vector control officials to coordinate surveillance and vector control efforts.

Vector control:

- Perform vector surveillance and control activities around the home and within a 100–200-meter radius of reported cases, including the neighborhood where the dengue case resides, and extend further to neighboring areas in case the virus is detected or cases are identified outside of the immediate neighborhood.
- Intensify source reduction efforts and potentially larvicide and adulticide treatments (as outlined in the vector control actions in areas with moderate probability of dengue transmission).
- Monitor the effectiveness of vector control efforts. More detailed information on vector control
 methods and surveillance are available in <u>Appendix</u> B. Strategies to *control* Aedes aegypti *or*albopictus.
- Appendix C. Recommendations for Entomological Surveillance and Surveillance and Control of Aedes aegypti and Aedes albopictus in the United States (cdc.gov).

• Enhanced surveillance:

- Offer DENV testing for other household members and ascertain information on any recent febrile illness episodes.
- Strongly consider enhanced surveillance around the household, particularly if the source of DENV introduction is unknown, including:
 - Conducting door-to-door case investigations in homes 100-200 meters of the confirmed local dengue case to identify and offer testing to people with elevated epidemiologic dengue risk based on symptoms. Inquire about travel history.

- Serosurveys among households within 100–200 meters of dengue case households can help identify more widespread dengue transmission and guide the geographic extent of vector control activities.
- Virological surveillance of *Aedes aegypti* or *Aedes albopictus* mosquitoes within 100–200-meter radius of the home or locations where the individual is likely to have been infected based on feedback from epidemiologists. Testing mosquitoes for arboviruses can help confirm local transmission. However, negative results are not conclusive, as virologic surveillance in mosquitoes has imperfect sensitivity and local transmission can occur in the absence of positive mosquito pools. See Appendix C. Recommendations for Entomological Surveillance for recommendations on the implementation of virological surveillance.
 - Virologic vector surveillance may be most useful in focal areas where DENV transmission is suspected but unprecedented (i.e., first evidence of mosquito-borne local DENV transmission in a non-endemic area). In Puerto Rico, evaluations of virologic surveillance in mosquitoes in areas with active DENV transmission have found ~7 DENV positive mosquitoes among every 10,000 mosquitoes captured. These findings indicate that it may be difficult to detect DENV in mosquitoes even in areas where transmission is occurring, and that negative results in mosquitoes should not be used to rule out local transmission. However, positive findings in mosquitoes, when available, can be very valuable in confirming local DENV transmission in an area and identifying the circulating DENV serotype. Sensitivity for DENV detection in mosquitoes can be increased by using higher numbers of traps (more mosquitoes captured) and maintaining surveillance for multiple weeks.

Healthcare provider outreach:

- o Intensify clinician outreach activities to enhance dengue detection, diagnosis, and management.
- o Inform healthcare providers to consider testing for dengue in patients exhibiting signs and symptoms that are highly compatible with dengue (e.g., fever and at least one of the following: thrombocytopenia, leukopenia, body aches, joint pain, or rash), regardless of recent travel history, and in the absence of another diagnosis, and provide them with dengue clinical management resources (See Appendix D. CDC Dengue Resources).

Communication:

- Provide updated epidemiologic reports to key stakeholders on the status of local transmission on a weekly basis.
- Continue mosquito control educational campaigns and tailor messaging to communities vulnerable to increased transmission.
- Conduct appropriate risk communication, following established principles (e.g., be first, be right, be credible).
 - Inform the public about what is known and what is not known.
 - Provide actions people can take to protect themselves and their families to reduce the risk of infection through mosquito bites including use of repellents.
 - Use available communication channels appropriate for the local community.

3.2 If multiple geographic areas are affected (>500 meters apart) or locally acquired cases are higher than expected compared to the median for previous years, the following actions can be pursued.

Vector control

- Implement area-wide larvicide and adulticide treatments by prioritizing areas based on the number of cases reported and vector surveillance results as outlined in vector control recommendations in section 3.1.
- Intensify community outreach and educational campaigns on effective mosquito control, the importance of clean-up campaigns to remove or reduce aquatic habitats and reporting possible mosquito sources to authorities, and personal protective measures.
 Monitor the effectiveness of vector control efforts.

Enhanced surveillance:

- In addition to enhanced surveillance activities outlined in section 3.1, STLT can consider:
 - Implementing syndromic surveillance in healthcare facilities around the areas of concern to enhance case finding, guide response decisions, and potentially develop a lower threshold for dengue testing among people with febrile illnesses (<u>Appendix E. Enhanced</u> <u>dengue surveillance for ongoing local transmission</u>).
 - Working with commercial labs to re-test specimens with positive or equivocal results for any of the assays (RT-PCR, NS1, IgM and IgG) from suspected dengue cases with NAAT and IgM to increase case capture and determine circulating serotype.
 - Implementing sentinel surveillance for dengue-like illness in high-risk areas and considering wastewater surveillance if resources are available in consultation with the CDC.

Algorithm C. Recommended actions for locally acquired dengue cases

Coordination

- · Coordinate with CDC and other agencies regarding local DENV transmission and response.
- Establish or strengthen communication channels between public health and vector control agencies to coordinate surveillance and vector control efforts.

Vector control

- Implement source reduction, larvicide treatment, and spray mosquito resting places and containers that cannot be eliminated around the home with residual insecticide in a 100-200-meter radius[‡] of reported case(s).
- Extend to neighboring areas in case the virus has spread beyond the immediate area.
- Monitor the effectiveness of vector control efforts.

Enhanced surveillance

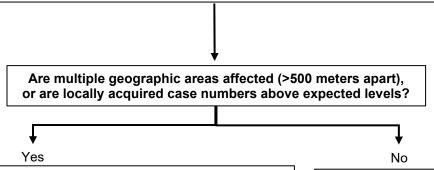
- · Offer DENV testing to household members with a recent febrile illnesses.
- Strongly consider enhanced surveillance around the household, particularly if the source of DENV is unknown, including:
 - Door-to-door case investigations to identify and offer testing to people with elevated risk based on symptoms, inquire about travel history.
 - Serosurveys among households within 100-200 meters of dengue case households.
 - Consider virologic surveillance of Aedes aegypti and albopictus mosquitoes within 100-200 meters[†] of the location where the patient is likely to have been infected if this is the first locally acquired dengue case in an area.

Provider outreach

- Intensify clinician outreach activities to enhance dengue detection, diagnosis, and management.
- Inform providers to suspect and <u>test for dengue</u> in patients with compatible symptoms, regardless of recent travel, and in the absence of other diagnosis.
- Provide them with dengue clinical management resources.

Communication

- Conduct appropriate risk communication, following established principles.
- · Provide updated epidemiologic reports to key stakeholders.
- Continue mosquito control education and tailor messages to communities at risk of increased transmission.



Expand vector control

- Implement area-wide larvicide and adulticide treatments by prioritizing areas based on the number of cases reported and vector surveillance results as outlined in vector control recommendations above.
- Intensify community outreach and educational campaigns on effective mosquito control, the importance of clean-up campaigns to remove or reduce aquatic habitats and reporting possible mosquito sources to authorities, and personal protective measures.

Expand enhanced surveillance

- In addition to enhanced surveillance activities outlined above:
 - Implement syndromic surveillance in healthcare facilities around the areas of concern.
 - Work with commercial labs to re-test positive or equivocal results by any test (RT-PCR, NS1, IgM and IgG) from suspected dengue cases with NAAT and IgM.
 - Implement sentinel surveillance for dengue-like illness in highrisk areas.

Continue steps above

† Average flight range of a newly emerged *Aedes* mosquito.

Appendices

Appendix A. Dengue Case Report Form

This form is intended as an example. Dengue cases should be reported into ArboNET using existing reporting mechanisms. For additional information, please contact dengue@cdc.gov.

	UE BRANCH USE ONLY VPP Date Received Specimen # Days post onset (DPO) Type Date Received
SAN ID GCODE \$1	ype Date Received Specimen # Days post onset (DPO) Type Date Received
SAN ID GCODE	
	/ \$3/
	/ / \$4 / /
Please read and a	complete ALL sections
Patient Data Hospitalized due to this illness: No Yes → Hospital	
Name of Patient: Lost Name First Name	Middle Name or Initial Fatal: Yes No Unik Mental status changes:
If patient is a minor, name of father or primary caregiver: Last Name	Fist Name Middle Name or Initial Yes No Unik
Home (Physical) Address	Physician who referred this case
-	Name of Healthcare Provider:
	Tel: Fax: Email:
	Send laboratory results to (mailing address):
City: Zip code:	_
Tel: Other Tel:	
Residence is close to:	
Work address:	
Patient's Demographic Information	Who filled out this form?
Date of Birth: Age:month Sex: M F	Name (complete)
	Relationship with patient: Tel: Fax: Email:
Must have the following information for sample processing	Additional Patient Data
Day Month Yes	How long have you lived in this city?
Date of first symptom://	Country of birth
Date specimen taken:	Have you been diagnosed with dengue before? Yes No Unk
Serum: First sample (Acute – first 5 days of liness – check for virus)	When diagnosed? Unk
Second sample	Gal Yellow Fever Vaccine Yes No Unk Year vaccinated
(Convalescent = more than 5 days after onset – check for antibodies)	During the 14 days before onset of illness, did you TRAVEL to other cities or countries?
Third sample	Yes, another country Yes, another city No Unk
Fatal cases (tissue type):/	WHERE did you TRAVEL?
PLEASE indicate below the signs and symptoms that th	ne patient has at the time that this form is being completed
Yes No Unk Evidence of capillary leak	Warning signs Yes No Unk
Fever lasting 2-7 days	Persistent vomiting
Fever now(>38°C)	Abdominal pain/Tenderness
Platelets ≤100,000/mm² Lowest serum albumin Lowest serum protein	Lethargy, restlessness
Platelet count: Lowest blood pressure (S8P/D	08P)/ Liver enlargement >2cm
Any hemorrhagic manifestation Lowest pulse pressure (systolic	ic - diastolic) Pleural or abdominal effusion
Perlechine Lowest white blood cell count Purpura/Ecchymosis	
Vomit with blood	Yes No Unk Digribes
Blood in slool	Conjunctivits
Nasal bleeding	Nasal congestion
Rhood in urine	Sore throat
Vaginal bleeding	Jaundice Jaundice
Positive urinalysis	
	Arthritis (Swollen joints)
Tourniquet test	

Appendix B. Strategies to control Aedes aegypti or albopictus mosquitoes.

Effective control of the mosquito vectors *Ae. aegypti* and *albopictus* can help reduce the likelihood of DENV transmission after importation of a travel associated case in areas with moderate probability of transmission or responding to locally acquired dengue cases. Effective mosquito control relies on an integrated vector management approach utilizing multiple interventions coordinated broadly across different social sectors.

When travel associated cases are reported in an area with moderate transmission risk, vector control efforts should be focused around the residence of cases. Priority should be given to performing *Aedes* larval source reduction around the home and within a 100–200-meter radius (the average flight range of a newly emerged *Aedes* mosquito) of reported cases.

If locally acquired cases have been reported, vector control activities need to include the neighborhood where the dengue case resides and extend further to neighboring areas in case the virus has moved outside of the immediate neighborhood.

1. Education and community engagement

- a) Educational campaign. Public messaging (newspapers, radio, TV, social media) informing people about measures that the population can take to prevent mosquito bites and mosquito breeding sites and to seek medical attention if dengue symptoms appear. Emphasis should be placed on a simple, easy to understand messages. Banners placed at community access points could be used to inform residents about the risk of dengue infections and disease, and to encourage them to participate in reducing mosquito habitats on their properties. The messages should specify what containers need to be removed or treated, with pictures and instructions.
- b) Clean-up campaigns. Local officials should conduct clean-up activities asking residents to clean their yards or patios and to offer help moving away heavy trash/junk objects (this should be conducted approximately every three months for prevention of new larval habitats). Some residents may need assistance to clear their yards (e.g., elderly, persons with disabilities, etc.).
- c) Community engagement. Residents should be asked for permission to inspect the property to eliminate or treat containers with larvicides that are not used for pet or human consumption. Residents should be encouraged to discard containers (provide a list/graphics of containers that produce Aedes mosquitoes) that accumulate water and other actions that would prevent producing mosquitoes on their properties.
- d) **Training** of public health professionals, emergency response personnel, and volunteers should be conducted in areas with local DENV transmission.

2. Traditional vector control

 Consider focal or area-wide treatments with larvicides and adulticides using application methods appropriate for the treatment area.

- Adulticides. Outdoor insecticide residual spraying using an appropriate insecticide for
 containers (not for pet or human consumption) and adjacent surfaces where mosquitoes
 land is highly recommended to disrupt transmission of DENV. Outdoor spaces include
 garages and other dark or protected areas where mosquitoes rest or land. It is not
 necessary to spray the entire outdoor walls, just below 1.5 meters from the ground,
 avoiding exposed surfaces to rain and sun. Integrated vector management programs
 should include an insecticide resistance management component.
- Larvicides. Wide area larvicide spraying (WALS) can be useful to treat abandoned lots, cemeteries, illegal dump sites, and houses whose residents refuse inspections or that are closed or abandoned. WALS alone, like other control agents/delivery systems, will not achieve sufficient control of Ae. aegypti and albopictus unless it is used as part of an integrated mosquito management approach. WALS alone will not interrupt active DENV transmission.
- **Environmental control.** Local officials should inspect and have septic tanks repaired, if applicable. Tire shops with outdoor stockpiles should be treated with larvicides/adulticides once a month and ensure that excess discarded tires are picked up and taken to recycling facilities as frequently as possible.
- Monitor the effectiveness of mosquito control. The effectiveness of pre-adult
 mosquito control is usually assessed by comparing the presence / absence or
 abundance of immatures in treated containers before and after treatment or by
 comparing with untreated areas. Adult mosquito surveillance can be used to monitor the
 effectiveness of mosquito control.

3. Protection against mosquito bites

- Installation or repair of screens as window and door screens have been shown to reduce the risk of dengue.
- Use of commercially available spatial repellents for houses without screens (available in hardware stores, pharmacies, etc.),
- **Topical repellents** (as recommended by <u>EPA</u>).

Appendix C. Recommendations for Entomological Surveillance

To better understand the risk of DENV transmission, health departments and vector control agencies can prepare by:

- Determining the abundance and seasonality of Aedes aegypti and albopictus vectors in their jurisdictions.
- Identifying main containers producing *Aedes aegypti* and *albopictus* to target clean-up campaigns and vector control measures.
- Conducting annual insecticide resistance assays (<u>CDC Bottle Bioassays</u>) to determine effective mosquito control strategies.
- Conducting educational campaigns on effective mosquito control, the importance of clean-up campaigns to remove or reduce aquatic habitats and reporting possible mosquito sources to authorities, and the use of personal protective measures.

In addition, some health departments with previously reported locally acquired dengue cases may coordinate with vector control agencies to conduct mosquito surveillance and control to identify areas at risk for transmission by:

- Identifying cumulative and interannual patterns of historical travel associated cases to determine if clusters of cases could be prioritized and targeted for *Aedes aegypti* and *albopictus* surveillance and control.
- Conducting enhanced mosquito surveillance in areas with historically high numbers of travel associated cases, including immature (larvae/pupae) surveys to identify the most productive aquatic habitats of *Aedes aegypti* and *albopictus* and target control measures towards these habitats.

Entomological surveillance for confirmed DENV infections

- For travel associated cases in areas with moderate probability of transmission, vector control programs may conduct surveillance of Aedes aegypti and albopictus mosquitoes within 100–200 meters of the home(s) of travel associated case(s).
- For locally acquired cases vector control programs should conduct surveillance of Aedes aegypti and albopictus mosquitoes within 100–200 meters of the home or locations where the individual is likely to have been infected based on feedback from epidemiologists. Vector surveillance may include the neighborhood where the locally acquired dengue case resides, and extend further to neighboring areas in case additional locally acquired cases are reported outside the immediate neighborhood. Mosquito surveillance will assist in evaluating the impact of vector control efforts.
- Mosquito virologic surveillance may be most useful in focal areas where DENV transmission is suspected but unprecedented (i.e., first evidence of mosquito-borne local DENV transmission in a non-endemic area). Testing mosquitoes for arboviruses can help confirm local transmission. However, negative results are not conclusive, as virologic surveillance in mosquitoes

has imperfect sensitivity and local transmission can occur in the absence of positive mosquito pools.

- Implementing mosquito population and virologic surveillance
 - There is currently no 'best practice' guidance on the type or number of traps to use. However, in previous dengue investigations, CDC scientists have placed 20-30 traps within 100–200 meters of the suspected site of infection. BG-Sentinel or Autocidal Gravid Ovitraps (AGO) have been shown useful in detecting infected container Aedes mosquitoes.
 - Traps should be serviced every day if using BG traps or twice a week for AGO traps to collect pools of *Aedes aegypti* and *albopictus* females for DENV testing and maximize chances of detecting the virus in mosquitoes. If the number of mosquito pools is high and straining resources of vector control programs, a super pool approach can reduce the number of RT-PCR tests required to detect dengue viral RNA in female *Aedes aegypti* and *albopictus* mosquitoes. A super pool consists of testing a pooled sample of aliquots taken from several individual mosquito pools (e.g., 10 individual pools; 1-20 individuals/pool). If a super pool is positive, then each individual pool needs to be tested, but if the super pool is negative there is no further testing.
 - Sensitivity for DENV detection in mosquitoes can be increased by using higher numbers of traps (more mosquitoes captured) and maintaining surveillance for multiple weeks.

Appendix D. CDC Dengue Resources

Healthcare providers:

- A Dengue Health Advisory was issued by CDC through the Health Alert Network, recommending having a high suspicion for dengue among people with fever and recent travel to dengue-endemic areas, and considering dengue among people without a history of travel who have signs and symptoms highly compatible with dengue (e.g., fever, rash, leukopenia, and thrombocytopenia): https://emergency.cdc.gov/han/2024/han00511.asp
- CDC Yellow Book, Dengue Chapter: <u>Dengue | CDC Yellow Book 2024</u>
- Dengue clinical courses, which are available from the CDC (<u>Dengue Clinical Case Management course (DCCM) | Dengue | CDC</u>) and the Pan American Health Organization (<u>Self-learning course</u>: <u>Clinical Diagnosis and Management of Dengue | Virtual Campus for Public Health (VCPH/PAHO)</u>).
- A Clinician Outreach and Communication Activity Call developed by the CDC (<u>Webinar Thursday</u>, <u>September 29</u>, 2022 <u>What Clinicians Need to Know about Dengue in the United States (cdc.gov)</u>).
- A dengue pocket guide to assist clinicians with clinical management of dengue
- A podcast from Emory University's Serious Communicable Disease Program and Project ECHO discusses a case of dengue fever tailored to clinicians (<u>A Case of Dengue Fever</u> <u>SCDP ECHO Podcast (simplecast.com</u>)).
- Travel Health Notices | Travelers' Health | CDC
- Additional resources can be found here: Dengue for Health Care Providers | Dengue |
 CDC.

In addition, health departments should coordinate with public health laboratories and healthcare providers to provide them with updated information on dengue testing practices, testing recommendations, available resources, and diagnostic kits (Clinical Testing Guidance for Dengue

Public

- Web site
 - o Dengue | Dengue | CDC
- Fact sheets
 - o Protect Yourself from Bites | Cómo protegerse de las picaduras de mosquito
 - Information for Dengue Patients | Información para personas con dengue
 - o Prevent Dengue During Pregnancy | El dengue durante el embarazo
 - o Protect your Baby | Su bebé tiene dengue
 - Mosquito Life Cycle | Ciclo de vida del mosquito
 - o Get Rid of Mosquitoes at Home | Elimine los mosquitoes en la casa
 - Septic Tank | Tanque séptico
 - Mosquito Control During an Outbreak | Control de mosquitos durante un brote
- Other materials

RESPONSE TO DENGUE

in Non-Endemic Areas of the U.S.

- Mosquito Bites Are Bad! (activity book) | Las picaduras de mosquitos son malas (libro de actividades)
- Door Hangers | Colgadores de puerta
- o Recursos Unidad Control de Vectores de Puerto Rico (prvectorcontrol.org)
- Social Media Posts
 - https://www.facebook.com/cdc/videos/1489280128601050
 - https://www.facebook.com/share/p/7EuR7HV3vVRXAGqM/?mibextid=WC7FNe
 - https://www.facebook.com/share/p/iGHNGLompJjuskC6/?mibextid=WC7FNe
 - https://www.facebook.com/story.php?story_fbid=862128545951156&id=1000646
 20552388&rdid=6fS1VqD44w8oSfsW
 - https://x.com/cdcgov/status/1778840531428167770?s=46&t=bR4uog4tb5sAuGv W34qPwQ
 - https://x.com/cdcespanol/status/1777384937974374683?s=46&t=bR4uog4tb5sA uGvW34gPwQ
 - https://www.instagram.com/p/C-di7ACurXr/
 - https://www.instagram.com/p/C95DbFjtLem/?img_index=1
 - https://www.instagram.com/p/C74haxNMck0/?img_index=1

Media

Press Kit: Mosquitoes | Mosquitoes | CDC

Appendix E. Enhanced dengue surveillance for ongoing local transmission

Some health departments may choose to conduct enhanced surveillance when locally acquired cases are detected. Approaches to consider are discussed below.

Active case finding around travel associated dengue cases

Active case finding can be implemented around travel associated or locally acquired dengue cases. Household members and persons with similar exposures (e.g., neighbors, work colleagues, schoolmates) of travel associated and locally acquired case patients can be interviewed about symptoms of DENV infection and urged to contact the local health department if symptoms develop. While household contacts of a dengue case may be most at risk, other settings in which persons with DENV infection may spend a large amount of time (e.g., workplace or school) may play a role in amplifying transmission. Special attention should be placed to settings in which transmission can amplify rapidly, such as densely populated encampments in urban areas where air-conditioning and mosquito screens are uncommon. Any persons with symptoms consistent with DENV infection who live near or in close proximity to a suspected human DENV infection case or reside within a 100–200-meter radius of a mosquito pool where DENV has been detected should be tested.

Implementation of syndromic surveillance for dengue

Emergency department electronic health records and other local sources of syndromic data could be evaluated prospectively and retrospectively to identify missed dengue cases. STLT Health Officers should work with facilities to sequester all blood specimens available from persons meeting dengue syndromic definitions for additional testing. The Florida Department of Health has developed syndromic definitions for dengue (available upon request). Using medical records of confirmed dengue cases could be useful to detect patterns to be used for case identification (e.g., fever plus leukopenia and thrombocytopenia). In addition, ICD-10 codes compatible with DENV infection can be queried to evaluate the potential for missed cases (available upon request).

Expanded diagnostic testing for DENV in areas with locally acquired dengue cases

State health departments in areas at higher risk for local DENV transmission can consider working with commercial laboratories to perform additional DENV testing by RT-PCR and IgM on the following:

- Specimens tested for dengue RT-PCR, NS1, IgM or IgG with positive or equivocal results
- Specimens tested for Zika or chikungunya with negative results that were not already tested for dengue

The CDC can coordinate with state health departments and public health labs to perform confirmatory DENV RT-PCR testing with serotyping and consider additional testing such as Plaque Reduction Neutralization Test (PRNT) if appropriate.

Sentinel site surveillance

State health departments can consider leveraging existing collaborations with hospitals or academic centers to test subsets of patients presenting with a dengue-compatible syndrome for DENV infection.

Wastewater surveillance

Recent findings from a feasibility study in Florida indicate that wastewater surveillance of DENV is possible (https://pubs.acs.org/doi/10.1021/acs.estlett.3c00769). However, limited data exist regarding the sensitivity of this method. Jurisdictions at increased risk of DENV transmission and with active wastewater surveillance activities could consider the implementation of protocols to better evaluate its utility in monitoring dengue transmission trends and detecting silent transmission in areas without reported human cases.