NC DEPARTMENT OF HEALTH AND HUMAN SERVICES

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To: NC Clinicians
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Background

In 2024, an increase in Oropouche virus (OROV) cases in both endemic areas and new, non-endemic regions, including Cuba has been reported. There is also a reported increase in severity of illness and potential vertical transmission. While travel-associated cases have been identified in the United States, there has been no evidence of local transmission to date. For more information, please see the CDC HAN. OROV, a member of the Orthobunyavirus genus, has historically occurred primarily in South and Central America. In Brazil, it is the causative agent of the second most common arboviral febrile disease after dengue fever [1].

Transmission

OROV is primarily an arthropod transmitted virus. In endemic regions, its primary vector is a biting midge (*Culicoides paraensis*). Some types of mosquitoes, including members of the *Culex* genus, are also capable of transmitting the virus. North Carolina insect vectors could include mosquitoes of the *Culex pipiens* complex, and at least one endemic species of midges in the *Culicoides* genus. Studies are currently underway to identify potential competent vectors in the United States. Vertical transmission from mother to fetus has been reported and is currently being investigated.

Clinical Presentation

Approximately 60% of people become symptomatic. Incubation is typically 3-10 days. Patients present with fever, chills, headache, myalgia, and arthralgia; other symptoms such as photophobia, skin rashes, and dizziness may also occur [2].

A large percentage of patients (~70%) experience recurrent symptoms several days to weeks after initial resolution of symptoms. Hemorrhagic and neuroinvasive manifestations are possible but less common (<5% of cases). In cases of vertical transmission of OROV, fetal death and congenital abnormalities, including microcephaly, have been observed.

Testing

Commercial testing for OROV is not available at this time. CDC is supporting clinical diagnostic testing using a Plaque Reduction Neutralization Test (PRNT) on serum and CSF (if patient has

neuroinvasive disease). OROV testing is available at CDC through the North Carolina State Laboratory of Public Health (NCSLPH). Testing will be restricted to individuals who meet criteria for clinical presentation and travel history (see "Should a patient be tested for Oropouche?" flow chart below).

Specimens sent to NCSLPH for OROV testing must include complete DHHS-3445: Special Serology and CDC 50.34 DASH forms, and a copy of negative dengue virus (DENV) test results if DENV testing is not requested through NCSLPH. These documents will be forwarded to CDC.

- To request OROV testing, choose "Other" on the Special Serology form and write in Oropouche. Select Arbovirus Neutralization Antibody CDC-10283 on the DASH Form. If also requesting DENV testing, choose that as well. Symptom onset date, travel dates, and travel locations must be included for testing to proceed
- OROV testing turnaround time is 4 weeks
- For questions, please call the Special Serology Laboratory at NCSLPH at 919-807-8623.

Treatment

There is no antiviral treatment available for OROV. Acetaminophen is the preferred first-line treatment for fever and pain; aspirin and NSAIDs should be avoided in patients with suspected dengue or OROV infection due to the potential risk of hemorrhage.

Control Measures

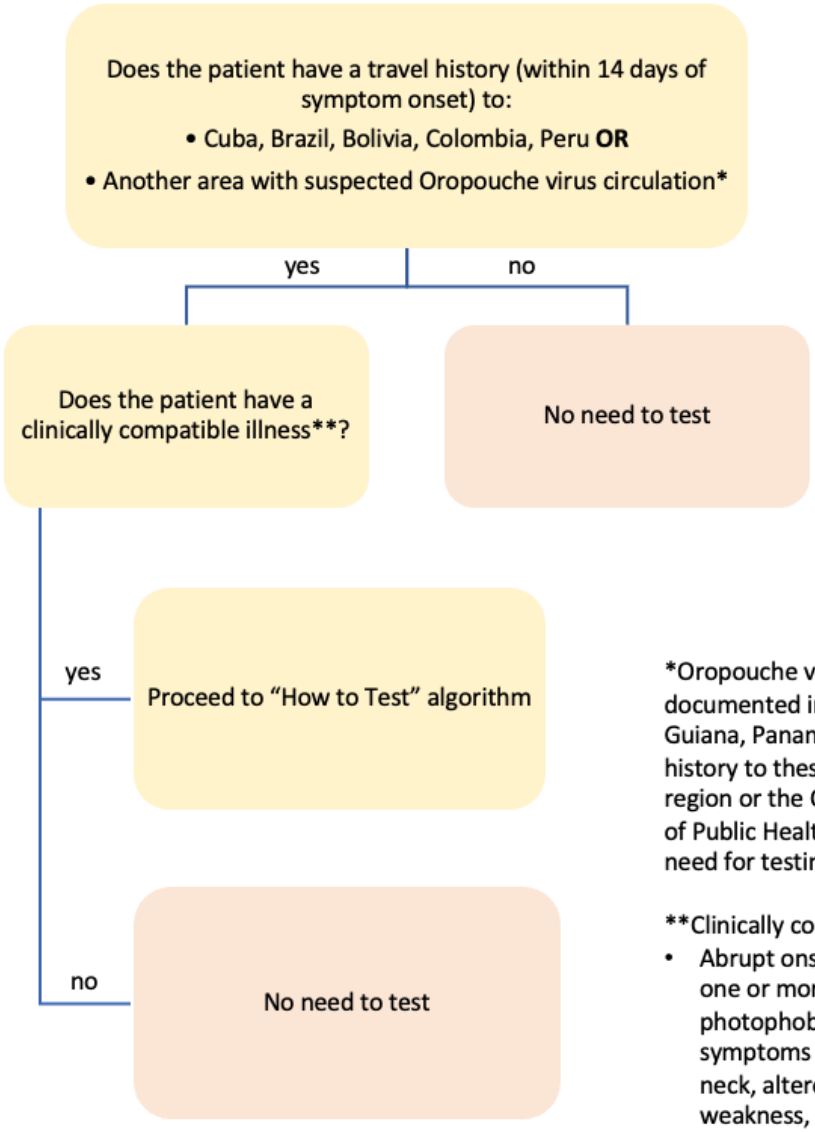
No vaccine is available. Returning travelers should take special precautions to avoid insect bites, including both mosquitos and biting midges (no-see-ums) for 3 weeks following return to the US. Advise use of EPA-approved insect repellants, protective clothing, and keeping windows and doors closed when possible, as biting midges can fit through most commonly used screens. Pregnant people should discuss travel plans with their healthcare provider and reconsider travel to countries with a Level 2 Travel Health Notice for OROV.

References and Additional Resources

1. Oropouche Fever: A Review. H Sakkas et. al. Viruses 2018, 10(4), 175.
2. Oropouche fever, an emergent disease from the Americas. D Romero-Alvarez and LE Escobar. Microbes and Infection 2018, 20(3), 135.

CDC/IDSA Clinician Update Call for Arboviral Diseases
Oropouche Virus Disease Among US Travelers – United States, 2024
Interim Guidance for Evaluating and Managing Infants Born to Pregnant People with Confirmed or Probable Oropouche Virus Disease

Should a patient be tested for Oropouche?

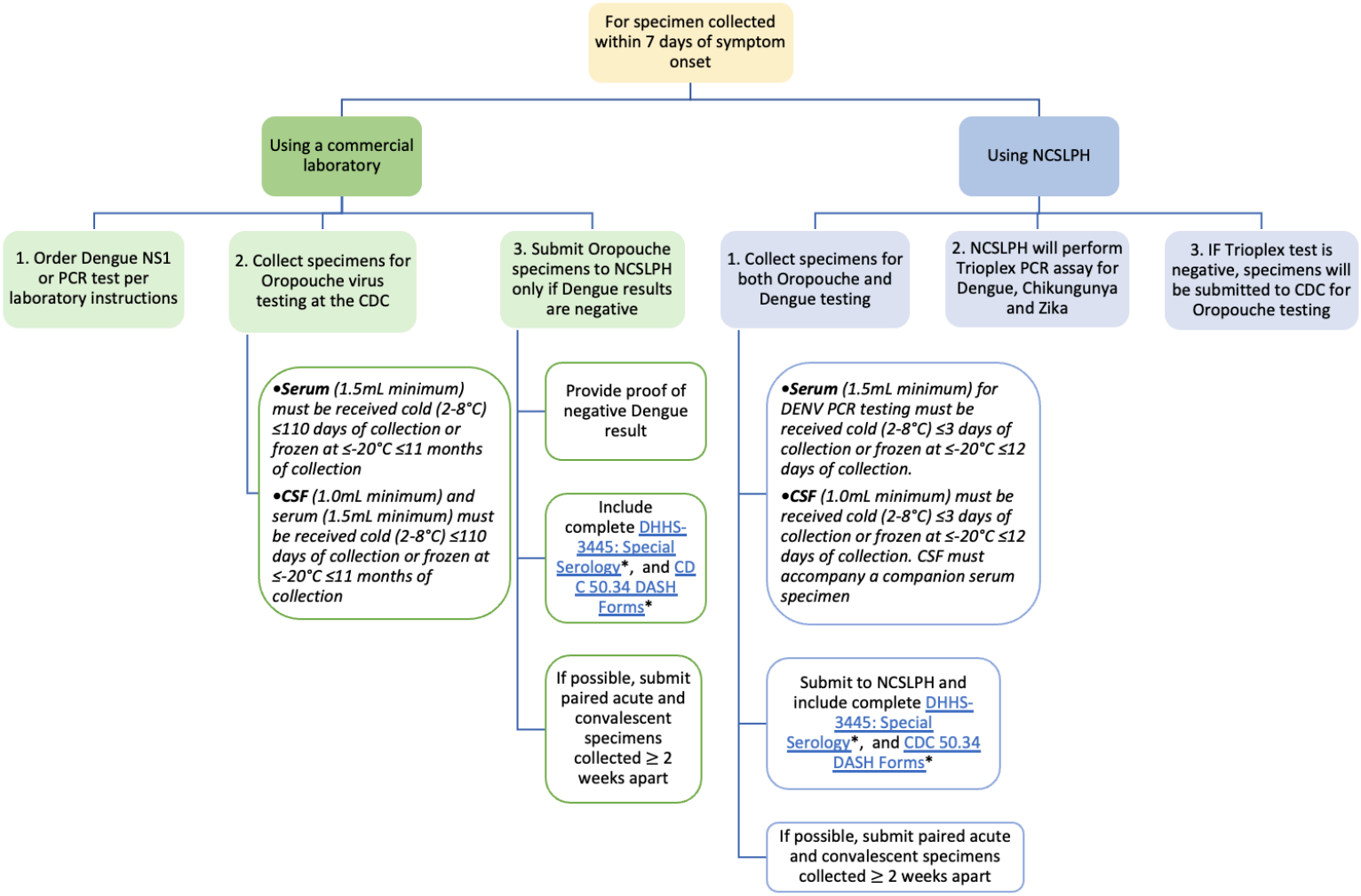


*Oropouche virus cases have previously been documented in Trinidad and Tobago, Ecuador, French Guiana, Panama, and Haiti. If the patient has travel history to these or other countries in the Amazon region or the Caribbean, please contact the Division of Public Health at 919-733-3419 to evaluate the need for testing on a case-by-case basis.

**Clinically compatible illness:

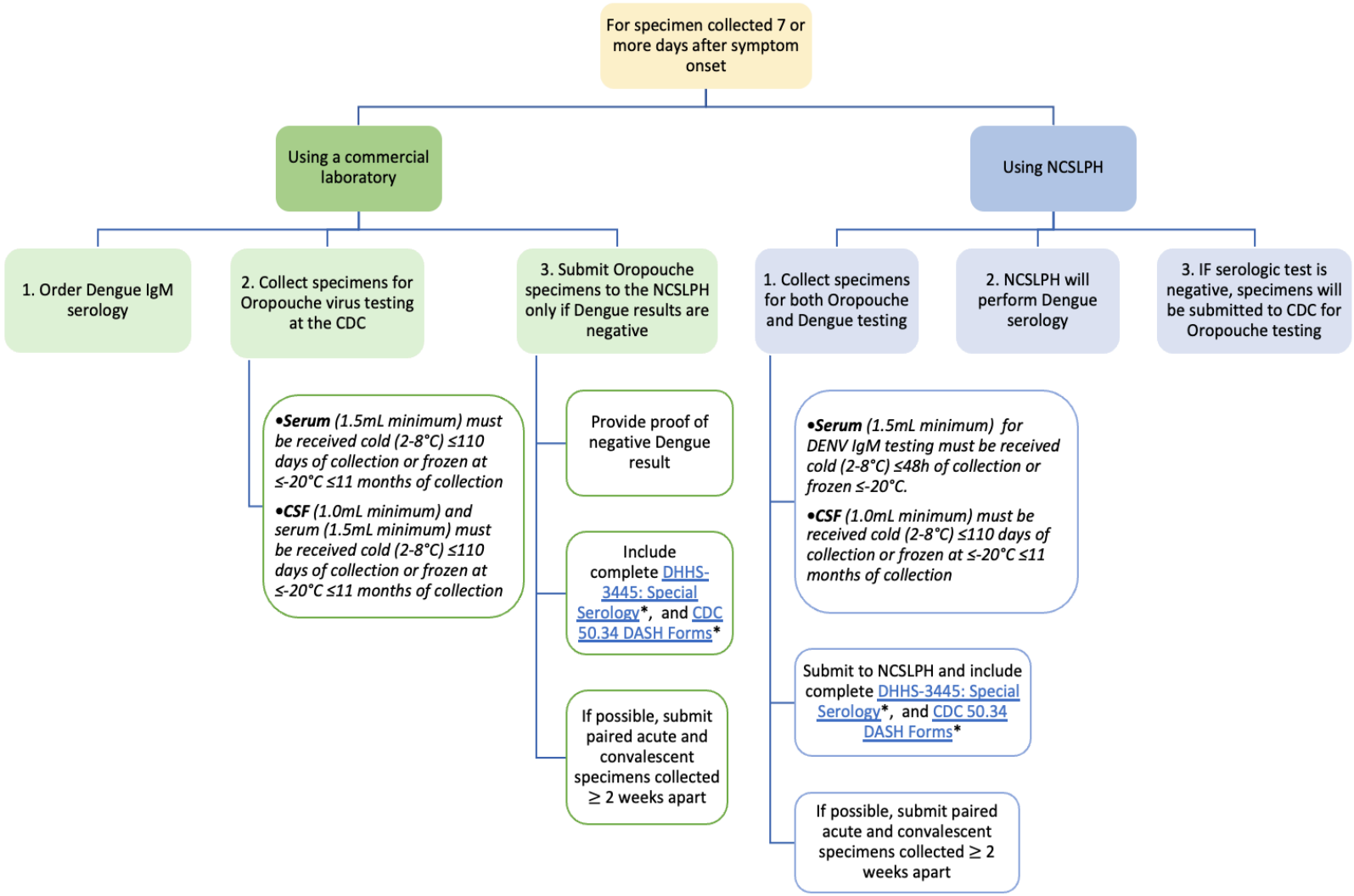
- Abrupt onset of reported fever, headache, and one or more of the following: myalgia, arthralgia, photophobia, retroorbital/eye pain, or signs and symptoms of neuroinvasive disease (e.g., stiff neck, altered mental status, seizures, limb weakness, or cerebrospinal fluid pleocytosis); **AND**
- No respiratory symptoms (e.g., cough, rhinorrhea, shortness of breath)

How to Test for Oropouche Algorithm
Part A: For specimens collected within 7 days of symptom onset



For any questions about testing, please call the NCSLPH Special Serology Lab at 919-807-8623.
*Links to NCSLPH Forms: DHHS-3445: Special Serology and CDC 50.34 DASH Forms

How to Test for Oropouche Algorithm
Part B: For specimens collected 7 or more days after symptom onset



For any questions about testing, please call the NCSLPH Special Serology Lab at 919-807-8623.
*Links to NCSLPH Forms: DHHS-3445: Special Serology and CDC 50.34 DASH Forms

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CDC HEALTH ADVISORY

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CDCHAN-00515

Increased Oropouche Virus Activity and Associated Risk to Travelers

Summary
The Centers for Disease Control and Prevention (CDC) is issuing this Health Alert Network (HAN) Health Advisory to notify clinicians and public health authorities of an increase in Oropouche virus disease in the Americas region, originating from endemic areas in the Amazon basin and new areas in South America and the Caribbean. Between January 1 and August 1, 2024, more than 8,000 cases of Oropouche virus disease were reported, including two deaths and five cases of vertical transmission associated with fetal death or congenital abnormalities. Countries reporting cases include Brazil, Bolivia, Peru, Colombia, and Cuba. In the United States and Europe in 2024, travel-associated cases have been identified in travelers returning from Cuba and Brazil. As testing and surveillance for Oropouche virus disease increase in the Americas, reports of cases from additional countries are expected. This Health Advisory advises on evaluating and testing travelers who have been in impacted areas with signs and symptoms consistent with Oropouche virus infection. It also raises awareness of the possible risk of vertical transmission (e.g., from gestational parent to fetus during pregnancy) and associated adverse effects on pregnancy and highlights prevention measures to mitigate additional spread of the virus and potential importation into unaffected areas, including the United States.

Background
Oropouche virus belongs to the Simbu serogroup of the genus *Orthobunyavirus* in the *Peribunyaviridae* family. The virus was first detected in 1955 in Trinidad and Tobago and is endemic in the Amazon basin. Previous outbreaks have been described in Bolivia, Brazil, Colombia, Ecuador, French Guiana, Panama, and Peru. One child was infected in Haiti in 2014. The current 2024 outbreak is occurring in endemic areas and new areas outside the Amazon basin; countries reporting locally acquired (autochthonous) cases include Brazil, Bolivia, Peru, Colombia, and Cuba. Although travel-associated cases have been identified in the United States (n=11), no evidence of local transmission currently exists within the United States or its territories.

Sylvatic (enzootic) transmission of Oropouche virus occurs in forested areas between mosquitoes and non-human vertebrate hosts (e.g., sloths, non-human primates, domestic and wild birds, and rodents). Humans can become infected while visiting forested areas and are likely responsible for introducing the virus into urban environments. Humans contribute to the transmission cycle in urban environments since infected humans develop sufficient viremia to serve as amplifying hosts. Biting midges (*Culicoides paraensis*) and possibly certain mosquitoes (*Culex quinquefasciatus)* are responsible for transmitting the virus from an infected person to an uninfected person in urban areas.

Approximately 60% of people infected with Oropouche virus become symptomatic. The incubation period is typically 3–10 days. Initial clinical presentation is similar to diseases caused by dengue, Zika, and chikungunya viruses, with acute onset of fever, chills, headache, myalgia, and arthralgia. Other symptoms can include retroorbital (eye) pain, photophobia (light sensitivity), nausea, vomiting, diarrhea, fatigue, maculopapular rash, conjunctival injection, and abdominal pain. Clinical laboratory findings can include lymphopenia and leukopenia, elevated C-reactive protein (CRP), and slightly elevated liver enzymes. Initial symptoms typically resolve after a few days, but a high proportion (about 70%) experience recurrent symptoms days to weeks after resolution of their initial illness. Although illness is typically mild, it is estimated less than 5% of patients can develop hemorrhagic manifestations (e.g., epistaxis, gingival bleeding, melena, menorrhagia, petechiae) or neuroinvasive disease (e.g., meningitis, meningoencephalitis). Neuroinvasive disease symptoms may include intense occipital pain, dizziness,

confusion, lethargy, photophobia, nausea, vomiting, nuchal rigidity, and nystagmus. Clinical laboratory findings for patients with neuroinvasive disease include pleocytosis and elevated protein in cerebrospinal fluid (CSF).

Although people exposed to biting midges or mosquitoes infected with the virus are most at risk for developing disease, the risk factors for more severe Oropouche virus disease are not well-defined. People at risk for more severe disease likely include those at risk for severe disease with other viral infections transmitted by vectors (e.g., people aged 65 years or older, or those with underlying medical conditions, such as immune suppression, hypertension, diabetes, or cardiovascular disease). Earlier this year, Brazil reported two deaths in otherwise healthy non-pregnant women, and five cases in pregnant people with evidence of vertical transmission of the virus to the fetus associated with fetal death or congenital abnormalities, including microcephaly. This was the first report of deaths and Oropouche virus vertical transmission and associated adverse birth outcomes.

Laboratory diagnosis is generally accomplished by testing serum. Cerebrospinal fluid can also be tested in patients with signs and symptoms of neuroinvasive disease. Diagnostic testing is available at some public health laboratories (e.g., Wadsworth Center, NYS Department of Health) and at CDC. CDC and other public health laboratories are currently working to validate additional diagnostic assays. Contact your state, tribal, local, or territorial health department for more information and to facilitate testing. For current testing and case reporting guidance, visit CDC's website. In many countries, outbreaks of dengue are occurring in areas with reported Oropouche virus transmission. For patients with suspected Oropouche virus disease, it is important to rule out dengue virus infection because proper clinical management of dengue can improve health outcomes. Other diagnostic considerations include chikungunya, Zika, leptospirosis, malaria, or infections caused by various other bacterial or viral pathogens (e.g., rickettsia, group A streptococcus, rubella, measles, parvovirus, enteroviruses, adenovirus, Mayaro virus).

No specific antiviral treatments or vaccines are available for Oropouche virus disease. Treatment for symptoms can include rest, fluids, and use of analgesics and antipyretics. Acetaminophen is the preferred first-line treatment for fever and pain. Aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) should not be used to reduce the risk of hemorrhage. Patients who develop more severe symptoms should be hospitalized for close observation and supportive treatment. Pregnant people with laboratory evidence of Oropouche virus infection should be monitored during pregnancy and live-born infants should be carefully evaluated.

Travelers to areas with Oropouche virus transmission should use prevention measures to avoid biting midge and mosquito exposure during travel and for 3 weeks after travel, or if infected during the first week of illness, to mitigate additional spread of the virus and potential importation into unaffected areas in the United States. Oropouche virus disease is not a nationally notifiable condition. However, CDC encourages jurisdictions to report voluntarily to ArboNET, the national arboviral disease surveillance system.

Recommendations for Healthcare Providers

- Consider Oropouche virus infection in a patient who has been in an area with documented or suspected Oropouche virus circulation within 2 weeks of *initial* symptom onset (as patients may experience recurrent symptoms), and the following:
    - Abrupt onset of reported fever, headache, and one or more of the following: myalgia, arthralgia, photophobia, retroorbital/eye pain, or signs and symptoms of neuroinvasive disease (e.g., stiff neck, altered mental status, seizures, limb weakness, or cerebrospinal fluid pleocytosis); AND
    - No respiratory symptoms (e.g., cough, rhinorrhea, shortness of breath); AND
    - Tested negative for other possible diseases, in particular dengue. If strong suspicion of Oropouche virus disease exists based on the patient's clinical features and history of travel to an area with virus circulation, do not wait for negative testing for other infections before contacting your state, tribal, local, or territorial health department.
- Contact your state, tribal, local, or territorial health department to facilitate diagnostic testing.

- Rule out dengue virus infection in travelers with suspect Oropouche virus infection because these viruses often cocirculate and cause similar clinical presentations during acute illness. Early clinical management of dengue can improve health outcomes.
- Be aware that a high proportion of patients (about 70%) with Oropouche virus disease may experience recurrent symptoms days to weeks after resolution of their initial illness.
- Be aware of the risk of vertical transmission and possible adverse impacts on the fetus, including fetal death or congenital abnormalities. Monitor pregnancies in people with laboratory evidence of Oropouche virus infection and provide thorough infant evaluations.
- Inform pregnant people of the possible risks to the fetus when considering travel to areas with reported Oropouche virus transmission. Counsel these patients to consider the destination, reason for traveling, and their ability to prevent insect bites.
- Pregnant people are currently recommended to reconsider non-essential travel to areas with an Oropouche virus Level 2 Travel Health Notice. If a pregnant person decides to travel, counsel them to strictly prevent insect bites during travel.
- Manage travelers with suspect Oropouche virus disease with acetaminophen as the preferred first-line treatment for fever and pain. Aspirin and other NSAIDS should not be used to reduce the risk of hemorrhage.
- Be aware that people who may be at higher risk for complications or severe disease include pregnant people, older adults (e.g., aged 65 years or older), and people with underlying medical conditions (e.g., immune suppression, hypertension, diabetes, or cardiovascular disease).
- Direct all travelers going to areas with Oropouche virus transmission to use measures to prevent insect bites during travel and for 3 weeks after travel, or if infected, during the first week of illness to mitigate additional spread of the virus and potential importation into unaffected areas in the United States.
- Report all suspected Oropouche virus disease infections to your state, tribal, local, or territorial health department to facilitate diagnosis and mitigate risk of local transmission. For after-hours contact information for health departments please visit: https://www.cste.org/page/EpiOnCall. Please follow standard procedures for reporting during normal business hours.

Recommendations for Health Departments

- Share Oropouche virus prevention messages for travelers and pregnant persons with healthcare providers, travel health clinics and the public.
- Perform surveillance for Oropouche virus disease cases in travelers who have been in areas with Oropouche virus transmission and be aware of risk of possible local transmission in areas where biting midges (*Culicoides paraensis)* and mosquitoes (*Culex quinquefasciatus)* are currently active.
- Keep current on CDC's evolving testing and case reporting guidance.
- Assist healthcare providers with obtaining appropriate testing for diagnosing Oropouche virus infection.
- Voluntarily report confirmed and probable Oropouche virus infections to CDC via ArboNET, the national surveillance system for arthropod-borne viruses.
- Contact CDC (eocevent495@cdc.gov) if concern exists for local transmission in a non-endemic area. Consider if the patient had contact with a person with confirmed Oropouche virus infection, lives in an area where travel-related cases have been identified, or has known vector exposure (e.g., mosquitoes or biting midges).

Recommendations for Travelers

- All travelers can protect themselves from Oropouche, dengue, Zika, and other viruses transmitted by insects by preventing insect bites, including using an Environmental Protection Agency (EPA)-registered insect repellent; wearing long-sleeved shirts and pants; and staying in places with air conditioning or that use window and door screens.
- Pregnant travelers should discuss travel plans, reasons for travel, steps to prevent insect bites, and potential risk with their healthcare provider.

- Pregnant people considering travel to countries with an Oropouche virus Level 2 Travel Health Notice should reconsider non-essential travel. If travel is unavoidable, pregnant travelers should strictly follow Oropouche virus prevention recommendations to prevent insect bites during travel.
- Travelers should be aware that the most common symptoms of Oropouche virus are fever and headache and that symptoms usually begin 3-10 days after being bitten by an infected midge or mosquito. Most people infected with Oropouche virus feel better within a week, but symptoms often come back.
- Travelers who have been in areas with Oropouche virus transmission should prevent insect bites for 3 weeks after travel.
- Travelers to areas with Oropouche virus transmission, including South America or the Caribbean, who develop fever, chills, headache, joint pain, or muscle pain during or within 2 weeks after travel, should:
    - Seek medical care and tell their healthcare provider when and where they traveled.
    - Not take aspirin or other NSAIDS (e.g., ibuprofen) to reduce the risk of bleeding.
    - Continue to prevent insect bites during the first week of illness to avoid further spread, especially in areas where mosquitoes or biting midges are active.

For More Information

- About Oropouche | CDC
- Travel Health Notices | CDC
- Preventing Mosquito Bites | CDC
- Find the Repellent that is Right for You | EPA
- Dengue: Guidelines for Diagnosis, Treatment, Prevention and Control | WHO

References

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2. Pan American Health Organization / World Health Organization. Epidemiological Alert: Oropouche in the Region of the Americas: vertical transmission event under investigation in Brazil, 17 July 2024. Washington, D.C.; 2024.
3. Pan American Health Organization / World Health Organization. Epidemiological Alert: Oropouche in the Region of the Americas, 1 August 2024. Washington, D.C.; 2024.
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11. Pan American Health Organization / World Health Organization. Public Health Risk Assessment related to Oropouche Virus (OROV) in the Region of the Americas, 3 August 2024. Washington, D.C.; 2024.

The Centers for Disease Control and Prevention (CDC) protects people's health and safety by preventing and controlling diseases and injuries; enhances health decisions by providing credible information on critical health issues; and promotes healthy living through strong partnerships with local, national, and international organizations.

Categories of Health Alert Network messages

Health Alert	Requires immediate action or attention. Conveys the highest level of importance about a public health event.
Health Advisory	Requires immediate action. Provides important information about a public health event.
Health Update	May require immediate action. Provides updated information about a public health event.
HAN Info Service	Does not require immediate action. Provides general information about a public health event.