

## Oropouche Virus – Interim Fact Sheet

### Disease Agent:

- Oropouche virus (OROV)

### Disease Agent Characteristics:

- Family: Peribunyaviridae, genus Orthobunyavirus (La Crosse virus is another example)
- Virion morphology and size: Enveloped, 80-120 nm in diameter
- Nucleic acid: OROV is a negative-sense, single-stranded RNA virus with a spherical lipid-enveloped genome consisting of three single stranded RNA segments called large (L) medium (M) and small (S) of 6,852; 4,385 and 958 nucleotides respectively similar to La Crosse virus.
  - There are four OROV genotypes, but it is suggested that infection with any will provide immunity against future reinfection.
- Physicochemical properties: other Orthobunyaviruses are inactivated by a number of disinfectants including sodium hypochlorite (household bleach), hydrogen peroxide, peracetic acid and ethanol. Heat and gamma irradiation have also been used.

### Disease Names:

- Oropouche fever

### Priority Level:

- Scientific/Epidemiologic evidence regarding blood safety: Theoretical
- Public perception and/or regulatory concern regarding blood safety: Very low
- Public concern regarding disease agent: Very low in non-endemic areas. Moderate in endemic areas where recent reports suggesting vertical transmission and fetal injury *in utero* have increased this concern.

### Background:

- Discovered in Trinidad in 1955. As many as 500,000 infections may have occurred since, based on serological studies. It is certainly underrecognized due to nonspecific clinical presentations, limited clinical suspicion and access to diagnostics.
- OROV is an arthropod-borne orthobunyavirus found in South America and causes Oropouche fever, a febrile infection similar to dengue. It is the second most prevalent arthropod-borne viral disease in South America after dengue. The main vector is the biting midge *Culicoides paraensis*, with a range as far north as the United States (US) suggesting the potential for OROV infection to expand geographically. *Culex quinquefasciatus* mosquitoes can also serve as a vector. The sylvan transmission cycle is incompletely understood, and vertebrate hosts include sloths, non-human primates and birds.
- Based on available data (2024), sustained local transmission risk in the continental US is considered low because of differences in vector ecology and human–vector interactions (e.g., mitigation by

- widespread availability of closeable windows and air-conditioning) compared with OROV–endemic areas.
- OROV is a BSL level 2 or 3 pathogen, depending on the country. In the US it is level 2.

#### **Common Human Exposure Routes:**

- Vector-borne
- No evidence for person-to-person spread before 2024 reports of vertical transmission *in utero*

#### **Likelihood of Secondary Transmission:**

- Appears low but vertical transmission described during pregnancy at the case report level during 2024 transmission season in Brazil
- A case report of virus isolation from semen has raised concern for the possibility of sexual transmission.

#### **At-Risk Populations:**

- Populations in endemic areas with exposure to vectors including travelers

#### **Vector and Reservoir Involved:**

- *Culicoides paraensis*, a small biting fly or midge is the main vector but culex and other mosquitoes have also been implicated.
- In the urban cycle, *C. paraensis* is the primary vector which has been implicated in large epidemics affecting up to 100,000 patients.
- Possible reservoirs in the sylvatic cycle based largely on antibody studies include sloths, non-human primates, rodents and wild and domestic birds.
- Potential vectors are widespread globally but there is little information about their competence for OROV transmission.

#### **Blood Phase:**

- The virus was originally isolated from acute phase serum injected intracerebrally into mice. Small numbers of cases with virus isolation from blood have been reported subsequently.
- Subsequent references to viremia are largely confined to demonstration of RNAemia but infectious virus is present during acute infection.
- The levels of both virus and RNA are highest early during symptomatic infection (peaking around day 2) and fall rapidly toward the end of the first week of illness. The virus may not be detectable by the time a patient seeks care.
- An appreciable rate of apparently asymptomatic infection ( $\approx 40\%$ ) raises the theoretical concern for transmission by blood and other substances of human origin.

#### **Survival/Persistence in Blood Products:**

- Unknown

**Transmission by Blood Transfusion:**

- Not reported to date from transfusion or transplantation

**Cases/Frequency in Population:**

- More than 30 epidemics have been recognized in Latin America and the Caribbean with the greatest number in Brazil. Autochthonous transmission has occurred in Peru, Panama, Colombia, Cuba, Bolivia, Venezuela, Haiti, French Guiana and Trinidad and Tobago.
- Extrapolation from serological studies suggest at least 500,000 infections had occurred by 2018.
- The prevalence of seroreactivity in affected regions can be as high as 20%.
- All genders and ages are affected.
- Since late 2023, OROV has caused large outbreaks in formerly endemic areas and new areas in South America.
- During January 1–October 15, 2024, more than 10,000 confirmed OROV clinical cases and 2 deaths were reported from 6 countries: Bolivia, Brazil, Colombia, Cuba, the Dominican Republic, Ecuador and Peru.
- To Oct. 15, 2024, 90 travel-associated cases related to travel from Latin America and Cuba have been reported among persons in the US, 2 in Canada, and 30 in Europe.
- Analyses of ~400 genomes revealed that the upsurge of OROV cases in the Brazilian Amazon coincides with spread of a novel reassortant lineage containing the M segment of viruses detected in the eastern Amazon region (2009-2018) and the L and S segments of viruses detected in Peru, Colombia, and Ecuador (2008-2021). The novel reassortant likely emerged in the Amazonas state between 2010 and 2014. Phylodynamic reconstructions showed that the current OROV spread was mainly driven by short-range (<2 km) movements consistent with the flight range of vectors as well as long-range (>10 km) OROV migrations consistent with viral dispersion by humans.
- The reassortant virus, responsible for the current outbreak, has several features that are different than the prototype strains: 100-fold higher titers in mammalian cell culture; earlier plaque formation with altered morphology; lastly, significant reduction in the neutralizing capacity of convalescent sera from prior infections.

**Incubation Period:**

- The incubation period is typically 3-8 days after exposure but there are reports extending to 14 days.

**Likelihood of Clinical Disease:**

- Seroprevalence studies suggest many infections are either asymptomatic or not recognized as Oropouche fever.

**Primary Disease Symptoms:**

- Approximately 60% of infected individuals become symptomatic. The appreciable rate of apparently asymptomatic infection raises the theoretical concern for transmission by blood and other substances of human origin.
- Oropouche fever closely resembles dengue virus infection and other arboviral infections like those

- of chikungunya or Zika viruses, and those resulting in malaria. Requires an index of suspicion and specific testing to diagnose.
- Symptoms include fever, myalgia, arthralgia, headache and photophobia, nausea and vomiting, malaise and dizziness.
- Unusual manifestations include rash and hemorrhagic signs.
- Neurologic complications, including aseptic meningitis and encephalitis can occur (in perhaps as many as 4% of recognized infections), mainly in immunocompromised individuals, and Oropouche should be considered when these syndromes occur in endemic/epidemic areas with serological and virologic examination of CSF considered.
- Mild recurrent symptoms may occur for up to three weeks.
- Postinfectious weakness and asthenia may last several weeks.
- Systematic data on the impact of *in utero* exposure are lacking, but concern has been raised during 2024 when a woman with compatible symptoms presented at 30 weeks gestation with fetal demise. She had serologic evidence of OROV infection (in addition to chikungunya and dengue), and serum and placenta were OROV positive by RT-PCR. OROV RNA was detected in cord blood and organ tissues from the fetus, in the absence of dengue, chikungunya, Zika and Mayaro viruses.
- As of 1 August 2024, a miscarriage, 4 (retrospective) cases of microcephaly, and 3 more possible vertical transmissions associated with fetal death are under investigation in Brazil.

**Severity of Clinical Disease:**

- Oropouche fever is generally relatively mild and self-limiting.
- More severe (e.g., CNS) illness can occur, especially in the presence of immunocompromise.
- The relationship to fetal injury and its spectrum is not clear.

**Mortality:**

- Mortality is highly unusual. During the current epidemic in South America, from reporting weeks 1 through 29, 2 deaths among 8078 cases have been reported, and these may be the first deaths attributed to OROV since its discovery.

**Chronic Carriage:**

- None

**Treatment Available/Efficacious:**

- Supportive; no specific anti-viral treatment is available

**Agent-specific Screening Question(s):**

- No specific question is in use.
- No sensitive or specific question is feasible.

**Laboratory Test(s) Available:**

- No FDA-licensed blood donor screening tests exist for OROV.
  - Diagnostic studies are available mainly after consultation with state and local public health laboratories.
- OROV is occasionally isolated in cell culture from the blood and/or CSF of symptomatic cases. Culturable virus is generally gone by the end of the first week of illness.
- Serological tests include EIAs (IgM and IgG) generally detecting antibodies to nucleocapsid antigens, PRNT, and immunoblots from blood or CSF. They are generally reactive from the 5<sup>th</sup> day after symptom onset. Cross-reactivity with related viruses can be an issue.
- Nucleic acid amplification assays are sensitive and specific and are the primary tests being used in epidemic areas.

**Currently Recommended Donor Deferral Period:**

- No FDA Guidance or AABB Standard exists.
- Prudent practice would be to defer until fully recovered. FDA, in an “Important Information”, has recently suggested 28 days from recovery when a donor volunteers a recent diagnosis of Oropouche disease.

**Impact on Blood Availability:**

- Agent-specific screening question(s): Not applicable
- Laboratory test(s) available: Not applicable

**Impact on Blood Safety:**

- Agent-specific screening question(s): Not applicable
- Laboratory test(s) available: Not applicable

**Leukoreduction Efficacy:**

- Unknown

**Pathogen Reduction Efficacy for Plasma Derivatives:**

- Multiple pathogen reduction steps used in the fractionation process have been shown to be robust in removal of enveloped viruses.

**Other Prevention Measures:**

- There is no licensed vaccine.
- Arthropod avoidance (e.g. repellants and barriers)
- No effective vector control measures have been described for the primary *Culicoides* vector.
- Timely detection and control should be prioritized to mitigate disease burden and stop its current spread.

**Suggested Reading:**

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