

## FOCUS ON

# Oropouche Virus in the Americas



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## Introduction

This document explores the re-emergence, epidemiology, and clinical presentation of Oropouche virus disease (also known as Oropouche fever). Oropouche virus disease is a zoonotic arboviral disease caused by Oropouche virus (OROV) and transmitted by biting midges and some mosquitoes, with patients experiencing an acute febrile illness that is often self-limiting and resolves within a week. Historically, Oropouche virus disease was reported primarily from the Amazon region of Brazil and Peru; however, now OROV is distributed more widely in the Caribbean, Central America, and South America.<sup>1</sup>

Public Health Ontario (PHO) developed this Focus On to raise awareness of OROV and Oropouche virus disease among Ontario public health partners and healthcare providers. This resource is both timely and essential, given the recent re-emergence of Oropouche virus disease in the Americas.

## Key Messages

- The putative species of biting midge and mosquito involved in OROV transmission are not found in Ontario, corresponding to a low risk of locally acquired Oropouche virus disease in the province; however, imported infections are possible in travellers returning from the Caribbean, Central America, and South America.
- Oropouche virus disease is typically a mild disease that resolves within a week; however, there is evidence of vertical transmission that can result in congenital abnormalities and fetal death.
- Travellers to affected countries should take appropriate personal protective measures, including using insect repellent, limiting time outdoors, covering up, wearing light-coloured clothing, wearing insecticide-treated clothing, and using bed nets.

## Background

Oropouche virus is a zoonotic arbovirus that causes Oropouche virus disease in humans. The virus was initially isolated from a patient in Trinidad and Tobago in 1955; the first Oropouche virus disease epidemic occurred in Belém, Brazil, in 1961 with approximately 11,000 cases.<sup>2</sup> Outbreaks have been sporadic since 1961 and primarily from the Amazon region of Brazil and Peru, with the largest in Manaus, Brazil, in 1980 with 97,000 cases.<sup>1</sup>

Since August 2024, imported Oropouche virus disease cases in individuals who had recently travelled to Cuba were reported in the Cayman Islands, Germany, Italy (plus cases from Brazil), Spain, United States (US) and Canada.<sup>3-7</sup> On Sept 3, 2024, the Public Health Agency of Canada (PHAC) updated a *Level 1 Travel Health Notice* for Oropouche virus disease in Bolivia, Brazil, Colombia, Cuba, and Peru, which was upgraded on Nov 4, 2024 to a *Level 2 Travel Health Notice* with Dominican Republic added to the list of impacted countries.<sup>8</sup> Similarly, the Centers for Disease Control and Prevention (CDC) have updated a *Level 1 Travel Health Notice* for Barbados, Bolivia, Brazil, Colombia, Cuba, Dominican Republic, Ecuador, Guyana and Peru on Dec 11, 2024; and a *Level 2 Travel Health Notice* was issued for Espírito Santo, Brazil on Dec 11.<sup>9,10</sup> Following the detection of 11 travel-associated cases in the US, on Aug 16, 2024, the CDC issued a *CDC Health Alert Network (HAN) Health Advisory: Increased Oropouche Virus Activity and Associated Risk to Travelers*.<sup>5</sup>

Given the relatively high numbers of travellers returning to Ontario from Cuba, there is a risk of imported cases for the province.<sup>11,12</sup> On September 20, 2024, the Public Health Agency of Canada published a *Rapid risk assessment: Oropouche virus (OROV), public health implications for Canada*, stating that the likelihood of OROV infection in Canadians travelling to or residing in affected countries in the next 7 months is assessed as low to moderate, varying by location, timing and duration of travel, as well as use of protective measures.<sup>6</sup>

## Methods

A literature search was conducted on Dec 17, 2024, in ProMed using the key word “Oropouche.” The exposures of interest were biting midges and mosquitoes and the outcome of interest was Oropouche virus disease. English-language peer-reviewed and non-peer-reviewed records that described OROV and its epidemiology were included. Out-of-scope for this document was the pathophysiology and immunology of Oropouche virus disease. The search concentrated on the epidemiological information relevant to Ontario.

# Results

## Virology

Oropouche virus is within the genus *Orthobunyavirus* and family *Peribunyaviridae*, further classified to the Simbu serogroup of viruses.<sup>1</sup> Oropouche virus is a spherical, enveloped virus composed of three single-stranded, negative-sense RNA segments.<sup>13</sup> Based on the molecular epidemiology of OROV isolates collected from the Caribbean, Central America, and South America (1960–2009), OROV likely emerged in Brazil about 235 years ago.<sup>14</sup> Several orthobunyaviruses circulate in Ontario (e.g., Jamestown Canyon virus); however, Simbu serogroup viruses, including OROV, do not circulate in the province.

Within a host, OROV and novel Simbu serogroup viruses can co-infect and undergo recombination, leading to reassortant viruses, including the Iquitos virus, Madre de Dios virus, and Perdões virus.<sup>2,15,16</sup> Whether or not exposure to reassortants confers some cross-protection from OROV is unknown.<sup>2</sup> The current hypothesis for the recent outbreak in Brazil is that a novel reassortment event occurred sometime between 2015 and 2024, in which the novel strain, compared to the prototype strain, replicates better in mammalian cells and is more virulent; serum samples from individuals infected in 2016 did not efficiently neutralize the new reassortant, meaning individuals previously infected with OROV are likely susceptible to reinfection with new variants.<sup>17</sup>

## Epidemiology

In a recent review of OROV, Wesselmann et al. (2024) noted that the epidemiology of the virus remains unclear, highlighting the need for more research into reservoirs, vector ecology, transmission cycles, immunology, and the natural history of infection.<sup>2</sup>

Oropouche virus circulates within two transmission cycles, the sylvatic cycle among non-human vertebrates in forested areas and the urban cycle among humans in metropolitan areas. Human infections acquired in forested areas provide sources for transmission in urban areas following movement of infected individuals. The sylvatic cycle is poorly understood, but involves non-human primates (e.g., capuchin and howler monkeys), three-toed sloths, and birds, with putative transmission by *Aedes serratus*, *Coquillettidia venezuelensis*, *Culex quinquefasciatus*, and species of biting midges in the genus *Culicoides*.<sup>18</sup> The primary vector in the urban cycle is considered the biting midge *Culicoides paraensis*, with involvement of the southern house mosquito (*Cx. quinquefasciatus*); neither of which are found in Ontario.<sup>13,19</sup> *Culicoides paraensis* eggs are laid in moist environments, hatching into larvae in 3–10 days; moist environments include dung, damp soil, tree holes, and decaying plant matter.<sup>19</sup> In the State of Rondônia, Brazil, increased biting activity of *C. paraensis* was associated with time of day (4–6 pm), the rainy season (January–June), high temperatures (30–32°C), and high humidity (75–85%).<sup>20</sup> Oropouche virus disease occurs mostly during the rainy season in affected countries.

*Culicoides paraensis* is found throughout most of South America, Central America, and the Caribbean, with populations extending north into the Central US (e.g., Missouri) and Eastern US (e.g., Virginia).<sup>1,21,22</sup> While *Culicoides* biting midges occur in Ontario, *C. paraensis* does not; however, climate change may contribute to a northerly range expansion of this species.<sup>23</sup> During laboratory studies, the vector competence was low for *Ae. aegypti*, *Ae. albopictus*, *Cx. tarsalis*, *Cx. quinquefasciatus*, and *C. sonorensis*.<sup>24,25</sup> *Aedes albopictus*, *Cx. tarsalis*, and *C. sonorensis* are found in Ontario in low numbers; the risk of local OROV transmission by these vectors is considered low for the province.<sup>26–28</sup> *Culicoides paraensis* and *Cx. quinquefasciatus* are found throughout Florida where imported cases have been reported; however, there is no evidence of local OROV transmission in the state.<sup>29</sup>



Prior to 2000, outbreaks of Oropouche virus disease were reported from Brazil, Panama, and Peru; however, since 2000, OROV has emerged in Argentina, Bolivia, Columbia, Cuba, Dominican Republic, Ecuador, French Guiana, Haiti, Paraguay, and Venezuela.<sup>1,13,30,31</sup> Given the wide range of potential reservoirs and vector species, along with population movement, the distribution of OROV is expected to expand.<sup>2,13</sup> Seroprevalence can be high in areas where OROV is not known to occur, representing unidentified outbreaks; for example, in Panama (1968–1978), antibodies against OROV were detected in 25% of the population.<sup>19</sup> Currently, outbreaks of Oropouche virus disease are occurring across the Neotropics. In Brazil, an outbreak of 8,639 cases (Jan–Aug 2024) occurred, which is 58.8 times the annual median of 147 cases (interquartile range [IQR]: 73–325; 2015–2023).<sup>17</sup>

Recent case reports indicate the potential for sexual transmission of OROV; however, there have been no reports of OROV sexual transmission.<sup>32,33</sup> Castilletti et al. (2024) reported on a male traveller returning to Italy from Cuba with Oropouche virus disease; viremia was prolonged for 16 days post symptom onset with replication-competent (live infectious virus recovered from culture) detected in semen.<sup>32</sup>

## Clinical Manifestations and Disease Severity

The incubation period for OROV is about 3 to 8 days following the bite of an infectious biting midge or mosquito.<sup>18,19</sup> Patients with Oropouche virus disease experience an acute febrile illness with symptoms including arthralgia, chills, dizziness, headaches, malaise, myalgia, photophobia, and retro-ocular pain.<sup>13</sup> In Peru, among 131 patients with serological evidence of OROV infection and fever, the most common clinical manifestations included headache (86%), myalgia (81%), arthralgia (73%), and loss of appetite (68%).<sup>34</sup> Oropouche virus disease is typically a self-limiting disease that resolves in 2–7 days.<sup>12,13</sup> Serious complications of OROV infection can extend the illness for several weeks, with estimates that less than 5% of cases may develop hemorrhagic manifestations (e.g., nosebleeds, bleeding gums) or neuroinvasive disease (e.g., confusion, dizziness, meningitis, meningoencephalitis).<sup>5,13</sup> In 30–70% of patients, symptoms return 2 days to 1 month following initial recovery and include dizziness, fatigue, fever, headache, meningismus, and myalgia.<sup>1,2,13,31,35</sup> Prior to the deaths of two non-pregnant women from Brazil in 2024, a death from Oropouche virus disease was last reported almost 70 years ago.<sup>1,5,36,37</sup>

On July 17, 2024, the Pan American Health Organization/World Health Organization (PAHO/WHO), given emerging evidence for the vertical transmission of OROV, alerted member states to report any cases of congenital malformation, miscarriage, and fetal death with unknown etiology.<sup>38</sup> The first documented cases of vertical transmission, which led to congenital malformations and fetal death, occurred in July 2024.<sup>5,36,39</sup>

Due to the similar clinical presentation of Oropouche virus disease and other co-circulating arboviruses (e.g., chikungunya [CHIKV], dengue [DENV], Zika [ZIKV]), underdiagnoses, misdiagnosis, and underreporting is likely high.<sup>18</sup> Efforts to develop a clinical prediction model for the diagnosis of Oropouche virus disease based on signs and symptoms alone did not perform well.<sup>40</sup> The challenge of clinical diagnoses contributes to a lack of disease awareness, which in turn leads to undetected outbreaks, and continued cryptic transmission. Identification of outbreaks are further hampered by a lack of adequate disease surveillance and multi-virus diagnostic panels.<sup>41</sup>

## Patient Demographics and Risk Factors

Patients with Oropouche virus disease are most often young (<40 years) and male (Table 1). In a study of 8,639 cases from Brazil (2015–2024), higher incidence of disease (>5 per 100,000 population) occurred in males 20–59 years old (Scachetti et al. 2024).<sup>17</sup>

**Table 1: Demographics of patients with Oropouche virus disease**

Location	No. patients	Age	Proportion male (%)
Bolivia <sup>42</sup>	356	20% of cases 30–39 years old	50
Brazil <sup>42</sup>	7,284	21% of cases 30–39 years old	52
Brazil <sup>43</sup>	27	Mean ( $\pm$ standard deviation): 43 years ( $\pm$ 17.7)	59
Columbia <sup>42</sup>	74	37% of cases 10–19 years old	49
Cuba <sup>44</sup>	89	Median (IQR): 35 years (18–51)	52
French Guiana <sup>45</sup>	41	Median (IQR): 38 years (16–51)	56
Peru <sup>42</sup>	290	40% of cases 30–39 years old	52
Peru <sup>40</sup>	97	40% of cases <15 years old	56
Peru <sup>46</sup>	131	25% of cases 18–39 years old	55

The risk factors for Oropouche virus disease are not described, but they are expected to be similar to other arboviruses (e.g., older age, those with immune compromise or underlying conditions). Outbreaks have been associated with urbanization, poor socioeconomic conditions, human migration, deforestation, and climate change (i.e., increased temperature and precipitation), factors that favour an increased likelihood of viral transmission.<sup>12,47–50</sup> In a recent study of the 2023–24 Brazil outbreak, Gräf et al. (2024) noted that outside of the Amazon region, case frequency was 3–9 times higher in small communities associated with banana and cassava cultivation.<sup>51</sup>

## Treatment and Prevention

There are no specific treatments for Oropouche virus disease and treatment is primarily supportive. Candidate treatments tested to date have not provided antiviral activity against OROV.<sup>1</sup> The development of vaccines against OROV is challenging due to the genetic diversity of the virus, however, several vaccines are in various stages of development.<sup>1,13,19</sup> On Dec 11, 2024, PAHO/WHO urged countries with ongoing transmission to strengthen epidemiological and vector surveillance and to reinforce prevention measures.<sup>7</sup>

Advice for the prevention of Oropouche virus disease among travellers focuses on pregnant women. In PHAC's *Level 2 Travel Health Notice* for Oropouche virus disease in the Americas, they recommend that "...pregnant people may want to be extra cautious and avoid travelling to areas where the Oropouche virus is present until more is known about how an infection could affect their unborn baby."<sup>8</sup> Similarly, the CDC *Level 2 Travel Health Notice* for Oropouche in Espírito Santo, Brazil, states "Pregnant people should reconsider non-essential travel to Espírito Santo, Brazil. If travel is unavoidable, these travelers should strictly follow Oropouche prevention recommendations."<sup>10</sup>

Prevention efforts in affected countries concentrate on increasing public and physician awareness, the development of laboratory diagnostics and human case surveillance, vector surveillance and management, and personal protection.<sup>1</sup> Travellers to affected countries should use insect repellent, limit time outdoors, cover up, wear light-coloured clothing, wear insecticide-treated clothing, and use bed nets.<sup>5,9,10</sup>

## Laboratory Diagnostics

Public Health Ontario's laboratory offers molecular testing (PCR) for OROV upon special request. To be approved for testing, patients must be screened for more common arboviruses, specifically CHIKV, DENV and ZIKV, and must have a relevant exposure and travel history. Serum is the preferred specimen type. In Oropouche virus disease, viremia can peak around day 2 of illness, however, OROV nucleic acids may be detected up to 7 to 10 days after symptom onset.<sup>31</sup> Serology testing is also available via the US CDC upon special request. Please see PHO's [testing information page](#) for further details.<sup>52</sup>

## Implications for Public Health

- In 2023 and 2024, OROV re-emerged in the Americas, with reports of vertical transmission from pregnant mothers to unborn children. The long-term impact of vertical transmission on the health of children is not known at this time.
- The primary OROV vectors (*C. paraensis*, *Cx. quinquefasciatus*) are not present in Ontario, making the risk of local transmission very low in the province.
- There are no formal surveillance mechanisms for OROV or Oropouche virus disease in Ontario.
- Travellers to affected regions should take appropriate precautions to prevent insect bites.
- Imported OROV infections are expected in travellers returning from the Caribbean, Central America, and South America.
- Clinicians should consider virus disease in their differential diagnoses for individuals with compatible symptoms and recent travel history to an affected area.

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