MONTHLY SCIENTIFIC REVIEW ON OROPOUCHE VIRUS

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General informations

This section details the history and latest developments of the outbreak, with significant events and updates on its current status.

The Oropouche virus (OROV) was first detected in 1955 in Trinidad and Tobago in the Caribbean near the Oropouche River. Since then, it has primarily affected South and Latin America, especially Brazil, Panama, Peru, Argentina, Bolivia, Colombia, Ecuador, and French Guiana. As of 2023, the virus has caused large outbreaks not only in historically endemic regions but also in new areas. By October 16, 2024, **the Americas reported 10,275 confirmed cases and 2 deaths** in six countries: Bolivia (356 cases), Brazil (8,258 cases and 2 deaths), Canada (2 imported cases), Colombia (74 cases), Cuba (555 cases), Ecuador (2 cases), Guyana (2 cases) Peru (936 cases), the Dominican Republic (33 cases) and the United States of America (90 imported cases).

Cuba reported its first Oropouche outbreak in June 2024 with 555 confirmed cases and over 10,000 suspected cases, according to PAHO by October 16. While this outbreak did not lead to severe cases, it marked an unprecedented geographic expansion of the virus. In the Dominican Republic, 33 cases, including 3 deaths, have been confirmed to date, according to PAHO as of September 23.

Additionally, imported Oropouche cases have been reported in countries in the European Region (30 cases).

Vertical transmission of Oropouche virus from mother to fetus had not been documented until five possible cases were identified in Brazil by July 30, 2024.

Scientific articles

This section presents relevant articles published on peer-reviewed scientific journals or pre-print platforms.

A Case of Vertical Transmission of Oropouche Virus in Brazil.

Garcia Filho C, Lima Neto AS, Maia AMPC, da Silva LOR, Cavalcante RDC, Monteiro HDS, Marques KCA, Oliveira RS, Gadelha SAC, Nunes de Melo D, Mota AGM, de Lima STS, Cavalcante KF, Duarte LMF, Cavalcante ÍJM, Mello LMS, Alencar CH, Rodrigues CDDS, de Oliveira CS, de Bruycker-Nogueira F, Naveca FG, Ribas Freitas AR, Cavalcanti LPG.

Published in *N Engl J Med* on 30 october 2024.
https://doi.org/10.1056/nejmc2412812

his case report describes a pregnant woman who tested positive for Oropouche virus (OROV) and suggests a potential link between the stillbirth and the ongoing OROV outbreak in Brazil. The findings underscore the significant risks associated with OROV infection during pregnancy, highlighting the need to consider this infection in pregnant women who present with fever or other symptoms suggestive of infection, especially those living in or traveling to regions where the virus is endemic or emerging.

Newborns with microcephaly in Brazil and potential vertical transmission of Oropouche virus: a case series.

As Neves Martins FE, Chiang JO, Nunes BTD, Ribeiro BFR, Martins LC, Casseb LMN, Henriques DF, de Oliveira CS, Maciel ELN, Azevedo RDS, Cravo LCC, Barreto ARF, Pessoa ALS, Filho AJM, de Sousa JR, Schuler-Faccini L, Quaresma JAS, da Costa Vasconcelos PF, da Silva Azevedo RDS.

Published in *Lancet Infect Dis* on 15 October 2024.
https://doi.org/10.1016/s1473-3099(24)00617-0

This case series investigates the potential link between Oropouche virus (OROV) and congenital malformations in newborns, particularly microcephaly, in Brazil. Of 68 newborns tested, six cases were positive for OROV, including one infant who died with OROV RNA and antigens detected in several tissues, including the brain. The findings suggest a potential vertical transmission of OROV, though further investigation is needed to confirm this. The study highlights the urgent need for comprehensive research on OROV's role in fetal harm, especially in areas affected by the ongoing outbreak.

Replication-Competent Oropouche Virus in Semen of Traveler Returning to Italy from Cuba, 2024.

Castilletti C, Huits R, Mantovani RP, Accordini S, Alladio F, Gobbi F.

Published in *Emerg Infect Dis* on 7 October 2024.
https://doi.org/10.3201/eid3012.241470

In this research letter, the authors report the observation of a febrile man in Italy who had traveled to Cuba in July 2024 and was diagnosed with Oropouche fever. Reverse transcription PCR detected prolonged shedding of Oropouche virus RNA in whole blood, serum, urine, and semen. Sixteen days after symptom onset, replication-competent virus was detected in semen, suggesting risk for sexual transmission.

Co-Circulation of 2 Oropouche Virus Lineages, Amazon Basin, Colombia, 2024.

Usuga J, Limonta D, Perez-Restrepo LS, Ciuoderis KA, Moreno I, Arevalo A, Vargas V, Berg MG, Cloherty GA, Hernandez-Ortiz JP, Osorio JE.

Published in *Emerging Infectious Diseases* on 2 October 2024.
https://doi.org/10.3201/eid3011.240405

In this study, the authors report human the co-circulation of 2 Oropouche Virus Lineages in the Amazon Basin in Colombia. They conducted phylogenetic analysis of the OROV L, M, and S segments isolated from patient samples by using available OROV genomes and sequences of the new clade from Brazil. OROV BR-2015-2024 from Brazil was present in 2 samples from Leticia municipality, designated as LET-2099 and LET-2102. Although the L and S segments of those 2 OROV samples each branched as paraphyletic clades basal to OROV PE/CO/EC-2008-2021, the M segment sequences were more closely related to OROV BR-2009-2018 sequences. The numerous mutations in OROV BR-2015-2024 RNA-dependent RNA polymerase and glycoproteins likely enhanced replication and immune evasion capabilities, increasing virus fitness and transmission. The identification of co-circulating strains of OROV exemplifies the evolving nature of orthobunyaviruses and raises concerns about future reassortment events and emergence of new lineages having more severe clinical phenotypes and enhanced vector competence.

Oropouche fever fatalities and vertical transmission in South America: implications of a potential new mode of transmission.

Sah R, Srivastava S, Mehta R, Khan SR, Kumar S, Satpathy P, Mohanty A, Ferraz C, Feehan J, Apostolopoulos V, Luna C, Rodriguez-Morales AJ.

Published in *Lancet Reg Health Am* on 25 September 2024.
https://doi.org/10.1016/j.lana.2024.100896

The 2024 Oropouche virus (OROV) outbreak is affecting 10 non-Amazonian states in Brazil, with confirmed fatal cases, including two adult female deaths. Vertical transmission of the virus, associated with congenital malformations like microcephaly and fetal deaths, has been observed but not yet definitively confirmed. Miscarriages and malformations have also been reported, particularly in the states of Pernambuco, Acre, and Pará. The lack of a specific antiviral treatment highlights the importance of enhanced surveillance and vector control measures. Further research is needed to better understand the impact of vertical transmission and its role in the evolution of the outbreak.

This section provides a digested list of a more extensive content accessible in Excel format here.

Relevant news

This section presents official reports from health agencies, manufacturers and press releases with reliable sources.

2024 Oropouche Outbreak

Published by CDC on 12 November 2024.
https://www.cdc.gov/oropouche/outbreaks/2024/index.html

From late 2023-2024, outbreaks of Oropouche virus disease (Oropouche) have been reported in several countries in South America and the Caribbean. Travel-associated cases among U.S. residents have been reported, but local transmission has not been detected in the United States.

Oropouche Virus and Possible Sexual Transmission

Published by CDC on 4 November 2024.
https://www.cdc.gov/oropouche/hcp/clinical-overview/possible-sexual-transmission.html

CDC will continue to review all available data, work closely with partners to obtain additional data regarding the likelihood of sexual transmission, and update these interim prevention recommendations as needed.

Response to Oropouche Virus Disease Cases in U.S. States and Territories

Published by CDC on 30 October 2024.
https://www.cdc.gov/oropouche/php/response-plan/index.html

CDC has developed a response plan to assist state, Tribal, local, and territorial health departments in investigating and responding to importation and potential transmission of Oropouche virus in U.S. states and territories in the Americas.

Unprecedented spread and genetic evolution of the Oropouche virus

Published by *Nature* on 28 October 2024.
https://www.nature.com/articles/s41591-024-03336-5

The current Oropouche fever outbreak has been traced to a novel reassortant virus that emerged about a decade ago, which highlights the importance of One Health surveillance in preventing, predicting, detecting and responding to emerging threats.

Fact sheets

This section provides a short overview of of the epidemiology, virology, clinical features and risk assessment related with the disease.

Oropouche disease is an arboviral disease caused by the Oropouche virus (OROV), a single-stranded RNA virus belonging to the *Orthobunyavirus* genus of the *Peribunyaviridae* family. This virus is endemic in several regions of Central and South America, as well as the Caribbean, where it actively circulates. Human transmission primarily occurs through the bite of small midges of the *Culicoides* genus (*Culicoides paraensis*), which inhabit forested and humid areas.

After OROV infection, **the incubation period ranges from 3 to 10 days**. Symptoms are often non-specific and can easily be confused with other arboviruses like Dengue, Chikungunya, or Zika. Patients may experience fever, headaches, nausea, joint and muscle pain, conjunctivitis, and abdominal pain. However, about **80% of infected individuals remain asymptomatic**. Recovery typically takes about a week, though it may extend for several weeks in some cases. Around 4**% of symptomatic cases may develop severe, neuroinvasive forms**, including meningitis and encephalitis. **Vertical transmission** of the virus, from mother to child during pregnancy, is still being studied.

Diagnosis of Oropouche disease relies on several methods. Virus detection via RT-PCR is possible between days 1 and 7 after symptom onset. Serological tests like ELISA can detect IgM and IgG antibodies, which appear from day 1 to two weeks after illness onset. Biological samples used for these tests include serum, saliva, and urine. In patients with signs of neuroinvasive disease, cerebrospinal fluid analysis can also be performed.

Treatment is primarily symptomatic, focusing on hydration, pain relief, and antipyretics. **No specific antiviral treatment** is currently available. As with Dengue, the use of aspirin and nonsteroidal anti-inflammatory drugs is discouraged to reduce the risk of bleeding. Although several antiviral candidates have been tested against OROV, none have proven effective. Ribavirin, tested in vitro on mice, showed no antiviral activity against OROV, though it was effective against other *Orthobunyaviruses* like Tacaiuma and Guama viruses. Favipiravir has not yet been tested against OROV but has shown efficacy against other viruses in the *Peribunyaviridae* family.

There is **currently no vaccine for Oropouche**. A preclinical study evaluated a vaccine candidate based on vesicular stomatitis virus (VSV) expressing OROV glycoproteins. This study demonstrated protection in mice, with reduced viral loads after exposure to the virus.

Diagnosis and care

This section offers a short overview of currently available countermeasures and recommendations for diagnosis, prevention and care.

Currently, Oropouche is an underdiagnosed disease because its clinical symptoms overlap with those of other arboviruses like Dengue, Chikungunya, and Zika, requiring laboratory confirmation, which delays diagnosis. Developing rapid diagnostic tests for OROV would enable early virus detection.

Moreover, no specific antiviral treatment is currently available, and very few clinical trials have been conducted in humans. Ribavirin, mycophenolic acid, and IFN-α have been tested for OROV. In vitro studies showed that ribavirin and mycophenolic acid lacked antiviral activity against OROV, unlike for two other *orthobunyaviruses*, Tacaiuma virus and Guama virus. IFN-α showed limited in vitro activity, dependent on dose and timing of treatment. Favipiravir has not yet been tested for OROV but shows promising activity against several related *Peribunyaviridae* viruses.

Developing an effective vaccine is also a priority, though studies are still scarce. Immunoassays have identified several epitopes for potential vaccine candidates, particularly T and B cell epitopes from the OROV polyprotein. Recently, a candidate vaccine based on vesicular stomatitis virus expressing OROV glycoproteins protected mice from viral challenge by reducing viral load. Cross-protection with existing vaccines against other viruses should also be explored.

Guidelines and practical information

This section lists official manuals of recommendations for clinical practice or public health policy published by leading health organizations.

4 Novembre 2024	Preventing Oropouche (CDC)
25 Octobre 2024	Interim Guidance for Evaluating and Managing Infants Born to Pregnant People with Confirmed or Probable Oropouche Virus Disease (CDC)
25 Octobre 2024	Clinical Overview of Oropouche Virus Disease (CDC)
20 September 2024	Updated Interim Guidance for Health Departments on Testing and Reporting for Oropouche Virus Disease (CDC)
10 September 2024	Interim Guidance for Evaluating and Managing Infants Born to Pregnant People with Confirmed or Probable Oropouche Virus Disease (CDC)
9 August 2024	Threat Assessment Brief - Oropouche virus disease cases imported into the European Union (ECDC)
3 August 2024	Public Health Risk Assessment related to Oropouche Virus (OROV) in the Region of the Americas. (PAHO)
17 July 2024	Recommendations for the Detection and Surveillance of Oropouche in possible cases of vertical infection, congenital malformation, or fetal death. (PAHO)