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Oropouche Fever on the Rise: Overview of a Reemerging Arbovirus in Latin America

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ABSTRACT: Oropouche virus is a reemerging arbovirus in Latin America, responsible for multiple outbreaks since its first identification in 1955. Following decades of sustained circulation in the Amazon region, it has recently spread to previously unaffected areas, particularly since late 2023, raising new public health concerns. Despite its growing relevance, it remains largely underdiagnosed, often confused with other arboviral diseases, and overlooked by surveillance systems.

This narrative review synthesizes current knowledge on Oropouche, drawing on literature published between 1962 and 2025, with particular focus on developments from 2023 onward. Sources were selected primarily from PubMed to provide an updated and concise overview of its epidemiology, transmission, clinical manifestations, diagnostic challenges and public health impact.

The virus is primarily transmitted by *Culicoides paraensis*, a biting midge, and has been reported in several South American and Central American countries, including Argentina, Barbados, Bolivia, Brazil, Colombia, Cuba, Ecuador, Guyana, Panama, Peru and Venezuela. Imported cases notified in North America and Europe highlight its potential for a wider geographic spread. Clinically, Oropouche fever usually presents as a self-limiting febrile illness that can mimic dengue, Zika or chikungunya. However, recent reports have described neurological complications, including meningitis and meningoencephalitis, as well as possible vertical transmission and congenital malformations, suggesting a broader disease spectrum. To date, five deaths have been attributed to the virus, with others under investigation. Diagnostic capacity remains limited, especially in endemic areas, and no specific treatment exists beyond supportive care.

The continued expansion of Oropouche, driven by climate change, urbanization and increased human mobility, underscores the need for improved surveillance and research. Without sustained attention, this emerging infection may evolve into a more serious threat to global health.

KEYWORDS: Oropouche Fever, Arbovirus, Public Health, Emerging Diseases, Epidemiology.

I. INTRODUCTION

Arboviruses, viral infections transmitted by arthropods, currently represent a growing threat to global public health — not only due to the increasing incidence reported over recent decades, but also because of their multifaceted and far-reaching societal impact[1]. Dengue is, undoubtedly, the most prominent example within this group, with an estimated 100 million cases per year and a broad geographic distribution, documented across all inhabited continents[2,3]. Its transmission dynamics vary regionally, ranging from sustained endemicity to sporadic or emerging outbreaks[4,5].

However, in recent decades, new arboviruses have continued to emerge and reemerge, with the potential to expand further and, although unlikely, reach the epidemiological scale of dengue[6,7].

Oropouche fever (OF) has emerged within this context as a reemerging arboviral disease, historically endemic in Latin America, particularly in the northern region of Brazil and the western Amazon basin, but still largely underrepresented in Western scientific literature [8–10]. The sharp increase in reported cases since late 2023, along with a recent geographic expansion — including imported cases in the United States, Canada and several European countries — has raised concerns regarding its potential for transcontinental dissemination[8,11].

II. ETIOLOGY AND TRANSMISSION CYCLE

This tropical disease is caused by the Oropouche virus (OROV), an arbovirus of the genus *Orthobunyavirus*, family *Peribunyaviridae,* and the order *Bunyavirales*. It is part of the Simbu serological group, which comprises various genetically related arboviruses of both medical and veterinary significance[9,12,13].

OROV exhibits a spherical morphology and is composed of a helical nucleocapsid that encloses the viral genome, itself surrounded by a lipid envelope. As observed in other members of the *Orthobunyavirus genus*, its genome consists of a negative-sense, single-stranded RNA, segmented into three parts: small (S), medium (M) and large (L)[9]. This segmented structure enables reassortment events to occur — a key driver of genetic diversity within this viral group. Reassortment takes place when two genetically compatible viruses co-infect the same host cell, facilitating the exchange of entire genome segments[2,14,15]. This mechanism contributes to the emergence of novel viral lineages with distinct genetic and phenotypic profiles, potentially altering pathogenicity, transmissibility and epidemiological dynamics. Among the best-characterized OROV lineages are the Iquitos, Madre de Dios and Perdões strains[14,15].

This vector-borne disease is primarily transmitted through the bite of *Culicoides paraensis*, a hematophagous dipteran species widely distributed across Latin America[16]. This species thrives in both natural environments and human-altered areas, including rural and urban settings[17]. The genus *Culicoides,* to which it belongs, has a global distribution and serves as a vector for a wide range of diseases, predominantly of veterinary importance. Notable examples include bluetongue virus (BTV), epizootic hemorrhagic disease virus (EHDV), Akabane virus (AKAV), bovine ephemeral fever virus (BEFV) and African horse-sickness virus (AHSV)[9,18].

Two distinct transmission cycles of OROV have been described: a sylvatic cycle, occurring in forested environments, and an urban cycle, associated with densely populated areas, ranging from small rural settlements to major urban centers. The urban cycle is particularly linked to settings involving either agricultural activity or proximity to large, forested areas[16].

In the sylvatic cycle, mosquitoes such as *Coquillettidia venezuelensis* and *Aedes serratus* —historically isolated in Trinidad and Brazil, respectively — have been identified as potential vectors. Reservoir hosts in this cycle include small mammals such as sloths, as well as primates, rodents and birds, as antibodies to OROV have been reported in all these animals. In contrast, the urban (or epidemic) cycle is predominantly maintained by the primary vector *Culicoides paraensis*. A key factor linking both cycles appears to be the human host, who, upon moving from the sylvatic environment to the urban environment and carrying a sufficiently high viremia, may act as the primary vertebrate reservoir, thereby sustaining urban transmission[6,9].

The transmission dynamics remain incompletely understood, particularly because the vectors and sylvatic hosts identified in the literature are based on historical isolations (mostly conducted in Brazil) that lack robust validation and contemporary confirmation[15,17,19]. Therefore, the most recent evidence suggests caution in determining the competent agents involved in vector-borne transmission[20]. To date, only *C. paraensis* has been conclusively demonstrated to be an effective vector. Recent entomological studies have also highlighted the susceptibility of *Culicoides sonorensis* to the virus under laboratory conditions. This finding is noteworthy, as it could signify an emerging shift in the geographical range of this arbovirus, considering that this vector is primarily distributed in temperate regions, particularly in central North America[14,20].

Mosquitoes of the *Culicidae* family, such as *Aedes aegypti*, *Aedes albopictus* and *Culex quinquefasciatus*, have been evaluated in experimental studies. However, to date, their vector competence has not been conclusively demonstrated[14,20]. Therefore, there is an urgent need for further research focusing on the vec-

tor competence of *Culicoides* species in both enzootic and non-enzootic areas, as well as other arthropods, particularly those belonging to the genera *Aedes* and *Culex*[20,21].

III. EPIDEMIOLOGY

Oropouche virus was first isolated in 1955 from the blood of a forest worker presenting with an acute febrile illness, residing in Vega de Oropouche, in Trinidad and Tobago[15,22]. In 1961, the first documented outbreak occurred in Belém, the capital of the state of Pará, Brazil, with over 11,000 reported cases, thereby demonstrating the epidemic potential of OROV. Initially confined to the state of Pará, the virus has progressively expanded within the Amazon region since 1981[6].

Sustained local transmission has extended across several countries in Latin America and the Caribbean over recent years, with reported cases in Argentina, Barbados, Bolivia, Colombia, Cuba, Ecuador, Guyana, Panama, Peru and Venezuela[2,11]. Since late 2023, epidemiological data have shown a significant increase in infections, with a total of 16,239 cases reported in 2024, including four deaths and five instances of vertical transmission. Of these, 13,785 were recorded in Brazil, accounting for 84.9% of all confirmed infections. Among the Andean countries, Peru reported 1,263 cases (7.8%), followed by Colombia with 626 cases (3.8%). For the first time, cases have been reported in North America (Canada and the United States) and in Europe (Spain, Italy and Germany). All of these were classified as imported cases, with a confirmed epidemiological link to endemic areas[11,23,24].

A large-scale outbreak is ongoing in the Americas[11,25]. According to the Pan American Health Organization (PAHO), by the fourth epidemiological week of 2025, a total of 3,765 cases had already been reported, with 97.7% occurring in Brazil (3,678 cases)[11]. Recent data released by the Brazilian Ministry of Health indicate a significant increase in case numbers compared to 2024. Between epidemiological weeks 1 and 20 of 2025, a total of 10,571 cases of Oropouche fever were reported in the country, representing a 57.9% increase compared to the same period in the previous year[26]. This upward trend confirms not only the persistence of active transmission but also the intensification of the epidemic cycle, potentially associated with changes in ecological, climatic and social conditions[6,25].

IV. CLINICAL MANIFESTATIONS

From a clinical standpoint, OF typically manifests as a sudden-onset febrile syndrome, following an incubation period ranging from 1–10 days. Clinical manifestations frequently include headache, myalgia, arthralgia, retro-orbital pain, nausea, vomiting and photophobia — features that closely mimic those of dengue fever. In some cases, a maculopapular rash resembling that of rubella may be observed, as well as mild hemorrhagic signs such as epistaxis, gingival bleeding or petechiae[2,21,27].

The symptomatic phase generally lasts between 2–7 days, marking the acute stage of infection. However, in approximately 60% of cases, a relapse of symptoms occurs after a brief asymptomatic interval of several days or weeks. The recurrent manifestations tend to mirror those of the initial episode, albeit typically with reduced intensity[15,27].

Although rare, Oropouche fever can evolve into more severe manifestations, such as aseptic meningitis or meningoencephalitis. These complications can present with intense occipital pain, dizziness, confusion, lethargy, photophobia, nausea, vomiting, nuchal rigidity and nystagmus[27]. Notably, among the reported neurological complications, an association between Oropouche fever and Guillain-Barré syndrome has been described in three patients in Cuba in the last year[28,29]. These findings highlight potential, though still poorly understood, neuroinvasive capacity of the virus[29].

This arboviral infection is often self-limiting and generally presents with a benign clinical course. Nevertheless, two fatalities were confirmed in 2024, in previously healthy young women, aged 21 and 24, whose clinical presentations resembled those of severe dengue[30,31]. Both patients developed headache, fever, nausea, vomiting, myalgia, abdominal pain, diarrhea and retroorbital pain. The younger woman also developed arthralgia and a red-colored rash, as well as hemorrhagic signs, such as petechiae and spontaneous bleeding from the gums, nose and vagina[30]. Both succumbed to OROV infection just four to five days after symptom onset, according to the clinical reports, due to severe coagulopathy and liver impairment[31]. The underlying pathophysiological mechanisms responsible for such severe manifestations remain poorly understood. One potential explanation for this outcome involves the co-circulation of distinct viral clades possibly eliciting a non-protective heterologous immunity, capable of trig-

gering the Antibody-Dependent Enhancement (ADE) as has been observed in severe dengue[2,32].

A more recent concern associated with OF is the possibility of vertical transmission. In Brazil, in 2024, four cases of fetal death and one case of congenital malformation were reported among pregnant women with a confirmed diagnosis of acute OROV infection, with several other cases currently under investigation[11,33]. In one stillbirth, viral RNA was detected in the umbilical cord blood as well as in fetal tissues including the placenta and central nervous system[33]. While the exact mechanism of intrauterine transmission remains unclear, current evidence suggests a link between maternal viremia and binding to placental surface receptors, which may facilitate transplacental passage into the fetal bloodstream[8,30]. Beyond the possibility of vertical transmission, OROV was identified in a semen sample from a previously healthy man following travel to Cuba, suggesting potential sexual transmission[8].

V. DIAGNOSTIC APPROACH AND THERAPEUTIC CONSIDERATIONS

The clinical diagnosis of Oropouche fever poses considerable challenges, primarily due to its nonspecific presentation and the significant clinical overlap with other arboviral infections, including dengue, Zika, chikungunya and Mayaro[21]. Diagnostic suspicion should be based on a thorough epidemiological assessment, considering recent travel to endemic regions, residence in areas with ongoing active transmission or documented exposure to known vectors[27].

Laboratory findings tend to be subtle and nonspecific, commonly encompassing leukopenia, lymphopenia, elevated C-reactive protein levels and mild to moderate elevations in hepatic transaminases[9,27]. According to the diagnostic protocol established by the Centers for Disease Control and Prevention (CDC), the gold standard method for diagnosis during the acute phase is reverse-transcription polymerase chain reaction (RT-PCR). Ideally, it should be performed within the first seven days following symptom onset, when viral RNA remains detectable in the blood or other clinical specimens[34]. During the convalescent phase, the gold standard serological method is the plaque reduction neutralization test (PRNT), owing to its superior specificity in distinguishing Oropouche virus antibodies from those of antigenically related *Orthobunyaviruses*[2,34]. While recommended, this method is not often used for patient diagnosis due to long turnaround times and the requirement for high-containment laboratory conditions[2].

Alternative immunoassays, such as enzyme-linked immunosorbent assay (ELISA), are often employed as complementary methods or substitutes for other serological techniques; however, their diagnostic utility is constrained by the risk of cross-reactivity, particularly in regions with co-circulation of related arboviruses[10]. In addition to the aforementioned methods, the literature describes other conventional serological techniques, such as hemagglutination inhibition, complement fixation and indirect immunofluorescence assay[9].

As previously mentioned, the diagnosis of Oropouche fever can be established through a wide array of laboratory tests. The selection of the most appropriate test should consider the clinical phase of the disease, the time elapsed since symptom onset and the availability of these diagnostic tools[34]. A major challenge lies in the decentralized availability of these diagnostic tests and the urgent need to develop rapid point-of-care testing solutions[2,9].

Treatment is symptomatic and is based on supportive care, including the use of analgesics and antipyretics, while nonsteroidal anti-inflammatory drugs should be avoided due to the risk of hemorrhagic complications, similar to those observed in other arboviral infections such as dengue[21]. Thus far, no antiviral agent has demonstrated sufficient efficacy to warrant clinical recommendation[2].

VI. PREVENTION AND CONTROL

Since Oropouche fever is transmitted through the bite of an arthropod vector, preventive measures primarily focus on vector control and the use of personal protective equipment[35]. Regular application of insect repellents, along with the use of appropriate clothing, such as loose-fitting and breathable garments that cover exposed skin, is strongly recommended. Furthermore, households should be protected with fine-mesh screens on doors and windows, a strategy that also contributes towards the prevention of other arboviral infections. In endemic regions, local authorities should also implement integrated environmental management and entomological surveillance programs to reduce vector proliferation[11].

Although the burden of Oropouche fever is predominantly concentrated in endemic areas, the current dynamics of human mobility and globalization present

significant challenges to international public health[21]. The potential for imported cases in non-endemic countries, such as Portugal, must not be underestimated, particularly considering previous reports of imported cases within Europe. Portugal may serve as an entry point for emerging and reemerging arboviruses, given the increasing volume of international travel and the effects of climate change, which favor the establishment of new vector species[24,36].

For this reason, in Portugal, efforts should be directed at early recognition of imported cases from endemic regions, which requires the promotion of medical literacy regarding the clinical manifestations of the disease, as well as the development of robust laboratory diagnostic capacities. OF must be considered in the differential diagnosis of acute febrile syndromes, neurological presentations or gestational complications in individuals with a recent travel history to Central and South America[24].

VII. RECENT ADVANCES, KNOWLEDGE GAPS AND RISK OF GLOBAL DISSEMINATION

In recent years, particularly since late 2023, Oropouche fever has attracted growing attention from the international medical and scientific community. This is reflected in the significant increase in recent scientific publications, as well as in the number of clinical guidelines and recommendations issued by international entities such as the World Health Organization, the Pan American Health Organization and the Centers for Disease Control and Prevention[11,37,38]. This collective effort has led to several advances in scientific literature and in the overall understanding of the disease, though various topics remain understudied.

Among the most relevant developments is the genetic characterization of the virus, including the identification of distinct viral lineages, notably the most recently described OROVBR-2015–2024 strain, which has been associated with the virus's recent reemergence in Brazil[8,16]. In addition, there has been a growing effort to elucidate the transmission cycle and to assess the vector competence of various hematophagous species, especially regarding the role of *Culicoides* species as vectors and their geographic distribution[14,20]. Furthermore, the increasing number of clinical case reports has also provided a better understanding of the clinical spectrum of the disease, helping to identify previously unrecognized manifestations[27,28,31,33,39].

Despite these advances, significant knowledge gaps remain. The pathogenesis of the virus remains poorly understood, often inferred from data on other *Orthobunyaviruses*, limiting our understanding of disease-specific mechanisms[14,40]. The sylvatic transmission cycle, including its reservoir hosts and secondary vectors, has yet to be fully characterized, with most of the current understanding based on historical and geographically restricted studies[8,9]. Diagnostic access continues to be a major obstacle in endemic regions, where Oropouche fever is frequently misdiagnosed as dengue or other febrile illnesses, contributing to significant underreporting and poor epidemiological visibility[2,21]. Moreover, no vaccine is currently available for Oropouche virus, further underscoring the urgent need for preventive strategies[2]. This represents a priority area for investment by public health authorities, particularly in the development of more rapid and cost-effective diagnostic tools[2,21].

According to the World Health Organization, the regional risk of OROV transmission is currently rated very high, particularly in Latin America, while the global risk remains low[37]. However, theoretical scenarios for broader dissemination should not be overlooked. These include the potential spread of infected vectors through human activities or environmental factors, and the possibility of viral adaptation to new arthropod species with broader geographic ranges, such as *Aedes aegypti*[20,37,41,42]. As such, continued surveillance, vector competence studies and preparedness measures are essential to anticipate and mitigate a potential expansion of Oropouche virus transmission beyond its traditional ecological niche[24,37,41].

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