# Clinical and ecoepidemiological situation of human arboviruses in Brazilian Amazonia

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**The main aspects of clinic manifestations and epidemiological data about human arboviruses in the Brazilian Amazonian region is reviewed. Thirty four types of arboviruses from 183 types isolated in the Amazonia have been associated with human diseases. Four of them are important in public health and are involved with epidemics; they are namely, Dengue (DEN), Mayaro (MAY), Oropouche (ORO) and Yellow Fever (YF) viruses. ORO and DEN are associated with human epidemic diseases in urban areas while MAY and YF in rural areas. Basically, ORO causes a febrile disease, sometimes accompanied with aseptic meningitis. MAY and DEN are associated with rash febrile disease, while YF determines hemorrhagic fever. Thirty other arboviruses are involved with febrile illnesses in a few and sporadic cases. All arboviruses (apart from DEN) are maintained within a sylvatic cycle in the forest, where several species of hemathophagous insects act as vectors and wild vertebrates are involved as hosts. DEN has a cycle where the *Aedes aegypti* mosquito is the vector and man is the host. With the exception of the four viruses associated with epidemics which determine great economical and social impacts, including death (as in the case of YF), the real involvement of these viruses as systematic agents of human disease is unknown. Further studies are needed to clarify unclear aspects of the epidemiological cycles of these viruses.**

*Os principais aspectos clínicos e ecoepidemiológicos das arboviroses associadas com doença humana na Amazônia brasileira são revistos. Trinta e quatro arbovírus dentre os 183 tipos até o momento isolados na Amazônia têm sido incriminados com doença humana. Desses, 4 são importantes em termos de saúde pública pois estão associados com epidemias; são os vírus Dengue (DEN), Mayaro (MAY), Oropouche (ORO) e Febre Amarela (FA). DEN e ORO estão associados com doença humana epidêmica em áreas urbanas enquanto MAY e FA em áreas predominantemente rurais. Basicamente, o vírus ORO determina um quadro febril algumas vezes acompanhado com meningite asséptica. MAY e DEN são responsáveis por quadros febris exantemáticos, enquanto o vírus FA determina, na sua apresentação clássica, uma sintomatologia típica de febre hemorrágica. Trinta outros arbovírus têm sido associados a doença febril benigna em poucos e esporádicos casos. Afora o DEN, todos os arbovírus envolvidos com doença humana na Amazônia brasileira são mantidos através de um ciclo silvestre desenvolvido na floresta, onde diversas espécies de insetos hematófagos e vertebrados silvestres atuam como vetores e hospedeiros, respectivamente. O vírus DEN tem um ciclo urbano em que o mosquito **Aedes aegypti** é o vetor e o homem atua como hospedeiro. Excetuando os quatro vírus associados a epidemias que causam um grande impacto socio-econômico, inclusive levando a morte (no caso particular da FA), o verdadeiro papel desses vírus como agentes sistemáticos de doença humana é desconhecido. Novos estudos são necessários para esclarecer aspectos ainda obscuros dos ciclos epidemiológicos da maioria desses arbovírus.*

The arboviruses constitute an ecological group of viruses some types of their representing a very important public health problem, worldwide. Very often, arboviruses have been responsible for large epidemics with serious impacts on human and veterinary health.

In Brazil, the arboviruses are spread in several regions. However, the number of types causing human diseases is low. Thus, of over 200 distinct serotypes isolated in Brazil, a few more than 30 have actually determined human disease. A small number has been incriminated as causative agents of epidemics. On the other hand, despite the low number of epidemic arboviruses, the social and economical impacts of these outbreaks are important.

Moreover, up to the present, in Brazilian Amazonia, 183 distinct arboviruses have been isolated up to the end of

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1991 (1). Of these, 34 have been associated, with human infections, on the basis of virus isolation or antibody detection. Twenty-seven of them, are members of 3 genus: *Alphavirus, Bunyavirus* and *Flavivirus*, and only 7 from other genera. With few exceptions, all the virus isolations have been obtained from individuals infected in nature. Three agents, however, have to date been isolated from people who had undergone a laboratory infection (Table 1). On the other hand, only four arboviral diseases are considered presently to be important to public health in Amazonia. They are, Oropouche (ORO), Dengue (DEN), Mayaro (MAY) and Yellow Fever (YF). All of them, have been associated with epidemic outbreaks, the first two (ORO and DEN) in urban areas, and the latter two (MAY and YF), mainly in rural areas. Certainly, these four arboviruses are responsible for over 90% of all cases of arboviral diseases in the Amazonia.

This account reviews our current knowledge about the pathogenic arboviruses to man in the Amazon region of Brazil, which will be discussed according to taxonomic status.

## Oropouche (ORO)

Oropouche fever virus is a *Bunyavirus* (Bunyaviridae), serologically related to the Simbu serogroup.

The outbreaks of Oropouche fever virus have caused important social and economic impacts, because the epidemics are explosive and, in a short time thousands of patients are attacked simultaneously. Patients sometimes present a severe disease including neurologic involvement (2), although, no fatality has been recorded to date due to ORO virus. When environmental (ecologic) and epidemiological (susceptibles, viral and vector circulations) conditions are favorable, the outbreaks begin. They have a cyclic occurrence, beginning during the rainy season (usually from January to June). Indeed, three outbreaks have been recorded in Belém during the last 30 years. The first, in 1961 (3), the second in 1968-1969 (4) and the third in 1979-1980, with several other localities also involved (5). Until 1980, all epidemics reported in Brazil had occurred in Pará State. From the end of 1980 to the first quarter of 1981, a large epidemic was reported in Manaus, Amazonas State. This outbreak was also extended to Barcelos county. A third epidemic was registered beyond the limits of Pará State, in Mazagão, a rural locality of Amapá State (6). In 1988, new areas were affected by epidemics of ORO fever. Porto Franco and Tocantinópolis, in Maranhão and Goiás States, respectively, reported thousands of cases (7). In 1991, a large epidemic was reported in Rondônia State in Ariquemes and Ouro Preto do Oeste towns. In these towns an epidemiological survey estimated that about 90,000 infections occurred during a 45-day period (8).

Based upon the population at risk during epidemics and estimated incidence rates taken from serological surveys, at least 500,000 people were probably infected by ORO virus in the last 30 years (1961-1991) in the Brazilian Amazon basin (1).

Clinical manifestation presented by infected patients is basically a febrile disease. Oropouche fever is characterized by an abrupt onset. Fever, headache, myalgia, arthralgia, anorexia, dizziness, chills and photophobia are the symp-

**Table 1** — Arboviruses isolated in the Amazon region which are responsible for human disease (in Amazonia and the Caribbean) according to type of disease and source of isolation.

| | | | | *Source of isolation* | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | *Human* | | *Vertebrate* | | |
| *Type* | *Genus* | *Antigenic group* | *Virus* | *Natural* | *Lab.inf.* | *Sentinel* | *Wild* | *Arthropod* |
| Febrile illness | Alphavirus | A | Mucambo | + | – | + | + | + |
| Febrile illness | Alphavirus | A | Pixuna | – | + | – | + | + |
| Febrile illness | Arenavirus | Tacaribe | Flexal | – | + | – | + | – |
| Febrile illness | Bunyavirus | Anopheles A | Tacaiuma | + | – | + | – | + |
| Febrile illness | Bunyavirus | Bunyamwera | Xingu | + | – | – | – | + |
| Febrile illness | Bunyavirus | C | Apeu | + | – | + | + | + |
| Febrile illness | Bunyavirus | C | Caraparu | + | + | + | + | + |
| Febrile illness | Bunyavirus | C | Caraparulike | + | – | + | + | + |
| Febrile illness | Bunyavirus | C | Itaqui | + | – | + | + | + |
| Febrile illness | Bunyavirus | C | Marituba | + | – | + | + | + |
| Febrile illness | Bunyavirus | C | Murutucu | + | – | + | + | + |
| Febrile illness | Bunyavirus | C | Nepuyo | – | – | + | + | + |
| Febrile illness | Bunyavirus | C | Oriboca | + | – | + | + | + |
| Febrile illness | Bunyavirus | California | Guaroa | + | – | – | – | + |
| Febrile illness | Bunyavirus | Guama | Catu | + | – | + | + | + |
| Febrile illness | Bunyavirus | Guama | Guama | + | – | + | + | + |
| Febrile illness | Bunyavirus | Simbu | Oropouche | + | + | + | + | + |
| Febrile illness | Flavivirus | B | Bussuquara | – | – | + | + | + |
| Febrile illness | Flavivirus | B | Ilhéus | + | – | + | + | + |
| Febrile illness | Phlebovirus | Phlebotomus fever | Alenquer | + | – | – | – | + |
| Febrile illness | Phlebovirus | Phlebotomus fever | Candiru | + | – | – | – | + |
| Febrile illness | Phlebovirus | Phlebotomus fever | Morumbi | + | – | – | – | – |
| Febrile illness | Phlebovirus | Phlebotomus fever | Serra Norte | + | – | – | – | – |
| Febrile illness | Vesiculovirus | VSV | Jurona | + | – | – | – | + |
| Febrile illness | Vesiculovirus | VSV | Piry | – | + | – | + | – |
| Rash febrile disease | Alphavirus | A | Mayaro | + | + | + | + | + |
| Rash febrile disease | Flavivirus | B | Dengue 1 | + | – | – | – | + |
| Rash febrile disease | Flavivirus | B | Dengue 2 | + | – | – | – | – |
| Rash febrile disease | Flavivirus | B | Dengue 4 | + | – | – | – | + |
| Encephalitis | Alphavirus | A | EEE | – | – | + | + | + |
| Encephalitis | Alphavirus | A | WEE | – | – | + | + | + |
| Encephalitis | Bunyavirus | Bunyamwera | Tucunduba | + | – | – | – | + |
| Encephalitis | Flavivirus | B | SLE | + | – | + | + | + |
| Hemorrhagic fever | Flavivirus | B | Yellow fever | + | – | + | + | + |

toms more observed. There may also be nausea, vomiting, diarrhea, epigastric pain, retrobulbar pain, conjunctival congestion and burning sensation. Rash is rare and has been observed only in about 5% of all patients (4,9). When the last outbreak occurred in Belém, neurologic involvement was also observed and was characterized as meningitis, which resolved fully and without sequelas (2). The disease persists for about 2 to 5 days. In the epidemic of 1980 in Belém, at least 63% and in Porto Franco about 56% of those infected suffered overt clinical symptoms (5,7). All attempts to isolate ORO virus during relapses have failed. Recurrence has been documented especially among people who quickly resume strenuous activities. There have been no documented cases of second infections with ORO virus (10).

The midge *Culicoides paraensis* is the urban vector of ORO virus during epidemics. The infected patients can transmit the virus to *C. paraensis* during the first two days of disease (viremic period). Viremia persists until the 5th day of disease, but only 23% of them have enough titer virus to infect the vector (4). It has been suggested that ORO is maintained in two distinct cycles; an urban (epidemic) in which man is the principal vertebrate host and the midge *C. paraensis* the vector. The second (sylvatic) cycle would be responsible for the maintenance of ORO in nature. This is a silent cycle where primates, sloths and birds are the vertebrate hosts. The vector is unknown (4). It is possible that *C. paraensis* itself, can be the vector, because this biting midge is also widely distributed in tropical rain forests and rural areas of the Amazon basin. Evidence of another vector has not been found, except for one isolation each, *of Aedes serratus* (Fig. 1) and *Coguilletidia venezuelensis*. Further studies are necessary to clarify this aspect of sylvatic cycle.

## Dengue (DEN)

Dengue viruses are included in genus *Flavivirus* (Flaviviridae). Antigenically, the four serotypes numbered 1 to 4 are members of group B of arboviruses.

Two large epidemics of dengue fever were reported in the Amazon region: *1)* in Boa Vista, Roraima, in 1982 (11) and *2)* in Araguaína, Tocantins, in 1991 (12). In Boa Vista, serotypes 1 and 4 were the causative agents (Note: this was the first documented epidemic based on clinical and laboratorial findings in 50 years in Brazil). About 12,000 people were infected (13). In Araguaína, DEN 2 was the serotype responsible for about 90,000 cases (12). It is important to emphasize that DEN 2 was isolated for the first time in Brazil from a febrile patient who arrived in Belém from Luanda, Angola, in February 1989 (14). In both outbreaks, the clinical manifestations were characterized by a febrile illness accompanied by rash. Hemorrhagic signs and symptoms were not found. The clinical picture presented was one of abrupt onset, with high fever, intense headache and chills, as well as malaise, backache, photophobia, myalgia and exanthema. Diarrhoea, nausea, vomiting and dizziness could be found in some patients. Clinical illness persisted from 3 to 10 days, more often for 4 to 6 days. Fatalities due to DEN viruses were not reported in the Brazilian Amazon region. *Aedes aegypti* is the single vector of DEN viruses found in this region.

***Figure 1. Aedes serratus is suspected to act as sylvatic vector of Oropouche virus.***

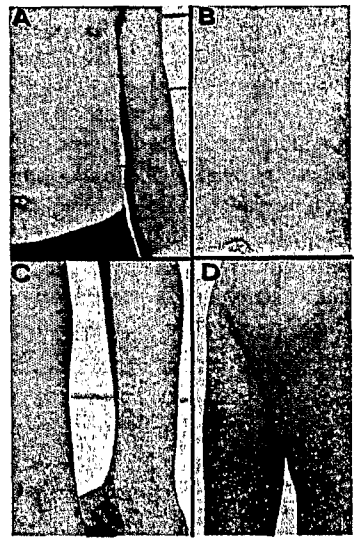


***Figure 2. Aspects of skin rash in Mayaro fever disease (Original photo from Pinheiro et al, Am J Trop Med Hyg 30: 674-681, 1981. Used with permission).***

## Mayaro (MAY)

Mayaro fever virus is an *Alphavirus* (Togaviridae), serologically related to group A of arboviruses.

MAY virus causes a severe febrile illness associated with arthralgia and skin rash. Mayaro disease is usually characterized by high fever, headache, epigastric pain, myalgia, arthralgia, rash, chills, nausea, photophobia and vertigo. Arthralgia and fever are present in all patients, while the maculopapular rash is present in about two thirds of them. The skin rash lesions usually appear on the 5th day of illness and last about 3 days. They are more frequent in children than older people and can be seen more prominently on legs, arms, chest and back (Fig. 2). Curiously, the face is less affected. Except for arthralgia which persists in some patients for about 2 months, all clinical manifestations lasted 3 to 10 days (15,16).

MAY virus is endemic in Amazonia and rates of antibodies are directly proportional to populations which maintain toilsome contact with forested areas. Immunity to MAY increases with age, and range in rural communities in the Amazon region from 10% to 60%. Between 20% to 47% of the populations of various Indian tribes in Amazonia display immunity to the virus (1,17). Despite high antibody rates, it is extremely difficult to isolate MAY, because the viremia determined by this virus is very short-timed (2-3 days), during which it is normally improb-

able to suspect MAY as the causative agent of the disease.

Presently, at least three epidemics of Mayaro fever virus were recorded in Amazonia, two of which in association with Yellow Fever virus (15,18). The MAY outbreaks are usually limited to rural areas near or inside forests, where *Haemagogus janthinomys* the main vector, is found in abundance. Thus, contact with the forest seems to be an important risk factor for infection with MAY virus. The vertebrate hosts of MAY are nonhuman primates. Birds can act as secondary hosts. These animals may be important for the dissemination of the virus.

## Yellow Fever (YF)

The YF virus is the prototype of genus *Flavivirus* (Flaviviridae). Because of its cross reactivity in the Hemagglutination Inhibition (HI) test it is a member of group B.

All nonhuman primates are highly susceptible to infection, many species frequently developing fatal disease. On the other hand, birds, rodents, marsupials, bats, amphibians and reptiles are highly resistant to YF virus infection.

Each year in Brazil, human cases of YF are recorded in endemic and/or epizootic areas, through sylvatic transmission. They can occur sporadically or as outbreaks. These jungle YF epidemics have been mainly caused by the mosquito species *Haemagogus janthinomys*. In most cases, humans play an important role in the dissemination of the virus to areas where there is no virus, but where vectors are abundant. Modifications of the forest environment through lumbering, agricultural work, cattle husbandry, road development, wood extractions and other activities augments the number of contacts between nonimmune humans and sylvatic vectors and are the main responsible for appearance of human YF in Brazilian Amazonia (19).

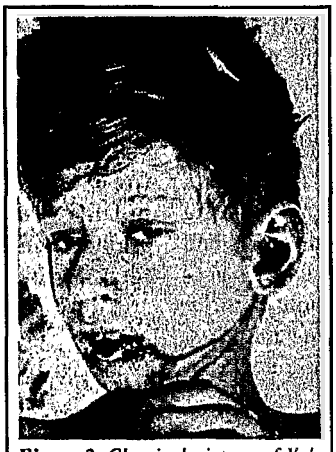

***Figure 3.** Classical picture of Yellow Fever. The hemorrhagic manifestations are severe.*

The urban cycle was eradicated from Brazil since 1942. However, as mentioned in the Dengue section, *Aedes aegypti* is now wide and intensively distributed in the country. Thus, since a viremic patient can arrive in a place with high densities of *A. aegypti*, an urban epidemic may start which will have catastrophic consequences. Around 80% of all people living in *A. aegypti* infested areas are susceptible to YF virus.

Clinically, the classical picture of YF is a disease of biphasic evolution, classified as hemorrhagic fever, and characterized by fever, headache, chills, nausea, vomiting, generalized myalgia, weakness and dizziness in the early phase or period of infection. These symptoms last about 3 days during which the virus can be recovered (viremia) from the blood. If mosquitoes bite a patient, they can become infected. Sometimes this phase is followed by a brief period of remission, in which patients have a sensation of improvement. Remission is especially found in severe forms. During abortive infections, symptoms and signs abate rapidly at this point. In the more serious cases, after the remission, it may install a second phase or period of toxemia when symptoms depend on the localization of YF in the liver and kidney. Jaundice, coffee grounds hematemesis as well as other hemorrhagic manifestations such as epistaxis, melena, gastrointestinal bleeding, may become evident (Fig. 3). Aminotransferases and bilirrubinemia rates increase. Renal failure manifests itself by albuminuria, oliguria, anuria and azootemia. The virus is normally absent from blood during this period, although antibodies appear. About 20% to 50% of the patients who enter this period have a fatal outcome, usually between the seventh and tenth days of illness. Atypical, fulminant cases can also occur with deaths as early as 3 days after onset (20). On the other hand, the patient can die after 2 to 3 weeks of disease. In both cases pulmonary and/or cardiac complications are responsible for the death.

In the last 19 years (1973-1991), 329 cases of YF were reported in Brazil (Cenepi, MS, 1992), of which 248 (75.4%) had fatal outcomes. The cases were distributed as follow: 146 (44.4%) in the Amazon region, 161 (48.9%) in the central part of Brazil and 22 (6.7%) in Minas Gerais State (southeast region). In the Amazon basin, Pará State had the highest prevalence, 56.2% of all cases in the region, which corresponds to 82 cases (Table 2).

The case-fatality rate of reported cases in these last 14 years was 75.4% (Table 2). We may comment that this high rate is due to the fact that, the majority of officially recorded cases were generally of severe ill hospitalized patients. In this circumstance, 329 cases is an underestimated number and the real number of inapparent or very mild infections is very high but, unfortunately, unknown. Therefore, the true impact of jungle Yellow Fever in Brazil and particularly in Amazonia is not available.

## EEE, WEE and SLE encephalitis

Eastern Equine Encephalitis (EEE) and Western Equine Encephalitis (WEE) are members of *Alphavirus* genus, which serologically are included in group A of arboviruses. Saint Louis Encephalitis (SLE) is a *Flavivirus* and is serologically related to group B of arboviruses.

Antibodies to EEE, WEE and SLE viruses have been detected in inhabitants of the Amazon basin, but only SLE has been isolated from sick humans, but without encephalitis (16,22). On the other hand, epizootics determinated by EEE in horses (21) and by SLE in sentinel monkeys (22) have been reported. Wild birds are the main vertebrate hosts of these arboencephalitis viruses. Indeed, a wide variety of species of wild birds seems to be susceptible to these viruses (22).

## Other arboviruses

**Bunyaviridae** — The family Bunyaviridae comprises 5 genera, of which three — *Bunyavirus, Phlebovirus* and *Hantavirus* — are found in the Amazon region. One genus, *Bunyavirus*, comprises over a quarter of the known arboviruses. From 70 Bunyaviruses isolated, 13 were obtained from natural infections of man (Table 1). These viruses are included in several serogroups. Except of Oropouche fever virus which has already been discussed, these viruses do not cause epidemics. All of them cause self-limited sporadic disease, disabling febrile illnesses in man, characterized by fever, headache, chills, malaise and prostration.

Table 2 — Distribution of jungle Yellow Fever diagnosed in Brazil by State between 1973-1991.

| *State* | *Cases* | *%* | *Fatal cases* | *%* |
|---|---|---|---|---|
| Acre | 2 | 0.6 | 2 | 100 |
| Amapá | 2 | 0.6 | 2 | 100 |
| Amazonas | 16 | 4.9 | 13 | 81.2 |
| Goiás | 114 | 34.7 | 88 | 77.2 |
| Maranhão | 12 | 3.6 | 7 | 58.3 |
| Mato Grosso | 26 | 7.9 | 25 | 96.1 |
| Mato Grosso do Sul | 21 | 6.4 | 19 | 90.5 |
| Minas Gerais | 22 | 6.7 | 11 | 50 |
| Pará | 82 | 24.9 | 54 | 61.4 |
| Rondônia | 11 | 3.3 | 10 | 90.9 |
| Roraima | 21 | 6.4 | 16 | 76.2 |
| **Total** | **329** | **100.0** | **248** | **75.4** |

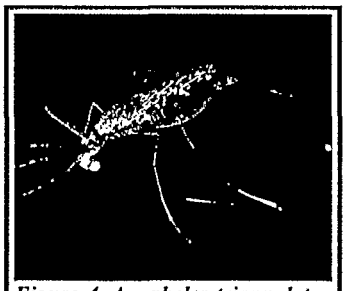

*Figure 4. Anopheles triannulatus mosquito, the main vector of Guaroa and Tocaiuma viruses in the Brazilian Amazonia.*

**Guaroa (GRO)** — Guaroa fever virus, included in California serogroup, is (except for Oropouche) the most widely distributed *Bunyavirus* in the Amazon region, as evidenced by HI test. An overall rate of 18% of positive sera have been found in several localities of the Amazon basin (16). Eleven strains of GRO virus have been obtained from sick people. With the exception of one obtained from transcutaneous hepatic biopsy, of a patient with paralytic disease (25), all isolates originated from blood of febrile ill people. Concomitant infections with malaria have been reported (23).

The mosquitoes *Anopheles triannulatus* (Fig. 4) and *A. nuneztovari* are the vectors of GRO virus in this region (24). Birds of a wide variety of species, included in several families, are suspected to be the vertebrate hosts, as is suggested by the high rates of HI antibodies which have been found in these vertebrates.

**Tacaiuma (TCM)** — Tacaiuma fever virus, a member of Anopheles A serogroup has been responsible for sporadic acute febrile illness of man. This disease has an abrupt onset and is characterized by fever, headache, chills, myalgia, arthralgia and weakness. Two cases have been associated with jaundice and malaria (23). Low rates of HI antibodies (1%) have been found in people living in a large variety of localities in the Amazon region (16). Antibodies to TCM virus were found in monkeys and horses of the Amazon basin. *Haemagogus* sp and *A. triannulatus* (Fig. 4) mosquitoes have each furnished two strains, and should be considered the main vectors of this virus (24).

**Tucunduba and Xingu (Unregistered)** — Tucunduba and Xingu viruses, belonging to Bunyamwera serogroup, were each isolated once from man. Tucunduba was obtained from an 18-month-old girl who presented a clinical picture, characterized by meningoencephalitis. Fever, headache, vomiting, symptoms and signs of central nervous system involvement, including paresis and coma have been observed (16). Xingu virus was isolated from a patient with an infection diagnosed as active hepatitis B (HBsAg positive). The severe disease was characterized by fever, jaundice and had a fatal outcome. Unfortunately, a second sample was not obtained and the definitive proof of the participation of Xingu virus as the causative agent of that disease was lost (16). Tucunduba is frequently obtained from pools of *Wyeomyia* mosquitoes. The vertebrate host of Tucunduba is unknown. Both vector and vertebrate host of Xingu are virtually unknown.

**Group C viruses** — Apeú (APEU), Caraparu (CAR), Itaqui (ITQ), Marituba (MTB), Murutucu (MUR), Nepuyo (NEP) and Oriboca (ORI) viruses, included in group C, have been isolated from man in Amazonia. The disease caused by these viruses is characterized by high fever, headache, chills, myalgias, photophobia and retrobulbar pain. The symptoms remained for 4 to 5 days. Surveys carried out in several localities of the Amazon region have shown a rate of 15% of immunity for group C viruses (16). Several species of Culicidae mosquitoes act as vectors of these viruses. Rodents are the main vertebrate hosts of group C viruses.

**Guamá (GMA) and Catu (CATU) viruses** — Guamá fever and Catu fever viruses, members of Guamá serogroup, have been isolated 9 and 11 times, respectively, from blood specimens of man. The disease determined by these viruses, has a sudden onset. Mild fever, dizziness, headache, muscle pains, arthralgia, photophobia and malaise are the main symptoms. The disease usually persists for 5 days. Recovery is uneventful (16). Both viruses are maintained by a sylvatic cycle, including *Culex* sp mosquitoes as the vectors and several rodents as vertebrate hosts.

**Phlebovirus** — At present 21 serotypes members of *Phlebovirus* genus, included in the Phlebotomus Fever serogroup, have been isolated in the Amazon basin. Of these, 4 were obtained from human beings. An interesting fact is that all phleboviruses until now isolated from man, belong to the Candiru complex. They were named Candiru, Alenquer, Morumbi and Serra Norte (26,27). Of each virus, a single isolate was obtained from the blood of man with febrile illness. The disease caused by these Amazonian phleboviruses is characterized by an acute, self-limited flu-like illness of 2 to 5 days duration. The disease usually begins suddenly with high fever, frontal headache, low back pain, generalized myalgia, photophobia, retrobulbar pain and malaise. Recovery is complete (16,27).

Phleboviruses are maintained in nature by a sylvatic cycle where the phlebotomine sandflies of several species, mainly members of the genus *Lutzomyia* act as vectors. The vertebrate hosts are virtually unknown.

## Flavivirus

**Ilhéus (ILH)** — Ilhéus fever virus is a *Flavivirus*, serologically a member of group B. This virus has been isolated from febrile ill man, mosquitoes and a large variety of animals, especially birds and bats. A total of 41 strains were obtained from blood of human beings, blood and tissues of animals and tissues of mosquitoes. The symptoms reported by patients were mainly of a sudden onset with fever, headache, chills, myalgia and weakness. Except for Yellow Fever and Dengue viruses, this is the *Flavivirus* with the highest rates of HI antibodies in the Amazon basin. Despite the high rates of antibody it is very difficult to isolate ILH from human beings. Actually, only 3 isolates have been obtained from man, because either the viremic period is quite short, or a great number of infections are asymptomatic, or both (16). ILH is maintained in nature by a sylvatic cycle in which *Psorophora ferox* (Fig. 5) mosquitoes act as principal vectors. Several species of wild birds included in a wide variety of families are the vertebrate hosts.

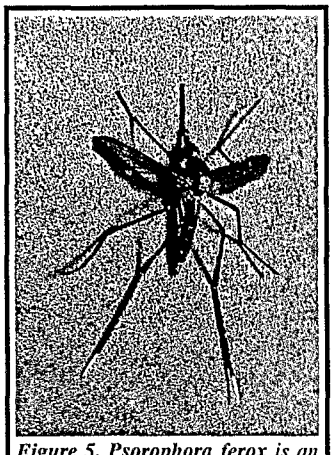

*Figure 5. Psorophora ferox is an important vector of the Ilhéus virus.*

## Alphavirus

**Mucambo (MUC) and Pixuna (PIX) viruses** — Mucambo fever and Pixuna fever viruses are members of the genus *Alphavirus*, and are serologically related to group A of arboviruses. MUC and PIX are the serotypes III and IV of Venezuelan Equine Encephalitis virus complex, respectively.

MUC and PIX have been isolated from human beings, seven times and once, respectively. All human isolates of MUC were obtained from naturally acquired infections, while the human PIX isolate was obtained from laboratory infection (16). Mucambo fever virus causes a disease characterized by a mild fever, headache, malaise and weakness. The symptoms remained during 2 to 3 days. Recovery is complete. In nature, MUC virus is maintained by a sylvatic cycle in which rodents are the main vertebrate hosts, especially *Oryzomys capito*. Several species of Culicidae mosquitoes act as vectors, mainly *Culex portesi* (16,22). Both vectors and vertebrate hosts of PIX are unknown.

## Arenavirus

**Flexal (FLE)** — Flexal virus is an *Arenavirus* and serologically is included in the Tacaribe serogroup. The prototype of FLE virus was obtained from an *Oryzomys bicolor* in 1977 in Itaituba at km 212 of the Transamazon highway (26). The human disease caused by this virus has been recorded once from a young female technician working in the laboratory. The clinical picture presented was one of a mild fever, malaise, weakness, severe headache for a week, generalized myalgia, nausea, vomiting, dizziness, diarrhea and alopecia. The symptoms remained for about 1 month. The patient recovered without sequelas (16). The sylvatic cycle responsible for the maintenance of FLE is unknown.

## Vesiculovirus

**Piry (PIRY) and Jurona (JUR) viruses** — Piry fever and Jurona fever viruses are included in the family Rhabdoviridae. Both agents are members of the genus *Vesiculovirus*. Serologically they are related to the VSV serogroup. The prototype of PIRY was furnished from tissues of a *Philander opossum* caught in Utinga forest. High rates of NT antibodies to PIRY have been found in Amazon immigrants from south regions and in people living in the south and southeast regions of Brazil, but it is rare in the Amazonian native. The human isolate was originated from a laboratory infection. The disease was characterized by an abrupt onset with high fever, headache, chills, photophobia, myalgia, arthralgia, dizziness and weakness. The blood sample from which the isolation was obtained, showed in the hemogram a leucopenia of 3,000 leucocytes. The disease remained for 1 to 2 days.

There is no other record of human disease, although frequently, a high prevalence of NT antibodies was found in people who have worked with this virus (16).

JUR virus has been isolated once from the blood of a 58-year-old man sampled in Costa Marques, Rondonia State, at the border with Bolivia. The disease was a febrile illness, whose blood smears for malaria search were negative. Other information about symptomatology as well as evolution were not obtained. JUR virus prototype was obtained from one pool of *Haemagogus* sp mosquitoes caught in the Belém-Brasília highway.

## Comments and perspectives for future researches

Arbovirus can be transmitted to man by infected arthropods in two distinct levels: the sylvatic cycle and the urban cycle. In the former, the vectors are infected and maintained in the jungle in determined areas (ecologic niche) where a transmission chain is responsible for the maintenance of arboviruses and, infected vectors can transmit arboviruses to nonimmune vertebrate hosts and vertically to other vectors. In this context, man is infected tangentially by the bite

of infected arthropods when intruding many times in an ecologic niche at some distance from his dwelling. This tangential mode of infection results in a few or sporadic cases. Generally, all cases are reported at the same site, usually in forests or near them (28). This mechanism is responsible for outbreaks of jungle Yellow Fever and Mayaro fever infections. In the second level (urban cycle), a person infected becomes an amplifying host in the transmission chain and initiates an epidemic (man-mosquito-man) in an urban area. In this context, domestic arthropod vectors are involved and they can transmit the virus to other persons, after an extrinsic incubation period. This is what happens, for example in Dengue and Oropouche epidemics.

On the other hand, the frequency of transmission of an arbovirus to man is a function of vector population density, vector competency, environmental factors (humidity, temperature) and other factors. The risk of transmission also depends on their geographic distribution. For some arboviruses, this risk is minimal and is limited to determined ecologic niches or regions, because such viruses have a limited distribution, while others can cause human disease in several regions; it is the case of Yellow Fever which can be transmitted inside a large epizootic area, as well as in urban centers, since the primary vector *Aedes aegypti* can become infected.

As we have seen, each arbovirus is maintained in nature through a well defined ecological niche where the vertebrate hosts and haematophagous insects play the most important role. Therefore, arboviruses are essentially zoonosis which the modifications of environment, facilitate, in an adequate period of time, the occurrence of human infections. So, arboviruses can effectively survive better in regions like Amazonia, where the populations of vertebrate hosts are high and relatively stable and where a large variety of mosquitoes may attain high densities. It is well known that arboviruses tend to have specific geographic distributions, and that each area studied thus far seems to have its own particular arboviruses fauna. In this context, therefore, why is it that Amazonia which occupies about half the extent of Brazil and has so many different arboviruses has only a few number of researchers studying them? Logically, new areas of research may be given more priority to establish all parametric variants involved in the maintenance of arbovirus in nature.

Since the pioneer studies, there is a concept that our knowledge of the majority of the arboviruses is lesser than that related to their ecology. Generally we have information only about the circumstances of the original isolation from nature. Further information is needed, based on more complete studies during epidemic phases and during interepidemic periods. As stated by Reeves: "we must mind that our ecologic knowledge of any arbovirus is incomplete and it would be a faulty concept to believe it ever will be" (29).

Logically, there must be certain thresholds of host densities and vector populations that are essential to maintain any arbovirus in this basic enzootic cycle in a favorable environment, and changes in these population levels, if downward, will disrupt the cycle and lead to disappearance of the virus; and if upward, will lead to an explosion of viral multiplication and wide dissemination (29). It is possible, that this latter phenomenon has been the mechanism responsible for new epidemic areas affected by Oropouche fever virus in the Amazon region.

New studies are needed on the various types of biotopes in each region of arbovirus activity. In view of the migration of a great number of birds and bats from one place to another, we must consider the possibility that migration of these animals can determine, in an adequate time, the evidence of arbovirus diseases to man and other animals.

Finally, we must remember that the intensive migration of man associated with colonization, exploration of subsoil and other activities, can determine changes in the environment. Moreover, the actions on the biotopes are each day more frequent and intensive and further researches must be done to achieve reliable evaluations of these changes. Thus, cross information through this interface can result in valuable information and should answer many questions about these fascinating agents of human diseases. ■

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# Modifications of arbovirus transmission in relation to construction of dams in Brazilian Amazonia

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**The Amazonian region of Brazil seems to be the world's richest reservoir of arboviruses. To date, 183 different types of arboviruses have been detected in the Amazonian region, accounting for more than one third of the 535 arboviruses reported in the world. Of these, 136 (74.3%) are endemic. The main objective of this paper was to evaluate what the effects of the construction and flooding of dams would be on the transmission and epidemiology of sylvatic arboviruses, in order to define the potential health hazards to which the human population would be subjected. Five areas were surveyed but only one could be thoroughly studied. Comparisons were made between surveys: *i)* inside the dam region, before, during and after the flooding period; *ii)* outside the dam region, in an area with a similar climate, landscape and vegetation, during the total time of the studies. The two chosen areas, namely Altamira and Tucuruí, were studied since 1974, and since**