ARBOVIRUSES PATHOGENIC FOR MAN IN BRAZIL.

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RESUMO

Os mais importantes aspectos clínicos e ecoepidemiológicos e aspectos preventivos acerca das arboviroses associadas com doença humana no Brasil são discutidos. Trinta e seis arbovirus dentre os tipos presentemente isolados no País têm sido incriminados como causadores de doença humana. Destes, cinco são importantes em termos de saúde pública pois estão associados com epidemias, são os virus Dengue (DEN), Mayaro (MAY), Oropouche (ORO), Rocio (ROC) e Febre amarela (FA). DEN e ORO estão associados com doença humana epidêmica em áreas urbanas enquanto MAY, ROC e FA especialmente em áreas rurais. Basicamente, o virus ORO determina um quadro febril algumas vezes acompanhado por meningite asséptica. MAY e DEN são responsáveis por quadros febris exantemáticos, sendo que DEN, nos últimos anos tem sido associado com quadros de febre hemorrágica, o que sabidamente é o mecanismo pelo qual o virus FA determina a sua apresentação clínica clássica e o ROC está associado com graves quadros de encefalite. Trinta e um outros arbovirus têm sido associados com doença febril benigna em poucos e esporádicos casos. Afora DEN e os *Arenavirus* Flexal e Sabiá (não são arbovirus), todos os arbovirus envolvidos com doença humana na Amazônia Brasileira, são mantidos em natureza através de um ciclo silvestre desenvolvido na floresta, onde diversas espécies de insetos hematófagos e vertebrados silvestres atuam como vetores e hospedeiros, respectivamente. O virus DEN tem um ciclo urbano em que o mosquito *Aedes aegypti* é o vetor e o homem atua como hospedeiro. Os arenavirus são transmitidos diretamente ao homem através de excretas de roedores que são seus principais hospedeiros. Excetuando os cinco virus associados com epidemias que causam um grande impacto socio-econômico, inclusive levando a morte, casos verificados com FA, DEN e ROC, o verdadeiro papel desses vírus como agentes sistemáticos de doença humana é ainda pouco conhecido. Novos estudos são necessários para esclarecer aspectos ainda obscuros acerca da epidemiologia da maioria desses arbovirus.

SUMMARY

The main aspects of the clinical manifestations and epidemiological data regarding human arboviruses in the Brazilian Amazon region are reviewed. Thirty-six arboviruses and other viruses of vertebrates have been associated with human disease among over 200 isolates made in Brazil. Five of them are important in public health and are involved in epidemics, they are the Dengue (DEN), Mayaro (MAY), Oropouche (ORO), Rocio (ROC) and Yellow Fever (YF) viruses. ORO and DEN are associated with epidemics of human disease in urban areas, while MAY, ROC and YF have been responsible for epidemics in rural areas. Usually, ORO cause a febrile disease, sometimes accompained by aseptic meningitis. MAY and DEN are associated with febrile disease and rash, while YF produces a hemorrhagic fever and ROC is an agent responsible for encephalitis. Thirty-one other arboviruses are involved in rare and sporadic cases of febrile illness. All arboviruses (with the exception of DEN and arenaviruses) are maintained by a sylvatic cycle in the forest, where several species of hematophagous insects act as vectors and wild vertebrates are involved as hosts. DEN has a cycle in which the *Aedes aegypti* mosquitoes are the vectors and man the vertebrate host. Arenaviruses are transmitted directly to man by rodents. With the exception of the five viruses associated with epidemics which are of great economical and social impact, and may be responsible for deaths, (e.g. of DEN, ROC and YF), the exact involvement of these viruses as systematic agents of human disease is unknown. Further studies are needed to clarify aspects of their epidemiology. Arenaviruses are directly transmitted to man by way of the excreta of infected rodents which are the reservoir-hosts of these viruses. Appropriate safety measures should be adopted when handling these viruses as they can be transmitted via the respiratory tract (droplet infection).

INTRODUCTION

Some arboviruses and other viruses transmitted by rodents, are important worldwide public health problem. They have frequently been responsible for extensive epidemics, with serious impact on human and veterinary health.

In Brazil, these viruses are spread over several regions, although, the number of types causing human disease is low. Only a few have been incriminated as causative agents of epidemics, but in spite of the relative infrequency of these epidemics, their social and economical impact is important. Thus, during epidemics of Dengue and Oropouche, many workers and students may become ill and there is consequently, a loss of productivity and high absenteism in the schools. This may have a great impact in a given community.

Up till the end of 1994, 200 diferent arthropod-borne and rodent-borne viruses have been isolated in Brazil. Based on virus isolation or antibody detection, 36 of these have been associated with human infections

(Table 1). Twenty-eight are members of the 3 genus; *Alphavirus* (6), *Bunyavirus* (14) and *Flavivirus* (8), and 8 belong to another three genera. With few exceptions, all these viruses have been recovered from people naturally infected. To date, four have been isolated only from persons acquiring accidental laboratory infection (Table 1).

Table 1. Arboviruses and other viruses transmitted by rodents isolated in Brazil associated with human disease according of type of disease and source of isolation, 1954-1995.

type of disease	genus	antigenic group	virus	Nat.Acq*.	Lab.Acq*.	wild host	sentinel	arthropod
Hemorrhagic	*Flavivirus*	B	Yellow fever	+	-	+	+	+
" "	*Flavivirus*	B	Dengue 2	+	-	-	-	+
" "	*Arenavirus*	Tacaribe	Sabiá	+	+	-	-	-
Febrile illness	*Alphavirus*	A	Mucambo	+	-	+	+	+
" "	*Alphavirus*	A	Pixuna	-	+	-	+	+
" "	*Arenavirus*	Tacaribe	Flexal	-	+	-	+	-
" "	*Bunyavirus*	Anopheles A	Tacaiuma	+	-	+	-	+
" "	*Bunyavirus*	Bunyamwera	Xingu	+	-	-	-	-
" "	*Bunyavirus*	C	Apeu	+	-	+	+	+
" "	*Bunyavirus*	C	Caraparú	+	+	+	+	+
" "	*Bunyavirus*	C	Itaqui	+	-	+	+	+
" "	*Bunyavirus*	C	Marituba	+	-	+	+	+
" "	*Bunyavirus*	C	Murutucu	+	-	+	+	+
" "	*Bunyavirus*	C	Nepuyo	-	-	+	+	+
" "	*Bunyavirus*	C	Oriboca	+	-	+	+	+
" "	*Bunyavirus*	California	Guaroa	+	-	-	-	+
" "	*Bunyavirus*	Guama	Catu	+	-	+	+	+
" "	*Bunyavirus*	Guama	Guama	+	-	+	+	+
" "	*Bunyavirus*	Simbu	Oropouche	+	+	+	-	+
" "	*Flavivirus*	B	Bussuquara	-	-	+	+	+
" "	*Flavivirus*	B	Ilhéus	+	-	+	+	+
" "	*Phlebovirus*	Phlebotomus	Alenquer	+	-	-	-	-
" "	*Phlebovirus*	Phlebotomus	Candiru	+	-	-	-	-
" "	*Phlebovirus*	Phlebotomus	Morumbi	+	-	-	-	-
" "	*Phlebovirus*	Phlebotomus	Serra Norte	+	-	-	-	-
" "	*Vesiculovirus*	VSV	Jurona	+	-	-	-	+
" "	*Vesiculovirus*	VSV	Piry	-	+	+	-	-
Rash febrile	*Alphavirus*	A	Mayaro	+	+	+	+	+
" " "	*Flavivirus*	B	Dengue 1	+	-	-	-	+
" " "	*Flavivirus*	B	Dengue 4	+	-	-	-	+
Encephalitis	*Alphavirus*	A	EEE	-	-	+	+	+
" "	*Alphavirus*	A	VEE I-F	-	+	+	+	+
" "	*Alphavirus*	A	WEE	-	-	+	-	+
" "	*Bunyavirus*	Bunyamwera	Tucunduba	+	-	-	-	+
" "	*Flavivirus*	B	Rocio	+	-	+	+	+
" "	*Flavivirus*	B	SLE	+	-	+	+	+

* Human infection.

Until now, only five arboviral diseases are considered to be of public health importance in Brazil, due to their capability of causing death or severe human illnesses. They are Dengue (DEN), Mayaro (MAY), Oropouche (ORO), Rocio (ROC) and Yellow fever (YF). All of them, have been associated with epidemic outbreaks, and at least three, DEN, ROC and YF, have been responsible for human disease with fatal outcome. ORO and DEN are active in urban areas, while MAY, ROC and YF, occur mainly in rural areas. These five arboviruses are responsible for over 95% of all human cases of arboviral disease in Brazil.

This account reviews our current knowledge regarding the taxonomic status and epidemiological data, concerning the arboviruses that are pathogenic for man in Brazil, and covers studies made over the past 40 years.

ALPHAVIRUSES

EASTERN EQUINE ENCEPHALITIS (EEE)

The virus

Eastern Equine Encephalitis (EEE) virus is member of the *Alphavirus* genus, family Togaviridae. Serologically, EEE belongs to the serogroup A, which has a distant antigenic relationship with the Highlands J virus of the WEE complex. EEE has only a single serotype causing human and animal diseases (Karabatsos, 1985).

Epidemiology

Antibodies to EEE have been detected in inhabitants of the Amazon basin, but no virus has been isolated from sick humans, with or without encephalitis. On the other hand, epizootics of equine mortality caused by this virus have been reported in horses from the municipality of Bragança, Pará State (Causey et al . 1962a). Wild birds are the main vertebrate hosts of this arboencephalitic virus. A wide variety of wild birds of several avian families seem to be susceptible, notably *Thamnophilus aethiops* and *Phlegopsis nigromaculata* (Formicariidae), and *Ramphocelus carbo* (Thraupidae) from which virus strains were also obtained. HI antibodies have been detected to the rate of 1.3%, or higher, in 23 other species of birds of several families (Vasconcelos et al., 1991). (Table 2). The epizootic vectors, in North America, is the mosquito *Culiseta melanura* (Morris, 1988), while in South America it is *Aedes taeniorhynchus*. *Culex pedroi* is the enzootic vector in Latin America (Theiler & Downs, 1973). In 1991, however, 14 strains of EEE virus were obtained from 96 pools of *Aedes albopictus* (total of 9,393 insects) caught in Florida, USA (CDC, 1992), indicating that this species may play a role in the maintenance of this virus and might become an important vector in tropical areas.

In Amazonia, EEE antibodies against are generally of low prevalence (approximately 1%), with exception of Cametá, in Pará State, where about 20% of people have been shown to be positive (Causey et al 1962a).

Table 2. Wild birds from which EEE virus was isolated and specific HI antibodies confirmed by N tests detected in Brazilian Amazonia.

Bird family	Bird species	number of strain	% positivity (sampled)
Formicariidae	*Phlegopsis nigromaculata*	2	0.5 (203)
	Thamnophilus aethiops	1	4.0 (8[illegible])
Thraupidae	*Ramphocelus carbo*	1	0.5 (8[illegible]4)
Tyrannidae	*Mionectes oleaginea*	1	0 (96)
Icteridae	*Cacicus cela*	1	0 (...)

Clinical features

EEE is associated with human and equine encephalitis. In man the spectrum of infection ranges, however, from asymptomatic to full-blown encephalitis. During an epidemic in New Jersey in 1959, the ratio of clinically apparent to inapparent cases was 1:23. Clinically, the course of disease due to EEE has two possibilities: systemic disease and encephalitis. In the systemic infection the patient has an acute infection characterized by high fever, severe muscle pains, chills, malaise and arthralgia. There is no Central Nervous System (CNS) involvement, and recovery is complete. In its encephalitic form the disease is usually more severe in children. The main symptoms of encephalitic form of EEE are irritability, restlessness, vomiting, cyanosis, convulsions, neck rigidity, tremor, and coma. Death usually occurs from 2 to 10 days after onset and the mortality is extremely high, especially during epidemics (Morris, 1988). In Brazil, a single case of EEE encephalitis has been reported in Bahia (Alice, 1956).

Prevention and control measures

During epidemic periods, the inseticidal control of adult mosquitoes is the most important measure. Vaccine is not easily found, and is presently used exclusively to immunize virus laboratory workers Sentinel animals can be used to demonstrate virus activity.

MAYARO (MAY)

The virus

Mayaro virus belongs to the genus *Alphavirus* of the family Togaviridae. Serologically, it is a member of the serogroup A (Karabatsos, 1985). Among the alphaviruses, MAY is included in the Semliki Forest complex as a species, with two subtypes, Mayaro and Una, based upon cross-reactivity by hemagglutination-inhibition (HI) test. Biologically it resembles Chikungunya virus (Pinheiro & Le Duc, 1988).

Epidemiology

The first isolations of MAY were obtained in Trinidad, in 1954, from five febrile patients. In Brazil, the first isolations were made in 1955, from several patients suffering a febrile illness in a community about 200 km east from Belém. MAY virus has also been associated with epidemic febrile disease in Bolivia, Colombia and Panama (Karabatsos, 1985), and infections, without virus isolations, have been reported in Suriname, Venezuela and French Guiana (Pinheiro & Le Duc, 1988). Mayaro virus activity has been documented only in the Americas.

In Brazil, MAY is largely distributed in the Central, Amazonian and Northeast regions. In Amazonia it is endemic and the higher rates of antibodies are associated with populations mainly composed of forest-workers. For this reason, the highest prevalence of antibodies has been found in the Brazilian indian communities, with 20% to 47% of the members of the tribes showing antibodies to MAY (Vasconcelos et al., 1992b). Immunity to this virus increases with age, and in rural communities in the Amazon region ranges from 10% to 60%. Despite high antibody rates, it is extremely difficult to recover MAY from man and other vertebrates (except in epidemics), because the viremic period shown by this virus to be very short-lived and lasted no more than 2-3 days. During this short time it is unlikely that MAY will be suspected as the causative agent of the disease. From mosquitoes, however, isolation of the virus, is relatively easy, especially from *Haemagogus* (Table 3).

Table 3. Strains of MAY virus according of source of isolation.

SOURCE OF ISOLATION	NUMBER OF STRAINS
MAN	66
Haemagogus sp	28
Haemagogus janthinomys	25
Sabethes sp	2
MONKEYS *	3
Other wild animals **	4

* two sentinels; ** two reptiles, 1 rodent and 1 marsupial.

At least four epidemics of Mayaro fever virus have been reported in Pará State, Amazonian region: in Guamá in 1955, Belterra in 1978, Conceição do Araguaia in 1981 and Benevides in 1991 (Pinheiro et al., 1981, 1986; Travassos da Rosa et al., 1991, unpublished data). MAY has a similar cycle to that of YF virus, and two outbreaks (Belterra and Conceição do Araguaia-PA) occurred in association with Yellow fever virus. Outside Pará State, two outbreaks were registered in 1987 and 1991 in Itaruma, Goiás State (Hoch et al., unpublished data) and in Peixe, Tocantins State (Vasconcelos & Travassos da Rosa, 1991, unpublished data).

MAY outbreaks are usually limited to rural areas near or within forest, where *Haemagogus janthinomys*, the main vector, is found in abundance. Contact with the forest seems to be an important risk factor for infection with this virus. The vertebrate hosts of MAY are nonhuman primates, although birds can act as secondary hosts. It is noteworthy, that these animals may be important for the dissemination of the virus, since many species that can carry MAY in the viremic phase, can cover large distances in a short time.

Clinical features

MAY disease is usually characterized by a sudden onset of 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. Infected persons usually complain that fever and headache are intense. The maculopapular skin rash usually appears on the 5th day of illness and lasts three after onset. The rash is more frequent in children than older people and is seen more prominently on the legs, arms, chest and back. Curiously, the face is less affected. Except arthralgia which may persist in some patients for about 2 months, all clinical manifestations last from 3 to 10 days (Pinheiro et al., 1981a; 1986).

Prevention and control

There are no practical control measures during an epidemic caused by MAY, although, individual measures can help to prevent human disease, such as avoidance of forested areas where virus transmission is occurring. It is important remember that the vectors are mosquitoes which bite between 09:00 to 16:00 hours when sunlight is pre-eminent, and that the vector is clearly sylvatic. To prevent MAY, the only feasible method is personal protection against mosquito vectors

VENEZUELAN EQUINE ENCEPHALITIS (VEE) COMPLEX

A. MUCAMBO (MUC) & PIXUNA (PIX)

The viruses

Mucambo fever and Pixuna fever viruses are members of the genus *Alphavirus*, and are serologically related to group A of the arboviruses. Both viruses are classified as subtypes of the Venezuelan Equine Encephalitis (VEE) virus complex. The HI test is extremely useful in separating subtypes of the VEE complex, and they have been classified by this technique as the subtypes III (MUC) and IV (PIX) of the VEE virus complex. The prototype of the MUC virus was obtained in 1954, in the Utinga forest, near Belém. The first strain of PIX was isolated from a pool of *Anopheles nimbus* collected at km 94 of the Belém-Brasilia Highway, Para State, in 1961 (Karabatsos, 1985).

Epidemiology

In nature, MUC virus is maintained by a sylvatic cycle in which rodents are the main vertebrate hosts, in particular *Oryzomys capito*. Several species of mosquitoes act as vectors, principally *Culex portesi*, from which strains have been consistently isolated in Brazilian Amazonia and French Guyana (Pinheiro et al., 1986; Vasconcelos et al., 1991). The virus is widely distributed in the Amazonia region and also in São Paulo State, where it is found principally in the Valley of Ribeira (Iversson et al., 1982).

PIX virus has been isolated three times in Amazonia. On two occasions it was from mosquitoes (the prototype and another isolate, from *Trichoprosopon digitatum*) and once from the viscera of rodent, *Proechimys guyannensis*. No signals of activity on the part of this virus had been detected since 1964, and both vectors and vertebrate hosts of PIX are poorly known.

Clinical features

MUC has been isolated 7 times from naturally infected human beings, and in one occasion from a laboratory acquired infection (Pinheiro et al., 1986). Mucambo fever virus causes a disease characterized by an abrupt onset with mild fever, headache, malaise and weakness lasting by 2 to 3 days. Recovery is complete. On the other side, PIX virus caused a febrile disease of 3 days of evolution.

Prevention and control measures

MUC and PIX viruses have not been associated with epidemics and no control measures are applicable. As they are only responsible for sporadic cases in rural areas, the most important way of preventing infection is the avoidance of such areas and the use of mosquito repellents.

B. VEE SUBTYPE I-F

The virus

This variety of serotype I of the VEE complex has been isolated in 1976 in the Ribeira Valley, São Paulo

State, from a pool of mosquitoes *Culex (Melanoconion)* sp. The serotype is largely found in São Paulo State, where antibodies against the virus are quite found, especially in people living near forested areas. Strains from human beings have not however been isolated in that region. A single isolate of VEE subtype I-F was obtained in Belém, in 1987, from a laboratory acquired infection (Travassos da Rosa et al., 1990)

Epidemiology

The vectors of this serotype are mosquitoes, principally *Culex (Melanoconion)* mosquitoes. Known vertebrate hosts include rodents such as *Proechimys* and *Oryzomys*, bats, and birds. A serological survey of wild animals carried out in the Ribeira Valley, São Paulo (Iversson et al, 1982), has recorded the presence of HI antibodies, particularly in rodents. In the same area, subtype I-F of the VEE complex was also isolated on a single occasion from a bat *Carollia perspicillata* and sentinel mice. Human sera collected at the same time commonly showed HI antibodies. The highest positive-rate being found in fishermen, with a positive rate of 26 % (79/303).

An outbreak of a febrile illness was caused by the virus, in 20 out 25 soldiers who were training in an area of the Ribeira Valley. No isolations were made, but the infection was confirmed by detection of IgM antibodies by MAC ELISA in two serum samples collected from military personnel (L.B. Iversson, personal communication).

Clinical features

In a patient from whom the virus was isolated, illness was characterized by an abrupt onset of high fever, chills, severe headache, myalgias (especially in back and neck), arthralgia and malaise. The disease lasted 5 days and the patient made an uneventful recovery (Travassos da Rosa et al., 1990). Among the above-mentioned soldiers, the most important symptoms observed were high fever, severe headache, malaise, diarrhea and sleepiness (L.B. Iversson, personal communication).

Prevention and control measures

The subtype I-F is an enzootic strain of VEE virus and only few cases of naturally acquired infection have been observed in a highly localised area: all cases were soldiers entering the enzootic zone. There is not available vaccine, and prevention or control measures are, once more avoidance of forest areas. As with all pathogenic viruses, safety measures are needed for laboratory staff working with this subtype.

WESTERN EQUINE ENCEPHALITIS (WEE)

The virus

Western Equine Encephalitis (WEE) virus is member of the genus *Alphavirus* of the family Togaviridae. Serologically, WEE is member of the serogroup A. Immunological studies have demonstrated that WEE virus is closely related to Sindbis, Aura, Fort Morgan and Highlands J viruses, that comprise the group (Karabatsos, 1985).

Epidemiology

WEE virus is widely distributed in the Americas, from Canadá to Argentina. In Brazil, antibodies against the agent have been found from Amazonia to the Southern region, and strains have been obtained from wild birds, the main vertebrate hosts of WEE elsewhere. In the USA, peridomestic *Culex tarsalis* is the principal epidemic and endemic vector, and virus transmission is basicly made in summer (Reisen & Monath, 1988). In Brazil, cases of human disease due to WEE have not yet been diagnosed. The absence or paucity of human disease in Brazil and other countries of South America has been attributed to ecologic factors, rather than, differences in strain virulence. HI antibodies rates in Amazonia have been found to be about 1% or lesser in the human population. In this same region, however, a high prevalence of HI antibodies has been found in wild birds belonging to the Formicaridae, especially *Phlegopsis nigromaculata* and *Hylophilax poecilonota*, and the Tyrannidae, mainly *Cocythopis torquata* from which virus strains have already been isolated (Vasconcelos et al., 1991). Another 28 species of various avian in Brazilian Amazonia serological positive-rate have showed a percentage of 5.1% or higher (Vasconcelos et al., 1991). These details is summarised in the Table 4. Although WEE virus has been isolated from single specimens of *Aedes fulvus*, *Culex taeniopus* and *Cx. portesi*, in Amazonia, the

arthropod vectors in Brazil, have not been thoroughly investigated and many other vectors may exist.

Table 4. Species of wild bird which furnished strains and specific HI antibodies confirmed by N tests to WEE virus in the Brazilian Amazonia.

WILD BIRD FAMILIES	BIRD SPECIES	NUMBER OF STRAINS	% POSITIVITY (SAMPLED)
Formicariidae	*Gonopophaga aurita*	1	2.7 (75)
	Hylophylax poecilonota	1	5.3 (360)
	Myrmotherula hauxwelli	1	0 (196)
	Phlegopsis nigromaculata	1	10.0 (203)
	Pyriglena leuconota	1	1.5 (223)
Tyrannidae	*Corythops torquata*	1	5.1 (164)

Clinical Features

In North America, WEE is associated with meningoencephalitis in man and equines, with a high morbidity and mortality. In man the infection has a spectrum which ranges from inapparent to full-blown encephalitis. The disease has an abrupt onset with high fever, headache and symptoms and signs of CNS involvement, lethargy, stiff neck, photophobia, drowsiness, vertigo, irritability, generalized convulsions, tremor and upper motor neuron deficits, and changes in mental status. The severity of the disease is dependent on the patient's age, with the illness frequently more severe in children than in adults (Reisen & Monath, 1988).

Prevention and control measures

In North America, where WEE has an epidemic cycle, control measures are important to prevent or interrupt virus transmission to man and domestic animals, especially equines. In Brazil, the disease has not yet been reported in man. However, the virus is enzootic, and to prevent acquisition of the infection it is best to avoid contact with the forest where the vectors may be present.

BUNYAVIRUSES

GUAROA (GRO)

The virus

Guaroa fever virus, included in the California serogroup is a member of *Bunyavirus* genus, family Bunyaviridae. It was isolated in Colombia in 1956 from the blood-stream of a 75 year-old woman who showed no evidence of illness (Groot et al., 1959). By HI and N tests GRO virus is most related to Trivittatus virus within the California serogroup (Karabatsos, 1985).

Epidemiology

GRO virus is (excepting Oropouche) the most widely distributed *Bunyavirus* in the Amazon region, as evidenced by the HI test. An overall rate of 18% positive sera has been found in several localities of the Amazon basin (Pinheiro et al., 1986).

Eleven strains of GRO virus have been obtained from sick people. With the exception of one obtained from transcutaneous hepatic biopsy, from a patient with a paralytic disease (Causey et al., 1962b), all isolates originated from the blood of febrile persons. In Brazil and Colombia, mosquitoes of the complex *Anopheles Nyssorhynchus*, especially *An. triannulatus* and *An. nuneztovari* are the main vectors of GRO virus (Dégallier et al., 1989). A wide variety of birds from several families, are suspected to be the vertebrate hosts, following the detection of high rates of HI antibodies. However, strains have not yet been isolated from any member of the sylvatic vertebrate fauna. Data concerning isolations of this virus are summarized in Table 5.

Table 5. Guaroa virus strains obtained in Brazilian Amazonia, until end of 1993.

SOURCE OF ISOLATION	NUMBER OF STRAINS
Man	11
Anopheles triannulatus	4
Anopheles nuneztovari	4
TOTAL	19

Clinical features

The disease has an acute onset with high fever, chills, headache, mylagias and malaise. Concomitant infections with malaria have been reported in two cases. All patients recovered after the illness had lasted from 3-5 days (Vasconcelos et al., 1990).

Prevention and control measures

Since GRO has not been associated with epidemics, there are no control measures applicable. The virus is responsible for sporadic cases in rural areas and the most important measure to prevent infection is personal protection against biting insects.

GROUP C VIRUSES

The viruses

Group C of the arboviruses was established by Casals and Whitmann in 1961 and originally consisted of five serologically related viruses isolated at Belém, Brazil, by Causey (1961). These were Apeú (APEU), Caraparu (CAR), Itaqui (ITQ), Marituba (MTB), Murutucu (MUR) and Oriboca (ORI). Later, a seventh stype was discovered (Shope & Causey, 1961). Several other types have since been described from Trinidad and Panamá, but only one of these, Nepuyo (NEP) virus has also been encountered in Amazonia (Shope & Whitmann, 1966).

Structural studies have shown that these viruses belong to the family Bunyaviridae. These viruses fall into four complexes: the Caraparu complex (Caraparu and Apeu viruses), the Marituba complex (Marituba and Murutucu viruses), the Oriboca complex (Oriboca and Itaqui viruses) and the Nepuyo complex (Nepuyo and Gumbo Limbo viruses). In the latter complex, Gumbo Limbo is a virus formerly not found in Brazil. It has been found in Florida (USA) as an infection of mosquitoes and wild rodents. It is believed that these viruses of the above-mentioned complexes have probably suffered a reassortment in nature, since they are transmitted in a compact ecosystem (Shope et al., 1988).

Epidemiology

The group C arboviruses are maintained in nature by cycles involving small forest mammals, principally rodents, and nocturnal mosquitoes which are mainly *Culex* species of the subgenus *Melanoconion*. One type, APEU, and one subtype, MTB, are preferentially transmitted in the forest canopy among arboreal marsupials and monkeys. With the exception of NEP, all have been isolated from man in Amazonia. Surveys among human communities carried out in several localities of the Amazon region have shown a rate of 15% positivity rate for antibodies against group C viruses (Pinheiro et al., 1986). Caraparu virus is certainly the most widely distributed group C virus in Brazilian Amazonia, and it has also isolated in São Paulo State, where has been associated with human illness. Several species of mosquitoes act as vectors of these viruses, in particular *Culex (Melanoconion)* mosquitoes, and especially, *Cx. (Mel.) portesi*. Rodents are the main vertebrate hosts of group C viruses, particularly *Proechimys guyannensis* and *Oryzomys capito*, and hundreds of strains have been obtained from these hosts and the mosquito vectors. Marsupials have an important role in the maintenance for Apeu and Marituba in nature (Shope et al., 1988). Table 6 summarizes the major data concerning isolations of these viruses in the Amazon region of Brazil.

Table 6. Group C virus isolates in Brazilian Amazonia until end of 1993.

SOURCE	ORIBOCA	ITAQUI	CARAPARU	APEU	MARITUBA	MURUTUCU	TOTAL
Man	13	2	14	6	5	5	45
Sentinel animals	186	407	894	66	67	120	1740
Wild animals	16	17	36	3	3	19	94
Arthropods	29	20	28	7	5	13	102
TOTAL	244	446	972	82	80	157	1981

Clinical features

Disease caused by these viruses is characterized by a febrile syndrome. Onset is usually sudden, and high fever, headache, chills, myalgias, photophobia and retrobulbar pain are the most common symptoms mentioned by the patients. The symptoms remain for 4 to 5 days, and although some patients complain of severe symptoms, recovery is uneventful (Pinheiro et al., 1986).

The single human strain of Nepuyo virus isolated to date came from a febrile Panamanian patient (Karabatsos, 1985).

Prevention and control measures

Outbreaks attributed to these viruses have not been reported, and consequently there are no applicable control measures. Individual measures to prevent human disease are, once again, avoidance of contact with areas where virus transmission is occurring, and the use of mosquito repellents and bed nets. There are no available vaccines.

GUAMA (GMA) & CATU (CATU) VIRUSES

The viruses

This group of viruses was also first established on the basis of new isolates made in the Belém Virus Laboratory (BLV). The group Guamá viruses are closely related by the CF test, but most serotypes are quite distinct by HI and N. Guamá and Catu viruses are the second and third most frequently encountered viruses at the BVL (after the group C virus Caraparu).

Guama and Catu viruses are members of the Guamá serogroup of the genus *Bunyavirus*, in the Bunyaviridae family (Karabatsos, 1985). The prototype strain of GMA was isolated from a sentinel mouse in 1956, and that of CATU was obtained from the blood of a sick man. These viruses have been isolated 9 and 11 times, respectively, from blood specimens of man.

Epidemiology

Presence of antibodies against these viruses, detected by HI is about 1% to 2% in Brazilian Amazonia, where they are prevalent. In the municipality of Breves and municipalities near it, however, people have shown a positivity-rate for HI antibodies against these viruses, as high as 50%, confirmed by neutralization tests Travassos da Rosa & Vasconcelos, unpublished data). The ecoepidemiology of these viruses is similar to that seen for group C viruses (Shope et al., 1988). The main vertebrate hosts are rodents, especially *Proechimys guyannensis* and *Oryzomys capito* and the vectors, *Cx. (Mel.) portesi* mosquitoes. Isolates have been consistently made from these vertebrate and invertebrate hosts in Brazilian Amazonia and the Caribbean forests. Table 7. summarizes the more important data concerning isolations of these viruses in Amazonia.

Table 7. Guamá group virus isolates until end of 1993.

SOURCE OF ISOLATION	CATU VIRUS	GUAMA VIRUS	TOTAL
Man	11	10	21
Sentinel animals	356	603	959
Wild animals *	58	92	150
Arthropods	50	88	138
TOTAL	475	793	1268

* Especially rodents

Clinical features

The disease determined by these viruses, has a sudden onset. Mild fever, dizziness, headache, muscle pains, arthralgia, photophobia and malaise are the most common symptoms described, and the disease usually persists for 5 days. Recovery is uneventful (Pinheiro et al., 1986; Shope et al., 1988).

Prevention and control

Since, GMA and CATU viruses have not been associated with epidemic diseases, there are no available measures to control human infections, and there are no available vaccines for medical use. Individual protection methods include use of mosquito repellents, bed nets and the avoidance of forest areas where infections have been reported.

OROPOUCHE (ORO)

Oropouche virus is member of the family Bunyaviridae, genus *Bunyavirus*, it is included in the Simbu serogroup of bunyaviruses (Karabatsos, 1985).A total of 21 distinct viruses is currently recognized within this serogroup, with isolates from most of the world, except Europe (Le Duc & Pinheiro, 1988).

Epidemiology

ORO virus was first isolated in 1955 in the West Indian island of Trinidad, from a febrile forest charcoal-worker. There were no signs of an epidemic at that time. In 1961 in the city of Belém, Pará, Brazil, 15 strains were recovered from patients during an epidemic calculated to have infected 11,000 people (Pinheiro et al., 1962), and a second epidemic was recognized in early 1968-69 in the coastal area of Bragança, Pará State. A third epidemic was registered in 1979-80, once again in Belém, in the same area of the city as recorded in 1961, with several other locaties also involved (Freitas et al., 1980). The epidemics commonly begin during the rainy season (usually from January to June in Belém).

The outbreaks of Oropouche 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 have severe disease including neurologic involvement (Pinheiro et al., 1982), although, to date, no fatality has been recorded due to ORO virus. When environmental (ecologic) and epidemiological (susceptibles and vector in high prevalence, and abundance of virus circulation) conditions are favourable, outbreaks occur. They have shown a tendency to occur in a cyclic modality. Thus, three outbreaks have been recorded in Belém during the last 33 years.

Curiously, until 1980, all epidemics reported in Brazil had occurred in Pará State, but from the end of 1980 to the first quarter of 1981, an extensive epidemic was reported in Manaus, Amazonas State, and extended to the municipality of Barcelos, in the State of Amazonas. A third epidemic outside Pará was recorded, in Mazagão, a rural locality of Amapá State (Borborema et al., 1982). In 1988, further areas were affected by epidemics of ORO fever, Porto Franco and Tocantinópolis, in Maranhão and Goiás States, respectively, reported thousands of cases (Vasconcelos et al., 1989). In 1991, a large epidemic was reported in Rondonia State in the towns of Ariquemes and Ouro Preto do Oeste. There, an epidemiological survey estimated that about 90,000 infections occurred during a 45 days period (Vasconcelos et al., 1992b) Finally, in 1994, an epidemic broke out in Serra Pelada, a gold-mining locality in the municpality of Curionópolis, Pará State. A total of over 4,000 cases was estimated in a population that did not exceed 6,000 (Travassos da Rosa et al., 1995).

Based on the population at risk during such epidemics and estimated incidence-rates based upon serological surveys, at least 500,000 people were probably infected by ORO virus in the last 33 years (1961-1994) in the Brazilian Amazon basin (Vasconcelos et al., 1992b).

It has been suggested that ORO is maintained in two distinct cycles; firstly in an urban (epidemic) in where man is the principal vertebrate host and the midge *C. paraensis* is the vector. The second (sylvatic) cycle is responsible for the maintenance of ORO in nature, and it is a "silent" cycle in which primates, sloths and birds are the vertebrate hosts, but in which vector is unknown. Possibly it is again *C. paraensis*, for this biting midge is also widely distributed in tropical rain forest and rural areas of the Amazon basin. Evidence of another vector has not been found, although single isolations have been made from *Aedes serratus* in Amazonia and *Coquilletidia venezuelensis* in Trinidad (Karabatsos, 1985). Table 8 shows the main data of ORO virus isolation.

Table 8. Oropouche virus isolates in Brazilian Amazonia until end of 1993.

SOURCE OF ISOLATION	NUMBER OF STRAINS
MAN	502
Edentata	4
Culicoides paraensis	11
Aedes serratus	1
Culex quinquefasciatus	2
TOTAL	520

Clinical features

Oropouche fever is characterized by an abrupt onset, and fever, headache, myalgia, arthralgia, anorexia, dizziness, chills and photophobia are the symptoms most observed. Nausea, vomiting, diarrhea, epigastric pain, retrobulbar pain, conjunctival congestion and burning sensation have also been reported . Rash is rare and has only been observed in about 5% of all patients (Pinheiro et al., 1981c; Pinheiro, 1983). During the last outbreak in Belém, neurologic involvement was also recorded and characterized as meningitis, which resolved without sequelae (Pinheiro *et* al., 1982). The disease persist for about 2 to 5 days and in epidemic of 1980, at least 63% in Belém and 56% in Porto Franco suffered overt clinical symptoms (Freitas et al., 1980; Vasconcelos et al., 1989). Recurrence has been documented, especially among people who quickly resume strenuous activities, but all attempts to isolate ORO virus during relapses have failed. . There have been no documented cases of second infections with ORO virus (Le Duc & Pinheiro, 1988).

Prevention and control

The most appropriate measure to prevent epidemics is the control of the vectors. These measures can be carried out by insecticide "fogging" during the period when *C. paraensis* adults are active. The use of mosquito repellents may be useful for individual protection, especially during epidemics. There are no vaccines available for human use.

TACAIUMA (TCM)

The virus

Tacaiuma fever virus, is a member of the genus *Bunyavirus*, family Bunyaviridae. Serologically it belongs to the Anopheles A serogroup, where is poorly related by CF with Anopheles A virus. The prototype strain was obtained from the blood of a sentinel monkey (*Cebus apella*) in the Oriboca forest near Belém in 1955 (Karabatsos, 1985).

Epidemiology

This virus has also been isolated in southeast São Paulo State, from a pool of *Anopheles cruzii* (Karabatsos, 1985). In Amazonia and São Paulo, antibodies to TCM are detected with difficulty by HI. In the Amazon region, where there is a higher prevalence, antibodies to this agent have been found in about 1% of the population, mainly in rural areas. Antibodies to TCM virus have been found in horses and wild animals, and horses appear to be important hosts judged by the prevalence of HI antibodies confirmed by N tests. Among wild animals, in the Amazon region, monkeys, rodents (*Nectomys* and *Oryzomys*), bats and forest birds have the highest prevalence of antibodies to the agent, and it is possible that they can act as vertebrate hosts. *Haemagogus sp* and *An. (Nys.) triannulatus* mosquitoes have furnished five and two strains, respectively, and can be considered as important vectors of this virus (Dégallier et al., 1989). Outside Brazil, immunity to TCM virus by HI tests has been found in a bird and a man, in Argentina (Karabatsos, 1985). Table 9, summarizes available data concerning strains of this virus obtained in Brazilian Amazonia.

Table 9. Tacaiuma virus strains obtained in Brazilian Amazonia, until end of 1993.

SOURCE OF ISOLATION	TOTAL OF STRAINS
MAN	3
Sentinel monkey	1
Haemagogus sp	6
Haemagogus janthinomys	1
Anopheles triannulatus	3
TOTAL	14

Clinical features

This virus has been responsible for sporadic, acute febrile illness of man. The disease has an abrupt onset and is characterized by fever, headache, chills, myalgia, arthralgia and weakness. Two cases occurred in association with malaria due to *Plasmodium falciparum*. These patients presented with jaundice and one of them died (Vasconcelos et al., 1990). It is believed that his death was caused by his malarial infection.

Prevention and control

The TCM virus is enzootic and only a few cases of naturally acquired human infection have been observed on enzootic Amazonian focus. To prevent human TCM infection, the only feasible approach is personal protection against vectors, by the use of bed nets and mosquito repellents.

TUCUNDUBA & XINGU (UNREGISTERED)

The Viruses

Tucunduba and Xingu are members of the family Bunyaviridae, genus *Bunyavirus*. Antigenically, these viruses are included in the Bunyamwera serogroup.Tucunduba is a closely related to the Wyeomyia virus, while Xingu is a subtype of the Cache Valley complex, indistinguishable from Maguari virus by the classical tests. The prototype of Tucunduba virus was obtained in the Oriboca forest from *Wyeomyia sp* mosquitoes in 1955. Xingu virus was isolated once from the blood of a man, along Transamazon Highway, in the municipality of Altamira, in 1978.

Epidemiology

Tucunduba has been isolated from numerous mosquitoes. Up to 1993, some 50 strains were isolated from arthropods, particularly from *Wyeomyia sp*, *Sabethes sp* and *Trichoprosopon digitatum*. It is believed that these mosquitoes play an important role in maintaining cycle of this virus. The vertebrate hosts of Tucunduba are unknown. CF antibodies were found in 3 apparently healthy members of the family of the encephalitic patient from whom Tucunduba was isolated (Vasconcelos et al., 1992b).

Both the vector and wild vertebrate host of Xingu are unknown.

Clinical features

Tucunduba virus has been isolated only once, from an 18 month-old girl who presented a clinical picture of meningoencephalitis. Fever, headache, vomiting, symptoms and signs of central nervous system (CNS) involvement were noted, including paresia and coma. The disease lasted two weeks, and left no CNS sequelae (Vasconcelos et al., 1992b).

Xingu virus was recovered from a man, whose blood was also positive to the Hepatitis B surface Antigen (HBsAg) and with a diagnosis of active hepatitis B. The disease was characterized by fever, jaundice, and had a fatal outcome. Unfortunately, the patient was not resampled and definitive proof of the participation of Xingu virus in this death was lost (Pinheiro et al., 1986).

Prevention and control

Since these viruses have not till now been associated with widespread epidemics and have been isolated on a single occasion, no control measures are indicated.

PHLEBOVIRUSES

The viruses

The immunological overlap of these agents has been largely demonstrated by HI studies and to a lesser extent by CF and N test studies. Robert Shope has been in large degree responsible for the creation of serogroups and the delineation of the intragroup relationships (Theiler & Downs, 1973).

At present, 21 Amazonian serotype members of the genus *Phlebovirus* genus, family *Bunyaviridae*, are included in the Phlebotomus Fever serogroup. Four phleboviruses (Alenquer, Candiru, Morumbi and Serra Norte) have been associated with disease in humans these viruses are known only from a single isolate, obtained from the blood of patients with febrile illness.

Epidemiology

Most of the phleboviruses have been recoverd from naturally infected sand flies and are presumed to be transmitted by these insects, mainly members of the genus *Lutzomyia*. However, these phleboviruses (Arumowot Itaporanga and Rift Valley fever) have been isolate repeatedly from mosquitoes in Nature. Isolations also have been obtained from the blood of sick persons, wild animals and sentinel mice. Antibodies to these viruses in wild mammals and man have been detected at very low prevalence (under 1%).

Clinical features

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. The viremia is short-lived and recovery has been uneventful.

Prevention and control

These agents are not associated with epidemic dicase and no control measures are indicated, no vaccine available. Personal protection by bed-nets and insects repellents are useful means of avoiding infections with these and other arthropod transmitted viruses.

FLAVIVIRUSES

DENGUE (DEN)

The virus

Dengue virus belong to the family Flaviviridae and the genus *Flavivirus*. There are four dengue serotypes designated DEN1, DEN2, DEN3 and DEN4.

Epidemiology

Extensive epidemics of dengue fever have been reported in Brazil: The first one occurred in 1981/82 in Boa Vista, Roraima, where serotypes 1 and 4 were the causative agents (Travassos da Rosa et al., 1982) About 11,000 people were infected (Osanai et al., 1983).

In 1986 to 1990, several outbreaks caused by DEN-1 were reported in the States of Rio de Janeiro, São Paulo and Minas Gerais states. In this region, Rio de Janeiro notified about 90% of all the cases. In same period, epidemics were registered in the Northeast of Brazil, mainly in the States of Alagoas and Ceará Almost 80% of the reported cases were from Ceará. With the exception of a few cases with hemorrhagic manifestations, patients presented with the classical dengue fever. In all episodes, DEN-1 was the causative.

From 1991 to 1994 other States in the North (Tocantins), mid-eastern (Goias, Mato Grosso and Mato Grosso do Sul) and North-east (Maranhão, Piauí and Bahia) reported epidemics. The serotype DEN-2 was responsible for about 85,250 cases in Araguaina, Tocantins, in 1991 (Vasconcelos et al., 1992a), although only 2,194 cases were reported (Table 10). DEN 2 was isolated for the first time in Brazil, in Belém, from a febrile patient arriving from Luanda, Angola, in February 1989 (Travassos da Rosa et al., 1989). and again in Rio de Janeiro, from an autochthonous patient in 1990 (Nogueira et al., 1990).

DEN-1 has been associated with dengue fever outbreaks in mid-eastern region of Brazil, and small outbreaks were reported in 1994 in Porto Seguro (Bahia) and Teresina (Piauí). Simultaneously, epidemics due to DEN-2 occurred in Alagoas and Ceará in 1994, and in 1990 Rio de Janeiro experienced DEN-2 epidemics in which several cases of DHF were notified. There are no available data regarding the notified cases of Alagoas State. In Rio de Janeiro 150 cases of DHF and 8 deaths were registered, while in Ceara, 26 cases were confirmed as DHF and 14 of them, had a fatal outcome (Vasconcelos et al., 1995). From 1982 to 1994, the Brazilian Ministry of Health, had registered 336,954 cases (FNS, 1994). However, the number of cases (Table 10) are clearly an underestimate and reflect a considerable undernotification. It has been more realistically calculated that about 3 to 5 million cases occurred during this period.

The diurnal, domestic mosquito *Aedes aegypti* has been the vector in all the epidemics reported in Brazil. Although the potential vector *Aedes albopictus* mosquito (the "Asian Tiger"), has been identified in areas where dengue transmission has been reported, no evidence has been obtained of transmission by this importan

Asian vector and no virus has been isolated from it. In Brazil, dengue is a seasonal illness of the rainy season (from December to June).

Table 10. Dengue fever cases reported in Brazil, by state and region, 1982-1994*

STATE	1982	1986	1987	1988	1989	1990	1991	1992	1993	1994	TOTAL
Roraima	12000	-	-	-	-	-	-	-	-	-	12000
Tocantins	-	-	-	-	-	-	2194	-	-	-	2194
North	12000	-	-	-	-	-	2194	-	-	-	14194
Ceará	-	4419	22513	55	4126	15656	6907	117	7	28670	82266
Pernambuco	-	2118	-	27	-	-	-	-	-	-	2145
Alagoas	-	9383	3225	65	60	294	1317	279	781	202	15606
Bahia	-	-	623	-	-	-	-	-	-	202	825
Northern	-	13802	28479	120	4213	15950	8020	396	786	29074	100842
M. Gerais	-	-	527	-	-	-	286	-	3863	-	4670
R. de Janeiro	-	33568	60342	60	1111	21005	78702	1117	321	164	196390
São Paulo	-	-	46	10	10	2081	3661	31	652	574	7065
Southeast	-	33568	60915	70	1121	23086	82649	1148	4836	738	208131
M. G. do Sul	-	-	-	-	-	1606	4346	771	570	720	8021
M. Grosso	-	-	-	-	-	-	-	900	892	634	2426
Goiás	-	-	-	-	-	-	-	-	-	3340	3340
Centro-west	-	-	-	-	-	1606	4346	1671	1462	4702	13787
BRAZIL	12000	47370	89394	190	5334	40642	97209	3215	7086	34514	336954

Source: FNS/DEOPE-GTFAD.

* Until, August 1994.

Clinical features

The clinical spectrum of dengue infection is wide ranging from asymptomatic or with manifestations from an indifferentiated fever to hemorrhagic fever with or without shock syndrome (DHF/DSS). It is noteworthy that the intensity of clinical features commonly depends on the age of patient. The most benign cases were diagnosed in infants and young children characterized by a febrile illness with or without a rash. In adults and older children the severity of disease increased and was characterized by an abrupt onset of high fever, intense headache and chills, malaise, backache, photophobia, myalgia and exanthema. Diarrhoea, nausea, vomiting and dizziness have been noted in some patients. Clinical illness persisted from 3 to 10 days, most often for 4 to 6 days. Fatalities due to DEN viruses from such patients are uncommon. Leukopenia and thrombocytopenia have occasionally been observed by other workers (WHO, 1986).

In DHF almost all patients have presented high fever, hepatomegaly, several hemorrhagic manifestations and circulatory failure. The severity of the disease also depends on age and children are often suffer an illness of intense severity. Two important symptoms found in DHF are gastrointestinal bleeding and shock. Thrombocytopenia (100,000) is present in almost all cases, as well as hemoconcentration (hematocrit increase 20% or moreover the basal value). Lymphadenopathy, myalgia, arthralgia, generalized abdominal pain and presence of a sore throat or injected pharynx are common symptoms. Splenomegaly is uncommon and most frequently seen in children. The most important hemorrhagic phenomenon is a positive tourniquet test. Petechiae are common on the extremities, soft palate, axillae and face, especially in early days of illness. Sometimes severe gum bleeding may be responsible for a fatal outcome. Other hemorrhagic signs usually observed in severe cases are epistaxis, melena and genital bleeding (WHO, 1986).

When DHF is accompainied by DSS, the condition of the patient deteriorates in a few hours. In such cases, there are signs of circulatory failure represented by circumoral cyanosis, a weak and fine pulse; clammy cold skin; restlessness; and often profound shock. If a prompt treatment is not available, the outcome is frequently fatal (WHO, 1986). As reported in Asian DHF, some patients in Fortaleza (Ceará State), had encephalopathy, characterized by somnolency, lethargy, restlessness, neck stiff and, in some cases, signs of encephalitis and coma. These symptoms, occur rather as a consequence of circulatory failure rather than virus damage to the

brain or other part of the CNS for no virus or dengue virus antigen was obtained from these tissues (Vasconcelos et al., 1995).

Prevention and control

Dengue epidemics have occurred in at least 12 States of Brazil, with more or less 90% of all cases reported in Rio de Janeiro, Ceará and Alagoas States: In these foci, thousands of susceptible people became immune to DEN-1 and/or DEN-2 viruses, the two serotypes presently circulating in Brazil, year by year. As there are no available vaccines, control measures to break these epidemics rely principally on reduction of the population of adult forms of *Aedes aegypti* and its maintenance at a reduced level (usually a Breteau index of 1% or less). Anti-mosquito measures include ultra low volume (ULV) spraying with residual insecticides, the spraying of breeding sites and environment sanitation to reduce or eliminate sites of larval development. The main objective is to interrupt virus transmission in a short time. Several studies have showed that ULV application of malathion is quite effective in reducing adult vector population.

In the inter-epidemic periods it remains important to monitor the vectors population-index to avoid an increase which may start another cycle of transmission. It is unfortunate that the attitude of the population as a whole makes such vector control difficult to achieve.Although some countries have obtained significative results with community planned programmes, attempts in Brazil have had poor results. It is hoped, however, that in the near future cost-benefit calculations may indicate that this is at the present the only way to control DEN viruses and their epidemics.

ILHEUS (ILH)

The virus

Ilhéus fever virus is a *Flavivirus* (Flaviviridae) and serologically is a member of group B. The prototype ILH strain was isolated in Ilhéus city, State of Bahia, Brazil, in 1944, from a pool of *Aedes* and *Psorophora* mosquitoes (Karabatsos, 1985). Subsequently this virus has been isolated from febrile patients, mosquitoes and a large variety of animals, particularly birds and bats. ILH is closely related to Rocio and Japanese encephalitis viruses. Cross-reaction with Rocio in the HI is common in Brazil, and infections can be determinated with precision only by the use of N tests

Epidemiology

In Brazilian Amazonia, a total of 41 strains have been obtained from the blood of human beings, blood and other tissues of animals, and the tissues of mosquitoes. Except for yellow fever and Dengue viruses, this is the *Flavivirus* with the highest rate of HI antibodies in the Amazon basin. Despite the high rates of antibody is, however, very difficult to isolate ILH from human beings, and only 3 isolates have so far been made from man. Either because the viremic period is quite short, or because a great number of infections are asymptomatic (Pinheiro et al., 1986). ILH virus has been also detected through specific HI antibodies, confirmed by N tests, in São Paulo State, particularly in people living in the Ribeira Valley (Iversson et al., 1982). The virus is maintained in nature by a sylvatic cycle in which *Psorophora ferox* mosquitoes act as the main vectors. Other species of *Psorophora* and *Aedes serratus* mosquitoes play a secondary role the maintenance cycle (Table 11). Several species of wild birds of a wide variety of families are the vertebrate hosts, but bats have been also found infected. Sentinel monkeys have furnished two strains of this virus.

Table 11. Species of mosquitoes from which ILH virus was isolated.

MOSQUITO SPECIES	NUMBER OF STRAINS	% POSITIVITY
Psorophora ferox	19	54.3
Psorophora albipes	6	17.1
Psorophora lutzii	3	8.6
Aedes serratus	4	11.4
Aedes fulvus	1	2.9
Aedes scapularis	1	2.9
Haemagogus leucocelaenus	1	2.9

Clinical features

The symptoms reported by patients are mainly of a acute illness. The disease onset is sudden an ! with high fever, severe headache, chills, myalgia and weakness. The symptoms persist for about 3 to 5 days, and recovery is uneventful (Pinheiro et al., 1986). Past experimental infections, have shown that ILH can be responsible for a mild encephalitic disease without sequelae.

Prevention and control measures

ILH is not associated with epidemic disease in Brazil, there are no control measures or vaccines available Some measure of personnal protection exist in avoidance of forest areas where vectors may be present, and a the use of mosquito repellents.

ROCIO (ROC)

The virus

Rocio virus is a *Flavivirus* (Flaviviridae) and serologically is closely related to Ilhéus, Saint Louis encephalitis, Japanese encephalitis and Murray Valley encephalitis viruses, from which it can be separated by serological tests. Western blotting studies, carried out recently, showed that ROC is most closely related to the Murray Valley encephalitis virus. The prototype strain was obtained in 1975 in São Paulo, from cerebellum and spinal cord tissues of a patient of a fatal case of encephalitis (Karabatsos, 1985).

Epidemiology

Almost all aspects of the ecoepidemiology of ROC virus are unknown. Some informations has been acquired from pontual studies carried out by Faculdade de Saúde Pública of São Paulo University and for long term surveillance by the Instituto Adolpho Lutz in the Iguape area of Ribeira Valley in São Paulo State. The most important findings have been obtained from human serology, at that region. HI and N tests surveys carried out after the 1976 epidemic until the time of writing this article, have shown for ROC, a wide distribution in the Ribeira Valley. Fishermen and agriculture workers were the people most affected, and almost all of them were living in the region when the epidemic started. In 1975-1977, a total of 1,021 cases were reported in the Santista Lowlands and Ribeira Valley (Lopes et al., 1978a,b; Iversson, 1988). Young men aged from 15-30 years-old were apparently at highest risk, since most infections were within this age bracket. Probably, this was because men of this age-group usually work outdoors and consequently, are most exposed to the vectors In contrast, the case-fatality rate was higher in older persons and this higher mortality was associated with a lower degree of inmune response to infection in this group. The serum of two fishermen obtained in 1983 and two children collected in 1987, were among material examined during a serological survey. All of these individuals, who lived in the Ribeira Valley, had IgM antibodies, but none of them showed symptoms of disease (Iversson et al., 1989). Outside the epidemic area, five ROC virus cases were diagnosed in Parana State in a border region near the Ribeira Valley (Iversson, 1988). What factors were responsible for the appearance and disappearance of the virus in the region remains a mistery. An exhaustive study to elucidate the maintenance cycle of ROC virus has not showed very encouraging results. ROC virus was isolated once from a ruffous-collared sparrow *Zonothrichia capensis* in the Ribeira Valley region, and antibodies in other species of birds of several different families have suggests that wild birds may play a role in the cycle. No strains, however, were isolated from these or other vertebrate groups. A strain of ROC was obtained from a pool of the mosquito *Psorophora ferox* collected during the outbreak in Cananeia, São Paulo. *Ps. ferox* collected in the areas where most cases occurred during the epidemics represented less than 1% of all mosquitoes captured of human bait, however, and it is unlikely, therefore, that this species can act as an important vector The isolation of a third strain from sentinel mice, during the course of the epidemic, in the same region (Lopes et al., 1978a,b), suggested that an infected vector to be present in the area . Other evidence of circulating virus was not obtained. Unfortunately, the available data, are not enough to firmly incriminate any vector or vertebrate host in the virus maintenance-cycle.

Clinical features

The pathology of ROC virus ranges from asymptomatic infection to full-blown encephalitis. Based on the studies of 12 cases in São Paulo City after their exposure in the endemic area (Lopes et al., 1978b), the incubation period was 12 days (ranging from 7 to 14 days). Typically, the disease begins suddenly with high

fever, headache, anorexia, nausea, vomiting, myalgia and malaise. Later, encephalithic signs abruptly appear, with weakness, abdominal distension, confusion, motor impairment and consequently difficulties in walking and equilibrium, meningeal irritation, and cerebellar syndrome. In parallel there is reflex disturbance with both hyperreflexia, hyporeflexia and absence of reflexes, as well as the presence of pathological reflexes, such as Kernig and Brudzinski signs. Some patients have presented muscular alterations, ranging from hypotonic to hypertonic, and convulsions. Other manifestations include urinary retention, photophobia, lachrymation, acrophobia, and arterial hypertension. The evolution of disease is usually fulminant with death in a few days. Sometimes, however, it may be prolonged, with the patients in coma for several days or weeks before death. Serious sequelae were also observed in surviving patients, especially those with encephalitis, with permanent neurological sequelae such as visual, olphactory and auditory disturbances, lack of motor coordination, equilibrium disturbance, paresthesia, difficulties in swallowing, sphincter incontinence and defective memory (Tiriba et al., 1976). Table 12, shows the main symptoms and signs presented in 234 hospitalized cases during the 1975 outbreak in São Paulo (Tiriba et al., 1976).

Table 12. The main symptoms and signs observed in 234 patients with encephalitis caused by Rocio virus, São Paulo, 1975 (Tiriba et al., 1976).

SYMPTOMS/SIGNS	NUMBER OF PATIENTS	POSITIVITY
Headache	219	93.6%
Fever	212	90.6%
Meningeal irritation	134	57.3%
Vomiting	120	51.3%
Alterations of consciousness	119	51%
Motor abnormalities	116	49.6%
Weakness	106	45.3%
Alterations of tendon reflexes	59	25.2%
Alteration of muscular tone	58	24.8%
Anorexia	55	23.5%
Abdominal distention	49	20.9%
Nausea	45	19.2%
Sore throat	45	19.2%
Hyperemia of conjunctivae	37	15.8%
Pathologic reflexes	32	13.7%

Prevention and control measures

Very little is known concerning the vertebrate hosts and arthropod vector of ROC virus, and so there are no effective control measures. Vaccines are not yet available. Mosquito adulticides and the use of larvicides in ditch water and other places where water may collect, may be helpful in controlling ULV. Personnel protection by the use of bed nets and mosquito repellents may be useful for people in or near the epidemic area, especially where there is the evidence of virus transmission.

SAINT LOUIS ENCEPHALITIS (SLE)

The virus

Saint Louis Encephalitis virus (SLE) is included in the genus *Flavivirus*, family Flaviviridae. By serological tests it is member of group B of arboviruses. The prototype strain of SLE was isolated in 1933, in Saint Louis, USA, from human brain tissue (Karabatsos, 1985). The first strain obtained in Brazil was isolated in 1960, from a pool of *Sabethes belisarioi* captured at the km 94 on the Belém-Brasilia Highway, Pará State (Theiler & Downs, 1973). SLE is closely related to Murray Valley, West Nile and Japanese encephalitis viruses.

Epidemiology

Widely ditributed in the Americas SLE virus, has been found from Canada to Argentina. It is responsible for encephalitis in human beings, but equines are not affected. It is the most widely distributed encephalitic arbovirus in USA, where it has caused more cases of encephalitis than EEE, WEE and California encephalitis

viruses put together (Luby, 1979). The case fatality rate during epidemics ranges from 5% to 20%, increasing with the age. Antibodies to SLE virus have been detected in inhabitants of the Amazon basin, and their prevalence in several small and large communities of Brazil, particularly in the Amazon region has been found to be about 5%. Recent studies in Ceará State (Northeast Brazil) in a randomized serosurvey during a large epidemic of dengue fever, showed a positivity of 10.1% by HI, with most of the positives confirmed by N tests (IEC, unpublished data). Although, it is difficult to isolate SLE from humans without encephalitis. In Belém, two strains have been obtained from the blood of sick humans with no signals of encephalitic involvement (Pinheiro et al., 1986). Epizootics in sentinel monkeys (Vasconcelos et al., 1991) have been reported in a forested area near Belém.

Wild birds are the main vertebrate hosts of SLE virus (Table 13), and a wide variety of species seem to be susceptible, particularly members of the families Formicariidae (*Formicarius analis*, *Conopophaga aurita*, *Thamnomanes caesius* and *Hylophylax poecilonota*), Pipridae (*Chiroxiphia pareola*) and Columbidae (*Geotrygon montana*), from all of which the virus has been isolated. In at least 15 species of birds, HI antibodies have been confirmed by N tests, with a positivity range of from 1% to 16.7%, and with six species having a prevalence higher than 5% (Vasconcelos et al., 1991). On the other hand, 86 other species, from several different families, have showed an antibody rate of 3.4% or higher. This data suggests that wild birds species play an important role in the maintenance cycle of SLE virus, which accounts for the wide distribution of this virus in the Amazon basin. Specific HI antibodies to SLE confirmed by N tests were also found in low prevalence in human beings and wild birds of São Paulo State (Iversson et al., 1982). *Culex coronator* and *Cx. declarator* mosquitoes have been frequently found infected, and doubtless play role in the maintenance cycle of this arbovirus. It virus has also been isolated from several other mosquitoes of different genera. These mosquito species possibly play a secondary role in the dissemination and maintenance of SLE virus in Brazil.

Table 13. Species of wild birds which furnished strains and specific HI antibodies to SLE virus in the Brazilian Amazonia.

Bird family obtained	species	strains	% positivity (sampled)
Formicariidae	*Myrmotherula hauxwelli*	1	2.3 (196)
	Formicarius analis	1	11.4 (79)
	Pyriglena leuconota	2	1.5 (273)
	Thamnomanes caesius	1	6.1 (95)
	Hylophylax poecilonota	2	5.1 (360)
	Hypocnemis cantator	1	3.0 (134)
	Conopophaga aurita	2	5.3 (75)
Pipridae	*Chiroxiphia pareola*	2	16.7 (84)
	Pipra pipra	1	0.7 (290)
Columbidae	*Columbina talpacoti*	1	0 (289)
	Geotrygon montana	2	3.4 (219)
Furnariidae	*Automolus infuscatus*	1	1.2 (98)
	Phylidor erytrocerchus	1	0 (23)
Tyrannidae	*Myiobius barbatus*	2	1.0 (196)
Galbulidae	*Galbula albirostris*	1	2.7 (78)
Fringillidae	*Saltator maximus*	1	2.1 (154)
Dendrocolaptidae	*Glyphorhynchus spirurus*	1	3.6 (408)

Clinical features

The typical clinical picture of SLE virus infection is one of severe encephalitis with, high mortality. The disease starts suddenly, with high fever, headache, malaise, and dizziness; in a short time the patient develops symptoms and signs of CNS involvement characterized by stiff neck, desorientation, tremulousness ataxia or generalized motor weakness, incoordination and coma. Dysuria and other disorders of micturation have also been reported. Whereas the disease severity and fatality increases with age, children and young adults may

show undifferentiated fever and aseptic meningitis, or even asymptomatic infection (Tsay & Mitchell, 1988).

In the two cases with virus isolation recorded in Brazil, the clinical picture was characterized by a febrile illness with jaundice, neither of them showing any signs of CNS involvement. The first patient's illness was characterized by hepatic failure accompanied by jaundice. Suddenly, he became febrile and this led to the suspicion of viral infection. There followed an acute leukemia and the patient died some days after his blood sample was taken. Convalescent serum was therefore not obtained. The second case was diagnosed during an epidemic of Oropouche fever. The patient developed a febrile disease accompanied of jaundice, abdominal pain, myalgia, arthralgia, chills and severe headache. The main laboratory finding were a bilirrubin level of 6.0mg/dl, and moderate elevation of SGOT, SGPT and urea levels. Recovery was uneventful after 16 days of disease (Pinheiro et al., 1981b; 1986) with seroconversion type secondary response to flaviviruses.

Prevention and control

In areas where SLE virus is epidemic the most important measure is the mosquito control with adulticides in ULV, or larvicides in ditches and other collections of water. Added to this, personnel protection with bed nets and mosquito repellent may be useful within the epidemic area, especially where there is evidence of virus transmission. In Brazil, SLE virus infection is sporadic and there are no control measures in operation. A synthetic polypeptide vaccine for human use is available in the USA, but evaluation of efficacy in an open trial is needed (Tsay & Mitchell, 1988).

YELLOW FEVER (YF)

The virus

The YF virus is the prototype of the genus *Flavivirus* in the Flaviviridae family, and antigenically, YF is a member of group B. The prototype strain (Asibi strain) of YF was isolated in Lagos, Nigeria, in 1927 from whole blood collected in Kpeve Village, Ghana, from a 28 year-old man with a mild form of the disease (Karabatsos, 1985).

Epidemiology

Many South American species of nonhuman primates become severely or fatally ill, whereas most African species have mild or inapparent infections. Consequently, monkeys play a most important role as the major vertebrate hosts for the vectors. On the other hand, birds, rodents, marsupials, carnivores, amphibiams and reptiles are highly resistant to YF virus.

Each year in Brazil, human cases of YF are acquired in endemic and/or epizootic areas, through sylvatic transmission. They can occur sporadically or in outbreaks. These jungle YF epidemics have been mainly transmitted by the mosquito *Haemagogus janthinomys*. Other *Haemagogus* mosquitoes, such as *Hg. albomaculatus*, are important vectors in the western region of Pará State (Travassos da Rosa et al., 1984), as well as *Sabethes chloropterus* and *Sa. soperi*. The latter have been indicated as important vectors, particularly in the State of Mato Grosso do Sul. These *Sabethes* species were the main mosquitoes responsible for transmission during an outbreak which occurred near Campo Grande and neighbouring municipalities in 1991/1992. They were found to be very abundant, and YF virus was isolated from several pools (Dégallier et al., 1992).

In most cases, it is man who plays important role of disseminating the virus to areas where there was previously no virus but where vectors and monkeys are common enough to start virus transmission. Modifications of the forest environment through lumbering, farming, road development, and other activities increase the contacts between nonimmune communities and sylvatic vectors, and are the mechanism mainly responsible for the occurrence of human YF in Brazilian Amazonia (Monath, 1988).

The urban cycle was eradicated from Brazil in 1942. As mentioned in the Dengue section, however, *Aedes aegypti* is now widely distributed in at least 21 States in this country. A viremic patient arriving in a locality which is outside the YF endemic area, but with a high density of *Ae. aegypti*, may start an urban epidemic. This may have a catastrophic consequences in a non-immune population. From 1930 until December 1993, 2440 cases of YF were notified in Brazil. Of these, 329 out of 332 were urban cases in the 30's, with three more (in State of Acre) in the 40's. The other 2,108 were of sylvatic YF (Table 14). In this period the only localities not reporting cases were Sergipe and Tocantins States, and the Distrito Federal. Table 14, is shows the main foci or risk areas for sylvatic YF in the past, e.g. Minas Gerais, Espírito Santo and São Paulo, and more recently, Goiás, Pará, Mato Grosso and Maranhão states.

Table 14. Yellow fever reported cases in Brazil, 1930- 1993, according with state and region.

STATE	1930-1939		1940-1949		1950-1959	1960-1969	1970-1979	1980-1989	1990-1993	TOTAL	
REGION	Urb	Syl	Urb	Syl	Syl	Syl	Syl	Syl	Syl	Urb	Syl
Acre	4	-	3	12	2	-	2	1	-	7	17
Amapá	-	-	-	-	-	-	-	2	-	-	2
Amazonas	3	7	-	6	1	3	4	13	1	3	35
Pará	8	19	-	21	21	3	35	51	10	8	160
Rondonia	-	-	-	1	1	-	6	8	-	-	16
Roraima	-	-	-	-	-	6	12	8	8	-	34
North	15	26	3	40	25	12	59	83	19	18	264
Goiás	-	49	-	93	63	5	75	42	-	-	327
M.Grosso	1	152	-	3	34	14	11	15	2	1	231
M.G. Sul	-	-	-	-	-	-	-	17	14	-	31
Central West	1	201	-	96	97	19	86	74	16	1	589
Alagoas	9	-	-	-	-	-	-	-	-	9	-
Bahia	6	4	-	10	1	-	-	-	-	6	15
Ceará	94	-	-	-	-	-	-	-	-	94	-
Maranhão	-	2	-	-	1	-	2	9	58	-	72
Paraiba	8	-	-	-	-	-	-	-	-	8	-
Piaui	29	1	-	-	-	-	-	-	-	29	1
Pernambuco	65	-	-	-	-	-	-	-	-	65	-
R.G. Norte	2	-	-	-	-	-	-	-	-	2	-
Northern	213	7	-	10	2	-	2	9	58	213	88
E. Santo	-	113	-	168	-	-	-	-	-	-	281
Minas Gerais	26	309	-	28	75	5	2	20	-	26	439
R.de Janeiro	73	59	-	6	-	-	-	-	-	73	65
São Paulo	-	15	-	-	129	-	-	-	-	-	244
Southeast	73	596	-	202	129	5	2	20	3	99	1029
Paraná	1	38	-	-	46	7	-	-	-	1	91
S. Catarina	-	29	-	2	-	9	-	-	-	-	40
R.G. do Sul	-	-	-	1	-	6	-	-	-	-	7
South	1	7	-	3	46	22	-	-	-	1	139
BRAZIL	329	897	3	351	374	58	149	188	111	332	2108

In a period of 21 years (1973-1993), 329 cases of sylvatic YF were reported in Brazil (FNS, 1992), 248 (75.4%) of which had a fatal outcome (Table 15). These cases were distributed as follow: 146 (44.4%) in the Amazon region, 161 (48.9%) in the Centro-West region and 22 (6.7%) in Minas Gerais State (Southeast region). In the Amazon basin, Pará State had the highest prevalence, with 82 cases (56.2%). The fatality-rate of reported cases in the last fourteen years was 75.4%, but this high rate is probably because the majority of officially recorded tend to be the severe ill, hospitalized patients. Notified cases are, therefore, underestimated. The real number (including the innaparent or very mild infections) must be very high indeed, but unfortunately unknown, and the true impact of jungle yellow fever in Brazil cannot be accurately estimated.

Table 15 Distribution of jungle Yellow fever cases diagnosed in Brazil and fatality rate by State between 1973-1993.

STATE	CASES	CASES(%)	FATAL	FATALITY
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
RONDONIA	11	3.3	10	90.9
RORAIMA	21	6.4	16	76.2
TOTAL	329	100.0	248	75.4

Clinical features

Clinically, the classical picture of YF is that of a biphasic disease classified as a 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 and, if mosquitoes bite the 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. After remission, in the more serious cases, there may be a second phase of toxemia when symptoms related to the localization of YF in liver and kidney may appear. Jaundice, "coffee ground" hematemesis and other hemorrhagic manifestations such as epistaxis, melene and gastrointestinal bleeding, may become evident. Aminotransferases and bilirrubinemia rates increase and renal failure manifests itself by albuminuria, oliguria, anuria and azootemia. The virus is normally absent from blood during this period, although antibodies do appear. About 20% to 50% of the patients who enter this phase of infection die, usually between the seventh and tenth days of illness. Atypical, fulminant cases can also occur, with death as early as 3 days after the onset of symptoms (Serié et al., 1968; Monath, 1988). On the other hand, patients may die after 2 to 3 weeks of disease. In both cases pulmonary and/or cardiac complications are responsible for the death.

Prevention and control

Urban epidemics of YF virus can be controlled by two main methods. Firstly, eradication sources of larval development of *Aedes aegypti* population or reducing it to a level sufficiently low to prevent virus transmission; and secondly by massive immunization programmes with 17D vaccine. In efficient programme of vector control, maintenance of the Bretau index below 5.0% level is generally sufficient to avoid virus transmission (Monath, 1988). Several measures may be adopted to attain this objective, such as, the use of ULV malathion insecticide against adults; the use of abate for control of larvae; the elimination of breeding sites (old cans, motor tyres, holding water, etc.); and educational pamphlets and talks for the local population; predatory fish which eat the larvae of *Ae. aegypti*, and the use of "autocidal" ovitraps and predatory *Toxorhynchites amboinensis* can be helpful (WHO, 1986).

OTHER VIRUSES -
VESICULOVIRUSES
PIRY (PIRY) & JURONA (JUR)

The viruses

Piry and Jurona viruses are included in the family Rhabdoviridae. Both agents are members of the genus *Vesiculovirus*, and are serologically related to the VSV serogroup. The prototype of PIRY was isolated in 1960 from the viscera of a *Philander opossum* trapped in the Utinga forest, while JUR virus was isolated in 1962 from a pool of *Haemagogus sp* mosquitoes collected at km 87 of the Belém-Brasília highway, Pará State (Karabatsos, 1985).

Epidemiology

High rates of NT antibodies to PIRY virus have been found in the Amazon region in immigrants from the South and in people living in the South and Southeast regions of Brazil: it is rare, however, in the local inhabitants of Amazonia. For this reason it is thought that PIRY is an imported virus from the Southern and/or South regions, probably during the construction of the Transamazon Highway, when many people from the Southern States came to Belém and neighbouring areas before travelling on new highway through the Amazon region to Altamira, Itaituba and Maraba during the colonization of the important Amazonian road. The single human isolate that has been made from a laboratory infection, and five other laboratory acquired infections have been reported. The vector and vertebrate hosts for this virus are unknown yet.

No antibodies to JUR virus have been detected in serum samples from birds, rodents or other wild vertebrate in Brazilian Amazonia, and no isolations of this virus were made from thousands of *Haemagogus* sp mosquitoes inoculated in mice. The single strain obtained from man originated from the blood of a febrile patient from the municipality of Costa Marques in the State of Rondonia (IEC, unpublished data). Immunity to the agent has not been detected in Amazonia or in other regions of Brazil.

Clinical features

The Piry disease was characterized by an abrupt onset of high fever, headache, chills, photophobia, myalgia, arthralgia, dizziness and weakness. The blood sample from which isolation was obtained showed a leucopenia of 3,000 leucocytes in the hemogram, and the symptoms lasted for 1 to 2 days. There is no other record of human disease, although a high prevalence of NT antibodies have been frequently found in persons who have worked with this virus (Pinheiro et al., 1986).

JUR virus has been isolated on one occasion from the blood of a 58 year-old man from Costa Marques, Rondonia State, on the border with Bolivia. The disease was a febrile illness, and blood smears examined for malaria were negative. Other information regarding simptomatology were not obtained.

Prevention and control measures

These viruses are not associated with epidemic and control measures or vaccines preparation are therefore not of great importance. For laboratory workers, however, the reported laboratory infections with Piry virus indicates care in handling these two viruses.

ARENAVIRUSES

FLEXAL (FLE) AND SABIÁ (UNREGISTERED) VIRUSES

The viruses

Arenaviruses are rodent-borne viruses not transmitted by insects.

Flexal (FLE) and Sabiá (unregistered) viruses belong to the *Arenavirus* genus, family Arenaviridae. Antigenically, are member of Tacaribe serogroup. The prototype strain of Flexal virus was isolated from the pooled viscera of the rodent *Oryzomys bicolor* (Hardwood), trapped, at km 212 on the Itaituba-Jacareacanga stretch of road, along the Trasamazon Highway, Pará State, in 1975 (Karabatsos, 1985). The Sabiá virus prototype was obtained from whole blood from a fatal case of haemorrhagic fever in São Paulo State in 1990 (Coimbra et al., 1994).

Epidemiology

FLE virus has been isolated three times from *Oryzomys bicolor* and once from *Oryzomys capito*, caught in the Itatituba-Jacareacanga area of the Transamazon Highway. Attempts to isolate FLE from other wild rodents in the same region were unsuccessful. CF antibodies were demonstrated, however, in 3 out 56 *Proechimys sp.*, collected in the same region, as well as in 2 out 88 apparently healthy men living near the area of isolation. No evidence of virus circulation has been obtained outside this locality. Three out 55 laboratory workers were positive for CF antibodies to FLE virus, suggesting that this virus can be easily transmitted to persons handling it, or infected animals.

The single Sabiá virus strain isolated was obtained from a 25 year-old woman from São Paulo State, and no other evidence of circulation of this virus has been found. Neither is there any available data regarding vertebrate hosts among the rodents that have been examined in São Paulo State.

Clinical features

The disease caused by FLE virus has an abrupt onset with fever, chills, headache, myalgia, dizziness and diarrhea. In the cases examined, fever was high and sometimes reached 39°C. Headache was severe, and diarrhea lasted for 7 days. The disease lasted for 4 weeks, and leukopenia was observed during the two first weeks. Recovery was complete.

The Sabiá virus infections has shown two different clinical picture: severe hemorrhagic fever, and a febrile illness without hemorrhagic manifestations. One patient has developed hemorrhagic fever similar to the clinical picture for other arenaviruses with the patient becoming ill suddenly with high fever, somnolence, inflamed oropharynx, chills, severe headache, myalgia, weakness and anorexia. Later, in the index case, the patient worsened, with haematemesis, vaginal bleeding and conjuntival petechiae. On the third day she developed increasing somnolence, tremors, difficulty in walking, generalised convulsions and coma. Death occurred on the fourth day (Coimbra et al., 1994). Another patient developed febrile disease but fortunately recovered after a 3 weeks illness (Gonzalez et al, unpublished data). A third patient developed an influenza-like illness characterized by high fever, chills, malaise, severe headache, generalised myalgia, sore throat, nausea, vomiting,

malaise, conjuntivitis, diarrhea, epigastric pain and leukopenia with lymphocytosis for 15 days. Recovery was uneventful (Vasconcelos et al., 1993).

Prevention and control

Arenaviruses have not been involved in epidemic spread in Brazil, and control measures including vaccines, have not been developed. As these viruses are transmitted by rodents, however, one measure to prevent transmission is the control of these animals and the avoidance of contact with them. These viruses are easily transmitted to laboratory workers via the excreta of rodents and by the aerosol route: it is important, therefore, that all safety measures (safety level III or IV) should be adoptted when handling of these viruses.

CONCLUSIONS

Arbovirus can be transmitted to man by infected arthropods in two distinct levels; the sylvatic cycle and the urban cycle. In the former, the infected vectors maintain the virus in a determined area of the jungle (ecologic niche) and can transmit arboviruses to nonimmune vertebrate hosts and vertically to other vectors. In this context man is infected tangencially, by the bite of infected arthropods when he intrudes into an ecologic niche which may be some distance from his dwelling-place. This tangential mode of infection results in a relatively rare or sporadic cases. Usually, all cases are reported from the same sylvatic site or near the forest (Brés, 1988). This mechanism is responsible for outbreaks of jungle yellow fever, Rocio and Mayaro fever infections. In the second level (urban cycle), an infected person becomes an amplifying host in the transmission chain and initiates an epidemic (man-arthropod-man) in an urban area. In this context, domestic arthropod vectors are now involved and they can transmit the virus to other persons after an extrinsic incubation period. This mode of transmission occurs, for example, in Dengue and Oropouche epidemics.

The frequency of transmission of an arbovirus to man depends on the vector population density, vector competency, and environmental factors such as humidity, temperature, etc. The risk of transmission also depends on the geographic distribution of the vectors. For some arboviruses, the risk of transmission to men is minimal and limited to determined ecologic niches or regions, due to the limited distribution of the these viruses. On the other hand, others can cause human disease in several regions: this is the case of yellow fever, which can be transmitted within a large epizootic area, as well as in an urban center, since the primary vector *Ae. aegypti* can become infected.

Each arbovirus is maintained in nature in a well defined ecological niche, where vertebrate hosts and haematophagous insects play the most important role. Arboviruses are essentially zoonosis facilitated over a period of time by modifications of the environment with result in the occurrence of human infections. Such arboviruses survive better in regions like such as Amazonia and the Ribeira Valley, where vertebrate hosts populations are high and relatively stable, and where a large variety of mosquito species may be found in high densities. It is well known that arboviruses tend to have specific geographic distributions, and each area studied, so far, seems to have its own particular arbovirus fauna.

Since the pioneer studies, there is a concept that our knowledge concerning the majority of the arboviruses is poor with regards to their ecology. Usually we only have information based on the circumstances in which the original isolation was made. Further information is needed, and more complete studies need to be made particularly during the ongoing epidemic phase and the interepidemic periods. Logically, there must be certain threshold densities of host and vector populations that are essential in maintaining a given arbovirus in a basic enzootic cycle in a favorable environment, and diminuishing changes in these population levels will disrupt the cycle and lead to disappearance of the virus. If the host and vector populations are substantially increased this will lead to an explosion of viral multiplication and wide dissemination (Reeves, 1963). It is possible, that this has been the mechanism responsible for new epidemic areas by Oropouche fever virus in the Amazon region.

New studies are needed on the various types of ecological niches in each region of arbovirus activity. In view of the migratory habits of a great number of birds and bats from one place to another, for example, we must consider the possibility that their movements may determine, in an adequate time, the presence of arbovirus disease in man and other animals. Longitudinal studies carried out in a given area for a reasonable period may furnish much needed answers to the complicated natural history and ecoepidemiology of the arboviruses.

With regards the arenaviruses, it is important to determine the transmission sites, since these viruses have a very localised focal and limited spatial distribution. An investigation of all patients with a clinical suspected picture of haemorrhagic fever without an aetiological diagnosis, should be routinely carried out to control human disease due to arenaviruses. Emphasis must be placed on the role played by rodents in the transmission of these agents in the environment, and the neccessity to control their population as a practical measure to avoid human infection.

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