

## Historical analysis of the records of sylvan yellow fever in the State of Amazonas, Brazil, from 1996 to 2009

**Maria das Graças Gomes Saraiva<sup>[1],[2]</sup>, Raul Diniz Souza Amorim<sup>[1]</sup>,  
Marco Antônio Sabóia Moura<sup>[1]</sup>, Eyde Cristianne Saraiva dos Santos<sup>[3]</sup>,  
Leônidas Sales Sampaio<sup>[4]</sup>, Maria das Graças Vale Barbosa<sup>[1],[2],[5]</sup>  
and Samira Bühner-Sékula<sup>[1],[6]</sup>**

[1]. Departamento de Epidemiologia e Saúde Pública, Fundação de Medicina Tropical “Doutor Heitor Vieira Dourado”, Manaus, AM. [2]. Faculdade de Medicina, Universidade Nilton Lins, Manaus, AM. [3]. Departamento de Engenharia Agrícola e Solos, Faculdade de Ciências Agrárias, Universidade Federal do Amazonas, Manaus, AM. [4]. Gerência de Vigilância de Doenças Transmissíveis no Amazonas, Fundação de Vigilância em Saúde, Manaus, AM. [5]. Escola Superior de Ciências da Saúde, Programa de Pós-Graduação de Medicina Tropical, Universidade do Estado do Amazonas, Manaus, AM. [6]. Instituto de Patologia Tropical e Saúde Pública, Universidade Federal de Goiás, Goiânia, GO.

### ABSTRACT

**Introduction:** Yellow fever is a non-contagious infectious disease, highly lethal, transmitted by the *Aedes*, *Haemagogus* and *Sabethes*. **Methods:** Descriptive retrospective study of the yellow fever cases in Amazonas, between 1996 and 2009. **Results:** Forty two cases of yellow fever were confirmed, with 30 deaths, 10% of which were foreigners. **Conclusions:** The presence of *Aedes aegypti* and *Aedes albopictus* in both rural Amazonas and its capital demonstrates the dispersion of these vectors and underscores the need for better and continuous epidemiological and entomological control.

**Keywords:** Epidemiological aspects. Spatial analysis. Vaccine.

Yellow fever is a non-contagious infectious disease, highly lethal disease of acute and short duration fever, whose etiological agent is a virus that belongs to the genus *Flavivirus*, family *Flaviviridae*<sup>1-3</sup>. A specific diagnosis is done through isolation and viral identification, detecting either viral antigens or nucleic acids, histopathological diagnosis (*post-mortem* specimens), and the serological complements pertaining to the viral identification<sup>3,4</sup>. The disease is transmitted to humans by the bite of infected mosquitoes of the genus *Haemagogus*, *Sabethes*, and *Aedes*<sup>5,6</sup>.

In the Amazon, the source of infection of this disease is related to non-human primates, of which the principal hosts are the monkeys of the genus *Cebus* (tufted capuchin), *Alouatta* (brown howler), *Ateles* (spider monkey) and *Callithrix* (tamarin)<sup>4</sup>.

Brazil presents the largest endemic area in the wild form, covering the basins of the rivers Amazonas, Araguaia-Tocantins and Paraná<sup>7</sup>. Between 1989 and 2008, 546 cases of yellow fever were registered in Brazil, responsible for 241 deaths, the highest registry being in the year 2000 (85 cases), all of which occurred in risk areas of the States: Acre, Amazonas, Pará, Roraima, Rondônia, Mato Grosso, Mato Grosso do Sul,

Maranhão, Tocantins, Goiás, Distrito Federal, Minas Gerais, São Paulo, Bahia, and Paraná<sup>8</sup>. The species *Haemagogus janthinomys* is the most common in the wild viral circulation and also has the largest geographical distribution in the country<sup>2,4</sup>. *Aedes albopictus* is held as a risk for the occurrence of yellow fever, by its susceptibility and ecological adaptability in rural areas, being capable of connecting urban and wild circles in the transmission of this disease<sup>9</sup>.

The presence of vectors provides favorable conditions for yellow fever outbreaks to happen. Besides the low vaccine coverage of the population that lives in endemic areas or otherwise in transition to sylvatic form, the presence of primates considered amplifiers and disseminators of the virus, and the displacement of susceptible people to endemic areas are critical factors in the spread of yellow fever<sup>4</sup>. It is a zoonosis therefore, impossible to eradicate. In Brazil, the disease control is seen as challenging due to the need of high vaccine coverage with consequent reduction of wild cases<sup>6</sup>.

The prevalence of yellow fever and its associated carriers, in municipalities of the State of Amazonas is presented.

A descriptive retrospective study was done from data collection of the following secondary sources: *Fundação de Medicina Tropical Doutor Heitor Vieira Dourado* (FMT-HVD), *Fundação de Vigilância em Saúde* (FVS)/*Secretaria Estadual da Saúde* (SES)-*Sistema de Informação de Agravos de Notificação* (SINAN).

We have included in this study all cases reported in the period of January 1996 to December 2009 which were confirmed for yellow fever through M antibody capture enzyme linked immunosorbent (MAC-ELISA) or histopathological laboratory testing.

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**Address to:** Dra. Maria das Graças Gomes Saraiva. Depto. de Epidemiologia e Saúde Pública/Fundação de Medicina Tropical “Doutor Heitor Vieira Dourado”. Av. Pedro Teixeira 25, Dom Pedro, 69040-000 Manaus, AM, Brasil.

**Phone:** 92 2127-3438; 92 9439-1290

**e-mail:** gracasaraiva@fmt.am.gov.br

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The identification of municipalities with the presence of *Ae. aegypti* and *Ae. albopictus* was done through the technical reports from FVS/SES and the scientific publications from FMT-HVD<sup>10-12</sup>.

The records of cases, vaccine coverage and vectors, were plotted in tables and figures, using the program ArcGIS®, whose themed maps help in observing the geographic distribution and spatial analysis.

Between 1996 and 2009, 42 cases of native yellow fever (NYF) were registered. In the evolution of NYF, in these cases, 71.4% (30/42) were fatal, 26.2% (11/42) were cured and 2.4% (1/42) survived asymptotically. Five fatalities were reported as having been vaccinated, 17 as not vaccinated and 8 were of unknown vaccinal status.

Of the cured patients, one declared being vaccinated and in 10 cases, patients claimed no knowledge of being vaccinated. Of the cases that were notified as having been vaccinated only one could show a vaccine certificate, however this patient died.

Of the 30 fatalities, 10% (3/30) were foreigners. The lethality rate in the study's period was 71% (30/42). From 1996 to 2001, 28 cases were registered with a fatality rate of 75% (21/28). From 2002 to 2009, after the implementation of the syndrome vigilance, 14 cases were registered with a lethality of 64% (9/14). The drop in the fatality rate during the period after the

vigilance was not significant,  $p=0.7171$  (**Table 1**). From the total, 98% (41/42) were autochthonous to Amazonas state, native to the 17 municipalities, and in one case imported from Juruti/Pará.

**Figure 1** shows the 31 municipalities where cases occurred and the presence of vectors. The rural areas for Manaus and Itacoatiara, registered similar counts of cases, 15% (6/42) in each municipality. Six of eight municipalities (Manacapuru, Manaus, Rio Preto da Eva, Itacoatiara, Novo Airão and Iranduba) from the metropolitan region of Manaus, concentrated 55% (23/42) of the cases. *Aedes aegypti* was found in 27 municipalities of the state, and *Aedes albopictus* was identified in nine<sup>10</sup>. Among the municipalities registered cases of sylvan yellow fever, 15 with *Aedes aegypti* infestation, of these three with both *Ae. aegypti* and *Ae. albopictus*, Manaus being one of them.

In the year 1996, there was the largest record of cases (15/42 - 36%), and only one record in between 2000 and 2006 (**Table 1**). Sixteen different professions were registered, 36% (15/42) being farmers. The male sex had the highest record with 83% (35/42) and 62% (26/42) of the cases were in the age group 20-49 (data not shown).

The accumulated vaccine coverage against yellow fever grew gradually, from 58.9% in 1996 to a peak during 2000 and 2005, however with a gradual reduction from 2006 (98.1%),

TABLE 1 - Annual vaccination coverage and accumulated in ten years, cases, deaths and fatality rate of Sylvan yellow fever, registered in the State of Amazonas, Brazil, in the period 1996 and 2009

Years	Vaccination coverage (%)				Fatality rate (%)
	annual	accumulated	cases	deaths	
1996	34.5	58.9	15	13	87.0
1997	17.1	72.3	0	0	-
1998	21.9	89.0	3	1	33.0
1999	12.8	96.2	5	4	80.0
2000	14.7	100.8	1	0	0.0
2001	11.5	103.7	4	3	75.0
1996 to 2001			28	21	75.0
2002	8.5	111.0	6	2	33.0
2003	8.0	113.0	0	0	-
2004	5.8	114.7	3	2	67.0
2005	7.2	117.2	2	2	100.0
2006	8.6	98.1	1	1	100.0
2007	9.3	97.1	2	2	100.0
2008	13.8	90.9	0	0	-
2009	7.3	87.0	0	0	-
2002 to 2009			14	9	64.0
Total			42	30	71.0

Source: PNI/FVS/SES/SINAN/SVS/MS - Programa Nacional de Imunizações/Fundação de Vigilância em Saúde/Secretaria Estadual da Saúde/Sistema de Informação de Agravos de Notificação/Secretaria de Vigilância em Saúde/Ministério da Saúde.

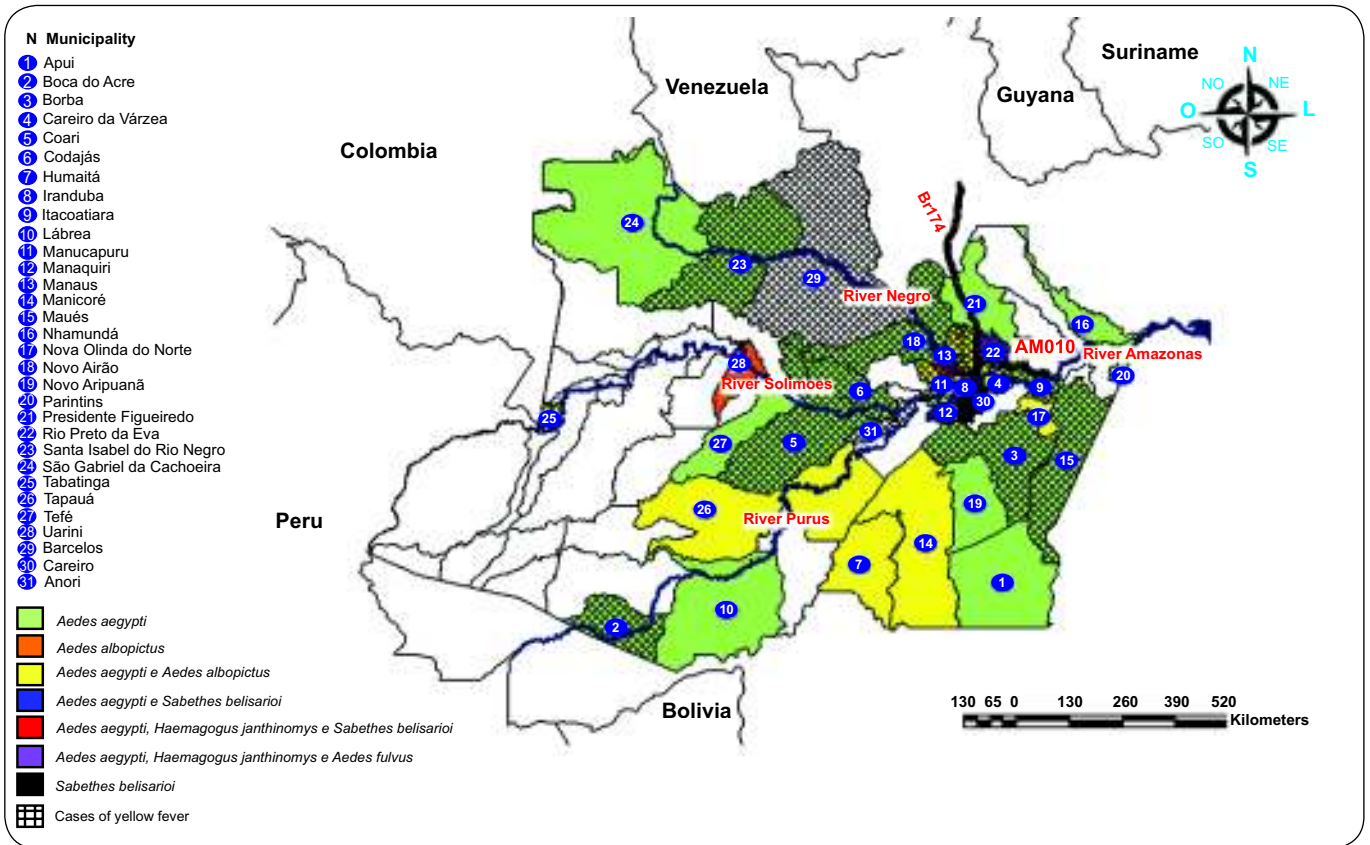


FIGURE 1 - Municipalities of State of Amazonas with the presence of vectors and sylvan yellow fever cases, period 1996-2009.

reaching 87% in 2009. In the years 1997, 2003, 2008 and 2009 there were no records of yellow fever (Table 1).

The specific diagnosis of patients suspected to have yellow fever is important to the epidemiological surveillance<sup>3</sup>, requiring laboratory surveillance in order to detect the presence of the virus prematurely, alerting the adoption of preventive measures and control<sup>4</sup>.

The lethality rate during the periods before and after the implementation of the syndrome surveillance dropped, but was not significant:  $p=0.7171$ . It could be due to an increase in case detection due implementation of surveillance activities. In the years 2008 and 2009 there were no cases reported; perhaps this was a reflex of the activities implemented by the surveillance or an under-notification of cases due to lack of diagnosis. The death of five vaccinated persons might indicate the possibility of compromising the quality of the vaccine due to cooling.

The male sex contributed to the largest portion of cases in the study, and the age group of 20-49 was the most common. One can note that in Amazonas, the occurrence of cases is related to the most productive age group, and to the male sex probably due to labor-related activities. Vasconcelos et al.<sup>13</sup> relates that in the Amazon and in Africa more than 80% of the cases of yellow fever occur in people of the male sex, aged between 14 and 35, and this preference is due to the largest exposure and not to susceptibility to the virus.

In Amazonas, since 2006, there has been a reduction of the vaccine coverage, while the difficulty in accessing the remote

rural areas due to the region's geographic characteristics, vast extension of the state, low population density and need of fluvial transport were present in the past. As an endemic region, it is important to increase the vaccine coverage of the populations and to maintain constant epidemiological-entomological surveillance<sup>14</sup>, especially for those who move between neighboring municipalities of Manaus, with the presence of *Aedes aegypti*, and increase the risk of urbanizing the disease<sup>11</sup>.

The study shows that during 2000 and 2005, when vaccine rates were high, 16 cases were registered, and only during 2003 there were no cases of yellow fever. The vaccine has a minimum validity of 10 years and the immunization program needs to stimulate the population constantly to keep the vaccine up to date. The vaccine coverage rarely hits a homogenous distribution and, therefore, does not guarantee the protection needed by all the populations exposed to the risk<sup>14,15</sup>. In spite of the high rates of coverage in the state, there are probably areas of low vaccine coverage as we observe occurrence of cases mainly affecting people from remote areas. Absence of reported cases could be due to lack of clinical suspicion and consequent lack of diagnosis.

In the spatial distribution of the cases, one can note cases in municipalities located primarily in the floodplains of the rivers Solimões and Negro, and on the AM-010 highway. The creation of the Manaus metropolitan region favors the dislocation of people to neighboring municipalities of the capital, through

the bridge that links Manaus and Iranduba, facilitating the accessibility of the populations, both in the rural and urban areas. Human infection by the yellow fever virus occurs accidentally when people enter the forest for leisure activities, for harvesting of plants/plant extraction<sup>11</sup>, or for agriculture (which comprise 36% of rural occupation). The fact that there were also cases involving professionals of high degree of education and foreigners, calls attention to the need of health education as well as requesting travelers to present proof of immunization.

The presence of *Aedes aegypti* and of *Aedes albopictus* in municipalities in the rural areas and in the capital of Amazonas suggests the dispersion of these vectors and reinforces the need to ensure high vaccine coverage, and maintain continuous and improved epidemiological and entomological vigilance. The record of *Aedes aegypti* in rural areas of Manaus characterizes the possible dispersion of this species, where the large number of people commuting between the rural and urban areas makes the anthropic transposition of this vector to these areas, enabling outbreaks of focal points of dengue and yellow fever. The presence of *Haemagogus janthinomys* in forest areas approximately 100 meters from residential areas leaves the population vulnerable to yellow fever that is characterized by the presence of *Aedes aegypti* intradomiciliary<sup>12</sup>. Entomological surveys revealed the presence of species of *Aedes fulvus* in Rio Preto da Eva, *Haemagogus janthinomys* in Iranduba and Rio Preto da Eva, and *Haemagogus leucocelaenus* in Careiro and Manaquiri<sup>11</sup>. Given the record of *Aedes aegypti* and *Aedes albopictus* and due to the accessibility of the populations to areas with the presence of transmitters of native yellow fever, especially in the metropolitan region of Manaus, vaccine coverage is indispensable, as well as georeferencing in the monitoring of these vectors; especially because of macro events such as the 2014 World Cup.

The complex urban areas and the high concentration of population contribute to higher poverty incidence, and as a consequence, the volume of litter and inefficient supply and storage of water in these areas, complicate the elimination or effective control of *Aedes aegypti*<sup>13</sup>.

The main methods for yellow fever control include: a vaccine coverage above 90% in all municipalities, a demand for proof of immunization from tourists upon entry, public awareness campaign through all media, which includes information not only on the disease but also for the the need to control *Aedes aegypti*.

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## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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