

# Yellow Fever

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*With the infestation by Aedes aegypti, urban yellow fever might already exist. This did not occur because of either the lacking of a sufficient contact between the diseased individual and the A. aegypti or perhaps because this, after sixty years without transmitting the virus, needs an adaptation phase to infecting again.*

Key words: yellow fever - urbanization - *Aedes aegypti*

Yet is discussed whether yellow fever has been originated either from Africa or America or simultaneously in both Atlantic sides, before existing any contact between them (Falcão 1971). It seems that the disease occurred in the American continent since the pre-Colombian era, under the jungle form and became urban (by man-to-man transmission), after the importation of *Aedes aegypti* from Africa (Franco 1969). In Brazil, it was surely identified by João Ferreira da Rosa, in the State of Pernambuco, in 1685 (Rosa 1694), and propagated to the State of Bahia in the following year. After this endemics, either isolated cases or small outbreaks were recorded (Franco 1969). The disease reappeared as serious epidemics in 1849 in Bahia, from where it spread out to the whole country (Meirelles 1907). In 1850, in the State of Rio de Janeiro, it sacrificed 4,160 lives and became endemic. Torres Homem (1885) stated that it was infectious but not contagious. Finlay (1881) showed that the transmission of yellow fever was done by *A. aegypti*, confirmed by Reed et al. (1901). It was also demonstrated that the disease was produced by a virus (Reed & Carroll 1902).

Based on Reed and cols' conclusions, several anti-mosquito campaigns were initiated by Gorgas (1903) in Havana and for the Panama Channel construction (Scott 1939), by Ribas (1903) in the State of São Paulo, and by Oswaldo Cruz (Cruz 1903) in Rio de Janeiro.

In despite of the excellent results of the control actions in certain areas, the disease continued in several regions of Brazil (Fraga 1930). With the

creation of the Rockefeller Foundation, it seemed that the yellow fever would be eradicated. This possibility has vanished with the discovery of the sylvan yellow fever. *A. aegypti* was seen in Brazil by the first time in 1898 by Lutz (1930) and in 1899 by Ribas (Franco 1969), its meaning only was recognized in the 30's decade (Soper 1977). For this, besides the case reports of yellow fever without the presence of *A. aegypti*, it was very important the result of about 400,000 viscerotomies performed in Brazil by unprofessionals, and the serological inquiries (Soper 1977). The two forms of yellow fever coexisted (Table I).

The good results of the *A. aegypti* control have indicated the feasibility of a mosquito eradication program, which was obtained in Brazil in 1955, the last focus been extinguished in April 2nd, in the rural zone of the municipality of Santa Terezinha, Bahia (Franco 1969).

The mosquito was eradicated in almost all the America, except the United States, Suriname, Venezuela, and a little part of Colombia, Cuba, Jamaica, Haiti and Dominican Republic (Soper 1977). The *A. aegypti* reinfested Brazil in 1967 (Frahia Neto 1967).

## EPIDEMIOLOGY

The yellow fever can be transmitted mostly by mosquitoes of both the genus *Aedes*, mainly *A. aegypti*, and of *Haemagogus*. Regarding to localization, the yellow fever can be either urban, rural or sylvan, presenting itself under the epidemic or endemic forms.

The urban yellow fever, transmitted by *A. aegypti*, has the man as the only known vertebrate host. It was extinguished in Brazil since 1942, with the last focus in Sena Madureira (State of Acre). When the mosquito is found in all the year seasons, as it happens in hot climates, and there is a great susceptible human population, as in great cities, it exists under the endemic form. Where there is both a difficulty for the mosquito survival as in

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Received 7 August 2000

Accepted 4 September 2000

TABLE I

Cases reported by viscerotomy in Brazil, Colombia, Peru and Bolivia, 1935-1949

<i>Aedes aegypti</i>	Cases
There were	41 (2.1%)
There were not	1,871 (97.9%)
Total	1,912 (100%)

Source: Taylor (1951)

the temperate zones, or insufficient human population, as in rural communities, it can be epidemic. It can be spread by infected people or mosquitoes. In other circumstances, the virus survival can be granted by the vertical passage through the mosquito egg (Monath 1995). In the past, the ships were the mainly source of propagation.

The yellow fever was primarily an enzootic or epizootic of sylvan animals, mainly primates, transmitted by mosquitoes generally of the genus *Haemagogus*. As the vertebrate viremia is of short duration, the mosquitoes are the very reservoirs of the virus.

In South America, the enzootic area (Fig.1) encompasses the Amazon hydrographic basins – Orinoco, Magdalena and Atrato – and a little area in the Ilhéus region (Taylor 1951). Periodically the epizootic spreads to the neighboring regions. Not always the virus is found in a certain point of the enzootic area. Within this, it circulates under the form of epizootics, the virus being maintained this way, as it happens with other viruses such as those of measles and rubella.

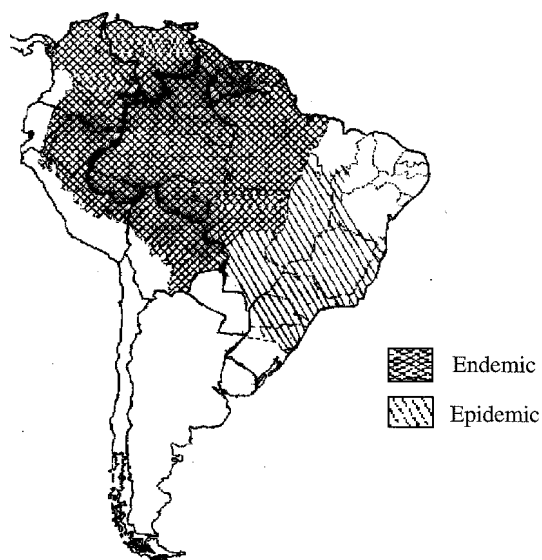


Fig. 1: sylvan yellow fever areas defined by World Health Organization

The human infection occurs in the endemic (enzootic) area, under the form of isolated cases or in little number when the men enter the forest.

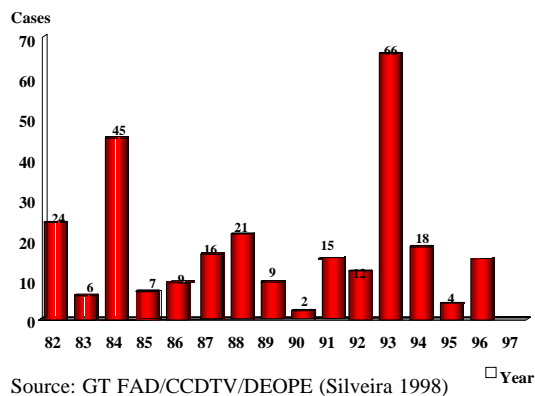
Periodically, each seven years approximately, suddenly the virus infects out of the enzootic area borders, in the epizootic zones, contiguous, thus considered as that enzootic area extension. So the epidemic occur. From the Amazon region, pass to south through the Paraná basin. These epidemics take place in hot and rainy periods, from September to March and may last for either one or some few years.

We have the opportunity of attending one of these epidemics occurred around Brasília, in the period from 1972 to 1973, when we saw more than 100 cases. The rapid way of epidemics spreading attracts the attention. The virus moves in a 6 km per day speed, considering the rhythm in which the human cases occur (Taylor 1951). In order to explain this fact, a possibility has been thought of, regarding the virus transportation by mosquitoes taken away by both the wind or acarids of birds (Taylor 1951). The cases acquired the disease near bordering stream woods, never 300 m far from these. Sometimes it was possible to observe people coming from the wood in the stream margins, with the mosquitoes coming together with them. The mosquitoes of the genus *Haemagogus* could be found within the houses near the bordering stream woods, thus possibilitating that occasionally perhaps a man-to-man infection could be transmitted, as priorly suggested (Bugher et al. 1944).

There are no evidences, but it is possible, that some sylvan yellow fever epidemics have been originated from some urban yellow fever focus. But the opposite has already been proved (Walcott et al. 1937, Guimarães 1974), comprehensively in Teófilo Otoni (1935), Lábrea (1936), Governador Valadares (1936), Cambará (1936), Xapuri (1937) and Sena Madureira (1942).

#### A. AEGYPTI THREAT

The sylvan yellow fever always existed in Brasil, in the past and even more recently (Fig. 2). As there is no possibility of extinguishing this disease, the way of preventing from has been (a) the vaccination of people who get in touch with endemic and epidemic zones, and (b) surveillance increase. No people should enter the Amazon Region without being vaccinated against yellow fever. The endemic zones; constitute permanent threat. They are of great extension but little inhabited. In the areas where there are epidemics, mainly in the states of Maranhão, Tocantins, Goiás, Mato Grosso do Sul, São Paulo, Paraná, Minas Gerais and Bahia, sometimes the vaccination is incremented only when yellow fever cases are di-



Source: GT FAD/CCDTV/DEOPE (Silveira 1998)

Fig. 2: sylvan yellow fever number of cases confirmed, Brazil, 1982-1997

agnosed. Despite being more inhabited, only the inhabitants who have contact with the stream bordering woods are infected. The initial diagnosis of the epidemics is generally postponed. In the epidemics of 1972-1973, the first cases have not been duly diagnosed, even when they occurred in hospitals. Nevertheless, the epidemics outbreaks auto-extinguish themselves because of the reduction of people susceptible to the infection.

The deeper concerns regarding sylvan yellow fever are the remembrances of the past and the fear that it may reach the cities, mainly the great cities of the non-endemic area.

Since 1967, when the *A. aegypti* was re-introduced in Brazil, there appeared the risk of yellow fever urbanization. This possibility increases as soon as the infestation by the *A. aegypti* spreads, mainly to the areas where there is sylvan yellow fever.

As soon as the re-infestation by *A. aegypti* occurred, the great risk was soon noted. With the dengue epidemics in Roraima, in 1982, another menace inherent to the reappearing of the mosquitoes was partially rendered concrete. As the number of cases of dengue and the circulation of more than one serotype has increased, the possibility of dengue hemorrhagic fever risk of occurrence also increased. The threats of epidemics of both dengue hemorrhagic fever and urban yellow fever, as well as the insufficiency of control actions assumed against *A. aegypti* scattering, motivated the decision of eradicating again the mosquito in the country. But the project was not implemented. Thus, the scenery propitious to the two threats concretizing remains installed.

The problem complicates with the finding, in the country, of *A. albopictus*, able to experimentally transmit the yellow fever virus (Theiler 1951).

### YELLOW FEVER URBANIZATION

Apparently existing favourable conditions to yellow fever urbanization, the fact that this has not occurred yet causes amazement. Fortunately, *A. aegypti*, until now, it has transmitted only the dengue virus. With so many variables in chain transmission, the existence of epidemiological conditions to the transmission of the disease can be theoretical, and also if there are hindrance factors related to either the host, or the virus or the transmitter as well.

*Geographical overlap of yellow fever cases and infestation by A. aegypti* - As mentioned above, there were many examples of urban yellow fever epidemics resulting from sylvan yellow fever epidemics. But we did not know the frequency of this occurrence. Now, *A. aegypti* started infesting again the majority of the municipalities of the country. Its activity as vector of other disease – dengue – is evaluated on the frequency of the number of cases notified.

The yellow fever virus can be isolated from the man infected, only in the first three or four days after the infection. Although sylvan yellow fever is acquired out of towns, the disease initiates suddenly, with a symptomatology that leads the diseased individual to looking immediately for medical care in the town. Even considering that, for each patient diagnosed, plenty of them are not notified, the number of cases, although constant, is relatively small. In the period of 1997 up 1999, this number was 147. Despite this, with the spreading of reinfestation by *A. aegypti*, it is difficult to admit that in this time no diseased individual with yellow fever has been pricked by the mosquito. In some states there are geographical superposition of the two diseases (Table II).

The features of the 147 cases of sylvan yellow fever, notified to the Brazilian Health Ministry in the period from 1998 to 1999, are shown in Table III.

TABLE II

States where sylvan yellow fever and dengue cases occurred from 1998 to 1999

States	Yellow fever		Dengue	
	1998	1999	1998	1999
Roraima	6	3	258	3,978
Pará	23	36	10,934	2,613
Amazonas	3	5	23,910	9,613
Maranhão	1	0	12,971	4,691
Tocantins	0	16	1,883	1,992
Goiás	0	10	6,412	2,550
Mato Grosso	1	5	8,787	2,662
Total	34	75	57,143	28,079

TABLE III

Features of the sylvan yellow fever cases diagnosed in Brazil, from 1998 to 1999

Sex		Age (year)				Deaths	
M	F	<10	10-19	20-49	>50	Yes	No
75	34	18	26	62	3	88	61

The frequency with which we saw diseased people, in the epidemics of 1972-1973, leads us to admit that unlikely the contact between them and *A. aegypti*, it could be avoided if they, on that occasion, had inhabited the dwelling houses as they do now.

Anyway, the likeliest explanation to the non urbanization of yellow fever in Brazil is that a sufficient contact between infected diseased individuals and *A. aegypti* would have not been occurred yet. Thus, the problem would be equated in statistical basis. But conjecturing on other possibilities is worthwhile.

Anyhow, it must be remembered that for an epidemic breaking out susceptible individuals are required.

*Virus* - There are many strains with pathogenic differences of yellow fever virus, either obtained in laboratory or selected in nature (Theiler 1951). Also the different pathogenicity for experimental animals among virus strains isolated in South America and Africa was already mentioned (Theiler 1951). The virus transmission to marsupials depends on their race. There is a virus strain, the D-17 one, which is used in vaccine against yellow fever, that was not reproduced and that is not transmitted by *Aedes*. The urban yellow fever virus is equal to that one of sylvan yellow fever, although it is believed that, from the clinical point of view, the disease of the latter is less severe than the former one.

Nevertheless, the urban yellow fever virus has disappeared among us and the sylvan yellow fever virus has kept circulating. But there is no evidence suggesting that virus strains can be interfering in the yellow fever urbanization.

*Aedes aegypti* - There is no evidence that the *A. aegypti* strain, now in circulation in Brazil, is different from that which circulated before the eradication. Nevertheless, two aspects must be considered. After the eradication, the mosquitoes which infested did not descend from those which were here and we did not know from where they did come, probably from neighboring countries.

Another aspect is that since about 60 years the mosquitoes do not transmit yellow fever, and we

do not know if there is some phase of adaptation, like occurs, for instance, with *Biomphalaria glabrata* in relation to *Schistosoma mansoni*. We believe that some study on the capacity of the *A. aegypti* found in Brazil, for transmitting yellow fever, at this moment, would be advisable.

*Absence of yellow fever in India and Far East* - It has been considered why some countries, like India and Thailand, have never had yellow fever, despite the existence of *A. aegypti* there. Many strains of *A. aegypti*, including those coming from Java and Red Sea, can transmit the yellow fever virus (Whithman 1951). Rhesus monkeys which served for experimental studies proceed from India. There is no evidence of racial resistance. It is assumed that the virus has never been introduced in the country. The time when the mainly via of yellow fever propagation were the ships, the long distance made difficult the virus survival in these boats. Besides, also in the East African seaport, yellow fever never existed in abundance. Another possibility may also be related: either to the *A. aegypti* strain or life habits prevalent in those regions.

*Vaccination* - As final considerations, we must have in mind that the urban yellow fever, like the sylvan one, spreads only where there are susceptible individuals. Also there is a vaccine of both with high efficacy and long lasting results against yellow fever. From the 109 cases of sylvan yellow fever notified in Brazil, from 1998 to 1999, only six informed that they have been vaccinated against yellow fever. In the epidemics which we follow in the period from 1772 to 1973, in the Brazilian Central Region, only two patients who have had the disease have been vaccinated; even so less than ten days ago. As a result, we have to vaccinate all the population of the country. This would be better together with other vaccines, including the vaccine against yellow fever in the national vaccination program.

## REFERENCES

- Bugher JC, Boshell-Manrique J, Roca-Garcia M, Osorno-Mesa E 1944. Epidemiology of jungle yellow fever in eastern Colombia. *Am J Hyg* 39: 16-51.
- Cruz O 1903. Prophylaxia da febre amarela. *Brazil-Med* 23: 482-484.
- Falcão EC 1971. *A Incompreensão de uma Época. Oswaldo Cruz Monumenta Histórica*, Vol. VI, Tomo I.
- Finlay C 1881. El mosquito hipoteticamente considerado como agente de transmisión de la fiebre amarela. *An R Acad Cien Med Habana* 18: 147-169.
- Fraga C 1930. *A febre amarela no Brasil*, Off. Graph. Insp. Demographia Sanitária, 361 pp.
- Frahia Neto H 1967. O recente reencontro do *Aedes aegypti* em Belém, Pará. *Rev Paul Med* 71: 259.

- Franco O 1969. *História da Febre Amarela no Brasil*. Ministério da Saúde, DNERU, Rio de Janeiro, 208 pp.
- Gorgas W 1903. A febre amarela e os mosquitos. *Brazil-Med* 17: 125-128.
- Guimarães JC 1974. *Febre Amarela Silvestre*. Thesis, Instituto de Microbiologia da Universidade Federal do Rio de Janeiro, Rio de Janeiro, 184 pp.
- Lutz A 1930. Reminiscências da febre amarela no Estado de São Paulo. *Mem Inst Oswaldo Cruz* 24: 127-142.
- Meirelles Z 1907. *Febre Amarela. Estudo Clínico*, H Garnier Livr Ed., Rio de Janeiro, 265 pp.
- Monath TP 1995. Flavivirus. In GL Mandell, JE Bennett, R Dolin (eds), *Principles and Practice of Infectious Diseases*, 4th. ed, Churchill Livingstone, p. 1465-1474.
- Reed W, Carroll J 1902. Etiology of yellow fever; supplemental note. *Am Med* 3: 301-305.
- Reed W, Carroll J, Agramonte A, Lazear JW 1901. Etiology of yellow fever; preliminary note. *Phil Med J* 6: 790-796.
- Ribas E 1903. Prophylaxia da febre amarela. *Brazil-Médico* 17: 343-400.
- Rosa JF 1694. *Tratado Único da Constituição Pestilencial de Pernambuco*, Miguel Manescal, Lisboa, 224 pp.
- Silveira AC 1998. Dengue: aspectos epidemiológicos e de controle. *Rev Soc Bras Med Trop* 31(Supl. II): 5-14.
- Scott HH 1939. *A History of Tropical Medicine*, Edward Arnold Co, Londres.
- Soper FL 1977. Ventures in World Health. *PAHO Scientific Publication* 355.
- Taylor RM 1951. Epidemiology. In GL Strode, *Yellow Fever*, McGraw-Hill Book Company Inc., p. 427-538.
- Theiler M 1951. The virus. In GL Strode, *Yellow Fever*, Mc Graw-Hill Book Company Inc., p. 39-136.
- Torres Homem FV 1885. *Estudo Clínico sobre as Febres do Rio de Janeiro*, 2a ed., Lopes do Couto Cia, 552 pp.
- Walcott AM, Cruz E, Paoliello A, Serafim JJ 1937. Epidemie of urban yellow fever which originated from case contracted in jungle. *Am J Trop Med* 17: 677-688.
- Whithman L 1951. The arthropod vectors of yellow fever. In GL Strode, *Yellow Fever*, Mc Graw-Hill Book Company Inc., p. 229-298.