

Full Length Research Paper

Yellow fever outbreak in central part of Senegal 2002: Epidemiological findings

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In 2002, a yellow fever (YF) outbreak occurred in the regions of Diourbel and Fatick, centre of Senegal. The index case was a young woman without any history of vaccination. Immunoglobulin M (IgM) specific of YF was detected in her blood by the Centre de Référence OMS sur la Recherche des Arbovirus et des Fièvres Hémorragiques (CRORA) in the Institut Pasteur of Dakar. According to specific case definitions, both active (investigation) and passive detection (surveillance) of human cases were performed and completed by entomological surveys. From September to December 2002, a total of 35 individuals recently infected by YF were identified out of 379 blood samples collected. During the investigation in October, 23 confirmed cases of YF were detected, including 11 deaths. All entomological indexes (Breteau, Container, House) were above the threshold of epidemic risk and 2 YF virus strains were isolated from *Aedes furcifer* collected in a village where YF cases and death were reported. Mass vaccination campaigns were urgently organized in all districts with positive cases to protect the populations.

Key words: Yellow fever, outbreak, mass vaccination, Senegal, West Africa, arbovirolosis.

INTRODUCTION

Yellow Fever (YF) is an acute viral hemorrhagic disease. The term "yellow" refers to the jaundice that affects some patients, causing yellow eyes and skin. The disease is endemic in tropical areas of Africa and Latin America, with a combined population of more than 900 million people. It is caused by the yellow fever virus (YFV), an enveloped RNA virus, belonging to the Flaviviridae family and the *Flavivirus* genus (Monath, 2001). The YFV is transmitted by the bite of certain mosquitoes of the genus *Aedes* (*Aedes aegypti* and other species). The mosquito gets infected when it feeds on viraemic animals in forests, such as monkeys. After the extrinsic incubation period (1 to 2 weeks), the infected mosquito becomes infecting, that is, it is able to transmit the YFV to another primate, in

particular a human being travelling through the forest (Vainio and Cuttis, 1998). The epidemic risk increases when infected humans return to the villages, semi urban areas or towns. Domestic populations of *A. aegypti*, living in close contact with human, are able to transmit the YFV both quickly and widely (Monath et al., 2008; Mutebi and Barrett, 2002; Staples and Monath, 2008). The infection results in asymptomatic form (Monath et al., 2008) or a wide spectrum of symptoms, from mild disease to severe illness and death (WHO, 2008). WHO estimates that 200,000 cases of YF occur every year in the world, causing 30,000 deaths. The number of YF cases has increased over the past two decades due to declining population immunity to infection, deforestation, urbanization,

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population movements and climate change. There is no specific cure for YF. The symptomatic treatment aims at reducing the symptoms for the comfort or survival of the patient (haemorrhage, organ failure). Up to 50% of severely affected people will die from YF, if intensive care is not quickly available. Vaccination is the most efficient preventive measure against YF. The vaccine is safe, affordable and cost-effective. It provides lasting and, in all appearance, lifelong protective immunity within one week for 95% of inoculated people (Staples and Monath, 2008; WHO, 2008).

YF is endemic in Senegal. The first well-described YF outbreak occurred in St. Louis du Senegal, in 1778 (Mutebi and Barrett, 2002). And, since the early 1930's sero-surveys have confirmed that Senegal was included in the YF endemic area of Africa. The implementation of YF vaccination decreases the burden of the disease, but, until now, several confirmed cases are regularly reported, in the centre and the south of the country (Digoutte, 1999; Digoutte et al., 1981; Salaun et al., 1981; Strode et al., 1951). In 2001, an epidemiological and entomological investigation has been carried out in the region of Diourbel (centre of Senegal) after the identification of 3 YF cases. The epidemiological investigation has revealed that an epidemic of YF did occur in the district of Bambey at the end of 2001 (14 new cases have been identified during the investigations). The entomological surveys have shown that *A. aegypti*, principal vector of YF, was ubiquitous in the investigated area and that all indices for the immature population of the vector (Breteau, container, house) were above the threshold of epidemic risk. Within the vector populations, a real risk of reappearance, even amplification of the epidemic during the following year was stressed. Again, in 2002, a new case of YF was confirmed in "Hôpital Principal" of Dakar: young woman, referred by the health centre of Touba (region of Diourbel) and hospitalized on the 15th September. The patient did not receive any recent vaccination, so that the presence of specific YF IgM permitted to confirm the diagnosis. The case was declared at the ministry in charge of healthcare in Senegal and a collection of blood samples was organized on hospitalized patients in the four health centers and some primary health units of the region of Diourbel. A total of 11 new cases of YF were identified out of 112 samples. Therefore, a multidisciplinary investigation was requested by the Ministry of health. It aimed to evaluate the number of cases of YF in the whole region of Diourbel and the risks of epidemic spreading into the bordering regions, in order to setup appropriate control measures and limit the impact of the diseases.

MATERIALS AND METHODS

This study took place from 4 to 13 October 2002. The investigation concerned the whole region of Diourbel (health districts of Touba, Mbacke, Diourbel and Bambey) and the health district of Colobane in the region of Fatick. It has been associated with an active

research of cases in the district of Niakhar and the villages of Dielmo and Ndiop, in the region of Fatick.

Case definition

A suspected case was defined as any person (1) presenting with acute onset of fever associated with jaundice appearing within 14 days of the first symptoms and/or (2) associated with hemorrhages and/or (3) deceased in a context of fever without any other etiology, since 1 July 2002. A confirmed case was a subject carrier of IgM specific of YF in absence of documented vaccination.

Search for and surveillance of human cases

Suspected and confirmed cases have been identified through laboratory results, health structures registers and interviews of doctors or nurses managing the health structures. The objective of the interview was to determine if the healthcare staff have seen or hear about cases presenting feverish jaundice, hemorrhagic fever, "malaria resisting to the treatment" and/or suspicious deaths, since 1 July. For each suspected case, the address was researched and he was visited at home. An active research of new cases was conducted in the neighborhood with the co-operation of village leaders and rural agents and villagers. They were questioned about people meeting the criteria of suspected cases or deaths associated with jaundice in the last three months. All suspected cases, patients with non-febrile illness (headache, nausea and vomiting, myalgia or lumbosacral pain) and asymptomatic people were proposed an inclusion in the sero-epidemiological study. Symptomatic individuals were examined by the doctors of the mission. An investigation form was filled out for all included people as well as a blood sample, to confirm or not the infection.

Serologic and entomologic investigations

With the agreement of the concerned people or their relatives, a questionnaire has been given to the suspicious cases and/or to a part of their close neighboring. Venous blood samples were obtained from these patients and randomly from healthy close neighboring persons in villages where probable or confirmed cases were observed. Sample collected in the field were stored and transported in liquid nitrogen to the Institut Pasteur of Dakar. Human blood samples collected were systematically tested for anti-YFV, dengue 2, Chikungunya fever, Rift Valley fever, Crimean-Congo and West Nile viruses IgM as previously described (Faye et al., 2007).

Tests for the presence of IgM specific to YF using Elisa and virus isolation on acute phase sera were performed in parallel with intracerebral inoculation of suckling mice and by inoculation on AP61 mosquito cell line.

An entomologic survey was conducted. Adult mosquitoes were collected at the evening from 18:00 to 21:00 pm after landing on immunized human volunteers. They were sorted and pooled by species and sex in the field and stored in liquid nitrogen. *Aedes* larval development sites were investigated in all localities indoor and outdoor of households randomly selected as well as in the peri-domestic areas. In the selected household, all containers holding both potable and non-potable water were inspected with a flashlight when necessary. For infested container, larvae or pupae were collected and taken to the laboratory (insectary) for rearing. The emerging adults were identified on a chill table and using a morphological keys (Edwards, 1941; Rueda, 2004).

The Breteau index (number of containers with larvae or pupae of *A. Aegypti* per 100 houses), container index (number of containers with larvae pupae of *A. Aegypti* per 100 water filled containers) and

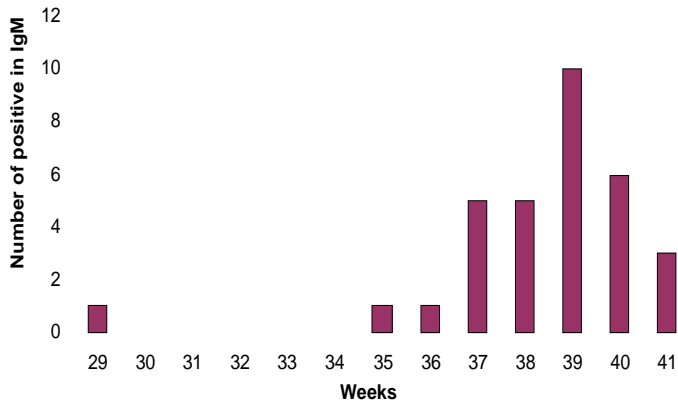


Figure 1. The epidemic plot includes the index case, the 11 detected cases before the investigation and the 23 cases identified during the investigation. For 3 individuals, the starting date of the symptoms is unknown. For the 32 other cases, the starting dates of the symptoms are spaced between 15 July 2002 and 9 October 2002 (weeks 29 to 41).

house index (number of positive houses per 100 by the houses) were calculated (WHO, 1986). The adult aggressiveness was expressed as the number of mosquito bite per person per evening.

The prospects have been done in the localities where cases of YF have been suspected and/or confirmed. In all, 6 villages of the Departments of Gossas (region of Kaolack), Bambey (region of Diourbel) as well as 7 districts of the towns of Touba and Mbacke (Department of Mbacke, region of Diourbel) have been visited.

RESULTS

Investigation of index case identified at principal hospital of Dakar

Aged 18 and residing in Touba (region of Diourbel), the young woman has started to present a febrile syndrome at the end of August with a *falciparum* malaria diagnosis. Her clinical signs worsened on 13 September with the appearance of jaundice and hemorrhagic syndrome (epitaxis and gingivorrhagies). She has then been hospitalized at the health centre of Touba. At the appearance of neurologic troubles (obsession), two days later, she has been addressed to Principal Hospital of Dakar (PHD), with a suspicion of YF among other hemorrhagic fevers. When she arrived at the PHD intensive care unit, she was presenting a febrile coma, a clear jaundice, an hematury, some vomito-negro, an anemic syndrome and a multi visceral failure. A blood sample has been addressed to Dakar Institute Pasteur at the Centre de Référence OMS sur la Recherche des Arbovirus et des Fièvres Hémorragiques (CRORA) which has shown IgM specific of YF. The patient recovered progressively.

That patient said she had not moved out of the district of Touba the month preceding her symptoms. However, her family is from Ndeme (district of Bambey, region of Diourbel), a village where the majority of YF cases had

been identified in 2001. Relatives living in this village have visited her a short time before her sickness. Moreover, two other people living with her have been ill at the same period.

Results of the mission of investigation in the field

The region of Diourbel involves 73 health structures with hospitals, health centers and primary health posts (19 for the health district of Diourbel, 21 for Bambey, 16 for Mbacke and 17 for Touba). The interviews with the medical personnel could take place in 70 health structures and registers could be consulted in 65. In all the 66,817, reports could be examined in the registers of the months of July, August, September and October.

Two hundred sixty six (266) blood samples were collected from individuals in villages where cases were detected. Twenty three individuals with specific IgM antibodies were considered to have had a recent YF virus infection. The epidemic plot includes the index case, the 11 detected cases before the investigation and the 23 cases identified during the investigation e.g., annex (Figure 1). For 3 individuals, the starting date of the symptoms is unknown. For the 32 other cases, the starting dates of the symptoms are spaced between 15 July 2002 and 9 October 2002 (week 29 to week 41). Among the 266 people included in the investigation and for which a blood sample could be obtained, the proportion of confirmed YF cases was identical according to gender (male: 12/130 versus female: 11/130). The cases were aged 3 to 38 and no case has been detected among the 54 people (aged 40 and more).

Entomological results

Table 1 shows the dominant species in the epidemic area and all potential vector of YF. A total of 654 adult mosquitoes belonging to 3 genera and 8 species were collected in the affected area. *Culex quinquefasciatus* (68.06%), *A. aegypti* (18.19%) and *Aedes furcifer* (12.07%) were the common species and constitute 98.3% of the fauna. Globally, *C. quinquefasciatus* was the most aggressive with density fluctuating between 0.42 bite per person per evening in Belel Doki up to 8.31 bite per person per evening in Darou Minam. Concerning *A. aegypti*, the most important aggressivities were recorded in the villages belonging to Bambey Departments like Ndione (2 bites per person per evening), Nguel (4.38 bites per person per evening), Ngascope (2.5 bites per person per evening). *A. furcifer* was much localised in the villages belonging to Gossas Departments where people received up to 2.83 bites evening in Belel Doki.

A total of 2 YFV strains were isolated from *A. furcifer* collected in Belel Doki. The minimum infection rate was 2.94% whereas the inoculation rate was 0.83 infected

Table 1. Adult mosquitoes collected in each community in the affected region, October 10 to 16th 2002.

Species	Number of mosquitoes collected (Number of specimen collection per person per evening)											Total
	Darou Miname	Darou Nahim	Darou Marnane	Foudaye	Ndione	Ngascope	Nguel	Refane	Mbacké	Colobane	Belel Doki	
<i>A. aegypti</i>	6 (0.38)	21 (1.31)	4 (0.25)	13 (0.81)	16 (2)	20 (2.50)	35 (4.38)	2 (0.25)	1 (0.13)	0	1 (0.04)	119 (0.53)
<i>A. furcifer</i>	0	0	0	0	0	1 (0.13)	1 (0.13)	0	0	9 (0.38)	68** (2.83)	79 (0.35)
<i>A. vittatus</i>	0	0	0	0	0	0	0	0	1 (0.13)	0	0	1 (<0.01)
<i>C. quinquefasciatus</i>	133 (8.31)	46 (2.88)	130 (8.13)	115 (7.19)	0	3 (0.38)	0	8 (1)	0	0	10 (0.42)	445 (1.99)
Others	1	1	1	1	4	0	0	0	0	0	2	10
Total	140	68	135	129	20	24	36	10	2	9	81	654

A. dalzieli. *A. gambiae*. *C. antennatus*. *C. tritaeniorhynchus*. **2 Yellow fever virus strains isolated.

Table 2. Aquatic stages investigation and YF epidemic risk indexes for each community in the affected region, October 10 to 16th 2002.

Department	Community	No. of houses	HU	No. of positive containers/No. of containers inspected						Total	BI	CI	
				Clay Jar		Barrel		Other**					
				Indoor	Outdoor	Indoor	Outdoor	Indoor	Outdoor				
Mbacké	Touba	Darou Nahime	20	44	0/1	0	0/1	0/1	0	16/27	16/30	36.4	53.3
		Darou Miname	22	94	0/1	6/9	1/1	0/1	0	6/8	13/20	13.8	65
		Ndamatou	20	112	1/2	4/5	0	1/1	0	17/21	23/29	20.5	79.3
		Madyana	20	114	0/2	1/3	0/1	1/1	0	16/19	18/26	15.8	69.2
		Keur Niang	20	93	0/1	3/10	0	1/2	0	8/18	12/31	12.9	38.7
		Forage Baye lat	21	100	0	5/9	1/1	4/6	0/1	13/15	23/32	23	71.9
Bambeye	Ngoye	Ndione	23	107	5/8	67/98	0	9/14	0	4/5	85/125	79.4	68
		Ngascope	20	82	3/3	47/66	0	2/6	0	0/2	52/77	63.4	67.5
		Nguel	8	59	1/1	30/39	0	4/7	0	2/3	37/50	62.7	74
		Refane	15	82	0/1	10/22	0/1	21/36	0/0	2/3	33/63	40.2	38.8
		Foudaye	15	51	0	12/19	0/1	14/24	0	0/2	26/46	50.9	56.5
		TOTAL	204	938	10/20	185/280	2/6	57/99	0/1	84/123	338/529	36	63.9

** Other includes tanks, chicken watering containers, discarded containers, tires, pots, bucket.

bite per evening meaning that *A. furcifer*, was responsible for at least 1.2 infected bites per person every fortnight.

Table 2 exhibits the results obtained in the 12

communities of the 3 department visited. In total, 650 containers mostly use for water storages were inspected in 204 houses corresponding to 938 habitation units. The main larval habitats

found in localities prospected were clay jars, plastic or metallic barrels and tanks.

The Breteau and container indices were variable according to the communities. The Breteau

indices ranged from a minimum of 13.8 in Darou Minane to a maximum of 79.4 in Ndione while the container indices ranged from 38.70 (Keur Niang) to 79.33 in Ndamatou. Except for Belel Doki, these indices indicate a high risk for yellow fever transmission in all communities.

The strong presence of *C. quinquefasciatus* and *A. Aegypti* in the localities of Bambey and Touba (despite pulverizing of insecticides) has also noted. However, in Belel Doki a village belonging to the Department of Gossas and where confirmed cases, among which a death, have been recorded, only wild vectors (*A. furcifer*) has been collected. Further two YFV strains were isolated from *A. furcifer* collected in this village.

DISCUSSION

YF is endemic in Senegal. Since 1950, several confirmed cases are regularly reported, in the Center and the South (Salaun et al., 1981). Clinical and serological arguments show that the outbreak that has affected the district of Bambey region of Diourbel in 2001 has been spread out in all the region of Diourbel and in the bordering regions in 2002. Previous studies had shown a high prevalence of IgG antibodies in human and simian populations which clearly indicated that increased sylvatic YF activity in Eastern Senegal has increased the risk of YF transmission among rural populations in Senegal.

Among the potential vectors of YFV, *A. aegypti*, *A. furcifer* and *Aedes vittatus* were recorded. *A. aegypti* is known as the main vector of urban epidemics of YF in Africa and South America. Its presence in the area of interest is already known and its involvement in YF epidemic transmission has already been described during previous epidemics (Chambon et al., 1967; Fontenille et al., 1997; Thonnon et al., 1999).

A. furcifer is known as a sylvatic vector but with its large flight range. It may contribute to both sylvatic transmission and virus dissemination from the forest zone to human habitats where the species is some time very abundant. The species play an important role in the transmission of YFV mainly during epidemic affecting rural area in Africa (Germain et al., 1980; Port and Wilkes, 1979). Concerning *A. vittatus*, the species is a proven experimental vector of yellow fever found associated with yellow fever virus in nature.

However, it is still considered a secondary vector since very little information has been obtained about its involvement during epidemics of yellow fever. The species was only incriminated as responsible of the YF epidemic that occurred in Sudan in 1940 (Kirk, 1941) and suspected as the main vector during the YF epidemic that occurred in Jos plateau in Nigeria in 1959 and 1969 (Lee and Moore, 1972).

The high densities of *C. quinquefasciatus* reflect the known anthropophilic behaviour of the species, associated to the human habitation in houses where collections of polluted water are frequent (latrines, wastewater

discharge channels). Although abundant, there is no risk related to this species since its involvement in the transmission cycle of YF virus has never been demonstrated.

It is possible that other YFV vectors exist in the area prospected. The short time dedicated to the study, the unfavourable environmental conditions coinciding to the end of the rainy season, related to the population dynamic of mosquito vectors may affect our list of species recorded as well as their representation.

Considering the species recorded in the affected area, we could conclude about an intermediate epidemic transmission involving *A. aegypti* and sylvatic vectors. This transmission cycle is the most common in the west African (Germain et al., 1980) and is the only one described to date in Senegal (Thonnon et al., 1999).

However, the distribution of the vector, indicate different transmission profile with the sylvatic vector *A. furcifer* displaying the main role in the zone of Gossas (Bele Doki land Colobane), while *A. aegypti* exhibit a major role in the department of Mbacke (Touba) and Bambey.

Conclusion

A. Aegypti, the epidemic vector of YF, has been present everywhere, in all the villages and towns prospected among which the town of Touba (main urban and commercial trade area of the region) and the index (Breteau as container), has been everywhere largely over the limit of the epidemic risk defined by WHO.

Taking into account the particularly important movement of travelers between the region of Diourbel and the rest of Senegal for commercial activities purpose, the health services in all the regions of Senegal have been alerted and have reinforced their surveillance system. Vaccination of all the population of Diourbel has been organized and spread out to the districts of Fatick where cases have been suspected. The surveillance setup has been permitted to collect 888 other samples and identify 36 new cases of some of these cases, which came from other regions than those previously infected: Dakar, Thies, Louga, Tambacounda and Kolda which indicated that the outbreak was more spread out than initially located.

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