

PLAGUE SURVEILLANCE IN BRAZIL: 1983 - 1992

Alzira Maria Paiva de ALMEIDA (1), Nilma Cintra LEAL (1), Francisco Gomes de CARVALHO (1),
José DANTAS SOBRINHO (2) & Célio Rodrigues de ALMEIDA (1)

SUMMARY

Plague caused by *Yersinia pestis*, has persisted in Brazil in several natural foci spread throughout rural areas in the States of Ceara, Paraíba, Pernambuco, Piauí, Rio Grande do Norte, Alagoas, Bahia, Minas Gerais and Rio de Janeiro. Nationwide surveillance of plague in Brazil based on serological testing started in 1983. We now present an update report of the examinations carried out in our laboratory from 1983 to 1992. The passive hemagglutination test for antibodies against fraction 1A antigen of *Y. pestis* and the passive hemagglutination inhibition control were employed for testing a total of 220,769 sera. Samples analyzed included 2,856 sera from clinically diagnosed plague cases or suspects, 49,848 sera from rodents of 24 species and 2 species of small wild carnivores (marsupials), 122,890 sera from dogs, and 45,175 sera from cats. Specific antibodies were found in 92 (3.22%) human sera; 143 (0.29%) sera from rodents of 8 species and from the two species of marsupials, 1,105 (0.90%) sera from dogs and 290 (0.64%) sera from cats. The presence of significant levels of specific anti-F1A antibodies among rodents and wild or domestic carnivores (dogs and cats) indicates that all the Brazilian plague foci remain active in spite of the absence of human cases in some of them.

KEYWORDS: Serology - Plague surveillance - *Y. pestis* - Brazil.

INTRODUCTION

Plague caused by *Yersinia pestis* is essentially a rodent-flea-transmitted disease. Humans can acquire plague through flea bite or direct contact with infected animals¹⁵. Plague may occur in domestic cats and dogs¹⁷. Cats are particularly susceptible to *Y. pestis* and they usually develop a severe illness^{12, 17}. Therefore, they have been responsible for human contamination, by direct respiratory contact, contact with exudates and occasionally by bites or scratches. On the other hand dogs seldom show clinical signs. However, both dogs and cats may carry fleas and flea-infested animals or carcasses into the peridomestic environment and into houses^{8, 15}.

Plague remains a public health problem in several countries in Africa, Asia and in the Americas¹⁰. In Brazil, it is well established in several natural foci spread throughout rural areas in the States of Ceara (CE), Paraíba (PB), Pernambuco (PE), Piauí (PI), Rio Grande do Norte (RN), Alagoas (AL), Bahia (BA), Minas Gerais (MG) and Rio de Janeiro (RJ)¹⁸. It was noticed that human plague in the Brazilian foci followed cycles of 5 to 10 years^{14, 18}. Between outbreaks it was assumed to be quiescent because it could not be detected, even when systematic bacteriological surveys of rodent-sentinels were carried out in most of the foci^{1, 2}. However, bac-

(1) Centro de Pesquisas Aggeu Magalhães/FIOCRUZ, Recife, PE Brasil.

(2) Fundação Nacional de Saúde (FNS).

Correspondence to: Dra. Alzira M. P. de Almeida, CPqAM/FIOCRUZ, Caixa Postal 7472, Cidade Universitária, 50670-420 Recife, PE, Brazil.
FAX (081) 271 2302, TELEPHONE: (081) 271 4000.

teriological surveys were shown to underestimate plague activities. Hence, serological testing has been recommended for surveillance programs in plague endemic areas ^{6, 11}.

Nationwide surveillance of plague in Brazil based on serological testing started in 1983. Most of the samples, collected by the teams of the plague control program, were processed in the Plague Laboratory of the "Centro de Pesquisas Aggeu Magalhães" (CPqAM) in Recife, Pernambuco.

We now present an update report of the examinations carried out in this laboratory from 1983 to 1992.

MATERIALS AND METHODS

A total of 220,769 sera from humans, rodents and wild and domestic carnivores from all the Brazilian plague foci were analyzed in the Plague Laboratory of the "Centro de Pesquisas Aggeu Magalhães" (CPqAM) in Recife, Pernambuco.

The sera were collected by the teams of the plague control program = "Campanha contra a Peste" (CCP),

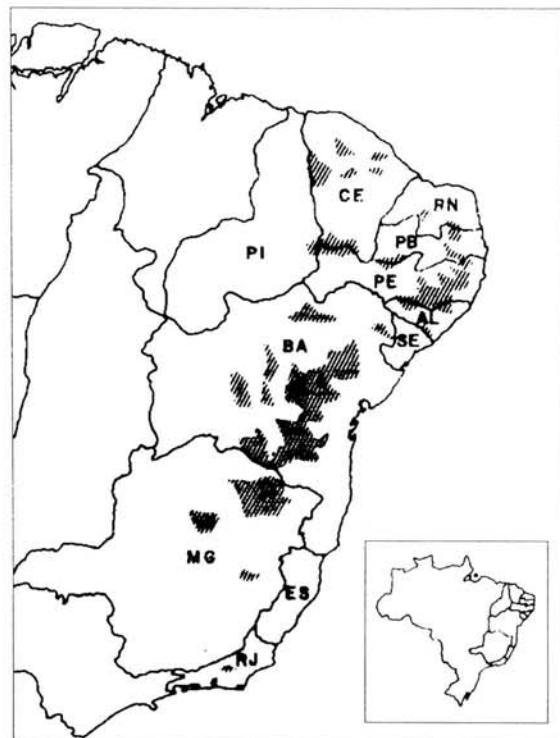


Fig. 1. - Map of Brazil showing the States where plague is endemic and from which sera samples were collected. Hatched areas are plague foci.

sponsored by the "Fundação Nacional da Saúde" (FNS), (former "Superintendência de Campanhas" = SUCAM) a branch of the Brazilian Health Ministry. The Brazilian States, where plague is endemic and from which sera samples were collected, are signalled in Fig. 1.

The normal field procedure involved collection of sera from animals, four days a week, throughout the years. However, some laxity of this procedure should be admitted mainly in the last years. The animals were from farms randomly selected in countries where any plague activity had been registered during the last five years. Human sera were obtained from plague-suspected persons, based on clinical symptoms, epidemiological evidence and their contacts. Eventually animal examination was focused in the areas of confirmed human outbreaks.

The passive hemagglutination test (PHA) for antibodies against fraction 1A (F1A) antigen of *Y. pestis* and the passive hemagglutination inhibition test (PHI), as control, were performed as recommended by WHO ¹⁹. Sera were considered positive only when repeated testing showed a PHA titre of $\geq 1:16$ that was four times or more higher than the PHI titre.

The program EpiInfo, was used to analyze the results, at confidence interval for properties at significance level of 95%.

F1A antigen was isolated from *Y. pestis* strain A1122 grown at 37°C as described by BAKER et al ⁷.

RESULTS

Human plague

A total of 2,856 sera from clinically diagnosed human-plague cases or suspects have been tested, 92 (3.22%) of which were antibody-positive (Table 1). Antibody-positive samples were originated from the foci in PB, BA, CE, RN and MG States. However, most of them were from the States of PB, BA and CE. All positive samples were obtained from 1983 to 1988 (Fig. 2).

Survey among rodent and small wild carnivores (*Marsupials*)

Sera from 49,848 rodents of 24 species and 2 species of small wild carnivores (*Marsupialia*) were tested. Table 2 shows the number of each species tested in the total sample, and the number and the percentage of the total with antibodies for each species. Antibodies were found in 143 (0.29%) animals of 10 species. These were:

TABLE 1

Distribution per State, of the number of sera from rodent plus marsupials, dogs, cats and humans, tested for antibodies to *Yersinia pestis* F1A antigen, number of antibody-positive sera and percentages of antibody-positive sera during the period from 1983 to 1992.

States	Rodents plus marsupials			Dogs			Cats			Humans		
	N° tested	N° positive	% positive	N° tested	N° positive	% positive	N° tested	N° positive	% positive	N° tested	N° positive	% positive
CE	11193	26	0.23	0	0	-	0	0	-	1235	19	1.54
PB	2498	61	2.44	15122	304	2.01	8275	184	2.22	804	53	6.59
PE	8119	2	0.02	56524	428	0.76	28227	87	0.31	24	0	-
PI	0	0	-	772	5	0.65	420	0	-	0	0	-
RN	6327	1	0.02	8546	73	0.85	4552	11	0.24	96	1	1.04
AL	1384	0	-	0	0	-	0	0	-	2	0	-
BA	4880	36	0.74	23165	169	0.73	760	2	0.26	671	18	2.68
MG	2049	1	0.05	15627	112	0.72	2909	6	0.21	12	1	8.33
RJ	13398	16	0.12	3134	14	0.45	32	0	-	12	0	-
Total	49848	143	0.29	122890	1105	0.90	45175	290	0.64	2856	92	3.22

Rattus r. alexandrinus, *Rattus r. frugivorus*, *Rattus r. rattus*, *Galea spixii wellsi*, *Akodon arviculoides cursor*, *Nectomys squamipes olivaceus*, *Oxymycterus quaestor*, *Oryzomys eliurus*, *Didelphis p. paraguayensis* and *Monodelphis d. domestica* from the States of CE, PB, PE, RN, BA, MG and RJ.

Plague antibodies were more frequently found among the plague-resistant *Cavidae*: *Galea s. wellsi* (1%) and *Marsupialia*: *Didelphis p. paraguayensis* and *Monodelphis d. domestica* (1.3%). By contrast, the presence of antibodies was less frequent among the *Muridae*:

Rattus r. alexandrinus and *Rattus r. frugivorus* (0.2%) and some species of *Cricetidae*: *Akodon arviculoides cursor*, *Nectomys squamipes olivaceus*, *Oxymycterus quaestor*, *Oryzomys eliurus*, (0.12%) and non-existent among the *Echymidae*.

The majority of positive animals originated from the same States (PB, BA and CE) and the same period (1983 to 1987) in which human cases were more numerous (Table 1 and Fig. 2).

Survey among domestic dogs and cats

Table 1 presents in detail the number of sera from dogs and cats tested on a State-by-State basis from 1983 to 1992, the number of antibody positive and the percentages.

To sum it up, plague antibodies were found among 290 (0.64%) out of the 45,175 cats tested and in 1,105 (0.90%) of the 122,890 dogs tested.

DISCUSSION

It appears from these results that plague activity has diminished in the Brazilian foci in the last years (Fig. 2). This decrease may be attributed to a manifestation of its natural cycle rather than to the laxity of the surveillance activities. Moreover, it confirms previous observations that plague follows different independent trends in each focus: in RJ, MG and AL States, plague activities have remained low. Low activity has also been maintained in PE State where it was very high not long ago^{1,2}. In BA and CE States small outbreaks have been coming about over the years. A severe outbreak came about in PB State between late 1986 and early 1988 which expanded to

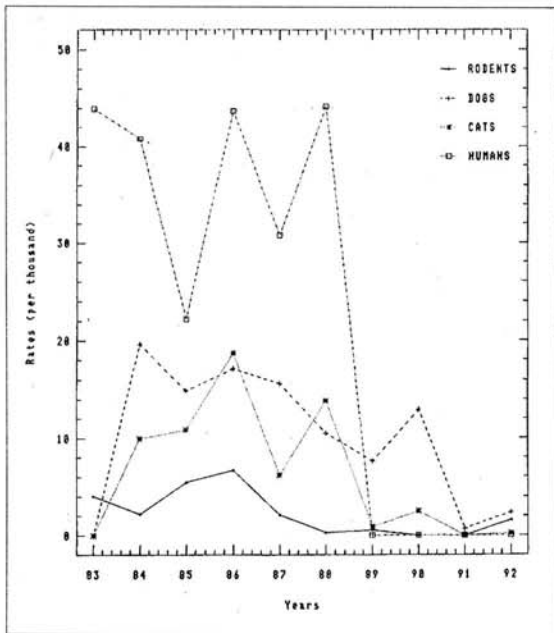


Fig. 2. - Rates of plague antibody-positive sera from humans, rodents, cats, and dogs from 9 Brazilian States, from 1983 to 1992.

TABLE 2
Rodents and marsupials tested for antibody to *Yersinia pestis* F1A antigen; 9 Brazilian States; 1983-1992.

Rodents	Species	N° tested	N° positive	% positive
Muridae	<i>Mus musculus brevisrostris</i>	73	-	-
	<i>Rattus rattus alexandrinus</i>	11733	16	0.14
	<i>Rattus rattus frugivorus</i>	17104	50	0.29
	<i>Rattus rattus rattus</i>	879	1	0.11
	<i>Rattus norvegicus</i>	26	-	-
Cavidae	<i>Cavia aperea aperea</i>	64	-	-
	<i>Galea spixii wellsi</i>	5210	53	1.02
Echymidae	<i>Euryzomatomys guiara guiara</i>	39	-	-
	<i>Proechimys albispinus albispinus</i>	21	-	-
	<i>Trichomys apereoides apereoides</i>	1138	-	-
Cricetidae	<i>Akodon arviculoides arviculoides</i>	225	-	-
	<i>Akodon arviculoides cursor</i>	4510	7	0.15
	<i>Bolomys lasiurus</i>	543	-	-
	<i>Calomys callosus</i>	144	-	-
	<i>Holochilus sciurus</i>	18	-	-
	<i>Nectomys squamipes olivaceus</i>	1000	2	0.20
	<i>Nectomys squamipes squamipes</i>	105	-	-
	<i>Oxymycterus quaestor</i>	1288	1	0.08
	<i>Oryzomys elurus</i>	3523	5	0.14
	<i>Oryzomys r. ratticeps</i>	169	-	-
	<i>Oryzomys subflavus</i>	665	-	-
	<i>Oryzomys utiariensis</i>	19	-	-
	<i>Thaptomys nigrata</i>	209	-	-
	<i>Thomasomys dorsali</i>	21	-	-
Marsupials	<i>Didelphis p. paraguayensis</i>	408	6	1.47
	<i>Monodelphis d. domestica</i>	215	2	0.93
Others	Without information	500	-	-
	Total N° tested	49848	143	0.29

bordering areas as RN State but after a while it declined ⁴.

However, it should be taken into account that an accurate comparison on a State-by-State basis is limited by built-in biases in sample collection. For example, the higher percentage of antibody-positive human sera from MG does not mean that plague was hyperactive there, but it was rather due to the quantity of sera tested. It is also noteworthy to emphasize that all antibody-positive human sera from PB State have been obtained during only one outbreak, whereas antibody-positive human sera had been found yearly in BA and CE, from 1983 to 1987. Furthermore, no human sera from CE have been examined in this laboratory after 1987.

As it was already pointed out ^{1,4} the rate of antibody-positive human sera is low. This could be due to the inclusion of inadequate samples for examination i.e., either the early collection of the samples, in a period in which antibodies could not supposedly be found yet or a misleading clinical screening. Actually, the patients

were supposed to be plague infected, mainly because they had buboes. But their buboes could be "bubonic leishmaniasis" ¹⁶ whose geographical distribution overlaps that of plague.

Certainly a good clinical screening of the patients leads to a higher rate of serological-positive results as it had been done during the outbreak in CE State in 1982 ³, contrasting with the results of the PB-1986 outbreak, when sera from asymptomatic and case contacts were included for examination ⁴.

Another possibility is that the PHA test is not sensitive enough to detect low levels of antibodies in the early stage of infection in which many sera were collected ⁴. This hypothesis is reinforced by the increase obtained in the percentage of positive results when some samples were re-examined by the Dot-Elisa, a more sensitive test ⁵.

Anyway, comparing the prevalences of antibody-positive humans, rodents, cats and dogs (Fig. 2 and

Table 1) it looks as though the human rate is higher. The lower rates of antibody-positive rodents and domestic carnivores result from the rather randomized collection of sera samples from these animals, including animals from infected and neighbouring areas.

Plague antibodies were more frequently found between the plague-resistant species. These results are in agreement with previous observations that resistant animals are more likely to develop plague antibodies. The susceptible ones usually die from their infections^{9, 13}. Accordingly, the bacteria *Y. pestis* is more frequently found among the sensitive species through bacteriological examination². Hence, searching for plague antibodies among the susceptible species is almost useless. In spite of the small number of animals examined, the incidence of positive plague antibodies was high among the two species of wild carnivores (*Marsupialia*) thus indicating that they are good sentinels for plague.

Antibody-positive domestic carnivores (dogs and cats) have been found yearly in each plague-endemic State where they have been searched for. Furthermore, their prevalence was higher in the States where the incidence of human plague was also higher. Antibody-positive percentages were higher among dogs than among cats in all, but PB State. Equally, high rates had been previously observed among cats during a plague outbreak in CE³. This may indicate that cats infect themselves easily and early but most of the infected ones disappear. As dogs are resistant and seldom die, after the outbreak, antibody-positive cats are outnumbered by them.

Although no evidence of plague transmission between humans and domestic carnivores in the Brazilian foci has been reported, it is noteworthy to recall that fleas, (*Ctenocephalides felis*) collected from a cat in a house where there were human plague patients, had once been found infected with *Y. pestis*².

As it was noticed elsewhere⁸, either wild and domestic carnivores have been shown to be better than rodents as indicators of plague in the Brazilian foci. Therefore they should be the preferred sentinel animal for plague surveillance.

The finding of antibody-positive animals indicates that enzootic plague still lingers on. Hence, even if human cases have not been numerous lately in the Brazilian foci, it is essential to keep each focus under

surveillance to detect any increase of plague activity in order to take precocious control actions. As plague eradication cannot still be expected and in view of its epidemic potential, its control is highly recommended.

RESUMO

Vigilância sorológica da peste no Brasil no período de 1983 a 1992.

A peste, infecção pela *Yersinia pestis*, se mantém no Brasil, em vários focos naturais, disseminados na área rural, dos Estados do Ceará, Paraíba, Pernambuco, Piauí, Rio Grande do Norte, Alagoas, Bahia, Minas Gerais e Rio de Janeiro. Desde 1983, o teste de hemaglutinação passiva para anticorpos contra a fração antigênica "F1A" de *Y. pestis*, vem sendo empregado ininterruptamente na vigilância da peste nos focos brasileiros. A especificidade do PHA é controlada pelo teste de inibição da aglutinação. No período de 1983 à 1992 foram examinadas 220.769 amostras de soro, sendo 2.856 de origem humana, 49.848 de roedores pertencentes à 24 espécies e de 2 espécies de pequenos carnívoros selvagens (marsupiais), 122.890 soros de cães e 45.175 de gatos. Anticorpos específicos foram encontrados em 92 (3,22%) dos soros humanos; 143 (0,29%) soros de roedores de 8 espécies e das duas espécies de marsupiais, 1.105 (0,90%) soros de cães e 290 (0,64%) soros de gatos. A presença de níveis significativos de anticorpos anti-F1A entre roedores e carnívoros domésticos (cães e gatos) e selvagens evidencia atividade pestosa nos focos apesar da ausência de peste humana em alguns deles.

ACKNOWLEDGEMENTS

We are grateful to Wayner de Souza and George Tadeu for their help with the computer and the figures.

REFERENCES

1. ALMEIDA, C. R.; ALMEIDA, A. M. P.; VIEIRA, J. B. et al. - Plague in Brazil during two years of bacteriological and serological surveillance. *Bull. Wld. Hlth. Org.*, 59: 591-597, 1981.
2. ALMEIDA, A. M. P.; BRASIL, D. P.; CARVALHO, F. G. & ALMEIDA, C. R. - Isolamento de *Yersinia pestis* nos focos pestosos do nordeste do Brasil no período de 1966 a 1982. *Rev. Inst. Med. trop. S. Paulo*, 27: 207-218, 1985.
3. ALMEIDA, A. M. P.; BRASIL, D. P.; MELO, M. E. B. et al. - Importância dos carnívoros domésticos (cães e gatos) na epidemiologia da peste nos focos do Nordeste do Brasil. *Cadern. Saúde. publ.* (Rio de J.), 1: 49-55, 1988.

4. ALMEIDA, A. M. P.; BRASIL, D. P.; LEAL, N. C. et al. - Estudos bacteriológicos e sorológicos de um surto de peste no Estado da Paraíba, Brasil. **Mem. Inst. Oswaldo Cruz**, 84: 249-256, 1989.
5. ALMEIDA, A. M. P. & FERREIRA, L. C. S. - Evaluation of three serological tests for the detection of human plague in Northeast Brazil. **Mem. Inst. Oswaldo Cruz**, 87: 87-92, 1992.
6. ARCHIBALD, W. S. & KUNITZ, S. J. - Detection of plague by testing serums of dogs on the Navajo Reservation. **HSMHA Hlth. Rep.**, 86: 377-380, 1971.
7. BAKER, E. E.; SOMMER, H.; FOSTER, L. E. et al. - Studies on immunization against plague. I. The isolation and characterization of the soluble antigen of *Pasteurella pestis*. **J. Immunol.**, 68: 131-145, 1952.
8. BARNES, A. M. - Surveillance and control of bubonic plague in the United States. **Symp. zool. Soc. Lond.**, 50: 237-270, 1982.
9. BUTLER, Y.; ALMEIDA, A. M. P.; ALMEIDA, C. R. et al. - Estudos sorológicos e experimentais da peste no nordeste do Brasil. **Rev. bras. Malar.**, 32: 26-35, 1980.
10. BUTLER, T. - The black death past and present. I. Plague in the 1980s. **Trans. roy. Soc. trop. Med. Hyg.**, 83: 458-460, 1989.
11. CAVANAUGH, D. C.; DEORAS, P. J.; HUNTER, D. H. et al. - Some observations on the necessity for serological testing of rodent sera for *Pasteurella pestis* antibody in a plague control program. **Bull. Wild. Hlth. Org.**, 42: 451-459, 1970.
12. GASPER, P. W.; BARNES, A. M.; QUAN, T. J. et al. - Plague (*Yersinia pestis*) in cats: description of experimentally induced disease. **J. med. Entomol.**, 30: 20-26, 1993.
13. HUDSON, B. W. & KARTMAN, L. - The use of the passive hemagglutination test in epidemiologic investigations of sylvatic plague in the United States. **Bull. Wildl. Dis. Ass.**, 3: 50-59, 1967.
14. MACCHIAVELLO, A. - Some special epidemiological and clinical features of plague in Northeastern Brazil. Washington, Public Health Reports, 1941.
15. POLAND, J. & BARNES, A. M. - Plague. In: STEEL, J. H., ed. **CRC handbook series in zoonoses**. Section A: bacterial, rickettsial and mycotic diseases. Boca Raton, CRC Press, 1979.
16. POMPEU, M. M. L.; GOMES, T. N. A.; PARISE, M. et al. - Leishmaniose bubônica causada por *Leishmania (Viannia) brasiliensis* - estudo histopatológico de 33 casos. **Rev. Soc. bras. Med. trop.**, 27 (supl. 1): 91, 1994.
17. RUST, J. H.; CAVANAUGH, D. C. & O'SHITA. - The role of domestic animals in the epidemiology of plague: I. Experimental infection of dogs and cats. **J. infect. Dis.**, 124: 522-526, 1971.
18. WORLD HEALTH ORGANIZATION. - Plague in the Americas. Washington, WHO/PAHO, 1965. (Scient. Publ. n. 115, p. 44-68) .
19. WORLD HEALTH ORGANIZATION. - Fourth report of the WHO Expert Committee on plague. **Wld. Hlth. Org. techn. Rep. Ser.**, (447): 23-25, 1970.

Recebido para publicação em 29/11/1994.
Aceito para publicação em 01/12/1995.