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REVIEW

Rodent hosts and flea vectors in Brazilian plague foci: a review

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Abstract

Plague, caused by the *Yersinia pestis* bacterium, has several foci scattered throughout a large area from the Brazilian territory that ranges from the Northeastern State of Ceará to the Southeastern State of Minas Gerais and another separated area at the State of Rio de Janeiro. This review gathers data from plague control and surveillance programs on the occurrence and geographic distribution of rodent hosts and flea vectors in the Brazilian plague areas during the period of from 1952 to 2019. Furthermore, we discuss how the interaction between *Y. pestis* and some rodent host species may play a role in the disease dynamics. The absence of human cases nowadays in Brazil does not mean that it was eradicated. The dynamics of plague in Brazil and in other countries where it was introduced during the 3rd pandemic are quite alike, alternating epidemics with decades of quiescence. Hence, it remains an important epidemic disease of global concern. The existence of a large animal reservoir and competent vectors demonstrate a need for continuous surveillance to prevent new outbreaks of this disease in humans.

Key words: fleas, plague, rodents, transmission, vectors

INTRODUCTION

It has been historically accepted that plague, caused by the bacterium *Yersinia pestis*, arrived to Brazil during the third pandemic through the seaport of Santos, located in the State of São Paulo. The first Brazilian case of plague was reported in October 1899, and from then onward up to 1906, it assailed almost all the great Brazilian harbors. Prompt control measures taken by the health authorities successfully controlled the infection in the ports. However, these measures did not prevent the disease from spreading to inland cities via railways and other means of transportation. During the decades 1920–1930s, the disease began to afflict small towns, farms, and ranches (sítios) in the rural areas (Pollitzer 1954; WHO 1965).

Recently, whole genome sequencing of several Brazilian *Y. pestis* strains isolated from different sources and periods revealed a rather low genetic diversity amongst the strains when compared to strains from other countries. These findings provided evidence that the plague spread throughout the Brazilian territory starting from a single introduction (Vogler *et al*. 2019). Similar patterns can be observed in other locations affected during the 3rd pandemic (Cui *et al*. 2013).

Entering through seaports, the infection afflicted first the brown rat-population of *Rattus norvegicus*, and in the rural zone of the Northeast, the commensal (*Rattus*

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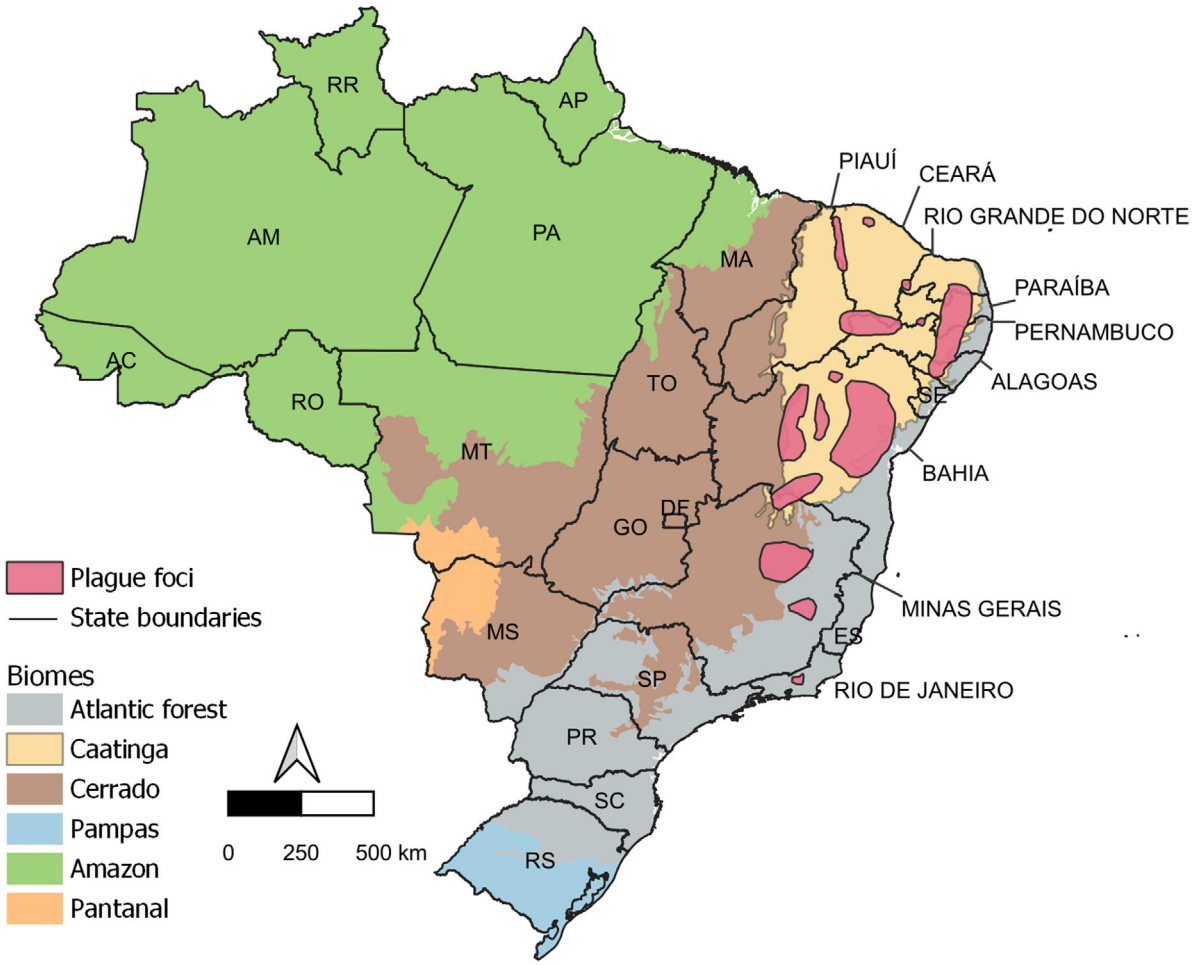

Figure 1 Map of Brazil showing the states, the biomes and the plague areas. The location of the Brazilian plague foci is shown in pink in the States of Piauí, Rio Grande do Norte, Paraíba, Pernambuco, Alagoas, Bahia, Minas Gerais, and Rio de Janeiro. Other colors represent the Brazilian biomes: Atlantic forest, Caatinga, Cerrado, Pampas, Amazon, and Pantanal.

rattus). Following its natural course, the infection encountered the susceptible autochthonous wild or sylvatic fauna and established several natural foci where the ecological conditions were suitable for its persistence (WHO 1965).

These foci persist until nowadays scattered through the Northeastern States of Ceará, Rio Grande do Norte, Paraíba, Pernambuco, Piauí, Alagoas, Bahia, and north of Minas Gerais, constituting the so called "Northeast focus." Another smaller and more isolated focus is located at the "Serra dos Orgãos" region in the southeastern State of Rio de Janeiro. (Giles *et al*. 2011; Almeida *et al*. 2020). The localization of the Brazilian foci is shown on Fig. 1.

Although no transmission to humans have been recorded in these areas since 2005 (Sousa *et al*. 2017; Zeppelini *et al*. 2018), the plague can still reemerge, due to its cyclical behavior, characterized by alternating periods of activity and quiescence (Stenseth *et al*. 2008). Understanding the determining factors for the occurrence of the infection is crucial to establish effective control measures to prevent spill over into human populations. Therefore, rigorous monitoring of host and vector populations allows an early detection of *Y. pestis* activity in the nature and consequently, a broader window of opportunity for triggering prompt control measures (Gage 2012).

Early records of plague in Brazil are sparse, as disease control was carried out by each State Department of Health. Only after 1935/1936, when the nationwide plague control and health policies were set, the data was properly collated and archived. Since 2002, disease control activities were decentralized to the municipal administrations (Tavares *et al*. 2012).

Over time, several studies have been carried out to assess the occurrence and distribution of the Rodentia and Siphonaptera faunas and to understand the possible role of different rodents and fleas in the maintenance, epizootization, and epidemization of plague in the focal areas. Biological features, susceptibility to infection, and vector ability were studied in laboratory using experimentally developed rodent and flea colonies (Karimi *et al*. 1974a,b; Almeida *et al*. 1981; Baltazard 2004; Tavares *et al*. 2012).

Following improvements in the understanding of geographical distributions, field behaviors, and genomic features, the nomenclature of small mammals has been updated and some of them were assigned to other genera or species (Burgin *et al*. 2018). As the accurate taxonomic identification is of utmost importance to understand the plague dynamics, the nomenclature of the rodent hosts was revised and updated following Bonvicino *et al*. (2015).

Here, we review and discuss information on the rodent hosts and flea vectors from the Brazilian plague foci gathered by the plague control and surveillance programs, between the years 1952 and 2019.

MATERIALS AND METHODS

Data collection

The present paper reviews the main features of plague rodent hosts and flea vectors, as well as their role in the dynamics of *Y. pestis* throughout the Brazilian territory during the last century. This work was carried out by consulting the literature and records from local control and surveillance programs, collected from 1952 to 2019, now available at the Nacional Reference Service of Plague (Serviço de Referencia Nacional de Peste) from the Aggeu Magalhães Institute (IAM, Recife, Brazil).

Rodents and fleas collection

Animal capture and handling methods varied according to the recommendations in each period. Further details can be found at the original publications (Freitas 1957; Bahmanyar & Cavanaugh 1976; Mills *et al*. 1995; Costa *et al*. 2017; Zeppelini *et al*. 2018). In short, rodents collection was carried out overnight using rodent live traps (type Chauvancy, Tomahawk, and Sherman); trapped animals were brought to a field processing site for collection of ectoparasites, sexing, and identification to species or genus; the ectoparasites were collected by brushing the rodents fur over a water container and transferred to small vials containing 2.5% saline for identification at the laboratory. The rodents were either kept in quarantine until death or euthanized.

Laboratory analysis

Dead animals were autopsied and examined for gross lesions, and tissue samples were taken for smear examination and culture for *Y. pestis* identification and isolation. Triturates of flea pools and rodent tissue samples were plated onto plain agar medium; the plates were incubated at 28 °C for 48 to 72 h and checked daily to observe the colony growth and the lysis by the anti-plague bacteriophage (Bahmanyar & Cavanaugh 1976; Karimi 1978). Serological surveillance was performed by the Hemagglutination assay (HA) with hemagglutination Inhibition control (HI) to detect specific antibodies for the *Y. pestis* capsular protein Fraction 1 or F1 (Chu 2000).

RESULTS AND DISCUSSION

Currently, the global incidence of human plague is the lowest reported by the WHO in 30 years (WHO 2019). The tendency of plague in Brazil also decreased since the years 1980, with the last confirmed human case in 2005 (Sousa *et al*. 2017; Almeida *et al*. 2020). However, it is not uncommon to observe a sudden reappearance of human cases after several decades of epidemiological silence in natural plague foci (Stenseth *et al*. 2008; WHO 2019). Therefore, understanding the disease dynamics is essential to establish effective surveillance strategies, capable of recognizing eventual epizootics that may precede spill overs to human populations. Hence, surveillance, monitoring, and control actions must be continued during plague silent periods (Gage 2012).

Due to the dissemination of *Y. pestis* from its original habitat to other regions of the globe, the dynamics of the pathogen–hosts–vectors interaction is unique in each ecosystem (Bramanti *et al*. 2016). To shed some light at the panorama of plague ecological features in Brazil, this review pinpoints the occurrence and distribution of plague-associated rodent hosts and flea vectors. We also discuss the possible roles of the different species in the dynamics of plague through an appraisal of the main studies carried out in different contexts from 1952 to 2019.

Inventory of wild-rodents fauna

In Brazil, the studies on wild rodents and their ectoparasites have become an important part of the activities of

the plague control programs as soon as the infection in the wildlife was surmised. The assessment of plague infection in wild rodents revealed a broad range of naturally infected species in the wild. These findings led to the development of experimental studies in the laboratory to determine the susceptibility of the most prevalent species and the vector capacity of the wild flea ectoparasites (WHO 1965). Several projects were carried out ever since: Inventory by the Nacional Plague Service (Serviço Nacional de Peste); Studies on the Chapada do Araripe plague focus; Plague surveillance program; Revaluation of the rodent populations.

From 1952 to 1955, the National Plague Service carried out a large inventory of the fauna of rodents and other small mammals and their ectoparasites in the plague areas of the Northeast to assess the occurrence and distribution of the Rodentia and Siphonaptera faunas. The collections were carried out in the peridomestic perimeter of rural areas (cultivated fields) and in sylvatic areas (remaining fragments of native vegetation) aiming to know the rodents diversity in different environments. The sylvatic ecotopes had higher diversity but lower abundance. During this study, 44 220 small mammals were caught, of which, 40 262 were rodents from 7 families and 22 genus and species (Freitas 1957).

From 1966 to 1974, a large research program took place in the plague focus of Chapada do Araripe plateau in the State of Pernambuco, focusing on understanding the mechanisms of the persistence, focalization, epizootization, and epidemization of plague in Brazil (Karimi *et al*. 1974a,b, 1976; Petter 1999; Baltazard 2004).

Other series of data on rodents occurrence was obtained along the activities of the plague surveillance program. For several decades the rodents were trapped, mainly at the peridomestic environment, for detection of the plague bacillus and/or antiplague antibodies. From 1978–1984, laboratory analysis and data collection were performed by the National Plague Reference Service. The surveys among the rodents were discontinued in 2007 due to new evidences that serological survey of plague antibodies among stray dogs is an efficient and more cost effective tool for plague surveillance (Tavares *et al*. 2012; Souza *et al*. 2017).

The last rodent inventory was carried out between 2013–2019 in the most prominent historical plague areas to assess the effects of both climate and anthropogenic changes on the plague-associated rodents populations (Costa *et al*. 2017; Zeppelini *et al*. 2018).

Rodents occurrence and distribution in the plague areas

The above inventories revealed the occurrence of 30 species of rodents distributed through 7 families: Cricetidae, subfamily Sigmodontinae (15 species), Caviidae (03 species), Echimyidae (05 species), Erethizontidae (01 species), Dasyproctidae (01 species), Sciuridae (02 species), Muridae (03 species). Figure 2 shows the distribution of the rodent species by the Brazilian states.

In the literature, some species can have their names modified through time, for example, *Necromys lasiurus* was previously named as *Bolomys lasiurus* and *Zygodontomys lasiurus pixuna)* (Bonvicino *et al*. 2015). Also the species *Pseudoryzomys* spp., *Euryoryzomys* spp., and *Oecomys* spp. were formerly misidentified as *O. subflavus*. Therefore, among the specimens referred to as *O. subflavus*, some individuals might be from any one of three genera (Costa *et al*. 2017). The genus *Oryzomys* was split into 11 genera and *Cerradomys* was coined to accommodate the *O. subflavus* group (Weksler *et al*. 2006). In this review, we followed the nomenclature revised by Bonvicino *et al*. (2015). The current nomenclature of the 30 species, caught in the peridomestic and sylvatic ecotopes from all the Brazilian foci can be seen in Table 1.

The commensal rat (*R. rattus*) is omnipresent in all plague areas from all the Brazilian states; they are found both inside the houses and in the peridomestic ecotopes and they are relatively resistant to the *Y. pestis* infection (Karimi *et al*. 1974a; Butler *et al*. 1982; Coutinho *et al*. 1982). Regarding the wild-sylvatic species, some were regularly caught in all the inventories while others were found fortuitously through an eventual sampling in specific biotopes directed to that species (Fig. 2).

In the Northeast plague area, *Necromys lasiurus* is by far the most common wild rodent among the Cricetidae/Sigmodontinae in all states (47.2%), followed in frequency by the species of *Cerradomys* (9.9%), *Oligoryzomys* (3.9%), *Wiedomys* (2.8%), *Akodon* (2.6%), *Calomys* (2.4%), and *Nectomys* (1.8%). Other species (*Holochilus, Oxymycterus, Rhipidomys*) occurred in very low numbers (Fig. 2).

In the plague area of the state of Rio de Janeiro, *Akodon* (37.4%) is the most prevalent species, followed by *Oligoryzomys* (18.9%), *Oxymycterus* (13.9%), *Nectomys* (10.4%), *Thaptomys nigrita* (0.8%), and others. Of note, of *T. nigrita* occurred only in this specific plague area while *Necromys* was absent (Fig. 2). Differences in the rodent and flea faunas from the two areas can be imputed to environmental differences between these biomes

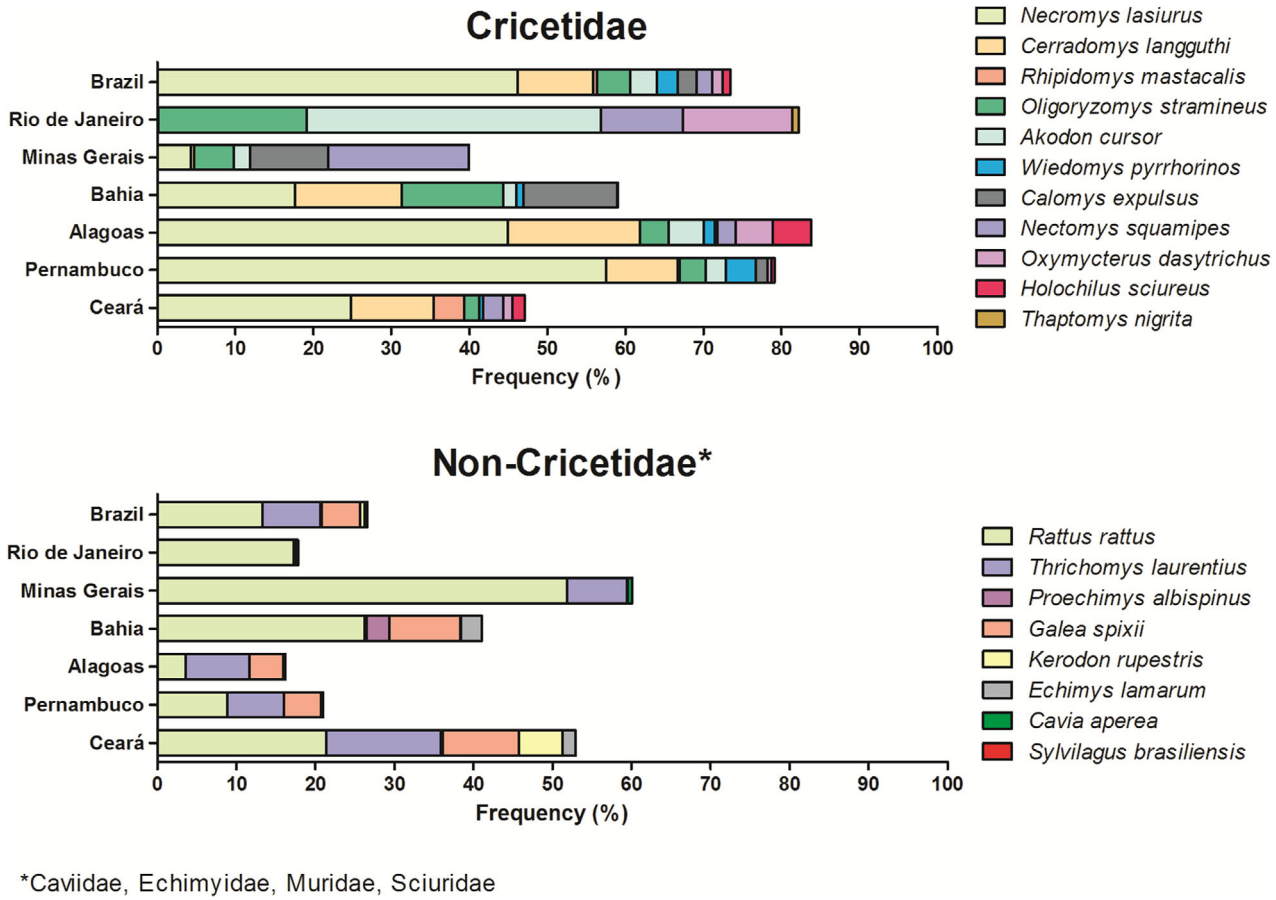

Figure 2 Distribution of the occurrence of the rodent species by Brazilian states. The bar labeled as Brazil represents the sum of the rodents from all the inventories in this review. Distinct species frequencies can be observed among the Rio de Janeiro (Southeastern) and the Northeastern foci; 176 × 130 mm (300 × 300 DPI).

(Fig. 1) and the primary or amplifier host is to be defined for the plague area of Rio de Janeiro.

It is noteworthy that some low prevalence species may eventually exhibit sudden and explosive pullulation or population growth named "ratadas." These phenomena are correlated with an unusual availability of a specific food (Sobral & Oliveira 2014). Two of these episodes were well documented in the State of Bahia, when two species that usually constitute a small fraction of the rodent population inventory (*Wiedomys pyrrhorinos* and *Calomys callosus*) were the major protagonists of the "ratadas" in 2002 and 2015, respectively.

Plague hosts and associated increasing in human plague risk

From the 30 rodent species described in the plague areas, 13 were found naturally infected, harboring either active infection or antibodies against *Y. pestis* (Table 1). The proportions of each species in positive rodents captured by the surveillance services in Brazil are represented on Fig. 3. Moreover, in addition to the 13 species, 5 others were presumed to be susceptible to have natural infection in the wild (Pollitzer 1954; WHO 1965), but the proof of the infection is yet to be established. Finally, there are no references of natural plague infection among the remaining 12 species (Table 1).

Results from studies performed at the Chapada do Araripe focus (PE) establish the species *Necromys lasiurus* as the epizootic (amplifier) host, spreading the infection to other species, even the less susceptible, as the commensal rat, and eventually causing spill overs to human populations. *N. lasiurus* is the more frequently infected by plague (Fig. 3) and carrying infected fleas (*Polygenis* spp.). They are highly plague susceptible, prolific, and ubiquitous; they shelter usually in sites covered by

Table 1 Rodent species from the Brazilian plague areas, current nomenclature, and status of natural infection

Natural infection with *Yersinia pestis*		
Confirmed[†]	Presumed[‡]	Undetected[§]
Cricetidae	**Cricetidae**	**Cricetidae**
Akodon cursor	*Wiedomys pyrrhorinos*	*Delomys dorsalis*
Calomys expulsus	**Caviidae**	*Euryoryzomys* spp.
Cerradomys langguthi	*Cavia aperea*	*Oecomys* spp.
Holochilus sciureus	*Kerodon rupestres*	*Pseudoryzomys simplex*
Necromys lasiurus	**Echimyidae**	*Rhipidomys mastacalis*
Nectomys squamipes	*Echimys lamarum*	*Thaptomys nigrita*
Oligoryzomys stramineus	**Sciuridae**	**Echimyidae**
Oxymycterus dasytrichus	*Sylvilagus brasiliensis*	*Euryzygomatomys spinosus*
Caviidae	**Muridae**	*Phyllomys* sp.
Galea spixii	*Rattus norvegicus*	*Proechimys albispinus*
Echimyidae	*Mus musculus*	**Sciuridae**
Thrichomys laurentius		*Guerlinguetus* sp.
Muridae		**Erethizontidae**
Rattus rattus		*Coendou prehensilis*
		Dasyproctidae
		Dasyprocta prymnolopha

[†]The species in which either active infection or plague antibodies were detected. [‡]Natural infection was not laboratory proved. [§]Without register of natural infection.

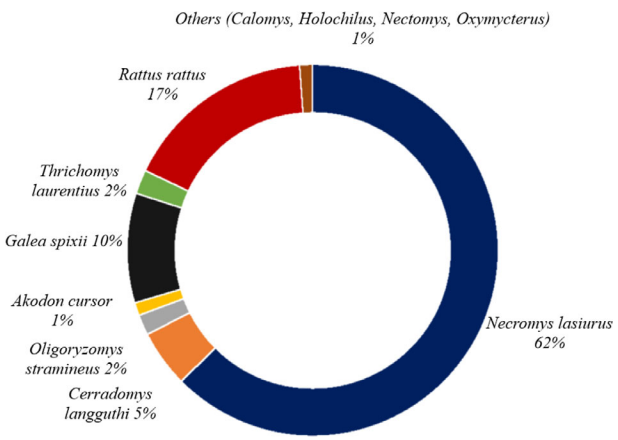

Figure 3 Species of rodents found naturally infected with *Yersinia pestis*. The values represent the proportion of each species in all either active infection or plague antibodies were detected; 158 × 130 mm (150 × 150 DPI).

a low and dense vegetation and in certain climatic conditions; they dig burrows. Their dispersal area overlaps the location of human cases. Therefore, the growth of *Necromys* population and the rise of its flea index (the ratio between fleas—the vector and rodents—the host) is acknowledged as a warning signal of the plague threat. Hence, permanent monitoring of the *Necromys* populations is recommended for the plague surveillance (Karimi *et al*. 1974a,b, 1976; Almeida *et al*. 1981; Baltazard 2004).

Factors of the persistence of the plague during quiescence

Several hypotheses have been proposed to explain the persistence of the plague bacillus during periods of quiescence: the traditional idea of rodent assemblage being the reservoir on the wild; survival of infected fleas in the burrows of the plague dead rodents; species or populations capable of developing a chronic infection (granuloma-like lesions) and infect vectors continuously (Gage 2012; Zeppelini *et al*. 2016).

These hypotheses can account for the conservation of the bacillus during short inter-epizootic periods but they

do not explain the decade-long silent periods that sometimes occur between two epidemics.

Other hypotheses can better explain this phenomenon: The maintenance of the bacillus could take place inside the rodent burrows, where the microclimate would allow its long-term survival on the carcasses of rodents, in the corpses of fleas, or in the bedding of dead animals or even in soil protozoa inhabitants. The epizootic would rekindle by reoccupation of the infected burrows by new rodents which would be contaminated by digging in these sites (fossorial and telluric mechanism) (Baltazard 2004; Drancourt *et al*. 2006).

Another possible explanation is that the infection could be maintained at the enzootic state in rodents and their fleas: After the term of the epizootic by depletion of susceptible hosts, the infection would remain in a chronic form in resistant populations. According to Karimi *et al*. (1974a, 1976), susceptible rodents are those whose mortality is almost 100% during an epizootic and resistant species are those in which at least 30% of animals survive the epizootic. Occasionally, the animals' resistance would be put at fault (aging, stress, famines, overcrowding). This failure could lead to a sepsis in a few animals from which fleas become infected. The fleas would be able to keep the bacilli until they meet new hosts. The transmission cycle would thus be kept at a low rate: there would be a long period of conservation of the bacillus in the rodent's organism and in the flea until the density of the populations of susceptible animals promotes transmission to an epizootic frequency (Poland & Barnes 1979; Gage 2012).

An attractive hypothesis for the long-term conservation of the *Y. pestis* in the Northeast foci was the permanence of the plague bacterium among the high populations of *Trichomys apereoides* (Echimyidae) and *Galea spixii* (Caviidae). These species find shelter into supposedly permanent habitats such as chinks and crevices of rocks. *T. apereoides* is highly plague-susceptible and could harbor, carry, and disseminate infected fleas. The *Galea* is plague-resistant and could maintain viable bacteria encapsulated into micro abscesses (Karimi *et al*. 1974a; Coutinho *et al*. 1982).

On the other hand, Petter (1999) assumed that the commensal *R. rattus* might play a role in maintaining the enzootic cycle. In the rural area they live either inside the houses where they make their nests in holes in the ground or walls and dig burrows on the soil, and in the peridomestic areas (Karimi *et al*. 1976). Moreover, they also could maintain viable bacteria encapsulated into micro abscesses (Butler *et al*. 1982; Coutinho *et al*. 1982), allowing periodic flea re-infection and consequently, reactivation of the epizootic cycle. In spite of the studies the enzootic (maintenance) plague hosts in the Brazilian plague foci is not yet defined nor the maintenance mechanism.

Studies about the fossorial and telluric plague

Several studies were performed to assess the hypothesis of conservation of the *Y. pestis* on the soil and the fossorial and telluric plague (Baltazard 2004; Drancourt *et al*. 2006). In our experiments, the plague bacillus was maintained successfully on sterile soil during 12 months into tubes tightly closed and buried into different environments in different conditions and analyzed at different time points. The fossorial ability and contamination with infected soil while digging was studied in experimental terrariums build with *Rattus rattus, Necromys, Thrichomys*, and *Kerodon* (Karimi *et al*. 1976; Almeida *et al*. 1981; Baltazard 2004). After the animals settled into the terrariums, laboratory infected fleas (*Xenopsylla* or *Polygenis*) were added; the terrariums were sealed and inspected afterward by introduction of naïve detectors and examination of samples of the soil and littering from the burrows. Furthermore, samples from soil and littering from the burrows from the fields were collected during the epizootic period and analyzed for *Y. pestis* detection (Karimi *et al*. 1976; Baltazard 2004). These experiments did not support the hypothesis and the plague fossorial and telluric was not demonstrated in Brazil.

A bias in these studies is that only traditional bacteriological techniques (culture and inoculation of laboratory animals) were then employed for the detection of the *Y. pestis* from the burrow or terrarium sample remains. The molecular biology techniques later introduced into the plague program were not available (Leal & Almeida 1999; Melo *et al*. 2003; Chioratto *et al*. 2007).

Rodent flea ectoparasites and role in plague transmission

The rodents collected through the several inventories harbored a total of 14 species from the families *Ctenophthalmidae* (01), *Pulicidae* (03), *Rhopalopsyllidae* (09), and *Stephanocircidae* (01). The same *Ctenophthalmidae* and *Pulicidae* species occurred in both plague areas (Northeast and Southeastern foci), but the *Stephanocircidae* only in the southeastern area. Different *Rhopalopsyllidae* species occurred in each area and one (*Polygenis tripus*) in both (Guimarães 1972; Brasil *et al*. 1989; Carvalho *et al*. 2001). The species of fleas and area of occurrence are given in Table 2.

Xenopsylla cheopis, the so-called rat flea and historically considered the classic plague vector, was prevalent

Table 2 Main flea species found in the plague foci in Northeast and Serra dos Órgãos (RJ), Brazil

Family/species	Northeastern foci	Serra dos Orgãos (RJ) focus
Stephanocircidae		
Craneopsylla minerva		X
Ctenophthalmidae		
Adoratopsylla antiquorum	**X**	X
Rhopalopsyllidae		
Polygenis atopus		**X**
Polygenis pygaerus		**X**
Polygenis pradoi		**X**
Polygenis rimatus		**X**
Polygenis roberti		**X**
Polygenis roberti roberti	**X**	
Polygenis bohlsi bohlsi	**X**	
Polygenis tripus	**X**†	**X**
Polygenis bohlsi jordani	**X**†	
Pulicidae		
Pulex irritans	**X**†	**X**
Xenopsylla cheopis	**X**†	**X**
Ctenocephalides felis	**X**†	**X**

†Naturally infected with *Yersinia pestis*.

among the commensal rats (*R. rattus*). It can also be found among the wild rodents but in very small number.

The vector capacity and the potential role of *Polygenis* spp. in the genesis of human plague was subject of debate (WHO 1965; Baltazard 2004). The species of *Polygenis* were considered inefficient vectors by the current notion that transmission of *Y. pestis* by blocked fleas represents the primary, if not almost exclusive, model by which flea-borne plague transmission occurs. This concept is often referred to as the proventricular blockage model or classical transmission model. Therefore, transmission by unblocked fleas generally was assumed to be minimal and relatively unimportant compared to transmission by blocked fleas (Gage 2012). Currently, other mechanisms of transmission are recognized such as mechanical transmission (mass transmission) by large number of flea bites and early phase transmission (EPT) or transmission by unblocked fleas during the first few days after becoming infected and before a complete blockage can form (Eisen & Gage 2011).

Studies on the plague transmission by *Polygenis bohlsi jordani* and *Polygenis tripus* using flea colonies raised in the laboratory (Baltazard & Eftekhari 1957) proved that they are efficient plague vectors and they might play important roles in the spread of plague during epizootics in the Northeast foci (Karimi *et al*. 1974b; Baltazard 2004).

As for *P. b. jordani*, the studies revealed that they survive for 30 days after a septicemic meal; one single specimen could transmit the infection to susceptible rodents; they are able to bite and to feed on humans (Karimi *et al*. 1974b). Therefore, besides the ability to transmit the bacterium among the rodents they also could transmit the infection from the rodents to the humans. The analysis of the occurrences during the epidemic period suggested that they could answer for numerous human infections. Therefore, they were considered the most effective vector on the northeast foci and their indices an efficient alarm signal of plague activities in the nature (Baltazard 2004).

In the foci of the Northeast, *P. bohlsi jordani* and *P. tripus* are the predominant species regarding the frequency among the wild rodents, while in the Serra dos Orgãos, the predominant species are *P. rimatus* and *P. pradoi* (Guimarães 1972; Karimi *et al*. 1974b; Brasil *et al*. 1989). The vector ability of these species remains unknown, as well as the role if any, of *P. tripus* on this focus.

CONCLUSION

Until the 1970s, Brazil experienced recurrent cycles of plague activity interspersed with 5 to 10 years of quiescent periods and geographic dispersion. However, some of the most relevant plague areas from Brazil had no reports of human cases for more than 50 years and tend to quiescence ever since. The absence of new cases must be accurately assessed, as there are no fair explanations. Considering the analysis of its secular tendency, this could be just a long-term cyclical phenomenon. Since 1986, the presence of *Y. pestis* bacterium has not been detected among the rodents or their fleas and serological surveillance of sentinel animals shows a decreasing trend. Of note, the amount of sentinel animals analyzed by serosurveys reduces every year, and declining rodent populations and flea index was also observed and no rodent die offs reported.

This panorama requires constant attention for eventual fluctuations on the rodent population as well as its ectoparasites that may be a signal of plague activity. Several hypotheses have been put forward to explain the persistence of the plague bacillus during periods of quiescence and the causes for re-emergence. An eventual reappearance of plague activities could derive from social

degradation, climate changes, expansion of rodents' population, and epizootization.

In summary, the dynamics of plague in Brazil and in other countries where the disease was introduced during the third pandemic are quite alike, alternating from epidemics to decades of quiescence. It is, however, of most importance to study the local population of reservoirs and competent vectors to comprehend how these species are affected by *Y. pestis* and how they can cause spill over to humans. Combined with continuous serologic surveys, these data provide key information for proper plague control in the given region. It is important to highlight that the absence of human cases nowadays in Brazil does not mean that it is eradicated and plague remains an important epidemic disease of global concern. The existence of a large animal reservoir and competent vectors demonstrate a need for continuous surveillance to prevent new outbreaks of this disease in humans.

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