## REFLECTIONS ON THE EPIDEMIOLOGY AND PREVENTION OF PLAGUE<sup>1</sup>

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In spite of the spectacular advances made in medicine, the ancient scourge of plague continues even today to be a constant threat to vast numbers of human beings in the underdeveloped areas of the world. The author traces its history, describes the cycle of transmission to humans through rodents and fleas, and furnishes data on its incidence.

#### Introduction

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Plague, a disease caused by *Pasteurella pestis*, is primarily and basically a zoonosis found in rodents, though human beings can contract the disease if they live in the same ecological environment as rodents that are reservoirs of the infection.

From time immemorial, plague has dogged man's footsteps, and at various periods in history it has taken a bitter toll of human lives. In some areas it has actually altered the social structure and upset the economic situation, and it is the disease that perhaps more than any other has caught the imagination of poets and writers and led them to depict its horrors.

Wu-Lien-Teh, reviewing the history of plague on the basis of Sticker's researches, cites the Bible (1 Samuel) as the earliest reference to the occurrence of plague, which decimated the Philistines in 1320 B. C.

Other references to the antiquity of plague are found in the writings of the physician Rufus of Ephesus, who speaks of the existence of plague in the year 1000 B. C. in Libya, Egypt, and Syria. Another ancient historical reference to the disease is the account of the plague that began at Pelusium in Justinian's reign in the fifth century.

Writing on the history of plague in China in more recent times, Wu-Lien-Teh (1936) tells how in 1792 at Chaochow, in Yunnan Province, Shih-Tao-Nan wrote a poem "Tien Yü Chi," a section of which, entitled "Rat Death," describes the scourge of plague in that area. The poet died of the plague a short time afterward. Later on, as recently as the end of the 19th century, a Moslem rebellion and troop movements in Yunnan Province brought the plague to Canton and Hong Kong in 1894, and the recent pandemic was propagated from that international port. It was not until the pandemic occurred, and obviously as a result of modern scientific development, that epidemiological research brought a knowledge of plague in all its aspects, including the reasons for its persistence in certain foci.

In spite of the enormous body of knowledge regarding plague and the technical resources now available for its prevention, even today—when the degenerative diseases, industrial accidents, air pollution, and contamination of natural water sources are emerging as the major health problems—this communicable disease continues to pose a permanent threat for vast population groups in developing areas.

## Natural Foci of Plague

#### Natural Primary Foci

The oldest and most active plague area in the world is the Central Asian Plateau, bounded on the south by the Himalayas, on the east by the Tien Shan mountain chain and Mount

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Altay, and to the northeast by the Shing-Shan and Stanovov ranges.

This area, regarded as the ancestral cradle of plague, with the marmot as the primary reservoir, lies between parallels 30 and 50 south latitude while in the east it stops short of the Pacific coast, reaching the middle course of the Sungari.

The area of the plague bacillus today in the Eurasian continent as a whole extends northward slightly beyond latitude 50 into the Transhaikal area, and in the extreme east to 51 degrees latitude, on the east bank of the Ural River.

In this vast region there are many natural foci (microfoci) where, as Kucheruk says (1967), the plague agent exists independently of human activity, being a normal and authentic member of the local biocenosis. The natural focus of the desert region of southcentral Asia (Kazakhstan) alone is 2 million square kilometers in area, stretching from the Ural River to the north of the Aral Sea, and ending at the western end of Lake Balkash. This area coincides with the northern edge of the desert region which is the habitat of the gerbil (Rhombomys opimus), the chief reservoir in that part of the world (Petrov, 1967).

The plague area is bounded on the extreme northwest by another focus, the Volga-Ural. less extensive in size (200,000 Km<sup>2</sup>), the reservoirs here being Citellus pygmeus, Meriones meridianus, and M. tamaricinus (Mironov, 1967); and in the southwest it fringes the Asia Minor focus, where the reservoirs are Meriones libycus, M. persicus (highly resistant), and M. tristami and M. vinogradovi (highly sensitive) (Baltazard, 1960).

The world map (Figure 1) shows the natural foci plague areas in Eurasia, Africa, and the Americas.

# Secondary Natural Foci

The area of distribution of P. pestis throughout the world comprises at the present time not only the vast primary natural focus of Eurasia. but the new areas of "sylvatic" or wild-rodent

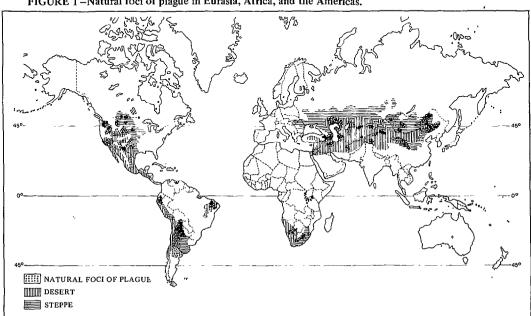


FIGURE 1 - Natural foci of plague in Eurasia, Africa, and the Americas.

Source: V. V. Kucheruk. "On the Paleogeness of Natural Foci of Plague" Proceedings of a Symposium, Prague, 1963.

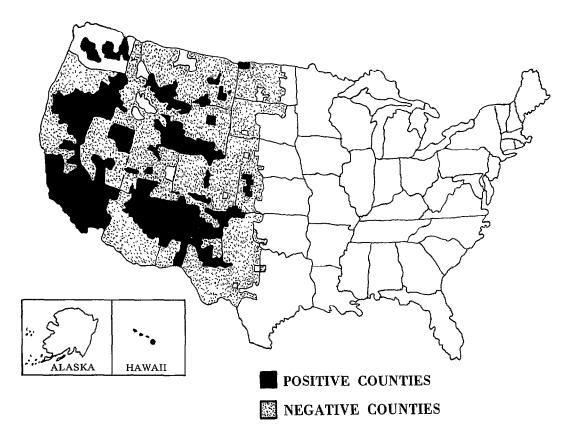
plague in Africa and the Americas, of recent origin. These foci, which have emerged since the recent pandemic, have come about as a result of the transference of the plague bacillus from common rats and mice to the indigenous wild rodents.

Africa. The natural foci here are situated in the southern part of the continent, in the Republic of South Africa, South West Africa, and Botswana, and also in the areas around Lakes Victoria, Albert, and Edward, in the Congo, Uganda, Kenya, and Tanzania.

In the African foci the primary reservoir is the gerbil (Tatera lobengulae) and intermediaries are *Mastomys coucha* and *Rhabdomys pumilio* (Jorge, 1928).

North America. The North American focus comprises approximately 40 per cent of the land area of the United States of America, embracing 131 counties in 15 of the western states (Figure 2). Ground squirrels of the species Citellus are the main reservoirs, but 10 wild rodent species and two Lagomorpha have been found infected: Citellus, Neotoma, Peromyscus, Eutamias, Tamiasciurus, Claucomys, Marmota, Thomomys, Microtus, Reithrodontomys, Lepus, and Silvilagus (Kartman, 1958).

FIGURE 2-Distribution of *Pasteurella pestis* infection in wild rodents and fleas in the United States of America, by counties, 1908-1964.



Source: Reproduction of figure in *Plague Epidemiology*, 1966. H. E. Stark, B. W. Hudson, and B. Pittman. National Communicable Disease Center, Atlanta, Georgia, 1967.

In 1939 plague was detected in Canada in areas bordering on the United States, and also in northern Mexico (Coahuila State) close to the U.S. border.

South America. The plague foci in South America, all of them independent, are situated in the following regions:

- a) Venezuela. The focus covers a small area of dry savannah in Miranda and Aragua States. Plague has been detected in *Sigmodon hirsutus* and *Heteromys anomalus* (De la Barrera, quoted in *Plague in the Americas*, PAHO, 1965).
- b) Peru-Ecuador. The focus is located in a continuous zone between northern Peru (Ayabaca and Huancabamba, Departments of Piura and Cajamarca) and southern Ecuador (Loja, El Oro, and Chimborazo a little farther north). The reservoirs are Akodon, Sigmodon, Oryzomys, and Sciureus (Macchiavello, 1955).

It is noteworthy that plague originating in this focus, situated in the mountainous inter-Andine region, has already reached the Amazon Basin, and in 1963 and 1964 cases occurred in humans in Bagua Province on the right bank of the Marañón River.

- c) Argentina-Bolivia. The focus extends from northern Argentina (Santiago del Estero, Córdoba, Tucumán, Salta, Jujuy) as far as Bolivia (Tarija, Chuquisaca, Santa Cruz). The reservoirs are *Caviidae* and *Graomys* (De la Barrera, 1965).
- d) Brazil. There are two independent areas of foci: the northeast focus, running along the arid zone of Bahia as far as northern Minas Gerais; and the Terezópolis focus, isolated and covering a small area of the Serra do Mar, in the districts of Terezópolis and Nova Friburgo.

Plague has already been found in the following wild rodents in Brazil: Zigodentomys pixuna, Cercomys cunicularius laurentius, Cercomys cunicularius inermis, Galea spixii, Hesperomys tener, Kerodon rupestris, Holochilus sciureus, Oryzomys subflavus, Thomasomys pirrhorhinus, Silvilagus brasiliensis, Cavia aperea (Silva, 1938; Macchiavello, 1941; Simond, 1951; Neves, 1956; De la Barrera, 1965).

Kucheruk (1963), studying the paleogenesis of the natural foci, gives his opinion that the North American focus is likewise primary, dating from a remote geological age, and related to the appearance of reservoir rodents of the same family (Sciuridae and Cricetidae) and also to the chief vector (Oropsyllus) in both continents. The distribution of the natural foci follows the desert and semiarid lands, the same being true of the foci of Africa and South America. Other authors (Jorge, 1928; Macchiavello, 1941; Pollitzer, 1954) consider that the foci in the Americas and in Africa originated with the pandemic that occurred at the beginning of the present century when plague-ridden Murinae from the synanthropic fauna were transported by the sea route (Rattus norvegicus, R. rattus, R. alexandrinus, R. frugivorus, Mus musculus).

If in fact the plague agent reached North America on earlier occasions via the Bering Strait, presumably it would first have infected the fauna of Canada (Pollitzer, 1954). Another point worth considering is the biochemical composition of the strains of *P. pestis*. The American race is glycerol-negative and of "oceanic" race (Berlin and Borzenkov, quoted by Korobkova, 1967) whereas the strain found in the Asian foci is of the "continental" race which acidifies glycerol media.

#### Structure and Dynamics of the Natural Foci

The research conducted by Pavlovski<sup>3</sup> on natural foci of communicable diseases has suggested new directions, since 1939, for the study of the structure and dynamic evolution of plague foci; and it has been demonstrated that the pathogenic agent, the reservoir, and the vector have a biological kinship in their biotypes, since they exist permanently in natural conditions as co-members of the local biocenosis.

If we apply Pavlovski's theory to the study of the ecology-epidemiology of plague foci, in

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<sup>&</sup>lt;sup>3</sup>Pavlovski, E. N. "On the Theory of Natural Foci of Diseases Communicable to Man." *J Gen Biol* (Moscow) 7:3-33, 1946.

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other words, if we investigate thoroughly all the ecological factors involved, we can learn something of the laws governing the process by which plague is perpetuated and propagated in nature, and thus acquire the necessary basic knowledge for combating and controlling the disease.

The mechanism by which *P. pestis* survives in the interepizootic periods is still an unknown factor. There are various hypotheses to explain the phenomenon, the one most commonly accepted being the permanent propagation of the plague agent through sporadic cases of acute and subacute infection, following the rodent-flea-rodent chain of transmission, with a more prolonged sojourn in the organism of the flea, especially during the cold season.

Petrov (1967), writing about the conservation of plague in fleas, says that they preserve the bacillus in their organism during the cold winter months and actively transmit it to animals during the hot season. He also says that the bacillus can be kept alive inside the rodent as well, and he demonstrated that "the process of infection among gerbils (M. libycus) can become chronic when the plague agent is kept for several months, without losing its virulence, inside the parenchyma, enclosed in a capsule of adipose abscess tissue. In due course, for unknown reasons the capsule disintegrates, and the process of general infection takes place, with growth of bacteria. This leads to the infection of the fleas and reactivation of the epizootic process."

The work of the Soviet researchers shows that "in a natural focus of plague the fleas are not only responsible for the transmission of the plague agent; they also help it to survive over a long period... adult fleas contaminated in natural conditions have been found to stay alive for a long time, up to 210 days being recorded in the warrens of the larger gerbils" (Bibikova, 1967). Under experimental conditions, even longer periods have been observed (Golov and Yoffe, 1928, and Mikulin, quoted by Bibikova, 1967). Macchiavello (1941) mentions the flea as a temporary reservoir in the Brazilian northeast.

The theory of the perpetuation of plague in a poly-host focus was launched in Russia in 1949 by Kalabukhov, who stressed the importance of this focus for the maintenance of the enzootic, since the varying degree of susceptibility in the different rodent species furnishes the plague agent with sensitive elements at all times (Kalabukhov, 1965).

The studies conducted by Baltazard et al. in the Kurdistan focus interpret the perennial nature of plague in foci of long standing as being the result of "the presence of the resistant rodent/susceptible rodent complex." The perpetuation of P. pestis demanded a dense population of highly resistant rodents capable of surviving the most virulent plague epizootic in large numbers, sedentary rodents capable of maintaining the infection of fleas in their warrens deep underground, which are permanent structures with a favorable microclimate (Baltazard, 1960).

Recently, in 1964, still researching in Kurdistan, Baltazard noted that *P. pestis* survives in the soil of rodents' warrens for a long time following an epizootic.

In 1967 Mollaret succeeded experimentally in keeping the plague bacillus alive in earth, in conditions similar to those of the microclimate of rodent warrens, and recorded *P. pestis* as surviving for more than seven months.

Experiments carried out by Baltazard's team (1964), in an attempt to reproduce the telluric cycle of plague, demonstrated the importance of the "burrowing of meriones in soil contaminated with a culture; they were literally stricken with plague."

## Incidence of Plague throughout the World

Following the epidemic outbreaks in the early decades of this century, urban plague has receded everywhere, as a result no doubt of development, more hygienic housing, the dying-out of plague in urban areas, and modern methods of reservoir and vector control.

In South America, urban plague had practically disappeared, but its incidence has been on the increase since 1960. Tables 1, 2,

TABLE 1-Reported cases of plague in Africa, 1950-1967.<sup>a</sup>

Country	1950-1954	1955-1959	1960	1961	1962	1963	1964	1965	1966	1967
Botswana	55	<del>_</del>			_					
Cameroon		_	_	1	_	_	_	_	_	_
Congo	172	102	26	3	4	4	2	16	8	7
Ghana	6	_	_	_	_	_	_	_	_	_
Kenya	76	127	36	3	3	2	1	_	_	1
Lesotho	11	-	_	_	_	_	_	_	_	_
Madagascar	834	120	6	4	28	9	6	38	9	8
Malawi		20	_			30	_			_
Mauritania	2	_	_	_	_		_		_	_
Namibia <sup>b</sup>			_	9	80	4	17	_	_	_
South Africa	90	26	1	1	7	_	1	_	_	_
Tanzania	848	10	_	_	2	_	513	1	_	_
Uganda	30	_		_	_		_	_	_	_
Upper Volta	_	_	_	_	_	_	-	_	1	
Zambia	10	29	_	_	_	_	_	_	_	

<sup>a</sup>World Health Organization. Epidemiological and Vital Statistics Report No. 20(5), 1967. World Health Statistics Report No. 21(4), 1968.

bFormerly South West Africa.

and 3 show (a) a falling-off in the incidence of plague in African and Asian countries, except in Vietnam, where 5,574 cases were recorded in 1967; and (b) an increase in the frequency of cases in the South American foci since 1960.

Plague in South America today is essentially rural; it is linked with the primitive type of rural dwelling, but it is widespread in the cultivated areas. The way of life of the rural dweller, engaged in tilling the earth and living in precarious housing built of materials that offer no protection against rodent infestation,

provides highly favorable conditions for the reservoir fauna that breed in the environment surrounding human dwellings. This has become the ideal "habitat," man-made for wild rodents, which find food in abundance in the harvested crops and shelter in the stone walls separating the fields.

In conditions so favorable for the propagation of the zoonoses, it is surprising that the endemic index is not even higher. The annual variation of incidence depends on many factors density of the rodent and flea population,

TABLE 2-Reported cases of plague in Asia.<sup>a</sup>

Country	1950-1954	1955-1959	1960	1961	1962	1963	1964	1965	1966	1967
Burma	3,488	887	22	41	73	34	11	36	48	117
Cambodia	38	15	_	_	_	_		_	_	_
India	22,450	891	78	404	686	205	109	14	11	6
Indonesia	11,444	520	_	_	_	_	_	_	_	_
Iran	50	12	_	-			_	_	_	
Laos	2	_		_	_	26	_		_	_
Philippines		2	_		_		_	_	_	_
Thailand	71	_	_		_	_	_	_		_
Vietnam	205	53	14	8	29	115	297	374	2,843	5,574

<sup>a</sup>World Health Organization. Epidemiological and Vital Statistics Report No. 20(5), 1967. World Health Statistical Report No. 21(4), 1968.

TABLE 3-Reported cases of plague in the Americas, 1950-1967.<sup>a</sup>

Country	1950-1954	1955-1959	1960-1964	1965-1967
Argentina	4	1		
Bolivia	96	48	134	155
Brazil	156	109	494	324
Ecuador	276	218	960	559
Peru	238	151	568	903
United States of America	4	6	6	16
Venezuela	14	3	7	

<sup>a</sup>World Health Organization. Epidemiological and Vital Statistics Report No. 20(5), 1967. World Health Statistical Report No. 21(4), 1968.

previous epizootics, meteorological conditions, agricultural production, etc.—which affect the reservoirs and/or vectors.

#### Incidence of Plague in Brazil

There is no record of the occurrence of plague in Brazil prior to the year 1899, when it invaded the country via the port of Santos. After infecting many cities along the coast, the disease reached the interior, especially the northeast, and gradually spread through the rural areas, where it found favorable conditions for survival and propagation in the fauna of indigenous rodents. Thus two independent plague foci were formed: the northeast and Terezópolis.

Northeast focus. This covers a wide area centered around the semiarid zone with a rainfall of under 1,000 mm, and stretches over the dry region into Bahia, as far as northern Minas Gerais.

The area is literally dotted with apparently independent foci, mostly located in the orographic system of the region, where conditions suit this particular zoonosis. The foci areas include the following:

Ceará: Regions of Serra de Ibiapaba, Serra de Baturité, Chapada do Araripe (north slope). Pernambuco: Chapada do Araripe (south slope), Araripina, Exu, Bodocó, Serra do Triunfo, Serra de Garanhuns, Bom Conselho, Aguas Belas, Caruaru, São Caetano, Pesqueira.

Paraiba: Serra da Borborema, Umbuzeiro, Campina Grande, Cuité, Cel. Ezequiel (R.N.). Alagoas: Palmeira dos Indios, Quebrangulo,

Arapiraca, Santana Ipanema, Mata Grande.

Bahia: Regions of Senhor do Bonfim, Feira de Santana, Jequié, Vitória da Conquista.

Minas Gerais: Medina, Pedra Azul, Salinas, Tumiritinga, Itanhemi.

Terezópolis Focus. This is an isolated focus, confined to a small area in the Serra do Mar, within the boundaries of the districts of Terezópolis and Nova Friburgo. It covers a tropical forest area where the rainfall is more than 1,000 mm (Figure 3).

The present endemic area covers approximately 230,000 km<sup>2</sup> with a rural population of more than 3 million and including 189 municipalities in eight states (Table 4). Between 1935 and 1967, 4,213 cases of plague were

FIGURE 3-Present endemic plague areas in Brazil.



TABLE 4-Endemic plague area in Brazil, foci in 1958-1967.<sup>a</sup>

State	Municipalities with plague foci	Rural population (1960)	Area in Km <sup>2</sup> (1960)	Focus centers
Ceará	27	462,340	21,907	186
Rio G. do Norte	5	48,670	922	21
Paraíba	9	147,857	5,195	30
Pernambuco	44	813,764	34,323	238
Alagoas	20	271,183	8,561	91
Bahia	68	1,180,668	129,066	328
Minas Gerais	14	188,396	28,154	75
Rio de Janeiro	2	37,052	1,858	2
Total	189	3,149,930	229,986	971

<sup>&</sup>lt;sup>a</sup>Prophylaxis Division, National Department of Rural Endemic Diseases.

TABLE 5-Reported human cases of plague, by state, Brazil, 1935-1967.

		States										
Year	Piauí	Ceará	R.G. do Norte	Paraíba	Pernam- buco	Alagoas	Sergipe	Bahia	Rio de Janeiro	S. Paulo	Minas Gerais	Total
1935 1936 1937 1938 1939 1940 1941 1942 1943 1944 1945 1946 1947 1948 1949 1950 1951 1952 1953 1954 1955 1956 1957 1958 1959 1960 1961 1962 1963 1964 1965 1966 1967	16 — — — — — — — — — — — — — — — — — — —	148 146 2 16 5 11 2 4 22 69 31 175 3 3 10 3 6 4 7 16 13 145 36 30 106 1043		19 4 5 5 1 19 4 	421 90 23 94 44 104 145 16 25 22 151 66 47 71 24 11 7 19 5 2 3 3 4 12 ——————————————————————————————————	19 555 83 112 13 366 9 2 17 255 1 19 3 41 2 — 5 — 13 12 1 3 60 4 6 553	1	72 5 2 57 36 20 257 52 17 4 1 3 4 20 20 25 16 13 15 14 12 37 13 10 785	12 -7 -7 	2 31 1 4 	3 3 7 9 	571 359 36 146 111 255 302 35 66 154 192 333 88 386 96 55 10 65 10 4 37 28 106 36 39 285 119 48 157

TABLE 6-Reported cases of plague, decade 1958-1967,<sup>a</sup>

	Posi	tive	Suspected			
State	Case	Death	Case	Death		
Ceará Rio Grande	353	15	49	4		
do Norte	21		13	2		
Paraíba	42	3	16	1		
Pernambuco	174	22	180	19		
Alagoas	99	8	41	7		
Bahia	155	37	414	95		
Minas Gerais	4	2	160	6		
Rio de Janeiro	11	2	-			
Total	859	89	873	134		

<sup>a</sup>Prophylaxis Division, National Department of Rural Endemic Diseases.

reported in 11 states (Table 5). During the 10-year period 1958 to 1967, 859 cases were reported, with 89 deaths, or a case-death rate of 10.4 per cent (Table 6).

# Some Aspects of Plague Prevention

The objectives of programs to combat plague are: (a) to reduce mortality (prompt treatment); (b) to prevent secondary cases (chemoprophylactic treatment of contacts); (c) to interrupt the domestic transmission cycles rodent-flea-man, rodent-flea-rodent, man-flea-man, and man-flea-rodent (disinsecting); (d) to carry out deratization (where possible with rodenticides); (e) to improve housing (health education measures).

Immunization is the measure recommended for preventing man from being infected in the fields in the event of a wild animal epizootic; but at present there is no vaccine of high immunizing potency available.

The vaccine considered to be the best is that prepared with the EV strain, but inoculation has to be repeated every year, which is not

practical, particularly as it would have to cover 90 per cent of the population to be effective.

Control measures are nearly always carried out late, generally after the epizootic has broken out, in other words, at the development stage.

Failure to take control measures in good time is the consequence of lack of field research, which can help to detect plague before the epizootic process is under way.

It should be pointed out that in the foci of underdeveloped areas today, antiplague campaign laboratories tend to be staffed and equipped for diagnosis only, not for research. Yet systematic field investigations are essential for detecting plague before its epizootic manifestations appear and determining where and when to take control measures.

## Summary

The author outlines the geographic distribution of the primitive or "natural" foci of plague, and discusses the spread of the zoonosis to rodent reservoirs in new areas. Emphasis is laid on the importance of the study of the epidemiological peculiarities of a particular plague focus, on the need to determine its structure and dynamics by means of research into the ecological environment in which P. pestis thrives, as a basis for the control of the disease. Data are given on the incidence of plague throughout the world during the period 1950-1967, and particularly in Brazil between 1935 and 1967, with special reference to the area where it is endemic, describing the larger and more important foci and giving corroborative data in a series of tables and figures. Various preventive measures that can be taken in underdeveloped areas are discussed, especially prompt treatment, interruption of the transmission cycles, destruction of the rodent and flea vectors, and improved Immunization is recommended as the answer to many of these problems, together with systematic research on vaccines and field investigations for the early detection of plague.

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