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PLAGUE STUDIES *

9. Epidemiology

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SYNOPSIS

Epidemiological aspects of (*a*) bubonic plague and (*b*) primary pneumonic plague are discussed separately in this study. The cause, spread, and persistence of bubonic outbreaks are dealt with.

In the case of primary pneumonic plague, the author systematically reviews the factors influencing the spread of the disease : climatic and social conditions, infectivity of the patients, immunity, and control measures. In discussing the cause of pneumonic plague outbreaks, the author deals with the possible influence of a special virulence of pneumonic strains, the role of the rodent and flea species involved, and the possibility of a pneumotropismus acquired by *Pasteurella pestis*.

The periodicity (cyclical and secular) of bubonic plague epidemics is discussed with a view to the possible forecasting of future epidemics.

The author indicates the influence of race, age, sex, and occupation on the incidence of both forms of the disease.

INTRODUCTION

In dealing with the epidemiology of plague, as has been seen in the fourth and the eighth of these studies,[65, 68] two fundamentally different forms of the disease should be considered :

(1) bubonic plague, produced, as a rule, by the bite of plague-infected insect vectors, mainly rodent fleas;

(2) primary pneumonic plague, due to a spread of the infection from man to man.

Even though " free-living " infected rodent-fleas may be temporarily important in the causation of bubonic plague in man, the continued existence of this form of the disease depends in the long run upon the persistence of

* This is the ninth of a series of studies which, when complete, will form a manual on plague and which will be published in separate editions in English and in French. — ED.

the infection in the rodents. The name of " zootic " plague recently recommended [88] for this form of the disease is therefore most appropriate.

Though initially dependent upon a spread of the infection from bubonic plague patients with secondary lung involvement to members of their families or other contacts, primary pneumonic plague is apt to spread, regardless of whether or not infected rodents and/or infective fleas continue to be present in the localities in question. In fact, purely pneumonic plague epidemics, due to the arrival of patients with secondary or primary lung involvement, have quite often been observed in localities where the rat populations were originally free from plague and where they remained entirely so even when the disease became rampant in man.

No doubt, therefore, primary pneumonic plague well deserves the recently proposed [88] designation of " demic " plague—the more so because, just as in the so-called bubonic outbreaks, cases without apparent buboes are met with, so in pneumonic epidemics, pulmonary cases without manifest lung involvement occur and rare bubonic cases may be produced through contact infection or, exceptionally, through the bite of infected human ectoparasites.

BUBONIC (ZOOTIC) PLAGUE

Cause of the Outbreaks

As noted in the sixth of these studies,[66] the Plague Research Commission was able, through a series of well-planned experiments, to disprove that infection through the air, through direct contact, or through contaminated inanimate objects was of any importance in the transmission of plague from rat to rat, and to establish, on the other hand, that plague was principally an insect-borne—and, particularly, a flea-borne—infection.

At the same time, the Commission adduced convincing proof that what had been established in regard to the spread of the infection among the rats, also held true for the conveyance of bubonic infection to man. As summarized by Lamb,[40, 41] the Commission found, in this respect in particular, that :

(1) A direct spread of the infection from bubonic patients was most unlikely, because (*a*) their excreta as well as those of the rats were found to be non-infectious when tested in the laboratory under conditions analogous to those in nature, and (*b*) the pus of healing buboes contained few, if any, virulent *Pasteurella pestis.*

(2) There was no convincing evidence to show that the human flea played an important role in the conveyance of the infection to man.

(3) Those attending bubonic plague patients remained singularly free from infection, the plague hospitals being in fact the safest places during the outbreaks.

(4) The contacts of patients who developed bubonic plague after arrival in a hitherto unaffected locality invariably remained well.

(5) The great majority of the patients whose history was accurately known had had no contact with previous cases before falling ill.

(6) If bubonic plague appeared in a settlement, in the great majority of instances not more than one case occurred per house.

(7) If multiple cases occurred in any house, they often appeared simultaneously, as if infected from a common source.

(8) If successive cases appeared in a house, invariably there was evidence of a higher rat-mortality than that found in houses yielding single plague cases.

The Plague Research Commission also established that close relationships existed between *Rattus rattus* epizootics and bubonic epidemics in time, in place, and in quantity.

As summarized by Wu Lien-teh,[98] in Bombay City, the average time-interval between the epizootics and the appearance of the epidemics was 10-14 days, and in a Punjab village, about a week—the difference being due to the fact that the Bombay figures were based on plague deaths, and those for the village on attacks.

The period of 10-14 days observed in Bombay comprised : (*a*) three days which, according to laboratory observations, had to elapse before the fleas, coming from the dead rats, were willing to attack man; (*b*) the average incubation period of human plague (three days); and (*c*) the average length of illness (5½ days).

The observations of the Commission also left no doubt that the places of infection in Bombay were the same in the case of *R. rattus* and in that of man. The same held true for the Punjab villages, but there account had to be taken of the close aggregation of the houses and the intercommunication of rat burrows between neighbouring habitations.

However, the Commission laid stress upon the fact that, evidently because many plague rats died in their burrows, infected fleas could be trapped in houses where no rat-falls had been noted.

A close relation in quantity was found to exist between the *rattus* epizootics and bubonic epidemics. If no rats with acute plague were found during the off-seasons, human cases were also absent. During the seasons the epidemic curve closely followed that of the *rattus* epizootics. An intimate relationship also existed between the number of plague rats found in a house and the appearance of human plague. Thus, in one of the villages studied, human cases occurred in only 3%-4% of the houses in which single plague rats had been found, whereas they occurred in 28% of the houses in which more than one plague rat had been found.

Generally speaking, the conclusions reached by the Plague Research Commission have remained unchallenged up to the present. In particular,

it has been confirmed through ample observations in various plague areas that, in contrast to the " demic " form of plague, the plague cases appearing during " zootic " outbreaks in individual houses usually remain single.

As has been discussed in the seventh of these studies,[67] some subsequent observers have maintained that in addition to, or even instead of, rodent fleas, human ectoparasites, particularly *Pulex irritans*, are of importance in the transmission of bubonic plague. While admitting that in places where these ectoparasites abounded, they might play a role in this respect, Pollitzer [67] stressed that in most plague areas, particularly those in China, India, and Madagascar, the part taken by human parasites in the conveyance of the infection was negligible, the transmission of plague to man depending upon the rat fleas. It was admitted, however, that the importance of wild-rodent fleas in the conveyance of the disease to man was not as universal, human infections in the " sylvatic " plague foci being partly due to direct contact with diseased rodents.

Attention was also drawn to observations showing that cases of tonsillar plague were found to be frequent among the Indians of Ecuador, who were in the habit of killing fleas and lice caught by them with their teeth.

A few observers, such as Durand & Conseil [18] and Nikanoroff,[56] conceived the idea that human convalescent or healthy carriers might be of importance in the perpetuation and spread of bubonic plague, the former two authors postulating that individuals harbouring *P. pestis* might develop plague bacteraemia if they became the prey of intercurrent diseases such as influenza or measles. However, no definite evidence has ever been brought forward to support these assumptions and there seems no reason, therefore, to revise the opinion expressed by Wu Lien-teh [98] that " like rodents with chronic plague, human carriers represent, so to speak, a sidetrack of the infection which ends blindly ".

While it is generally admitted that even though plague-infected rats are found in individual houses or compounds, human cases do not invariably follow in them, the opinion, held by most workers, that rat plague may exist in a community without leading to the appearance of the disease in man has not been universally shared. Petrie,[60] in particular, seems to have been sceptical in this respect. Discussing the discovery of " clandestine " foci of rat plague in Java by Swellengrebel & Hoesen,[85] he pointed out that the absence of human cases in these localities might have been merely apparent, because the methods available for case-finding were far less exact than the pooling tests used to detect the presence of *P. pestis* in the rats and their fleas.

There can be no doubt, however, that—as proved by recent experiences—rat epizootics may run their course without leading to human plague. The paucity, or even absence, of human cases in foci of wild-rodent plague also deserves great attention in this connexion.

Trend of Epidemics

In correlation with the slow evolution of the causative epizootics and the consequent restriction of the number of flea vectors initially available for human infection, the onset of bubonic epidemics is, as a rule, rather gradual. Hand in hand with an increasing rodent mortality and a corresponding increase of the " infection quantum " represented by infective rodent fleas, the outbreaks spread and reach the stage of their full development. This period of maximal morbidity and mortality is followed by a third stage of gradual decline of the epidemics (Dieudonné & Otto [16]). The evolution of bubonic outbreaks is thus markedly different from that of pneumonic epidemics, which develop far more rapidly. However, in contrast to the latter which, though apt to become rampant, are usually of an episodic nature, bubonic manifestations, because they serve, so to speak, merely as an index of a persisting rodent infection, tend to recur—often over prolonged periods—whenever conditions for a transition to man become suitable. From what has been discussed in the sixth and seventh of these studies,[66, 67] it will be gathered that this periodic or, one should say more accurately, " seasonal " incidence of bubonic plague outbreaks is governed by changes in the climatic conditions which, mainly by altering the infectivity of the flea vectors, exert a powerful influence upon the trend of the epizootics and, consequently, a most marked though indirect, influence upon that of the epidemics.

The data furnished in the first of these studies [63] regarding the seasonal incidence of plague in the recently or currently affected areas may thus be supplemented and summarized :

Area	*Plague seasons*
China	*North China.* Outbreaks started in late summer or autumn, sometimes extending into the cold season (Wu Lien-teh [98]). *Fukien Province.* Commencement in spring (usually between April and June). Epidemics lasting until early autumn, sporadic cases occurring as late as October and November (Park [59]). *Kwang-tung Province.* February-June (Park [59]). *Hainan Island.* February-April (Landauer [42]).
Burma	The usual plague season falls in the period November to April, with a peak in February in Upper Burma, and in March in Lower Burma, where there may be a secondary rise in July (Park; [58] Wilcocks [95]).
Viet Nam (South)	The first three quarters of the year, with a peak in April-May (Park; [59] Herivaux & Toumanoff [32]).
Thailand	According to Bangxang,[3] case incidence begins to increase in September, reaching its highest point in February and March. Low level from May to September, particularly during the wet months of June and July.

Area	*Plague seasons*
Java	Seasonal incidence not pronounced because, despite the presence of a dry and a wet monsoon, the temperature remains practically uniform throughout the year. Still, plague mortality begins to increase in the third quarter of the year, reaching its maximum in December or January (middle of wet season), commencing to decrease in February, and continuing to decrease in May and June (dry season) (Park [59]).
India	Dealing merely with the areas which were chiefly affected within recent times, Park [58] stated that : " Although plague is at a minimum during the hot and dry summer months, which in general all over India are from March to May, the incidence during the colder months varies in the different provinces owing to the varying rainy season, which in turn controls both the lowering of temperature and the rise in humidity ... The South-west Monsoon breaks on the west coast of India early in June, and provides suitable climatic conditions to permit in Bombay Presidency a peak incidence in October. Thereafter, the infection maintains a fairly high level till the end of the year, only to decline in the heat of March-April of the following year. Madras Presidency is subject to both the South-west and the North-east Monsoons and its seasonal incidence is thus more complicated, but on the whole it provides a peak incidence much later than Bombay in January, in common with the neighbouring States of Hyderabad and Mysore. The North Indian Provinces of United Provinces and Bihar are seen to have their peak incidence in March, and in common with the rest of India, the incidence declines sharply with the dry heat of the second quarter."
Egypt	As stated by Kamal [37] (see also Wakil, quoted by Pollitzer [63]), the months of maximal plague prevalence are : in northern Egypt (which has a Mediterranean climate), June and July; in middle Egypt, May; in upper Egypt (which has a hot and dry climate tempered by northern winds), March and April.
Tunisia	Outbreak at Ferryville observed by Magrou [48] lasted from August 1944 until March 1945. Percentage incidence of *Xenopsylla cheopis* was, according to Meunier,[51] highest in summer.
Algeria	Incidence highest in August (mean temperature 80°F (27°C)), plague then declining with the increased rainfall and falling temperatures from September onwards (Davis [13]).
Morocco	According to Davis [13] it could be noted " that plague is most prevalent at Casablanca in May and at Marrakesh in June and that in both areas there are two peaks during the year—namely, in May-June and October at Casablanca and in June-July and November at Marrakesh. The hot weather of midsummer seems to have a depressing effect on plague incidence in both areas ".
Senegal	Davis [13] stated that : " The most prominent feature of the seasonal epidemiology of plague in Senegal is the sharp rise after the dry period January-February (when the dry harmattan winds blow) to a peak in June before the onset of the rainy season during July-September. There is a noticeable recession in the two hottest months of the year—namely, September and October. The rise in temperature and relative humidity before the rains seems to favour human-plague transmission, which is checked by high temperatures at the end of the rainy season (October). "

Area	*Plague seasons*
East Africa (Belgian Congo, Uganda, and Kenya)	Dealing with the three following East African plague regions, Davis [13] stated that the equatorial climate at relatively high elevations with rather slight variations in mean temperature throughout the year appears to favour a uniform distribution of human plague without marked seasonal peaks. *Belgian Congo.* Case incidence lower between December and April, higher between May and November with a slight recession in August and September; the periods of lower incidence correspond to the drier times of the year and the first months of the long rainy season which follow the dry season of December and January (Davis [13]). *Uganda.* Seasonal plague incidence similar to that in the Belgian Congo. According to Hopkins,[33] all endemic foci are situated in areas with a rainfall above 45 inches (1,140 mm). *Kenya.* Though cases were recorded in all months, Roberts [70] found during an outbreak at Keruguya a rise in the case incidence at the time of the harvest, the incidence becoming highest between the two rainy seasons.
East Africa (Tanganyika)	As emphasized by Davis,[13] in contrast to the fairly uniform seasonal distribution of plague incidence in the above-mentioned East African regions, there is a well-marked plague season in Tanganyika which, lasting from February to April, corresponds to the single rainy season. The tropical climate prevailing during the rest of the year obviously prevents an incidence of human plague.
Madagascar	According to Robic,[72] the climatic conditions prevailing in the hot and damp coastal areas are unsuitable for the persistence of plague, while the relatively cool and moist weather on the high plateau creates a most favourable environment for its continued existence. Though cases occurred there throughout the year, plague regularly assumed epidemic features during the period of October to March, when, as recently summarized by Girard,[30] free-living *X. cheopis* abounded in the houses where plague cases had occurred, and were frequently infective. During the cool and rainless winter months, when the fleas appeared to be inactive, the incidence of bubonic plague was lowest, However, as stated by Le Gall [43] and by Girard,[30] pneumonic plague cases were comparatively more frequent in winter.
South Africa	As stated by Davis,[12] in the Union of South Africa, plague epizootics may be in progress at all times of the year. Likewise the secondary infections of commensal rodents, which are directly responsible for human manifestations of the disease, may take place at any time. Nevertheless, human attacks were most frequent in summer. The seasonal incidence of human plague in Basutoland, in South-West Africa, in the Bechuanaland Protectorate, and in Northern Rhodesia corresponded to that in the Union of South Africa (Davis [13]).
USA (western States)	According to Meyer,[52] epizootics among the ground-squirrels, which led to the appearance of sporadic plague cases in man, began early in spring, rose in intensity during the summer months, and slowly declined during autumn to disappear entirely during the winter in regions where the animals hibernated. However, in some localities young ground-squirrels, which were apt neither to aestivate nor to hibernate, could be found plague-infected in December and January.

Area	*Plague seasons*
Hawaii	As summarized by Mohr,[53] the *cheopis* infestation of the Honolulu Norway rats was lowest in October and highest in January. June also appeared to be a high month, but May and July showed low infestation-rates. Mohr added that, since temperature and humidity at Honolulu were high, but not too high for *X. cheopis*, infestation of the rats with this flea was marked.
Venezuela	As noted in the first of these studies,[63] the 1943 plague outbreak in Aragua State appeared in July, i.e., one month after an increased incidence of *X. brasiliensis* had been noted.
Brazil	From the first of these studies [63] it may be gathered that bubonic plague was most frequent at São Paulo in the south of the country in summer with a peak in January. In the north-east of Brazil, on the contrary, the incidence of the disease was comparatively highest from July to October, while the onset of the epidemic season in Ceará, which is still farther north, was in May and June. Dealing with the epidemiology of plague in Brazil in general, Barreto & Castro [6] noted an increase of the case incidence in spring or autumn when, following periods of heaviest rainfall, the temperature ranged from 19°C to 26°C (66°-79°F) and the relative humidity from 66%-83%.
Argentina	While, as maintained by Villafañe Lastra et al.[91] the plague incidence was formerly highest in summer, the recent rural outbreaks occurred mainly in winter (Sussini; [84] Barrera [4]).
Bolivia	According to Siles,[78] both summer and winter outbreaks of plague were observed.
Peru	Generally speaking, the annual plague epidemics in Peru tended to reach their peak during the summer months, but in areas where the winter months were warm, the plague seasons fell into an earlier period than in localities with a colder climate (Eskey [19]).
Ecuador	Plague was generally most rampant in December, of low incidence in June. However, the outbreaks in Loja Province occurred mainly during the dry season from May to December (Moll & O'Leary [54]).

At first glance, the data assembled in the above tabulation appear to be rather contradictory, because it will be noted that in some of the plague areas the case incidence was highest during the warm seasons and in others during the cool seasons, and that the prevalence of rain sometimes favoured and sometimes cut short the spread of the infection to man. However, whenever it is possible to correlate the statements made in regard to the seasonal incidence of bubonic plague with adequate meteorological data, it will be found that invariably the epidemics occurred during seasons in which the temperature was moderately high and the saturation deficiency of the air low. Though some exceptions appear to exist, as a rule bubonic plague epidemics occurred at times when the prevailing climatic conditions were within the limits found suitable by Brooks [7] for the occurrence of such outbreaks in India. As stated in the seventh of these studies,[67] Brooks concluded that :

" (1) Plague did not establish itself when the temperature rose above 80°F (27°C) accompanied by a saturation deficiency of over 0.30 inch (7.6 mm.).

" (2) Plague epidemics were rapidly brought to an end in the presence of a high saturation-deficiency, even when the mean temperature throughout, and after the termination of, an epidemic had been below 80°F (27°C).

" (3) Plague epidemics could commence and increase in intensity when the mean temperature was well above 80°F (27°C), provided that the saturation deficiency was below 0.30 inch (7.6 mm) ".

Spread and Persistence of Outbreaks

The consequences of plague invasion of the various recently or currently affected countries which, as can be gathered from the first of these studies,[63] was due mainly to importations by the sea-route varied according to local conditions. Whenever the climate prevailing at the time of the invasion or throughout the year was unsuitable, the infection failed to entrench itself. It is noteworthy, however, that even though, owing to such unfavourable conditions, plague was unable to gain a permanent foothold in the coastal regions of Madagascar, it still managed to penetrate into the interior of the island where almost ideal conditions for its persistence existed.

The prevalence, or sole presence, of comparatively inefficient vector fleas was also apt to impede the spread of plague, particularly its transition to man. Thus, as pointed out by Eskey,[20] in Seattle, Wash., USA, where *Nosopsyllus fasciatus* was the vector, plague smouldered among the rats for ten years, and yet only three human cases were recorded throughout this period.

However, instances such as those referred to above were exceptions rather than the rule. Usually, the invasion of a sea-port by the maritime route (or, as shown in the case of Hong Kong and Canton, even by the land route) was followed not only by an often prolonged, though gradually decreasing, local occurrence of plague, but also almost invariably by a spread of the infection to the hinterland. Practically without exception this led first to the involvement of inland towns connected with the ports by major traffic routes—particularly railways and rivers—and secondly to a further spread of the infection to rural areas which, because it usually depended upon a transport of infected fleas by primitive means of communication, was apt to take place in a rather haphazard manner. For reasons which will be discussed later, plague, while tending gradually to disappear, or to become minimal, in the urban centres of the hinterland as well as in the coastal towns, showed a most marked tendency to remain endemic in rural areas. Quite often, the infection, sallying forth from these strongholds, produced epidemics in adjacent areas which no longer permanently suffered from the disease.

Although it is legitimate to consider the above-described mode of plague propagation, which has been observed regularly in widely distant countries, as typical, many local variations of the process have been found to exist, owing principally to differences in the rodent species which served as reservoir of the infection. While in some of the countries commensal rodents continued to harbour the infection when rural areas became involved, in others the infection spread to wild-rodent species. Foci of true " sylvatic " plague could thus be formed, dangerous to man only when he penetrated into the remote haunts of the species concerned. In other cases, however, the wild rodents involved lived so near to man that their fleas could cause human infections within the settlements or could at least infect commensal rodents which in their turn brought the disease into the houses.

Under these circumstances, it is not surprising to find that different authors proposed different schemes for classifying the various stages of plague. Thus Devignat [14] distinguished three levels (" plans ") on which plague could develop—the " domestic-murine " (" murin domestique "), the " sylvatic murine " (" murin selvatique "), and the " human " ("humain") —which could be independent of one another or could be brought into relation by different modes of transmission.

In a valuable study, Macchiavello [47] distinguished four main stages in the propagation of plague in South America, namely : (*a*) invasion of the ports; (*b*) spread by railways and other means of communication to the towns of the hinterland; (*c*) subsequent involvement of adjacent rural areas; and (*d*) transition of the infection to wild rodents.

Important though the latter classification is for historical surveys, it suffices for the purposes of the present disquisition to give separate consideration only to : (*a*) urban manifestations; (*b*) rural manifestations, including under this heading, besides rat-caused outbreaks, those of a " peridomestic " origin, due to an interchange of the infection between commensal and wild rodents or to proximity of the latter to human habitations; and (*c*) wild-rodent plague in the strict sense of the term. These three main categories will now be dealt with seriatim.

Urban manifestations

As stated before, for various reasons, particularly owing to untoward climatic conditions or to the lack of efficient flea vectors, plague may fail to gain a foothold, or at least a permanent foothold, in the urban centres into which the infection has been introduced. However, as shown by many examples, given a suitable climate, a sufficiently large and susceptible rodent population, and the presence of a sufficient number of capable vectors, plague often became firmly entrenched among the rats of the affected cities or major towns, and persisted in the rodent populations for

at least a number of years, not rarely for many years. If, as was often the case, the prevailing climatic conditions did not favour perennial epizootics, plague assumed epizootic proportions whenever suitable seasonal changes of the weather took place. The high mortality of the rats during these seasons led to the liberation of infective rat fleas and, consequently, to the appearance of human plague manifestations, which, at least during the period immediately following the introduction of the infection, practically always assumed epidemic proportions.

During the off-seasons, when, as a rule, the surviving rats were capable of attracting the fleas which had left the few animals that succumbed to plague, human cases, if occurring at all, were few and far between.

Several reasons have been adduced to explain the gradual diminution and ultimate disappearance of the infection, which are characteristic for urban zootic plague. Thus some authors, such as, recently, Macchiavello,[47] stressed that a decimation of the rats through severe epizootics might greatly diminish or even abolish the chances of infection among the scattered survivors. However, the importance of this factor is limited, because urban plague often spreads in an irregular manner so that, even in severely-affected precincts, groups of rats may remain unscathed. Moreover, unless the reduction of the rat population becomes extreme, an increased fertility of the survivors is apt to lead soon to a re-establishment of the former population level or even to an increase in population. As maintained in the sixth of these studies [66] a vicious circle may exist in this respect, a decrease of the rat population through an epizootic leading to more frequent births during the following off-season, which in their turn help to promote the next epizootic.

One must fear that the procedures employed hitherto for rat destruction play an ambiguous role in the control of urban plague, since they also often act as a stimulus for a high compensatory fertility among the survivors. That, generally speaking, one should not think too highly of the routine methods formerly used for plague control, is exemplified by the observations of Uttley [90] in Hong Kong. He concluded that the decrease of plague in that port, and its final disappearance in 1923, could not be ascribed to the measures taken, because simultaneously the incidence of the disease decreased in the adjacent parts of south China, where no, or at least no intensive, control work had been done.

Even at best, the influence of the factors considered above is of limited importance compared to that exerted by the gradual extinction of plague-susceptible rats which, taking place in the course of the successive epizootics, leads to an increasing prevalence of plague-resistant rat strains and finally to the exclusive presence of rats refractory to the infection. The evidence adduced in this respect in the sixth of these studies [66] leaves no room for doubt that during the present pandemic, as well as in historical times, this gradual replacement of susceptible rats by resistant rats exerted a

profound influence upon the trend of the urban zootic plague outbreaks, and finally led to their disappearance.

As has been stated in the sixth of these studies,[66] not much information is available as to how long this herd resistance was apt to continue in the absence of autochthonous plague. It stands to reason that, in such cases, a gradual multiplication of a few susceptible rats, which had been spared during the past epizootics, might take place, and that, likewise, susceptible imported rats might have a chance to multiply. As was shown in the sixth study, such an evolution actually took place in Bombay. As also observed there, a change in the situation may likewise be effected by a multiplication of rodents other than the common rats, which, because formerly less numerous, have suffered little in the past rat-epizootics and, therefore, have not lost their herd susceptibility to plague.

That under such circumstances a reimportation of plague may create a dangerous situation for man, has been proved by recent experiences in Bombay, which may be recorded thus :

	Plague-infected rodents found		*Plague cases*
Year	*R. rattus*	*Gunomys kok*	*among residents*
1948	2	42	14
1949	4	2	2
1950	0	0	2
1951	0	0	0
1952	0	0	1

It will be noted that, owing no doubt to a reimportation of the infection from Bombay State, an enzootic was present among *Bandicota bengalensis kok* (*Gunomys kok*) and, to an apparently lesser extent, also among *R. rattus* in 1948 and 1949, and was obviously responsible for a number of plague cases among residents of Bombay who had never left the city. Though no infected rodents were found afterwards, the epizootic probably continued, because further plague cases among residents were recorded in 1950 and 1952 respectively. It should be noted in this connexion that so far no pooling tests have been used for rat examination in Bombay.

In assessing the importance of these observations, one must admit that (*a*) an unusually favourable situation for the reappearance of plague has been created in Bombay through the recent multiplication of the fully susceptible *B. bengalensis kok*, and (*b*) as proved by the almost all-yearly occurrence of imported human cases, chances for reimportation of plague into the city were considerable.

Nevertheless, though they are probably exceptional, these findings show that zootic plague may become re-established in an urban community comparatively soon after it has become extinct.

The extent to which plague-affected urban communities serve as distributing centres of the infection may vary considerably. Apart from the

degree to which the cities and towns are affected, which often shows seasonal variations and is apt to decrease in due course, the role which these centres play in the distribution of plague depends, in the first place, on their commercial importance and on the means of communication they possess. If railways or steamers are available for traffic, a spread of plague from seriously-affected urban centres, particularly from those of great commercial importance, is practically inevitable and is apt to lead to an importation of the infection into even quite distant towns, which then become secondary plague-distributing centres. Vice versa, the extent to which these secondary centres spread the infection decreases pari passu with their lessened importance for commerce and traffic. If they possess only primitive means of communication, they may distribute the infection merely in their immediate environs. Naturally, such a spread to surrounding rural districts is bound to take place also in the case of important plague-infected centres, in addition to a long-distance spread of the infection by modern means of communication (" peste urbano-rural " of Macchiavello [47]).

Rural manifestations

In contrast to purely " sylvatic " plague, the epidemiology of which will be dealt with separately, the rural manifestations of zootic plague—due to a presence of the infection in commensal and also in " peridomestic " wild rodents—have no independent standing in so far as, practically always, their initial appearance, and sometimes even their recurrence, is due to an importation of the infection from some plague-affected urban centre. Greenwood,[31] studying the outbreaks in the Punjab, maintained in this connexion that such an importation of the infection was most likely to occur in the case of villages which were large and situated near major lines of communication. The proportion of small villages which remained free from infection when plague became epidemic in an area was therefore much higher than that of larger villages or towns.

The problem of the persistence of plague in rural areas has been studied by numerous workers. Confirming and supplementing observations made in this respect by the Plague Research Commission and other early investigators, Kunhardt,[38] in a paper read in 1912 at the Second All-India Sanitary Conference, held at Simla, India, drew a distinction between "incomplete" and "complete" rural plague outbreaks. If the infection was introduced late in the season into a large settlement, an "incomplete" outbreak was apt to result and plague was likely to be carried over into the next season. On the contrary, "complete" outbreaks, as they occurred in small villages or in large communities which had been affected early in the plague season, were not carried over, apparently because the rat population had been decimated to such a degree that a further spread of the infection among the scattered survivors had become impossible. Kunhardt had actually found that

during the period 1899-1904 only 17 villages in the Poona district (Bombay State) had carried over the infection during the off-seasons, none of them more than once. He disbelieved, therefore, that plague was endemic in the rural parts of the district.

Browning-Smith,[8] in a paper read at the same conference, was not in agreement with Kunhardt, stating that, in the Punjab at least, the factors determining the local appearance of plague seemed to be very complex. He admitted, however, that plague rarely appeared in autumn in a place which had had a " complete " epidemic early in the year. Turkhud,[89] who also made a report during the 1912 conference, concluded from careful observations made in the Satara district (Bombay State) that, during each off-season, plague was carried over only in one village, whence the infection spread to the other villages which became involved in the same year. A different village was found to be the fountainhead of the infection in each subsequent year.

Acting upon the recommendation, made in 1910 by the Punjab Plague Committee, that in plague control work attention ought to be concentrated on places in which " incomplete " outbreaks had occurred, Kunhardt & Chitre [39] worked out a scheme for predicting the carrying-over of epidemics, based upon (1) the size of the communities in question, and (2) the month when the first autochthonous human-plague case had occurred. As summarized by Wu Lien-teh,[98] the two workers found that a carry-over of plague was possible under the following conditions.

Population of more than	*Date of first autochthonous plague case*
25,000	November
10,000	December
4,000	January
1,800	February
800	March

Strickland,[83] while agreeing in principle with Kunhardt & Chitre, pointed out with much reason that the figures arrived at by these two workers were not generally valid, but that, on the contrary, a separate formula had to be worked out for each plague district. Thus in his experience in the Belgaum and Dharwar districts (Bombay State), a carry-over took place in settlements which were much smaller in size and had been infected earlier than had been found by Kunhardt in the near-by Poona area. Strickland [83] also suggested that the transportation of grain after the harvests, because it facilitated the transportation of rats and fleas, might lead to an increased number of village infections.

According to the observations of George & Webster,[24] the villages of the Cumbum valley in southern India also did not suffer from plague " equally from year to year ". It was, no doubt, due to this inconstancy of the plague manifestations that, as established by these two workers, the

rats of the Cumbum valley were almost invariably susceptible to cutaneous or subcutaneous inoculations with *P. pestis* (97.5% positive results in 320 rats tested).

Observations similar to those recorded above were also made by workers in China. Landauer,[42] discussing the plague situation in Hainan, came to the conclusion that, in that island,

" the infection of the villages represents a distinct phase in the epidemiology of plague. The towns are infected first, but the disease has a tendency to become extinct after a series of more-or-less violent eruptions. The second stage (which does not follow necessarily) consists of an invasion of the country, where the disease assumes a different character. The small number of rats implicated leads to an uninterrupted chain of sporadic cases or of small epidemics, comprising at most 10 persons per locality. Once the disease has reached this stage, it rarely shows a tendency to disappear spontaneously from the regions thus affected and very often towns which had been free from plague for a number of years are reinfected from the villages ".[a]

Similar conclusions were reached by Yang et al.[101] who worked in the Fukien Province. They maintained that

" . . . scattered cases typical for the offseason are never found in towns. They sometimes occur in the outskirts of towns, especially among the hut population, but are most frequent in isolated farms or small hamlets. Due to their isolation, number and small size, such farms rarely become infected twice. Their rat populations have had no chance to become immune and may be likened to small piles of firewood scattered over the whole region. Sparks in the form of infected fleas or rodents set them on fire and when the large fire in the town has burnt out long ago for lack of combustible matter, there is always a new pile of fuel available in the country side ".

The excellent descriptions of the trend of rural plague outbreaks given by Landauer [42] and by Yang et al.[101] are all the more important in view of the opinion held by some observers that the appearance of the rural manifestations is invariably the result of an importation of the infection from a plague-affected urban centre. Thus Sharif & Narasimham,[75] recently studying the ecology of plague in two districts of Bombay State, maintained " that the idea that plague is more a rural problem is fallacious ". In their opinion, the big grain centres received the infection from some infected village through fleas imported with grain, and caused a dissemination of plague, mainly through grain, to other villages. Usually, the grain centres themselves did not become seriously involved in this progress of the infection because, owing to past epizootics, a large proportion of their rats was plague-resistant.

It is undeniable that at a late stage of their infection plague-affected towns may, as it were, serve as relay stations for the spread of the disease

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a " . . . l'infection villageoise représente une phase distincte dans l'épidémiologie de la peste. Les villes sont infectées les premières mais la maladie a tendance à s'éteindre après une série d'éruptions plus ou moins violentes. La seconde étape (qui ne doit pas nécessairement faire suite à la première) consiste dans l'invasion de la campagne, où la maladie prend un caractère différent. Le petit nombre de rats impliqué conduit à une chaîne ininterrompue de cas sporadiques ou de petites épidémies, comprenant au plus 10 personnes par endroit. Arrivé à ce stade, il est extrêmement rare de voir la maladie s'éteindre spontanément dans les régions ainsi infectées et très souvent des villes qui ont été exemptes de peste pendant un certain nombre d'années sont réinfectées par les villages."

from one rural area to another without markedly suffering themselves. However, as proved by the above-quoted observations in China, rural plague may persist and spread after the infection has become extinct in the adjacent towns, and may be responsible, in due course, for a reinfection of the latter.

Pollitzer,[62] who during the second World War had fairly ample opportunities of observing the evolution of plague in hitherto unaffected districts of south China ab initio, found that if a new country became invaded, as a rule rat plague, followed in due course by human infection, first became manifest in the county (" hsien ") capital or some other centre like a market town. Occasionally, however, the disease first appeared in some village situated close to a previously infected district. If so, the " hsien " capitals or other important towns almost invariably became involved in their turn and then served as distributing centres. As in other countries, plague in the towns gradually decreased and then disappeared, but occasionally the infection was reintroduced from adjacent rural foci.

Plague was as a rule shortlived in the numerous villages attacked. Appearance of the infection early in the season led to a " complete " outbreak with numerous rat-falls and human victims, the marked reduction of the susceptible rat population often resulting in a total disappearance of the disease. If importation took place late in the season, limited epizootics, with little or even no human plague, developed. Rat-falls became few and far between after the end of the season, but almost inevitably such " incomplete " outbreaks led to a carry-over of the infection and thus to conspicuous outbreaks in the following season.

The local reappearance of plague in more than one season was rare but, though not persisting for long, the infection was often carried from the affected to hitherto unaffected villages, usually through the transport of infected fleas in rice cargoes.

The conclusion reached by Pollitzer was that, while in the rural areas a local endemicity was exceptional,

> " the great tendency of the infection to spread to hitherto plague-free localities creates a condition of what might be termed *area-wide* endemicity, characterized by marked changes in the localization and extent of the individual outbreaks from season to season ".

Several workers besides those in India and China apparently referred to the existence of such an " area-wide " endemicity. Thus, as stated by observers such as Robic [72] and Sorel,[82] plague in an " endemo-epidemic " form is widely spread on the Madagascan plateau where, as stated by Girard at the second session of the WHO Expert Committee on Plague, even in the city of Tananarive the rats continue to be susceptible to the infection. Discussing the peculiarities of plague in the Belgian Congo, Devignat [15] upheld that in the Ituri region the infection was not immobilized but constantly moved from place to place in a fairly large territory, causing

only isolated human cases, which were unconnected with one another in time and space.

To judge from statements made by Villafañe Lastra et al.[91] and by Macchiavello,[47] an area-wide endemicity existed also in some of the South American plague foci.

In a valuable study on the spread of plague in the southern and central divisions of Bombay State, Sharif [74] reached the important conclusion that two types of epizootic could be observed in these regions. In the warm tablelands and plains the infection was often severe, leading to a heavy rat mortality and, consequently, to the disappearance of the disease within a short time. On the other hand, in the cooler regions, comprising the watersheds of the Western Ghats, plague spread slowly but, owing to a lower rat mortality, persisted for a long time. In the opinion of Sharif, these areas, which have a moderately moist and cool climate throughout most of the year, and also the hilly part of Hyderabad State, were endemic centres responsible for the occasional appearance of epidemic plague in the other parts of the affected area of Bombay State.

Since, according to the observations of previous workers who have been quoted above, an area-wide endemicity seems to have existed in districts of Bombay State now found by Sharif to suffer from occasionally imported epidemics only, one might postulate that the establishment of endemic foci in the hilly parts of the State represents the ultimate stage in the progress of the infection from the coast to the hinterland.

Be this as it may, it is certain that, in marked contrast to urban plague, rural plague, because it is usually unable to cause a gradual extinction of the susceptible host populations, is not a self-limiting disease but is apt to last for very long periods. It is important to stress this point, particularly because some observers, such as, recently, Baltazard et al.,[2] believe that, in contrast to plague manifestations caused by certain wild-rodent species, rat-caused plague manifestations are invariably of a rather ephemeral character. It may be claimed that the evidence adduced above does not support this view.

As stated earlier in this study, wild rodents of peridomestic habits may take part in the causation of rural plague manifestations as well as the commensal rats. Macchiavello [47] distinguished accordingly between two types of rural plague in South America, namely :

(1) " Pure " or " campestral " rural plague, in which *R. rattus* and *X. cheopis* alone played a role; and

(2) " Agrestial " rural plague (" peste rural agreste "), in which epizootics among peridomestic wild rodents were added, " as a temporary and transitory epiphenomenon ", to those among *R. rattus*.

Outbreaks of the former type were far more persistent than the manifestations of " agrestial " plague, because the fleas of the peridomestic

rodents were inefficient vectors and the climatic conditions in the open fields were favourable for *X. cheopis* at certain times only. However, as observed in Argentina for instance, the presence of " agrestial " plague was apt to lead to an entrenchment of the infection among " sylvatic " rodent species.

As has been discussed in the seventh of these studies,[67] Roberts [70, 71] found that *X. brasiliensis* was the principal vector of *P. pestis* in the rural areas of Kenya where plague was endemic in type, whereas *X. cheopis* was mainly, or even solely, involved in the urban manifestations of the disease, which were of an epidemic character. Similarly, it was maintained by Sharif & Narasimham [76] that *X. brasiliensis* was the main vector in the endemic areas situated in the Western Ghats of Bombay State, where plague showed a marked tendency to spread slowly but to persist. On the contrary, *X. cheopis* appeared to play the principal role in the low and warm tablelands of the State, where the outbreaks were of an explosive nature but did not last long.

In view of the fact that *X. brasiliensis* is at least as efficient a plague vector as *X. cheopis*, these different roles of the two flea species cannot be ascribed to differences in their vector capacity. As pointed out by Roberts,[70, 71] *X. brasiliensis*, because it infested mainly the rats which sheltered in the thatched roofs of houses, was bound to prevail in the rural areas of Kenya, whereas *X. cheopis*, which mainly infested the rats living underground, found a suitable habitat in the towns. There can be no doubt as well that the climatic conditions in the hilly districts of Bombay State were more favourable to *X. brasiliensis* than those in the tablelands, whereas the more adaptable *X. cheopis* could thrive in the latter.

" *Sylvatic* " *plague.* As aptly stated by writers such as Lobo & Silvetti,[45] the fundamental epidemiological difference between rat-caused and wild-rodent plague is that the presence of the infection among the rats is apt to lead to the appearance of collective human cases in settlements, whereas wild-rodent plague in the strict sense is, as a rule, responsible merely for the occurrence of sporadic cases in persons who have entered the haunts of the species concerned. Nevertheless, in view of the often enormous extent of the wild-rodent plague foci, the aggregate number of human infections contracted in them may be considerable, and the case-mortality is apt to be high since the patients often receive no adequate treatment, either because they live away from centres of civilization or because, owing to its sporadic incidence, the presence of the disease is not recognized. It must also be kept in mind that importations of the infection from the wild-rodent plague foci in Transbaikalia or Mongolia into hitherto unaffected areas of China have led to the most disastrous pneumonic plague outbreaks on record in modern times.

Periodicity of Outbreaks

Cyclical periodicity

Since the severity of zootic plague outbreaks in a given locality depends largely on the number of susceptible rodents available, one would expect that a marked depletion of this fuel for the spread of the infection through a severe initial epizootic would lead to a lesser incidence of the disease until the rodents had become numerous once more. In other words, one might assume a priori that, unless particularly suitable conditions for a rapid re-establishment of the rodent population exist (as may be the case in urban communities), zootic plague would show a cyclical periodicity, years in which a severe outbreak occurred being followed by a period of one or two years during which the infection causes less havoc.

In the course of an investigation on plague in the Punjab, Greenwood [31] found that this surmise was only in part justified by statistical evidence. There was no marked regularity in the succession of severe and mild outbreaks and, therefore, " it would not be safe to predict that a province seriously ravaged in one year will escape lightly in the following season ". He admitted, nevertheless, that an exhaustion of susceptible rats exerted some, possibly a considerable, influence on the trend of plague, while climatic changes played a less, probably a much less, important role in this respect. However, in Greenwood's opinion, there remained " a *tertium quid* which is not apt to be placed in evidence by statistical inquiries based on existing data ".

However, observations made by subsequent workers have shown that in India, as well as in other areas, plague outbreaks may show a marked cyclical periodicity. Thus Sharif [74] stated that :

" In the non-endemic areas [of Bombay State], such as are found in the Sholapur District, few localities get infected in one plague season, and then a very large number of them in the next one or two plague seasons. In the third or fourth plague season, only a few of them suffer, and then plague disappears for about a year or two. "

Hence, as maintained by Sharif, " the peak year in the Sholapur District appears to recur about every five years, with complete absence of plague for a year or two ".

Dealing with the epidemiology of plague in north-east Brazil, Macchiavello [46] stated :

" It is believed that an area in which plague has died out because of a lack of susceptible material may be reinfected if the rodent population happens to become sufficiently great at the same time that an opportunity for reintroduction of the plague organism occurs, such as the migration of infected rats. If this happens, however, at a time when one of the periodic nonplague epizootics has practically wiped out the rodent population, reinfection will not occur, but may skip several years until another opportunity arrives. This would explain the reappearance of plague in 5- or 10-year cycles in certain areas."

Silva,[79] studying the situation in Ceará State in particular, found that a reactivation of plague foci which had been dormant for two to five years was not infrequent.

Plague manifestations caused by wild rodents in Argentina showed, according to Barrera,[5] a cyclical periodicity of two years.

In South Africa, Davis [12] found :

" A periodicity of 5-6 years in the incidence of human plague points to the existence of a general periodicity in the fluctuations in numbers of the wild-rodent population in the Union as a whole; this shows signs of breaking down as human outbreaks become more and more associated with certain limited hyperenzootic areas . . ."

Quite possibly, the seriousness of the plague situation existing in the Punjab at the time during which Greenwood made his statistical investigations was, in essential respects, comparable to that present in the hyperenzootic areas of South Africa.

Secular periodicity

Ample evidence has been furnished in the first of these studies [63] to prove that the plague pandemics, following the same laws as individual outbreaks of the disease, showed a well-marked " secular " periodicity : a stage of gradual rise and spread was followed by a period of full evolution during which the disease, because it appeared mainly in the form of major epidemics, exacted a grievous toll in lives; and this period was followed in turn by a stage of gradual decline. The information supplied in that study also leaves no room for doubt that the present plague pandemic has reached the period of decline.

However, even though plague, which but a few decades ago ranked high among the diseases decimating mankind, now occupies a rather inconspicuous place in the fatality lists, it would be wrong to assume that this infection has altogether lost its sting.

Indeed, reconsidering this problem in the light of what has been discussed in the foregoing pages, one is led to ascribe the great reduction in the incidence of plague largely to the fact that this disease, which earlier in the present pandemic raged in urban communities, has now almost disappeared from these centres of population, and mainly occurs in rural areas where, as a rule, the case incidence is rather low. It follows that the spectacular decrease in the incidence of human plague is not by any means accompanied by a corresponding restriction of the areas in which the infection is present among the rodents. On the contrary, it must be realized that the extent of the areas in which the rodents are affected has become greatly enlarged during the present pandemic, because, progressing almost invariably from newly invaded coastal regions to the hinterland, plague has become entrenched among the rodent populations, and not rarely among the wild-rodent populations, of vast areas which had been unaffected before onset

of the pandemic. This is a situation which cannot be viewed with equanimity, the less so because there is reason to believe that, in some areas, plague among rural rodents, particularly among the wild species, has not yet reached the limits of its possible regional extent, and because it is certain that some of the foci of wild-rodent plague are much larger than is usually assumed.

Forecasting of Epidemics

Attempts to forecast the appearance of bubonic plague epidemics have been made in various ways.

As noted previously, Kunhardt & Chitre [39] proposed a scheme for predicting the reappearance of outbreaks due to a carry-over of the infection from the preceding plague season. However, Strickland,[83] while approving of this method, emphasized that the formulas worked out for this purpose had only local validity.

Forster (quoted by Wu Lien-teh [98]), while admitting that in the Punjab a drop in the plague mortality during November and December indicated a slight, or at most a moderate, incidence in the following spring, stressed also the importance of climatic factors. Prolonged periods without rain during autumn and winter, because they adversely affected the reproduction of fleas, were apt to reduce the plague mortality in the following spring. The absence of rain during November in particular seemed of great importance in this respect.

Comparing the plague statistics for different areas of India with the corresponding meteorological data, Rogers [73] found that seasonal variations in mean temperature and saturation deficiency exerted an important influence on the seasonal plague incidence, obviously by acting on the vector fleas. Rogers established, in particular, that the climatic factors of the previous year influencing the incidence of the disease were (*a*) the mean temperature during the hot weather and monsoon seasons, and (*b*) the saturation deficiencies in both these seasons as well as in November and December. If these values were low, plague incidence was favoured. However, as was to be expected, Rogers noted that the effect of favourable climatic influences was less marked after years of high plague incidence than after a period of low incidence of the disease.

Rogers found it possible to use such meteorological observations as a basis for forecasting plague epidemics in certain parts of India and obtained, as stated by Wu Lien-teh,[98] satisfactory results during the period 1930-2. However, no further advantage seems to have been taken of this method.

Convenient though it would be, it is not possible to base forecasts of plague epidemics upon observations of seasonal changes in the incidence of the vector fleas. It is true that, as stated in the seventh of these studies,[67] in regions where *X. cheopis* is the sole important vector, plague does not

assume epidemic proportions as long as the *cheopis* index remains below one, and that in localities where the index is constantly above this critical level, seasonal changes in the frequency of *X. cheopis* are often observable, which may be of value in assessing the plague situation. It has to be stated, however, that periods during which plague epidemics occur need not necessarily coincide with those during which the *cheopis* incidence is highest and that indeed it is a high incidence of actually infective fleas and not the frequency of potentially dangerous vector species which is of paramount importance in the spread of flea-borne plague.

As discussed in the fourth of these studies,[65] Shih & Pollitzer [77] found that observations on the frequency of rats showing signs suggestive of plague at autopsy and/or marked bacteriological evidence of the infection were apt to serve as a yard-stick for assessing the seriousness of the plague situation in the localities in question. The value of this simple method, which gave satisfactory results even when only a limited number of animals was available for examination, should not be underrated.

Race, Age, Sex, and Occupational Incidence

Most workers are agreed that differences in the race and sex incidence of bubonic plague cases, as well as the occasionally observed increased incidence of the disease among certain occupational groups (e.g., dock workers handling grain cargoes), are due merely to differences in the degree of exposure of the various groups to the infection and not to intrinsic causes. The validity of this opinion is well illustrated by observations on the sex incidence of the disease. In some plague areas, for instance according to Norman White [93] in India, females were found to be more frequently affected; in others, in South Manchuria for example, males were more frequently affected, while in a third group of foci the incidence of disease in the two sexes was about the same. Landauer [42] found that while this was the case in the towns of Hainan, in the rural areas of that island more females than males fell victims to the infection.

Gill [26] maintained that the often observed rarity, or even absence, of bubonic plague in young children was due to a state of resistance to the infection, engendered through the secretion of an endocrine gland which ceased to function when the children reached the age of about five years. However, the fact that sometimes cases among young children were comparatively not rare speaks against this assumption. For instance, Favarel,[21] in Madagascar, found 104 cases in children up to two years of age out of a total of 2,994 bubonic and septicaemic cases (3.1%).

In the experience of most observers, including Favarel,[21] the incidence of bubonic plague was highest in adolescents and in adults up to the age of about 45 years. That this rule is not invariable, however, is shown by

the observations of Barreto & Castro [6] who found that out of 746 plague patients, 724 of whom had bubonic plague, 25.7% were in the age-group of 0-9 years and 28.2% in that of 10-19 years.

There can be no doubt that this unusual age incidence of the disease in Brazil was due to peculiar extrinsic conditions and not to intrinsic causes.

PRIMARY PNEUMONIC (DEMIC) PLAGUE

In opposition to the usual opinion, some workers postulated that primary pneumonic plague might arise de novo, man contracting the infection more or less directly from plague-affected rodents without the intervention of human cases of zootic plague with secondary lung-involvement.

Thus, it was suggested by Simond [80] and by Zabolotny [102, 103] that an introduction of the infection into the mouth by means of fingers soiled either by the faeces of plague-infected fleas or by handling plague-affected wild rodents might lead to pneumonic plague. Connal & Paisley [11] and Nikanoroff [57] maintained that dust contaminated with the faeces of plague-infected rodents might also produce a primary lung-infection.

Scrutinizing the above-mentioned and other statements made regarding the existence of " original " cases of primary pneumonic plague, Wu Lien-teh [96, 97] and Wu Lien-teh & Pollitzer [100] found that, as a rule, such claims had not been substantiated by sufficiently accurate observations. The diagnosis was often based merely upon the history of the patients; complete autopsies were exceptional and thorough histological investigations had never been made in such cases. As proved by observations on " tonsillar " plague, the fact that oral infection of man with *P. pestis* led as a rule not to primary pneumonic plague, but to bubonic plague often followed by secondary lung-involvement, also deserved great attention.

Nevertheless, a number of instances were found which deserved the benefit of the doubt, while the " originally " pneumonic character of a few such cases—due almost invariably to infections contracted in the laboratory—could be taken for granted.

As has been stated in the eighth of these studies,[68] one should not be categorical in denying the possibility that patients with so-called primary septicaemic plague may occasionally be instrumental in passing respiratory infection to persons coming in contact with them, and the same might hold true exceptionally for patients with uncomplicated " tonsillar " plague or even for apparently healthy individuals harbouring *P. pestis* in their sputum or fauces. There can be no doubt, however, that in most instances primary pneumonic plague infection is due to contact with patients who suffer from bubonic plague with secondary lung-involvement.

Cause of Epidemic Outbreaks

The problem of why pneumonic plague epidemics arise received early attention on the part of the Indian Plague Commission,[34] who

" noted that there are difficulties in the way of assuming a simple interrelation between the inhalation of plague bacteria in the lungs and the supervention of primary plague pneumonia ".

Endeavouring to substitute a more adequate theory, the Commission suggested :

" (*a*) that there may be something, either in the form or in the manner in which the infectious material escapes from the body, which favours the conveyance of the infection into the lungs of persons in attendance on cases of plague pneumonia; (*b*) that there may be something specific in the infective material which conditions the supervention of plague pneumonia when the material is introduced into the lungs."

The Commission emphasized that there was no specific difference between the bacilli causing bubonic and pneumonic plague respectively. There might be a difference in virulence, but the evidence regarding this was contradictory. The Commission stressed, however, that

" the plague bacillus may, in the case of infective material derived from a pneumonic case, be associated with some other bacillus which favours its growth and contributes to the production of plague pneumonia ".

The opinion of the Indian Plague Commission that intrinsic causes are responsible for the rise of pneumonic epidemics has been endorsed by many other workers, whose views may be presented as follows.

Specific character of the causative organisms

Practically all later observers agreed with the Indian Plague Commission that, as far as is known, no specific difference exists between strains causing zootic and pneumonic (demic) plague respectively. Wu Lien-teh [98] aptly stated in this connexion that

" it is as easy to cause primary pneumonic plague in suitable animals by inhaling them with a strain from a purely bubonic human case, as to produce bubonic plague in laboratory animals by percutaneous or subcutaneous infection with freshly isolated pneumonic strains or even directly with sputum or material obtained at the postmortem of lung victims ".

This opinion was endorsed by Girard, who stated in a recent summary [30] that the oneness (" l'unicité ") of the plague bacillus causing pneumonic, as well as bubonic, plague manifestations could no longer be contested.

Special virulence of pneumonic strains

The question of whether or not the *P. pestis* strains causing primary pneumonic plague are endowed with a particularly high virulence has been

answered differently by different workers. As will be discussed later in this study, some observers are of the opinion that the virulence of the causative organisms increases during the outbreaks but, as rightly stated by Wu Lien-teh,[98] such an exaltation of the virulence, gradually taking place in the course of the epidemics, could not explain their rise.

Mixed infection

The opinion of the Indian Plague Commission, that primary pneumonic plague might be the result of a mixed infection, has been shared by some subsequent workers.

Thus Norman White,[94] on the basis of theoretical considerations, conceived the idea that

" the plague bacillus *alone* does not, and cannot cause widespread epidemics of pneumonic plague . . . and that it seems more than probable that there is an additional organism at work—in other words, the plague bacillus in symbiosis with another organism is responsible for epidemic manifestations of pneumonic plague, which is a disease *sui generis* ".

Adopting this idea, Nicolle & Gobert [55] expressed the opinion that an association of the influenza virus with *P. pestis* might be of importance in the rise of pneumonic plague epidemics. A similar conclusion was recently reached by Sokhey,[81] who stated that pneumonic plague was a combined virus and bacterial infection, and that the virus factor made the disease highly infectious, whereas plague pneumonias, as they occurred as complications to bubonic infection, were not infectious.

Dealing with the statement of Norman White,[94] Wu Lien-teh [98] pointed out with much reason that " no line of distinction can be drawn between sporadic and epidemic manifestations of pneumonic plague . . . Whether pneumo-pest *spreads* or not depends upon extrinsic and not upon intrinsic factors."

In regard to the claim of Nicolle & Gobert,[55] who maintained that in Tunis a close connexion existed between outbreaks of influenza and pneumonic plague, Wu Lien-teh stated that :

" Influenza is not always prevalent at the time of pneumonic epidemics. In fact only very few instances are on record where a simultaneous existence of both diseases was noted. In many others, where special attention was paid to a possible co-existence of influenza during pneumonic epidemics, the former disease was conspicuous by its absence."

This opinion was endorsed by Girard,[29] who emphasized that in Madagascar the seasonal occurrence of influenza did not provoke an increased incidence of pulmonary complications in the course of plague outbreaks.

Contrary to the opinion of Sokhey, it is impossible to consider only patients suffering from primary pneumonic plague as infectious, in view

of the fact that, as a rule, epidemics of this form of the disease have been caused by bubonic patients with secondary pneumonia. It is not surprising that a spread of the infection by the latter patients was less frequent in India than in countries or plague areas with a cooler climate.

Pneumotropismus of Pasteurella pestis

As summarized by Wu Lien-teh [98] and by Girard,[28] some observers tried to explain the peculiarities of pneumonic plague by the assumption that *P. pestis* could become specially adapted to the lungs, with the result that strains of this nature would produce lung involvement even when entering the body through the skin. However, the experimental evidence presented in this respect is not convincing, and it is also noteworthy that secondary lung-manifestations were by no means particularly conspicuous in the few patients who contracted bubonic plague during pneumonic epidemics through contact with the sputum of the sufferers or in other ways, e.g., through direct contact or through the bite of infected human parasites.

Moreover, it is clear that this supposed pneumotropismus of *P. pestis*, which could develop only through repeated passage from lung to lung, could not be responsible for the rise of pneumonic plague outbreaks.

Role of the rodent species involved

Claims were made by some workers that human infections derived from certain wild-rodent species, especially the Siberian marmot, were particularly apt to result in secondary lung-involvement and that this peculiarity might account for the frequent appearance of primary pneumonic plague manifestations in the areas in question. However, the evidence available in this respect is by no means convincing. Thus, as can be gathered from the information collected by Wu-Lien-teh,[96] the incidence of secondary pneumonic plague was not particularly high in Transbaikalia, where the tarabagan was the main reservoir of the infection and commensal rats played no role in the causation of the disease. Among 280 plague patients in that area, whose histories could be studied, only 10 might have suffered from primary pneumonic plague.

More important still, pneumonic plague manifestations have been found to be frequent in countries where ordinary rats alone formed the reservoir of the infection, for instance in Madagascar.

Role of the flea species involved

No evidence exists to show that the species of vector fleas involved exerted any influence upon the appearance of pneumonic plague manifestations in man. *X. cheopis* is the only vector of the infection in Madagascar where pneumonic plague is frequent.

It is of interest to note, in this connexion, that according to Eskey [20] lung involvement was particularly marked in experimental animals which had been inoculated with pooled fleas, collected in the USA for the purpose of plague diagnosis, or with fleas infected with *P. pestis* in the Plague Laboratory of the US Public Health Service (San Francisco). It would not seem, however, that this peculiar feature was of any practical importance. As noted in the first of these studies,[63] pneumonic plague was not unusually conspicuous in the USA, and most of the cases of wild-rodent origin occurred singly.

As will be gathered from the statements made in the foregoing pages, it has not been possible to ascribe the rise of pneumonic plague epidemics to any peculiar property of the causative organisms or to a mixed infection. There is also no convincing evidence to show that the presence of the infection in any particular rodent or flea species is of special importance in the causation of such outbreaks. Since, however, as aptly stated by Wu Lien-teh,[98]

" apart from rare instances, primary pneumonic plague is not passed directly from rodents to man, but arises from human cases with secondary lung involvement, it becomes clear that factors which help to mould such secondary pneumonic features deserve our serious consideration ".

Discussing this problem, Wu Lien-teh [98] stressed the fact that, as a rule, pneumonic plague outbreaks could be traced back to a single patient —or, at most, a few patients—suffering from bubonic plague with secondary pneumonia; quite often outbreaks were traced to a traveller who developed such manifestations while proceeding from an infected to a hitherto uninfected locality. Clearly, therefore, the rise of pneumonic plague epidemics depends not so much upon the frequency with which any kind of lung-involvement is present in the bubonic patients in general, as upon the appearance of well-marked secondary pneumonia, leading to frequent cough and a copious expectoration of *P. pestis* in individual sufferers.

It has been maintained, in this connexion, that an unusual susceptibility to respiratory infections in general was apt to influence not only the frequency, but also the severity, of secondary pneumonia in bubonic plague patients, and consequently the rise of primary pneumonic outbreaks. Thus Girard [27] expressed the opinion that differences in the susceptibility to pneumococcal infections helped to explain why pneumonic plague was rare in the coastal areas of Madagascar and rampant on the high plateau. Similarly, Wakil [92] believed that an increased susceptibility of the dark-skinned inhabitants of Upper Egypt to lung affections in general was partly responsible for the high incidence of pneumonic plague in that region.

It has to be noted, however, that this factor, although apparently exerting an influence in some plague areas, was found to be of no importance in others. Thus, it is noteworthy that the Chinese in Manchuria, while apt to fall an easy prey to pneumonic plague, were rather resistant to pneumococcal infections (Wu Lien-teh [98]).

Factors lessening the resistance to plague infection are, no doubt, of universal and great importance for the evolution of marked secondary lung-involvement in bubonic patients.

Attention was paid to this point by some early workers such as Simond [80] who maintained that plague pneumonia might develop in individuals whose lymph-nodes were unable to hold back the causative organisms introduced by the bite of infected fleas. A similar view was also put forward in 1905 by Elliot (quoted by Wu Lien-teh [98]).

Far more important than such rather remote possibilities is the well-established fact that travellers who fall ill with bubonic plague before leaving an infected locality, or en route, are particularly prone to develop marked secondary lung-involvement. Petrie & Todd [61] maintained that the appearance of these lung manifestations was due to the muscular efforts made by such people which, causing the detachment of infected thrombi from blood-vessels round the buboes, led to lung embolism. No doubt, however, extrinsic factors, such as cold or rainy weather and defective nutrition during the journey, may also be of importance in the development of marked secondary pneumonia in travellers.

Petrie & Todd [61] postulated that, generally speaking, malnutrition, particularly vitamin deficiencies, might enhance the susceptibility to plague infection. They assumed that these factors might have been partly responsible for the frequency of pneumonic plague during the pandemic known as the Black Death.

Seyfarth (quoted by Wu Lien-teh [98]) drew attention to the fact that not only travellers, but also patients suffering from " ambulatory " plague, might develop lung complications when their resistance was impaired in some way, e.g., when they caught colds.

An elaborate hypothesis of Petrie & Todd [61] was that a high saturation deficiency of the air, because it caused an excessive evaporation of moisture from the pulmonary mucous membranes, might lead to the development of secondary pneumonia.

Whether differences in racial susceptibility to plague infection might account for the rise of pneumonic plague epidemics, as has been claimed by some observers, seems rather doubtful. Presumably, the differences ascribed to this cause were really due to extraneous influences, such as differences in nutrition or other standards of life, or to differences in susceptibility to respiratory infections in general.

While, as shown above, an increased susceptibility to respiratory infections in general, or a lessened resistance to plague infection, is apt to exert an influence on the rise of pneumonic plague epidemics, the appearance of such outbreaks is also greatly promoted by extrinsic factors, such as adverse weather conditions or unfavourable standards of life, which lead to close contact between patients suffering from bubonic plague with marked lung-involvement and their families and friends.

Factors Influencing the Spread of Pneumonic Plague

Infectivity of the patients

Being caused by an entry of *P. pestis* through the lower parts of the respiratory tract, primary pneumonic plague is almost invariably contracted only by persons coming within close range of the patients, and usually results from the spraying of the infective material by the cough of the sufferers. Though persons who were near the patients for but a short time occasionally contracted the disease, as a rule infection was found to take place in those individuals who had had prolonged contact with the sufferers.

Since the frequency of the cough and the quantity of the plague bacilli sprayed by it may show most marked differences, depending upon a greater or lesser severity of the respiratory involvement, it is not surprising to find that the opinions held by different observers in regard to the infectivity of primary penumonic plague vary greatly. It is true that patients in the early stage of primary pneumonic plague, i.e., the stage during which cough and *P. pestis* in the expectoration are rare or even absent, and similarly patients suffering from " pulmonary " plague without lung consolidation, are practically innocuous and that those suffering from slight pneumonic plague, in which cough is often inconspicuous and plague bacilli may be scanty in the sputum, are not highly dangerous. However, the reverse holds true for patients suffering from the typical form of the disease, in which cough is frequent and the sputum teems with *P. pestis*. Still, it is noteworthy that even the contacts of such patients may escape infection when, consciously or unconsciously, they adopt precautions which, as Wu Lien-teh [98] put it, may seem useless from a theoretical point of view.

Immunity

While, as noted in the third of these studies,[64] there can be little doubt that instances of natural resistance to pneumonic plague infection exist, these are of such rare occurrence as to be of no practical importance. The same holds true for the few apparently healthy persons found to harbour virulent *P. pestis* in their sputum or fauces who, one must suppose, have acquired an immunity against the infection. How long persons who have been cured of primary pneumonic plague remain immune is still unknown.

It has been claimed by some observers that certain races, particularly European ones, are not liable to contract pneumonic plague. That such an apparent resistance to the infection is due merely to extrinsic causes, however, is well illustrated by the fact that during the 1920-1 epidemic hundreds of Russians living under unfavourable conditions fell victims to the disease.

There can also be no doubt that the comparative rarity of pneumonic plague in children and in aged people, as well as the sometimes observed absence of the disease in other groups of the population, are due merely to less close contact, or to absence of contact, with patients.

Climatic conditions

Though it is generally agreed that the spread of pneumonic plague is most markedly influenced by the prevailing climatic conditions, some differences of opinion exist as to the manner in which these factors exert their influence.

Fraser [23] and Jennings [35] maintained in this connexion that an excess of carbon dioxide, likely to be present in overcrowded and ill-ventilated houses, might favour the spread of the disease because, as had been shown by Marsh,[50] this gas exerted in vitro a favourable influence on the growth and virulence of *P. pestis.*

According to Manaud [49] lung changes were more marked in plague-infected laboratory animals kept at lower temperatures (15°-18°C) than in those kept at about 30°C. He also established that guinea-pigs which had been made to inhale frozen particles of *P. pestis* suspensions were apt to develop primary pneumonic plague, whereas those which had been made to inhale fluid suspensions of the organism at room temperature developed cervical buboes. Manaud postulated, therefore, that human infections during the 1910-11 Manchurian outbreak had been effected by the inhalation of frozen sputum particles which, he contended, remained more easily suspended in the air and penetrated more deeply into the respiratory tract than liquid particles.

Teague & Barber [87] concluded from inhalation experiments made at different temperatures and under varying degrees of humidity that a lower water deficit of the atmosphere, such as is present during cold weather, caused the sputum droplets to float longer in the air—a feature which, in the opinion of the two workers, favoured the spread of pneumonic plague. Teague [86] maintained in this connexion that the water deficit in the badly heated houses of Manchuria was not higher than that of the outside air.

In the opinion of Chabaneix,[9] the 1910-11 epidemic was probably stopped by the dry weather prevailing in March and April.

Scrutinizing this evidence, Wu Lien-teh [98] pointed out with much reason that pneumonic plague epidemics had occurred not only in cold weather but also in countries with a warmer or even a hot climate where the weather conditions considered as essential by Teague & Barber [87] did not exist, and that—far more important still—a mediate infection, as presupposed by these two workers and also by Manaud,[49] was of rather limited, if any, importance as compared to direct infection contracted in the immediate vicinity of the patients.

An influence of bad ventilation, combined possibly with that of an excess of carbon dioxide in the air, deserves attention but it is not easy to separate the influence of these factors from that of overcrowding, brought about by absolutely or comparatively unfavourable weather conditions, such as cool or rainy seasons, or marked differences between day and night temperatures.

Social conditions

Unfavourable economic conditions, or other factors of a social nature, which lead to overcrowding, play side by side with, or sometimes even in place of, adverse weather conditions a most important role in the spread of pneumonic plague. The people's habit of congregating round the sick and holding much-attended and prolonged burial ceremonies—a common practice in many countries—also exerts an ominous influence in this respect.

That adverse social influences may promote the spread of pneumonic plague, even in localities with a warm climate, is well proved by the observations of Wakil [92] in Upper Egypt. He noted that, owing to the system used for irrigating the fields in the southern areas of Upper Egypt,

" during the month of March, April and May, when plague is most prevalent in Southern Egypt, as well as in the subsequent months, great numbers of inhabitants are obliged to remain idle in their badly ventilated houses. There is thus a greater risk of the propagation both of bubonic and pneumonic plague than in other parts of Egypt."

This overcrowding of the houses was all the more dangerous because people hailing from the regions concerned often went to work in the then infected ports of Egypt, but almost invariably went back to their native places when they contracted a disease. If they had become plague-infected, they often arrived " with pneumonic plague complications caused by the long and tedious journey from the extreme north to the extreme south of the country ".

Control measures

One must fully agree with the statement of Wu Lien-teh [98] that " there is probably no infectious disease which, theoretically, is so easy to suppress as lung plague ". Indeed, even in the past, when no effective means for abortive treatment existed, isolation of the patients, combined with segregation and careful observation of their contacts, was bound to cut short the outbreaks. Unfortunately, however, the people, resenting the hospitalization of the patients and still more their own segregation, often did all they could to hide the presence of the disease.

It has to be noted, on the other hand, that in certain remote regions (e.g., Mongolia), the people themselves often devised surprisingly adequate methods of protection against pneumonic plague.

Concluding remarks

As will be gathered from the foregoing pages, various factors influence the spread of pneumonic plague, the comparative importance of them being apt to vary from locality to locality. If adequate facilities for control work are available, outbreaks of this disease may be quickly terminated or may even be nipped in the bud. Failing such facilities, the infection is apt to spread, particularly if—or as long as—cases of a highly infectious character prevail and if untoward weather conditions or adverse social conditions or, as is frequently the case, a combination of both these factors lead to overcrowding.

Local and Extramural Spread

The local spread of pneumonic plague is usually of a familial character. Appearing first in one or, at most, a few households, the infection is carried by visiting relatives or friends to other houses in the same community which are then apt to become subsidiary centres for the spread of the disease. A transport of the infection per saltum often takes place simultaneously, effected by persons who are incubating pneumonic plague or who are already actually ill. As is well illustrated by a comparative study of the pneumonic plague epidemics in Mongolia and China, the intensity and rapidity of this extramural spread of the infection depend upon the density of the population and the kind of communications available. In Mongolia, which was sparsely populated, and in Shansi, where the means of communication were primitive, a slow spread took place. A much more rapid spread, not rarely characterized by long-distance sprints of the infection, could be observed in Manchuria which possessed a railway system.

Rat Plague during Pneumonic Outbreaks

Dealing with plague in the Punjab, Gill [25] stated that the mode of spread of the pneumonic type " is direct from man to man, but, owing to the readiness with which rats become infected, it is liable to give rise to a rat epizootic, which in turn gives rise to a bubonic plague epidemic ".

The validity of this statement, which stands in marked contrast to the opinion reached by most other workers, appears to be rather questionable if it is considered that (*a*) at the time when Gill made his observations, rat-caused bubonic, as well as pneumonic, epidemics occurred in the Punjab, and (*b*) it is often rather difficult to prove the persistence of rat-plague during the off-seasons. It seems most likely, therefore, that the appearance of epizootics during pneumonic outbreaks, as observed by Gill, was due to the recrudescence of pre-existing enzootics and not to a recent spread of the infection from pneumonic patients to the rats.

For similar reasons, no credence can be given to the claim of Allain [1] that the rat epizootic leading to the 1920-1 plague outbreak in Madagascar was due to the infection of a few rats in the vicinity of a hospital where some earlier pneumonic-plague patients had been confined. Girard [27] was rather disinclined to agree with Allain's contention.

As proved by observations made during the 1910-11 and the 1920-21 epidemics in Harbin and in Vladivostock respectively, in very rare instances rats may contract plague during pneumonic epidemics. It must be emphasized, however, that this transition of the infection never led to the appearance of epizootics. It seems altogether unlikely, therefore, that rats, even if they should become infected during such epidemics, could prove dangerous.

Occurrence of Bubonic Cases in Pneumonic Plague Epidemics

As noted before, rare bubonic cases which were definitely not due to an infection derived from plague-affected rodents, have been observed in the course of pneumonic epidemics. According to their pathogenesis, or probable pathogenesis, these cases may be classified as follows :

(*a*) *Infection through the bite of a patient.* This unique instance, recorded by Leumann,[44] concerned a hospital employee in India who had been bitten in the thumb by a delirious pneumonic-plague patient. The employee developed an axillary bubo on the corresponding side, but recovered.

(*b*) *Skin infection through pneumonic plague sputum.* One instance of this kind observed by Jettmar [36] concerned a woman who, having wiped away the sputum of a pneumonic-plague patient, developed a cubital bubo, and died.

(*c*) *Entry of plague sputum into the eye*, as referred to in the eighth of these studies.[68]

(*d*) *Contact infection through the skin.* Two cases of this kind are on record, concerning patients who had kissed pneumonic-plague victims and, developing plague carbuncles on the face, succumbed to the infection (Wu Lien-teh [96]).

(*e*) *Contact infection through the oral or faucial mucosa.* The three patients whose records Wu Lien-teh [96] was able to obtain showed "tonsillar" plague and cervical buboes. One of them recovered.

Reference has also to be made to a case observed by Fimayer.[22] The patient in question, who had contracted infection through contact with pneumonic-plague patients, developed a submaxillary bubo. It was considered uncertain whether the infection had entered through the oral or faucial mucosa, or through the eye.

(*f*) *Infections apparently due to the bites of human parasites.* One must agree with Wu Lien-teh [96] that the few patients with groin buboes observed

during the Manchurian pneumonic epidemics had been infected through the bite of human parasites. As stated by this author,[98] the rarity of such cases proved " that rat-fleas alone are of practical importance in the transmission of bubonic plague ".

Age, Sex, and Occupational Incidence

Statistics collected during the 1920-1 epidemic at Harbin [10] showed the following age incidence in 1,252 patients suffering from primary pneumonic plague :

Age (years)	*Number of cases*
0-10	21
11-20	83
21-30	593
31-40	385
41-50	130
51-60	33
61-70	6
71-80	1
Total	1,252

It should be noted that the incidence of the disease was highest (78.1 %) in the age-group of from 21 to 40 years. Cases among young children and aged people were rare but, as noted before, it is certain that this was due merely to lessened chances of contact and not to intrinsic causes.

All but 67 of the 1,252 patients admitted to the Harbin Plague Hospital were males, and 1,139 of them were labourers. However, this peculiar sex —and occupational—incidence of the disease is explained by the fact that the infection spread mainly among members of the labouring class who, leaving their wives and children behind, had come to Harbin in search of work, and lived there under most unhygienic conditions in overcrowded shelters. Experience elsewhere showed that pneumonic plague has no predilection for either sex.

Decline of the Outbreaks

There can be no doubt that extrinsic factors exert a most marked influence upon the decline as well as upon the spread of pneumonic plague outbreaks. If good facilities for control work are available, the outbreaks are bound to terminate rapidly, while less well controlled, or uncontrolled, outbreaks are apt to last much longer. It is also obvious that epidemics which started or gained impetus at a time when the weather was inclement will decline and eventually terminate when the climatic conditions become favourable, because then the contact between the people will be less intimate than when cold or rainy weather compels them to crowd together in the

often rather narrow space of their closely shut habitations. Thus it was often held that the major pneumonic outbreaks in China, which had invariably become widespread in winter, declined as soon as the temperature began to be warmer in spring, and terminated when the weather had become good.

The question of whether, in addition to these extrinsic factors, intrinsic causes for the decline and termination of pneumonic plague epidemics also exist, is a most interesting one. A few observers believed that a termination of the outbreaks might be brought about by a gradually decreasing virulence of the causative organisms. There can be no doubt, however, that, if such a decrease in virulence took place at all, it occurred only in exceptional instances. Generally speaking, the virulence of *P. pestis* remained high throughout the epidemics or, as some workers, such as Wu Lien-teh,[96] Girard,[27] and Duffau & Lallement,[17] maintained, even gradually increased.

It would seem impossible, at first glance, that under these circumstances a spontaneous decline of pneumonic plague epidemics could take place. However, observations made at the end of the 1921 epidemic in Harbin and also in Vladivostock showed nevertheless that pneumonic plague outbreaks might decline spontaneously. As noted in the eighth of these studies,[68] it was found that, whereas the victims on whom autopsies were performed during the course of the outbreak at Harbin showed evidence of lung consolidation, most of the autopsies carried out at the end of the epidemic revealed no such signs, but only congestion of the lungs and the deeper parts of the respiratory tract, in which case, however, the blood-stained exudate, usually met with in the cases with pneumonic foci, was absent. One patient, afterwards found to have succumbed to this pulmonary form of the disease, had actually had no cough or expectoration.

As summarized by Wu Lien-teh et al. in 1924,[99] similar observations had also been made during the pneumonic plague outbreak in 1921 at Vladivostock. There the incidence of " septicaemic " plague cases, as the Russian workers called cases showing no evidence of lung consolidation, was not high during the course of the epidemic, attaining a possible maximum of 15.2%. However, except for a few bubonic patients and some doubtful ones supposed to have suffered from intestinal plague, practically all victims seen at the end of the outbreak showed features of " pulmonary " plague.

Since the patients suffering from this type of the disease were obviously little capable or incapable of producing respiratory infection in their contacts, Wu Lien-teh and his colleagues felt entitled to assume that the prevalence of such cases at the end of the outbreaks at Harbin and Vladivostock was at least partly responsible for the termination of these epidemics.

That pneumonic plague epidemics may be really self-limiting was proved by a further observation of Pollitzer & Li [69] in Hunan Province, China, where such an outbreak was seen to end before any control measures had been taken—obviously because the last patients in each of the two first-affected households, and all patients in the subsequently affected families,

had no sputum, and in four out of nine instances also no cough. The spread of the infection in this epidemic, which was due to an importation of the disease by a traveller, may be illustrated thus :

Source of infection	*Number of cases*
Contact with patients having cough and bloody sputum	13
Contact with patients having only cough but no sputum	2
Contact with patients having neither cough nor sputum	0
Total	15

The reason why such " pulmonary " cases become prevalent at the end of the outbreaks is not clear. In view of the rapidity with which the change from the pneumonic to the " pulmonary " form took place in the epidemic observed by Pollitzer & Li,[69] it is difficult to believe that this transition is due to an increased virulence of the causative organisms, produced through their direct passage from man to man. It is hoped that further work will throw light upon this interesting and important problem.

RÉSUMÉ

L'épidémiologie des deux formes principales de la peste humaine — bubonique et pneumonique — fait l'objet de cette étude.

La peste bubonique (ou zootique) est en relation étroite avec l'infection des rongeurs, par l'intermédiaire des puces qui la propagent. La transmission d'homme à homme est fort improbable : les excreta humains et murins ne sont pas infectants ; le pus des bubons ne contient que peu de bacilles, voire aucun; les puces humaines ne jouent en général pas un rôle important. Il y a, au contraire, une relation géographique et quantitative étroite entre l'épizootie murine et l'épidémie humaine. Cette dernière se manifeste 10-14 jours après la première : 3 jours entre le moment où les puces quittent les rats morts et piquent l'homme, 3 jours d'incubation de la peste humaine, 5-6 jours de durée de la maladie. Dans une agglomération humaine, on n'observe le plus souvent qu'un cas par maison. L'épidémie humaine évolue parallèlement à l'épizootie : elle augmente avec la mortalité chez les rats, atteint un maximum et décline. Les conditions climatiques influent sur le pouvoir infectant des puces vectrices et déterminent l'évolution de l'épizootie et celle de l'épidémie. Si elles sont défavorables ou si les espèces de puces vectrices font défaut dans une région donnée, la peste humaine ne s'y implante pas. L'épizootie murine peut suivre son cours sans donner lieu à des cas de peste chez l'homme.

L'infection des ports entraîne en général celle de l'arrière-pays; par les villes, étapes du trafic, la peste atteint les régions rurales. Il peut arriver que l'infection passe des rongeurs domestiques aux rongeurs sauvages. Des foyers de peste selvatique se forment, qui ne sont pas directement dangereux pour l'homme lorsqu'il ne pénètre pas dans les retraites des animaux. Une certaine périodicité des épidémies — de 2-6 ans — a été observée dans les régions d'endémie pesteuse, mais elle n'est pas constante. L'histoire révèle, par contre, une indéniable périodicité séculaire des épidémies, la période présente

correspondant à une phase de déclin. Bien que le danger que présente actuellement la peste soit considéré comme secondaire, il serait erroné de penser que la maladie a perdu son acuité. Elle a presque disparu des grands centres urbains, il est vrai; mais son aire de répartition chez les rongeurs n'a guère diminué. Il est possible, au contraire, qu'elle ait augmenté; la maladie s'est implantée maintenant parmi les populations des rongeurs dans des arrière-pays indemnes avant la dernière pandémie. La peste des rongeurs sauvages n'a pas encore atteint sa limite d'expansion et il se pourrait que les foyers soient plus importants qu'on ne l'imagine.

Diverses méthodes ont été préconisées, qui devraient faciliter la prévision des épidémies. L'auteur analyse la fréquence de la peste en relation avec la race, l'âge, le sexe, la nature des occupations.

Il est généralement admis, malgré quelques observations contradictoires, que la peste pneumonique (ou démique) a pour origine des complications pulmonaires de la peste bubonique, et qu'elle se transmet d'homme à homme par les expectorations. Le bacille, agent des deux formes, constitue une seule espèce. L'« unicité » du bacille pesteux est considérée comme incontestable. Certains auteurs ont expliqué la virulence et la contagiosité de la peste pneumonique par l'association du bacille pesteux avec un virus, celui de la grippe par exemple ; cette hypothèse n'a cependant pas été confirmée par la clinique ou l'épidémiologie. La réceptivité plus grande de certaines populations aux affections pulmonaires ne semble pas être un facteur constant dans la propagation de la maladie. Plusieurs facteurs interviennent, probablement, dont l'importance relative varie d'une localité à l'autre.

Le passage de la peste pneumonique sur les rats, qui serait à l'origine d'une épidémie de peste bubonique, n'a pas été confirmé.

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