

## REMARKS

ON

## PLAGUE IN THE LOWER ANIMALS.

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THE association of epidemic disease in human beings with disease in the lower animals is as old as the history of epidemic disease itself. The spirit of modern inquiry is, however, far from content with the scanty and superficial evidence which has too often in the past been considered sufficient to establish the identity of a disease in animals with that prevailing in man. The great historical epidemics of influenza, cholera, and small-pox have frequently been associated in this indefinite way with a murrain among horses, cattle and sheep, and, at times, with a disease in wild animals. But this coexistence of disease in man and brute appears to have been most often and most definitely met with in the case of plague.

Modern research, while throwing doubt upon some of the earlier historical statements, has clearly established the fact that the infection of plague not only can produce a disease closely resembling plague in man when artificially introduced into the tissues of certain animals, but that it not infrequently does so under natural conditions. What these animals are it will be the object of this paper to show. Each group of animals will be discussed in turn, and the phenomena presented by the disease in them in nature and in the laboratory will be discussed separately.<sup>1</sup>

Not only the great group of *Vertebrata*, but also certain families of the *Invertebrata* have been shown to be either liable to an attack of plague or to be capable of affording growth to the plague bacillus when artificially introduced into their tissues. Among the *Vertebrata* the mammalia are more susceptible to plague than either birds, reptiles, or fishes; it is indeed open to doubt whether any of the last three groups of vertebrates are capable of becoming the hosts of the plague bacillus, at any rate under ordinary conditions.

Amongst the *Mammalia* the group of animals most often affected by the disease, and apparently the most susceptible to the plague poison, is that of the rodents. It will, however, be more convenient to consider the various groups of animals in the descending order of the zoological scale, beginning with the Primates.

## MONKEYS.

*a. Under Natural Conditions.*—On at least three separate occasions monkeys have been observed to sicken and die from a disease resembling plague at the time of an epidemic of that disease in man, and on each occasion the specific nature of the disease in these animals was proved bacteriologically. The first instance was at Kankhal, near Hardwar, in the Saharanpur district of the North-West Provinces. In October, 1897, a considerable number of these animals died, and in several of the bodies the plague bacillus was discovered by Mr. Hankin, the Government bacteriologist.<sup>2</sup> It was impossible to kill the surviving monkeys on account of the religious feelings of the natives, but a large number were trapped and kept in confinement until the epizootic was at an end. The outbreak lasted some fifteen days. Mr. Haffkine<sup>3</sup> has stated in regard to this outbreak that "out of 21 monkeys found dead in the streets, and 50 which died in captivity, only 6 showed buboes, and contained microbes similar in appearance to the plague bacilli." "In none," he adds, "was the microbe finally identified." But as just stated Mr. Hankin successfully isolated the plague bacillus in some instances, and there appears, therefore, to be no doubt that the disease in these animals was the plague.

The second instance occurred in Jawalapur, apparently about the same time. In at least one monkey the plague bacillus was abundant in the nasal secretion, and was isolated from the internal organs after death.

The third instance occurred in Gadag, near Dharwar, in the Bombay Presidency, in December, 1898. In the course of a few weeks as many as 7 of these animals were seen to fall dead from the trees. In 2 the discovery of a bubo and the isolation from the tissues of the plague bacillus left no room

for doubt as to the cause of death. These monkeys were thought to be the bonnet monkey (*Macacus sinicus*)<sup>4</sup>.

*b. Under Artificial Conditions.*—Both the common brown and the common grey monkey are very susceptible to the action of the plague bacillus when pure cultures are artificially introduced into their tissues. The grey monkey (*Semnopithecus entellus*) was found by the German Plague Commission to be very much more susceptible to the disease than the brown (*Macacus radiatus*).<sup>5</sup> Both these species were largely employed by the German and Russian Plague Commissions for experimental purposes. The latter found them so sensitive to the bacillus that an invisible prick in the palm of the hand with a needle moistened with a culture of plague bacilli invariably produced death.<sup>6</sup>

It will be seen from the above that the monkeys most commonly met with in India can and do suffer from plague. There is, however, little proof that they act to any considerable extent in spreading the disease. In view of their unusual susceptibility to the disease under artificial conditions<sup>7</sup> it is, indeed, surprising that they apparently suffer so rarely under natural conditions. It is clear, however, that they can aid, and perhaps have aided, in spreading the disease, and the fact is one that cannot be forgotten in plague administration.

## INSECT EATING MAMMALS AND BATS.

There is, so far as I am aware, no evidence that any of these animals have ever become the hosts of the plague bacillus, either under natural or under artificial conditions.

## RODENTS.

The *Rodentia* are, as already stated, the most susceptible to plague of all animals. The principal rodent animals in which plague has been observed to occur, either naturally or experimentally, are: Rats, bandicoots, mice, squirrels, guinea-pigs, porcupines, and marmots. Each of these may be briefly considered separately.

*Plague in Rats.*

*a. Under Natural Conditions.*—It has been proved beyond question that rats frequently suffer and die from plague, and it can scarcely be doubted that they play a considerable part in the spread of the disease from one part of a town or village to another. Until recently it appeared possible that the rat was among the most important factors in the spread of plague, and the fact that the geographical distribution of plague had corresponded hitherto, to some extent, with that of a particular species of rat, the *Nesokia*, lent some colour to this belief. The recent spread of plague, however, to the southern hemisphere, and particularly to Madagascar and to South America, where the *Nesokia* is unknown, has rendered the view that the distribution of plague on a large scale is dependent upon the movements of these animals no longer tenable.<sup>8</sup>

When rats are attacked with plague they usually leave their underground habitations and migrate, often for a considerable distance. This migration may perhaps in some instances precede the occurrence of disease in them, but of this there is no certain evidence. Migrations of rats are not uncommon apart from disease, and under these circumstances they may sometimes be seen advancing in immense numbers over fields or along country lanes, even in this country. An occurrence of this sort in connection with the appearance of plague among rats has not, so far as I am aware, been recorded. The migrations which undoubtedly occur appear to be on a smaller scale, less organised, and more prolonged and gradual. In most instances the actual migration is not observed, and its occurrence is only inferred from the disappearance of rats from one neighbourhood and their appearance in unusual numbers in some other neighbourhood. This was what occurred in Bombay in 1896.<sup>9</sup> A similar observation was made in Karachi,<sup>10</sup> and in Hyderabad (Sind).<sup>11</sup> In Calcutta, where plague appeared in the city in April, 1898, the rats almost disappeared from the native quarters, where before they had swarmed. Among those which remained a considerable mortality occurred, which was proved in certain instances to have been due to plague.

This appears to be what usually happens when plague breaks out as an epidemic and epizootic; the larger number

of rats migrate, the remainder are attacked by the disease. It certainly occurred in Karachi<sup>12</sup> as well as in Calcutta and Bombay. It was also observed in Canton in 1894.<sup>13</sup>

The extent of the mortality in rats is not easy to determine. An increase in rat mortality may be partly apparent, due to the observer's attention being specially called to these animals in times of plague, and partly artificial, as the result of a campaign against rats when plague is prevalent. In some instances very large numbers of rats are said to have been infected, apparently more or less simultaneously. At Mengtze, in the Chinese province of Yunnan, such rats are said to have left their holes "in troops."<sup>14</sup> The same was observed at Pakhoi.<sup>15</sup> On the shores of the Yangtze, opposite Nanking, in 1881, rats died "in hundreds," and baskets and boxes were filled with them.<sup>16</sup> In Mandvi, the quarter of Bombay first attacked, "thousands" of rats were said to have died about a month before the plague appeared in human beings.<sup>17</sup> In a single infected house in Mokundpur, in the Punjab, as many as 200 dead rats were discovered.<sup>18</sup> In Canton the dead bodies of 22,000 rats were brought in as the result of an offer of a small reward for every rat killed.<sup>19</sup> More often the rats die in small numbers; the epizootic extends more slowly and is prolonged over a considerable time. This was certainly the case in Calcutta in the summer of 1898 and early part of 1899.

The symptoms of plague in rats under natural conditions appear to vary considerably. Buboes, it is known from *post-mortem* examinations, may occur in rats. Whether rats may be affected by the pneumonic form of the disease in nature would appear to be uncertain.<sup>20</sup> That it can be produced in them artificially has been conclusively proved.<sup>21</sup> The disease appears usually to become septicæmic before the death of the rat, and the bacillus can be found in many parts of the body. Severe affection of the nervous system is also evidently present, just as in man, as indicated by spasmodic and paralytic symptoms, and by a dazed appearance and staggering gait. Sometimes there is a limping jerk or spasm of the hind legs,<sup>22</sup> and sometimes the hind legs are dragged along the ground as though paralysed.<sup>23</sup> In some instances rats have been seen to rush about madly without fear of man, and after capering round the room to fall dead at the feet of the observer.<sup>24</sup> At other times they have been seen to move about listlessly in back gullies, sinks, and bathing places,<sup>25</sup> or to jump up suddenly and, turning round, to fall dead, or to "spring continually upwards from their hind legs as if they were trying to jump off something."<sup>26</sup>

The appearances after death vary. In a rat which I dissected in Calcutta, and from whose tissues I obtained plague bacilli in pure culture, the following were the principal *post-mortem* appearances:

The rat was recently dead, rigor mortis was present and fairly marked. The animal lay prone on its belly, with all four limbs extended. (Rats dead from ordinary causes are more usually found lying on one side, with the limbs flexed.) The body was not swollen, and there was no external sign of the cause of death. On opening the body the lungs were found deeply engorged; on section they exuded frothy blood; they were crepitant throughout, and there was no pneumonic consolidation in any part of them. The spleen was much enlarged and deeply engorged with blood. The liver was intensely congested; it was not enlarged; its outer margin presented a mottled appearance; on section it was found to be full of blood, and the liver substance was somewhat friable.<sup>27</sup> No hæmorrhages were seen anywhere. Agar tubes were inoculated with blood from the lung, spleen, and liver. The lung tubes showed contaminations, but from the spleen and liver pure cultures of the plague bacillus were obtained. No buboes, it should be added, were present in this rat. They have, however, been frequently observed in other rats.<sup>28</sup>

#### SOURCES OF INFECTION OF RATS.

The most important and obvious sources from which these animals might be expected to contract the disease are the following:

- a. The soil.
- b. Grain or other food stuffs.
- c. The tissues of other animals (including human beings) dead from plague.
- d. Infected rags, articles of clothing, or dressings from plague patients.
- e. Infected insects.

#### a. From the Soil.

That rats may become infected from the soil is probable. It is among the oldest beliefs in regard to the causation of plague that the disease arises from some miasmatic exhalation from the earth. Modern observation lends little support to this view; but it has shown that the soil or its surface can, under

certain conditions, receive and retain for a time the virus of plague in an actively infective state. That the plague bacillus ever passes deeply into the earth must be doubted, as it appears to be an organism requiring abundance of oxygen for its growth. Yersin claimed to have found the bacillus in the soil at a depth of 5 cm.; but though this bacillus presented all the morphological, cultural, and staining characteristics of the plague bacillus, it was not toxic to animals.<sup>29</sup> Lowson and Takaki failed to find the plague bacillus in earth.<sup>30</sup> Kitasato only once succeeded in infecting an animal with plague by injecting into its tissues the dust of an infected room.<sup>31</sup> Okada failed in his experiments with dust obtained from a like source, but succeeded in a certain number of instances with soil obtained from the surface of earthen floors, and from "below the floors" of rooms in which plague patients had lain. With soil obtained from 26 different sites, 57 mice in all were inoculated; of these 14 died of plague, as shown by the discovery of the plague bacillus in their tissues; 8 died of tetanus; 3 of malignant œdema; 6 from some other cause, the plague bacilli not being found in their tissues; and 24 remained alive and healthy. This author concludes that if the soil is rich in organic matter, contains a certain amount of moisture, and is only slightly exposed to air (*sic*) and light, it may retain the plague bacillus for a considerable period. In some of his successful experiments the soil was kept for as long as eleven days before being inoculated.<sup>32</sup>

It may be regarded as proven, then, that the soil may, under certain circumstances, contain the virus of plague. Rats, living in burrows in the soil, and when on the surface constantly grubbing with their noses in the dust and surface layers of the soil, might in this way become infected. The ease with which the earthen floors of native houses in India and China may become infected from the discharges, etc., of plague patients scarcely requires to be pointed out.<sup>33</sup>

#### b. From Grain.

The possibility of rats contracting plague from infected grain cannot be overlooked. When a rat epizootic is once started, diseased animals must almost certainly infect any grain stores to which they gain access, either by means of their dejecta,<sup>34</sup> their sputa, or by the dead bodies of such as die among the grain. Whether a rat epizootic can be started by infected grain brought from a distance is less certain. Hankin's<sup>35</sup> experiments tended to show that the plague bacillus, when artificially mixed with grain of various kinds, or with flour, dies out in from four to six days, but that it may survive for periods extending up to thirteen days. He failed to find the bacillus in specimens of grain from many sources, including grain which had been exposed to infection by rats sick and dead from plague. Negative evidence of this character is, of course, only presumptive and not conclusive proof that grain does not, under natural conditions, sometimes harbour the plague virus. The behaviour of the plague bacillus obtained from cultures on artificial media is probably quite different from its behaviour in nature, and the plague bacillus is probably very difficult to detect in grain as it is certainly difficult to detect in soil. On the other hand, the frequent occurrence of rat epizootics in the neighbourhood of grain stores or other food stores (as observed in Bombay, Calcutta, Alexandria, Mauritius, and innumerable other places), is no proof that the disease is started or spread by infected grain or other food, as a rat epizootic must of necessity be observed where rats most abound, that is to say, in the neighbourhood of grain or other food stores. For the present, therefore, it must be regarded as very probable, though as not absolutely proved, that rats can be and are infected with plague from grain or other food.

#### c. From the Flesh of Other Animals.

That a plague epizootic in rats may start, and also be perpetuated by their eating the dead bodies of infected animals—including human beings and also other rats—is certain. An instance of rats becoming infected through eating the tissues of a human plague cadaver came under my own observation in Calcutta. A native died early in the morning of June 15th, 1898. I saw the body at 7 A.M., four hours after death. The *post-mortem* signs and the history of the illness left no doubt that the man had died from plague, and this was further proved by the isolation of plague bacilli from the bubo (in the

left groin) and from the liver. In examining the body I observed that one big toe had been partly eaten away, evidently by rats. In the godown where the body had lain, three dead rats were discovered shortly after, and dead and dying rats were seen on the adjoining premises during the next week or two. On June 30th—fifteen days after the occurrence of the first case—a European sickened with plague in the adjoining house. In this case—which will be referred to again later in connection with the question of dogs and plague—the patient stated that, two or three weeks before his illness, his dog brought a dead rat and put it on his bed; the patient had touched the rat in removing it from his bed. Seven days after this patient sickened, a Eurasian female, living in a house four doors from where he lived, and three doors from the house of the original patient, was attacked with plague. It was ascertained that dead rats had been found in her garden, and that she was in the habit of gardening, and of spending much time among the flower beds where the dead rats were found. Dead rats were also seen in the premises of the next house to hers. Thus, in five out of six houses, in one street and all adjoining, a mortality among rats was observed immediately subsequent to the incident above described—the consumption by rats of the tissues of a human plague cadaver. Human cases of plague occurred in three of these houses (including the original case). There is scarcely room for doubt that the disease was spread by the rats.<sup>36</sup>

An incident of precisely the same character is reported to have occurred at Khankhanan in the Punjab. The patient in this case was an elderly native woman; she died, and the body was locked up in a room to await medical inspection. Next morning it was found that the nose and part of one cheek had been eaten away, almost certainly by rats. During the next few days, in every house in the block of buildings in which the corpse had lain, cases of plague developed, and many dead rats were found in these houses when they came to be disinfected.<sup>37</sup>

Possibly other instances of this nature have been observed elsewhere. The risk which plague cadaver offers as a means of infecting rats is recognised in most plague hospitals, where a cover of wire or other material is or should be provided to protect bodies from the attacks of these animals.

That rats may also contract plague from feasting on the bodies of other rats dead of the disease is exceedingly probable, though I am aware of no positive proof of their ever having done so. In earlier times it was believed that birds and beasts of prey would not touch the body of an animal that had died of, or in times of, pestilence, as though some instinct warned them of the danger to themselves; but in regard to rats there is certainly no evidence of any such squeamishness or cautiousness, and it is very unlikely that such notorious cannibals as these animals are would refuse to eat the body of another rat that had died of plague.

#### d. From Rags.

The possibility of rats becoming infected by sniffing at or eating rags, clothing, or poultices or dressings from a plague patient is obvious, though whether such an occurrence has been absolutely observed I am not in a position to say.

#### e. By Insects.

Finally there is very good reason to believe that plague may be and is spread to rats from other rats, and perhaps from human beings, by insects, of which probably the flea is the most important.

#### MODE OF INFECTION IN RATS.

The manner in which the virus of plague enters the tissues of a rat is uncertain. It probably enters either through the respiratory organs, through a discontinuity of skin, or through the alimentary canal. The absence of conclusive evidence that a primarily pneumonic form of plague develops in rats under natural conditions may be held to indicate that the first mode of invasion—through the respiratory organs—is at least rare. The presence of a bubo or of many enlarged lymphatic glands in some rats would point to an invasion through the skin, with consequent production of the disease in its bubonic or septicæmic form. The discovery of marked changes in the alimentary canal, and in at least one instance of sand and earth in the stomach,<sup>38</sup> would point to an invasion of the virus through the alimentary passages.

#### Transmission of Infection from Rats to Man.

If the manner in which rats contract plague is to a great extent uncertain, it is no less uncertain how the disease is usually transmitted to man from these animals. That it is sometimes so transmitted is certain. In rare instances it has seemed possible to state definitely that an infected rat has given the disease directly and immediately to a human being, either under circumstances which leave no doubt as to the manner in which the infection is transmitted (as by a bite) or in some manner less obvious (as by merely touching the animal). But in the large majority of instances the mode in which the infection passes from rat to man is quite uncertain, and there is often much room to doubt whether any such transmission has in fact taken place, or whether men and rats have not both caught the infection from some common source to which they have been exposed.

Direct transmission of plague from rat to man by means of a bite from an infected animal must be extremely rare. I am aware of only two instances in which such an occurrence has been observed. In one the patient had been bitten by a rat on both great toes; the skin was penetrated, and blood oozed from the wounds; an attack of plague followed, from which he ultimately recovered.<sup>39</sup> The second instance occurred in Mandvi (Bombay) about the same time. In this case gangrene developed round the wound, and the patient died.<sup>40</sup> Details are, however, lacking to prove that the rats who bit these persons were infected, and that the disease was the result of the bite, and not due to other causes. This mode of infection from rats, from the extreme rarity of the conditions under which it can occur, may be passed over with little comment. The part such a mode of infection plays in spreading plague must be infinitesimal.

Of much more common occurrence is the development of plague in persons who have actually handled a living or dead rat infected by the disease. Many examples of this kind have been recorded from the time of the epidemic in Jehangir's reign to the present day. Unfortunately in most of these instances details are wanting to show how the infection may be supposed to have passed from the animal to the human being, and this is equally true of the two cases of rat-bite just mentioned. It would be all-important to know whether in these cases the bubo developed in the upper extremity of those persons who have touched the rats, and on the same side as the hand which touched the animal (when only one hand had done so); or in the glands corresponding to the limb bitten by the rats in the other cases. It is conceivable that when a person handles an infected animal, alive or dead, some of the infecting material may be conveyed directly from the body of the rat to the person's hand, and may be subsequently rubbed in to some minute scratch or hang-nail or other skin-discontinuity; or it may be transferred to food (Indian natives invariably convey their food to their mouths in their fingers), and so gain access to the mouth and upper alimentary or respiratory passages. But that this does occur is at present only a matter of speculation and inference.

In the vast majority of instances where plague in rats is associated with or followed by plague in human beings there is no evidence that the affected persons have touched these animals, and it is necessary to suppose either that the transmission of the disease from rat to man has been effected in some mediate manner—as, for example, through the soil, food, fomites, or insects—or that the rats and the persons affected have become so from some infected source common to both. Probably both occur. Of the four mediate means of transmission just named, it is very possible that insects will prove to be the most important. A very plausible case has, indeed, been made out for the spread of plague from rats to man by means of insects. This question is briefly referred to later.

#### RAT SICKNESS AND HUMAN PLAGUE.

A very large number of instances of the association of sickness and death among rats with a plague epidemic in human beings have now been recorded; and though it has not been proved, in a large proportion of these instances, that the sickness and death among rats were due to plague, this has been conclusively established in a very considerable number. It is, therefore, exceedingly probable that, even in those instances where it has not been proved, the affection of rats

was nevertheless of a specific character. The following, among other examples, came under my own observation in Calcutta.

1. A punkah coolie employed in a European house was attacked with plague on May 17th, 1898. The house was a fairly good-class masonry building, but the servants' quarters where the patient was in the habit of sleeping were very close and insanitary. The smell of dead rats had been noticed since April 30th, and in the interval the bodies of four dead rats had been found about the premises. As the smell continued, I had some boards taken up in the floor of the drawing-room, and here the decomposed bodies of four other rats were discovered. This room was a ground-floor room, and the servants' quarters were just opposite its windows, and separated from it by about 10 feet. The house was temporarily evacuated and disinfected and there was no recurrence of rat mortality. The inmates all stated that the death of these rats was a most exceptional occurrence and that they had never known the like to happen before.

2. A similar instance occurred about the same time and in the same neighbourhood as the one just described. A native employed in a small *modi* shop, the principal wares of which were grain, flour, oil, spices, and similar articles of food, suddenly died. An examination of the body left no room to doubt that he had died of plague. On inquiry I learnt that twelve dead rats had been found on the premises during the preceding "week or two" (closer accuracy was impossible). The shop and its contents were thoroughly disinfected, and some of the latter burnt—measures which raised a storm of abuse in the native press, but which were successful in preventing any further spread of the disease in that neighbourhood.

3. A little later, on May 31st, 1898, a death occurred in a shop of exactly the same character as the last, but even smaller, closer, and darker than that one had been. This shop formed part of a native bazaar, made up, as most such bazaars are, of a series of narrow passages with stalls on either side. Meat, fish, fruit, vegetables, stuffs, and dry goods of various kinds were exposed for sale, mostly upon low, wooden platforms, raised about one foot from the surface of the earth. The passages were either unpaved or imperfectly paved, and the earth could be seen riddled with rat-holes in all directions. Upon inquiry from the caretaker of the bazaar I learned that rats had been dying in considerable numbers for some time before the death of the native in question occurred; the bazaar was closed and locked up at night, and on opening it each morning the dead rats were found on the stalls or in the passages. As many as 25 rats had been found on one day. A similar mortality in rats had never been known to occur there before. The bazaar was disinfected, and I made arrangements to have the whole floor of the bazaar watered daily with a disinfecting solution. The rat mortality ceased, and there was no recurrence of it for at least six months afterwards. On July 4th, however, a case of plague occurred in a native hut some fifty yards from the bazaar, and at the opposite end from where the first death had occurred. No dead or dying rats had been seen in this or the adjoining huts, and the source of infection in this case could not be ascertained. Possibly the rats had been driven out of the bazaar by the measures of disinfection adopted, and had carried the infection to this hut.

4. On March 12th and 13th, 1899, two boys, brothers, were attacked with plague. They were the sons of the Madrassee butler in a very large European house in one of the best parts of Calcutta. They lived in a small but very clean masonry house in the compound. They were attacked about a fortnight after returning from Madras to Calcutta. Both were removed to hospital, where both subsequently died. The houses from which they were removed, and some of the neighbouring out-houses and surface drains, were thoroughly disinfected. On March 24th, ten days subsequent to the removal of the boys to hospital, I learnt that two dead rats had been found on the previous day on the premises of another large European house on the opposite side of the road from the first. I then made personal inquiries at several of the neighbouring houses, and learnt that at one (one of the leading clubs) two dead rats had been found on the 23rd and a dead cat on the 24th; a dead cat had also been found "about a fortnight" previously. At another house, though no dead rats had been observed before, one was reported to me on the 26th, and the body was kept for my inspection. In this rat I found the *post-mortem* appearances already described, and isolated the plague bacillus from liver and spleen. In the meantime there had been no observed rat mortality on the premises where the two boys had died, nor was there subsequently. Those premises had, it will be remembered, been thoroughly disinfected, and equally thorough disinfection was practised on the other premises where the rats had died. No further rat mortality and no subsequent cases of plague in human beings were observed in the neighbourhood. To explain this sequence of events it seems almost necessary to suppose that the thorough disinfection in the first instance drove the rats away from the premises first infected to the adjoining premises, where a small, localised epizootic was slowly developing when it was cut short by the measures of disinfection put in practice there.

A very large number of examples analogous to those just adduced might be quoted, both from my own notes and from the recent literature of plague. For the present it must, I think, be admitted that rats can and do suffer from plague under natural conditions; that they can and do act as a means of diffusing infection and transmitting it to man; but that the extent to which they are responsible for the diffusion of the disease and the distance over which they diffuse it is uncertain. It is probable that they are an important, but not the sole, means of spreading the disease.<sup>41</sup> In a group of 32 cases of plague which I investigated on this point in Calcutta in 1898, I found positive evidence of the death of rats in 7 only. It is, however, quite possible that in many others rat mortality had occurred; in many of the cases it was most difficult to get any accurate or trustworthy information at all, and most of the patients were drawn from a class of slaves

who would probably pay little attention to the discovery of a sick or dead rat.

In like manner it is uncertain how far rats may carry the infection of plague. In Bombay they were believed to have carried the disease from Mandvi, on the south-east of the island, to Malabar Hill on the west, some three miles away; to Sion, Worli, Mahim, etc., on the north, some six miles away; to Bandra, some eight miles away; and to many places on the island of Salsette, a dozen or more miles away. Whether, however, a single rat, or troops of rats, could carry the infection so far is uncertain. In all these instances the spread was not particularly rapid, and there was time for the occurrence of successive short emigrations of rats, with successive production of local epizootics farther and farther removed from the original outbreak. I am aware of no instance in which migrating rats have been proved to carry plague infection over longer distances than this; or in which infected rats have been carried by train (in grain or goods waggons, for example); or, finally, in which rats have been proved to carry plague infection from one port to another on board ship.

In regard to the possible carriage of living infected rats by train, with consequent introduction of infection into a place from a distance, the matter is not a wholly simple one, and it has, perhaps, not yet received the attention which it deserves. I have not succeeded in finding any published observations bearing upon this point; those which I was myself able to make related to but one town and one set of circumstances, and they led to a negative result.

My inquiries related to the outbreak of plague in Calcutta in 1898; they were made of the station master, goods superintendents, passenger and goods guards, and clerks attached to the godowns of the Howrah Station, the terminus of the lines of railway which bring all the goods and passenger traffic from the west of India to Calcutta. I learnt that grain (with which rats are so constantly associated) is packed in sacks and not in bulk; and that goods and grain waggons travel very slowly, taking fourteen or fifteen days to accomplish a journey done by passenger trains in two days. None of my informants could recall a specific instance in which he had seen a live or dead rat in a waggon, but more than one thought he might have seen one and forgotten, as he would not pay much attention to such an occurrence. One guard had seen a very large dead rat on the footboard of a waggon; he thought it had been carried some considerable distance in that position, but how far he could not say. It would be possible for a rat to gain access to a waggon while it was being loaded, as a flap connects it with the platform, and a waggon might be left for a time with the doors open and the coolies away. Once inside and the door sealed, it is a question how long a rat could survive; there would be abundance of food and probably of air, but there would be no water, and in India the heat would be intense. On one occasion, shortly before my inquiries were made, a dog had been accidentally shut up in a waggon, and travelled for twelve hours before the sound of its whining led to its release. Supposing a plague-infected rat to gain access to a waggon, it would probably not survive any great length of time; it would die and its body would be found at the end of the journey. How long the plague bacillus can survive in the body of a dead rat is uncertain; I have never succeeded in finding it in bodies where decomposition had already set in.

It would seem probable, then, that the infection of plague might be carried by train in the body of an infected rat over a distance which a goods train can traverse in one day or, probably at the most, two days. It is unlikely that a plague-infected rat would survive longer than this and be in a condition to escape at the end of the journey and diffuse the infection amongst its fellow-rats in the new locality. It is very unlikely that a plague-infected rat would be carried in a passenger train. There remains the possibility of the plague virus being carried by train in grain or other goods contaminated by the dejecta of plague-infected rats.

Whether the plague infection has ever been carried over short distances by train in the bodies of living infected rats, or over longer distances in rat dejecta, I am aware of no evidence to show. Plague has often been carried by train in the bodies of infected persons, but I know of no proved instance in which it has been carried by train in the bodies of rats or in rat dejecta.

## RATS ON SHIPBOARD.

In regard to the carriage of plague-infected rats on board ship from one port to another, such a mode of transport of infection is generally believed to be possible. The fact that in Calcutta, Bombay, Alexandria, Oporto, Mauritius, and many other places, the earliest cases of plague occurred in the neighbourhood of the docks, or in persons employed among shipping, lent great probability to the view that the infection was in these instances imported by sea; and as in no instance was it possible to prove its introduction in the body of an infected person, or in infected fomites, and as in some of these instances a rat mortality near the docks accompanied or preceded the outbreak in human beings, it has seemed exceedingly probable that infected rats, or articles contaminated by them, have been the means of introducing the infection. There is great difficulty, however, in finding proof of such an occurrence. On no recent occasion, it would seem, has it been possible to trace an outbreak of plague to a definite introduction of the infection by sick or dead rats upon a certain known ship. On the other hand, sickness and death of rats might so easily occur on board a ship without being discovered, or, if discovered, without their significance being realised, that this negative evidence is no proof that the infection has not been brought by sea in infected rats or articles contaminated by them. A plague epidemic always takes some time to develop, and by the time it is recognised the ship which brought the infection may have left the port; or such an ordinary circumstance as the finding a few dead rats on board many weeks before may have been quite forgotten.

I am aware of only three recorded instances, though probably others have escaped my notice, in which the development of human plague cases on board a ship has been associated, or believed to be associated, with a mortality among rats. They are the following:

a. The ss. *Shannon* left Bombay for Aden some time in March, 1898; the day before she sailed "several dead rats" were found in the purser's storeroom on board, and the day after she sailed a postal official on board developed symptoms of plague.<sup>42</sup>

b. A French barque, the *Duchesse Anne*, arrived at San Francisco from Hong Kong on October 28th, 1898, having been seventy-four days on the voyage. According to the telegrams to the daily press at the time, the captain had died on board of plague "in August," a member of the crew had died of the same disease "in September," and "all the rats" on board had died of what was believed to be plague. Fuller details of the incidents, however, throw great doubt on all these statements. The captain, it is true, died on the fifth day of the voyage, but of what disease could not be ascertained. A sailor died on the thirty-fifth day out of what appeared to have been phthisis. One or two rats were trapped (when is not stated), but no dead ones were found. There was no reason to suppose that the captain had died from plague.<sup>43</sup>

c. In May, 1898, several cases of plague occurred among the crew of the ss. *Mahallah*, a ship belonging to the Khediviah Company, and employed on postal service in the Red Sea. The infection seemed to cling to this ship in a remarkable manner, successive cases of plague developing during a whole month, in spite of repeated disinfections. During the earlier disinfecting processes dead bodies of rats were, it is stated, found in the boat, and other rats were seen, still living, which ultimately died of what was believed to be plague. Sick animals were seen even after the second process of disinfection.

The details hitherto published in regard to all these cases are too scanty to allow of any deductions being drawn as to the parts played by the rats in their production. In the other published instances of plague occurring on board ship at a distance from an infected port—such as those in the Thames in 1896, on the *Golconda*, *Carthage*, *Bhundara*, *Caledonia*, *Dilwara*, *Patna*, *Peninsular*, *Berenice*, *J. W. Taylor*, *Kilburn*, or *Montevideo*—the accounts which have appeared in the daily or weekly press have either made no mention of sickness or death among the rats on board, or have definitely stated that nothing of the kind had been observed.

## INFECTION OF RATS UNDER ARTIFICIAL CONDITIONS.

The high degree of susceptibility of these animals to plague has been shown experimentally by a large number of observers. The disease has been communicated to them by inoculation with pure cultures of the bacillus, by implantation of fragments of organs from plague cadavers under the skin of rats, by feeding with infected material, by intraperitoneal injection of plague material, and by placing fragments of organs or a portion of a pure culture of the bacillus in the nostrils or in the conjunctiva.<sup>44</sup>

*Plague in Bandicoots.*

This animal (*Nesokia bandicota*), which is common enough in India, though much less common than the ordinary house rat, has been known to become the subject of plague. Re-

corded observations of the kind are, however, scanty, and I am aware of only one positive instance in which these animals contracted the disease. Mr. Hankin<sup>45</sup> has stated that in Upper Colaba, a district of Bombay, in the twentieth week after plague first appeared in that city, an outbreak of the disease occurred in bandicoots in a particular house. The symptoms of the disease in these animals and the numbers attacked are not given. A servant who each day disinfected the house and removed the dead animals contracted plague, and Mr. Hankin himself developed an attack of the disease six days after investigating the occurrence. I have never observed plague in bandicoots in Calcutta, nor was any sickness or mortality recorded as occurring in these animals in that city during 1898 or the early part of 1899. It would appear that though bandicoots may occasionally become infected by plague, they cannot be regarded as of the same importance as the ordinary house rat in the spread of this disease.

*Plague in Mice.*

Though mice of all kinds are very susceptible in the laboratory to plague, there is little evidence that they suffer from it to any great extent under natural conditions. The fact is a remarkable one, for these animals would appear to be quite as much exposed to the ordinary sources of infection as rats, and in the laboratory they are quite as sensitive to the plague bacillus as rats are; yet in the wild state they have not hitherto been observed to contract the disease to anything like the same extent as the larger animal. In Bombay there has been no evidence of any epizootic among mice during the successive epidemics of plague which have visited that city. In 1896-97 it was definitely observed that the mice were well and lively, while the rats were dying in large numbers.<sup>46</sup> In one or two instances the discovery of a dead mouse was associated with the occurrence of plague in a human being.<sup>47</sup> At Bandra, near Bombay, some dead mice were found, while plague was epidemic, but no proof has been published that they died from plague.<sup>48</sup> In Calcutta, in 1898 and the early part of 1899, I never heard of a single instance of mice dying under suspicious circumstances, although rats were undoubtedly dying of plague. At Kankhal and Jawalapur, where a smart outbreak of plague occurred in 1897, only two dead mice were seen, and in neither could the plague bacillus be detected.<sup>49</sup>

On the other hand, in some recent instances of plague elsewhere, a mortality among mice has been observed to coexist with plague mortality in rats and human beings. Thus at Tai-Ho-Kou, in Formosa, in September, 1897, both rats and mice are said to have died at the same time as the indigenous cases of plague occurred in human beings.<sup>50</sup> In like manner, during the small outbreak of plague at Jeddah in March, 1898, large numbers of sick mice are said to have been seen. Some were so ill that they could be caught by the hand. In four dead mice the plague bacillus was detected in their tissues (whether more were examined with negative results is not stated).<sup>51</sup> In Alexandria dead mice were found, in addition to dead rats, in a certain rag and bone store, in March, 1899, at a time when plague was believed to be in the city. No proof is, however, offered that the animals had died from plague.<sup>52</sup>

Plague epizootics in mice would, then, appear to be rare, though other instances might be quoted from the accounts of past epidemics—as, for example, in the outbreak of plague in the Punjab and Kashmir about 1611,<sup>53</sup> and the more recent occurrence of mortality among mice (and rats) in Barkuri village, Danpur Pargana, Kumaon, a known centre of *mahamari*, or hill plague, though this mortality was not at the time accompanied by any mortality from plague in human beings.<sup>54</sup> Generally it would seem that mice play a very much less important rôle than rats in spreading plague.

*Plague in Squirrels.*

On at least one occasion these animals have been proved to contract plague in the wild state. In December, 1898, a grey-striped squirrel was picked up dead at Gadag, in the southern portion of the Bombay Presidency, where plague was at the time prevalent. There was no bubo in this animal, but the spleen was enlarged and plague bacilli were isolated from its tissues.<sup>55</sup> On another occasion, in Poona, two dead squirrels were picked up in the lines of the 2nd Bombay Lancers,

among whom plague was at the time prevailing. The belief was expressed that the animals had died from plague, but no positive proof of this is adduced.<sup>36</sup> Experimental evidence of the susceptibility of squirrels to plague is apparently lacking. These animals are extremely common in India, and the rarity of recorded instances of their contracting the disease must be taken to indicate that they are not highly susceptible to the virus. The part they take in its spread must be an extremely small one.

#### Plague in Guinea-pigs.

In the laboratory these animals are very susceptible to the virus of plague, and they are among the most convenient for experimental purposes. I am aware of no published evidence that these animals have contracted the disease in a natural state.

#### Plague in Porcupines.

The single reference that I have seen to the occurrence of plague in these animals is the following brief statement published last autumn: "It is reported at Mysore that several porcupines have died in the Zoological Gardens from bubonic plague."<sup>37</sup> In view of the great susceptibility of other rodents to plague, there is no *a priori* reason why porcupines should not be liable to it. Detailed observations upon the manner in which animals with so impenetrable an epidermic covering contracted the disease should prove interesting.

#### Plague in Marmots.

In the Transbaikal province in Eastern Siberia, a marmot known as the Tarbagan (*Arctomys bobac*) suffers at times from a disease believed to be plague, and this disease is occasionally transmitted to human beings. In an endemic plague centre in Eastern Mongolia there is also some evidence that these animals contract the disease. I have elsewhere<sup>38</sup> discussed in detail what is known of these two centres of disease and the part taken by the marmot in its spread.

#### Rabbits.

These animals, though susceptible to the disease in the laboratory, do not appear to have ever contracted it under natural conditions. Should plague, which has now for the first time in history reached Australia, spread at all widely there, it will be of great interest to observe whether these animals, which abound so in Australia, suffer at all from the disease.

#### NOTES AND REFERENCES.

<sup>1</sup> The present discussion of the subject will be confined to recent evidence. <sup>2</sup> *Thirtieth Annual Report of the Sanitary Commissioner with the Government of the North-West Provinces*. <sup>3</sup> *Ibid.* <sup>4</sup> *Indian Medical Gazette*, March, 1899. <sup>5</sup> *Plague in Monkeys and Squirrels*. By Alice Corthorn, M.B. <sup>6</sup> *Report of the German Plague Commission*, p. 299. <sup>7</sup> *Report of the Russian Plague Commission*, p. 15. <sup>8</sup> In at least one instance a monkey has been artificially infected by being allowed to chew a piece of sugarcane which had been smeared with a pure culture of plague bacilli. (Wilm, *Indian Medical Gazette*, June, 1897.) <sup>9</sup> The principal families of the *Murinae*, the zoological group to which rats and mice belong, are the *Mures* and *Stenomurinae*. The former are confined to the Old World, the latter to the New World and Madagascar. The most noteworthy genus of the *Mures* is the *Neosokia*, of which the most remarkable member is the pig-rat or bandicoot (*Neosokia bandicoota*) (*Encyclopaedia Britanica*). It was the last-named animal whose geographical distribution was believed to coincide to some extent with that of plague (Cantlie, *Epidem. Soc. Trans.*, N. S., vol. xvi, p. 19). The recent spread of plague to countries where the bandicoot is unknown, and the infrequency with which this animal is infected in countries where it exists have shown that this view can no longer be held. <sup>10</sup> The course of the rat migration in Bombay is traced in detail in the Municipal Commissioner's report for that city, 1896-7, pp. 9-10. <sup>11</sup> *Indian Medical Gazette*, 1897, p. 207. <sup>12</sup> Surgeon-Lieutenant-Colonel Henderson, on Plague in Sind. <sup>13</sup> *Ibid.* <sup>14</sup> Rennie, quoted by Cantlie (*loc. cit.*). <sup>15</sup> Baber, in Parliamentary Papers, 1878. China, p. 6. <sup>16</sup> Lowry, *Medical Reports of the Chinese Imperial Maritime Customs*, No. 24. <sup>17</sup> McGowan, *Ibid.* <sup>18</sup> *Times of India*, September 30th, 1896. <sup>19</sup> *Report of the Sanitary Commissioner with the Government of India*, 1897, p. 91. <sup>20</sup> Whether a large proportion, or any, of these rats had died from plague is not stated. <sup>21</sup> Lowry (*loc. cit.*) found the lungs of rats dead from plague deeply congested; the same was observed at Lienchow, and in the districts of the southern Kiangsi in 1886, but no mention is made of pneumonic patches in the lungs. During the prevalence of plague in Yunnan nearly a century ago "it happened that in the daytime strange rats appeared in the houses, and lying down on the ground perished with blood spitting," which may have indicated a lung affection. (Mr. Kumagusu Minakata in *Nature*, February 16th, 1890.) <sup>22</sup> Batzaroff, *Annales de l'Institut Pasteur*, May, 1890. <sup>23</sup> Cantlie (*loc. cit.*) for Hong Kong. <sup>24</sup> A. Happer, *Chinese Customs Medical Reports*, 1880. <sup>25</sup> *Bombay Plague Committee Report*, 1898, p. 205. <sup>26</sup> McGowan, *loc. cit.* <sup>27</sup> Baber, *loc. cit.* <sup>28</sup> Compare the description of a necropsy on a rat dead from plague, by A. Rennie. (*Medical Reports of the Chinese Imperial Maritime Customs*, No. 48, p. 69.) <sup>29</sup> *Municipal Commissioners' Report*, Bombay, 1897, p. 9. Also Rennie, *loc. cit.* <sup>30</sup> Yersin, *Annales de l'Institut Pasteur*. <sup>31</sup> *Epidem. Soc. Trans.*, N. S., vol. xvi. <sup>32</sup> Kitasaki, *First Report on the Cause of Bubonic Plague*. <sup>33</sup> Okada, *Sei-i-Kwat Medical*

*Journal*, Tokyo, October 31st, 1899. <sup>34</sup> It is beyond the scope of the present article to discuss the many other questions connected with the infection of soil with plague virus. So far as published experiments indicate it would seem that it is only the soil of rooms in which plague patients have lain, or in which rats have perhaps died of plague that becomes infected. There is nothing to support the view that the virus spreads through the soil of a district or country like a patch of ringworm spreading from a centre, as some have suggested. <sup>35</sup> The plague bacillus has been found in the dejecta of rats. <sup>36</sup> Government of India, *Report upon Plague in India*, 1896-7, Appendix I. <sup>37</sup> The diagnosis in the cases of plague in human beings was beyond doubt. Unfortunately an acute attack of fever, followed by absence from Calcutta on sick leave, prevented me from obtaining any bodies of the rats for bacteriological examination, and from investigating the series of events until a week or more after their occurrence. <sup>38</sup> *Report of the Sanitary Commissioner with the Government of India*, 1897. <sup>39</sup> Rennie, *loc. cit.* <sup>40</sup> McCabe Dallas, quoted by Weir, *Indian Medical Gazette*, 1897; this or the following is possibly the same case as that referred to by Dr. Weir at p. 55 of the *Municipal Commissioners' Report on Plague in Bombay*, 1897. <sup>41</sup> *Ibid.* <sup>42</sup> It can scarcely escape notice that in a large number of historical epidemics no mention is made of an affection of rats: that in some recent local prevalences of plague in India no affection of rats has been observed; and that a plague epidemic, once started, can last a long while after all the rats have apparently left the place in which it is raging. <sup>43</sup> *Indian daily press of March 19th, 1898*. <sup>44</sup> *Public Health Reports*, Marine Hospital Service, Washington, 1899, p. 1345; report of Dr. M. J. Rosenau, dated Angel Island, California, November 12th, 1898. <sup>45</sup> The literature of experimental plague in rats and other animals is very extensive; among the published observations upon this subject may be mentioned those of the German and Austrian Plague Commissions; of Haffkine and Hankin in India; of Lowson, Wilm, and Yersin in China; of Roux and Simond in France; of Vysockovitch and Zabolotny and others in Russia; of Batzaroff, of Roumania, and many others. To have attempted in the text to summarise, however briefly, the results obtained by these observers would have extended the present paper far beyond its intended limits. <sup>46</sup> *Annales de l'Institut Pasteur*, November, 1898. <sup>47</sup> *Health Officer's Report on Plague in Bombay*, 1896-7, p. 70. <sup>48</sup> Childe has recorded a doubtful instance of the kind (*Report of the Bombay Plague Research Committee*). <sup>49</sup> Simond, quoted by Hankin, *loc. cit.* <sup>50</sup> Hankin, *loc. cit.* <sup>51</sup> J. J. Matignon, *Janus*, July-August, 1898. <sup>52</sup> Noury Bey, *Annales de l'Institut Pasteur*, September, 1898, p. 604. <sup>53</sup> La Peste à Alexandrie en 1899 (report of the Commission appointed to inquire into the origin of the epidemic), p. 19. <sup>54</sup> *Bombay Gazetteer*, vol. iv, chap. xii. <sup>55</sup> Hutcheson, *Transactions of the First Indian Medical Congress*. <sup>56</sup> Dr. Alice Corthorn, *Indian Medical Gazette*, March, 1899. <sup>57</sup> *Report of the Sanitary Commissioner with the Government of India*, 1897, Section III, p. 83. <sup>58</sup> *Lancet*, September 30th, 1899, p. 910. <sup>59</sup> *Journal of Tropical Medicine*, February, 1900, Plague in Siberia and Mongolia and the Tarbagan; by the author.

(To be continued.)

## AN ACCOUNT OF SOME RESEARCHES INTO THE NATURE AND ACTION OF SNAKE VENOM.

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### II.

#### ON THE SOURCE OF IMMUNITY WHEN COBRA VENOM IS TAKEN BY THE MOUTH.

In a paper published in the BRITISH MEDICAL JOURNAL of July 17th, 1897, Professor Fraser wrote as follows:

The failure of so highly toxic a substance (serpents' venom) to produce poisoning when it is administered by the stomach might be due to chemical changes produced upon it by the secretions of the stomach and intestines, or to non-absorbability into the blood from the stomach and intestines. It is already known that the toxicity of venom is not reduced materially by gastric digestion.....As serpents' venom introduced into the stomach is not rendered innocuous by the stomach secretions, while notwithstanding it fails to cause poisoning, it may be assumed that the stomach walls are incapable of absorbing it also. If, like other poisons, it can be absorbed from the intestines, the explanation of the failure to produce toxic symptoms when it is administered by the stomach might depend on a chemical or physiological destruction of its toxic properties by some substance or substances which it encounters soon after entering the intestinal canal, and most probably, therefore, by the bile or the pancreatic secretion. To explain the innocuousness of stomach administration fully would accordingly require that the effects on venom of the biliary and other intestinal secretions should be investigated, and also the absorbability of venom through the intestinal walls.

As a contribution to the settlement of the question I have made a number of experiments with the biliary secretion, and whatever may be the influence of the other secretions, or of intestinal absorption, that of the bile has been found to be so decided as to be in itself sufficient to account for the innocuousness of stomach administration.

The object of the present paper is to fill in some of the gaps suggested by Professor Fraser in the above very interesting sentences.

Another possibility occurred to me—namely, that the source of protection might perhaps lie in the action of intestinal epithelium during absorption. This idea was suggested by the fact that the epithelium of the serpents' venom glands has the power of so altering the fluid passing through it as to