I. EXPERIMENTS UPON THE TRANSMISSION OF PLAGUE BY FLEAS.

PART I.

HISTORICAL INTRODUCTION.

That outbreaks of plague are associated with a more or less simultaneous mortality amongst rats is an observation of great antiquity. After the discovery of the bacillus by Yersin and Kitasato this concomitant disease of rats was identified as plague, and during the last twelve years the association of rat plague and human plague has been shown to be almost invariable. The relationship has been so striking that many observers who have studied the question on the spot, *e.g.* Yersin, Ogata, Simond, Thompson, Koch, Gaffky and many others, have arrived at the opinion that from an epidemiological point of view one must regard plague as essentially a rat-disease in which human beings may participate.

The relationship of the epizootic and epidemic has been particularly carefully studied for the outbreaks in Sydney by Ashburton Thompson (1902, 1903, 1904), in Port Elizabeth by Blackmore (1902), in Hong Kong by Hunter (1904), as well as in Cape Colony by Mitchell (1906), in Queensland by Baxter-Tyrie (1905), and for Calcutta by Pearse (1905). Other observers have recorded the coincidence of rat and human plague in many places[1].

In India the importance of the epizootic in the spread of plague in Bombay was early recognised by Snow and Weir (1897), Hankin (1898), and the German Commission (1899). As the disease advanced into

[1] A historical account of the relationship of rat plague to human plague with a good summary of the literature (excepting, however, many important Indian observations hidden away in official reports and not easily available) is to be found in a paper by Carlo Tiraboschi, "Die Bedeutung der Ratten und Flöhe für die Verbreitung der Bubonenpest." *Zeitschr. f. Hygiene*, 1904, vol. XLVIII. p. 513.

the country districts many valuable observations bearing on this question were collected by the various Sanitary Officers, notably by James (1899), and are to be found in their official reports to the Indian Government. At the present time the almost universal opinion of Sanitary Officers in India who have been engaged in dealing with the epidemics seems to be that the epizootic is principally responsible for the spread of plague.

The present Commission is also engaged in determining the relationship of the epizootic to the epidemic by extensive observations in Bombay and in two isolated Punjab villages. These observations are at present incomplete: they will extend over one year and will be published in due course. At the present time, however, it may be stated that they fully confirm the observations of Ashburton Thompson in Sydney and Hunter in Hong Kong, that the human outbreak is *preceded* by the extensive development of an epizootic of plague amongst the rats.

If the fundamental importance of plague amongst rats be admitted, the study of the epizootic becomes of essential importance. The Commission has, therefore, occupied itself, amongst other problems, with the question of the means whereby plague is spread from rat to rat and from rat to man. That the disease may be conveyed from rat to rat by one animal devouring the carcase of another is undoubted, but from experiments made in this direction this would appear to be an uncertain method which usually requires the ingestion of large doses of infected material, and it is obviously impossible to explain in this way the transference of the disease to man.

The possibility of insects playing some rôle in this transfer no doubt occurred to many investigators. Yersin (1894), Hankin (1897) and Nuttall (1897) showed that the dejecta of flies and ants fed on infected organs contained virulent plague bacilli. Nuttall also fed bugs upon plague-infected mice and subsequently allowed them to bite healthy mice without, however, conveying the disease. The bugs harboured virulent bacilli as long as three days after feeding on plague-infected mice. Ogata (1897) crushed fleas from rats which had died of plague and injected them into two mice, one of which died of plague after three days. He suggested, from epidemiological considerations, that plague was mostly conveyed by suctorial insects such as mosquitoes and fleas.

Simond (1898) found organisms indistinguishable morphologically from the plague bacillus in the stomachs of fleas fed upon rats and mice dying of plague, and succeeded in infecting a mouse by injecting an

extract of crushed fleas taken from a plague rat. From his observations on plague in India during the previous year Simond arrived at the idea that plague was transferred from rat to man by means of fleas, and he made some experiments to try to convey the disease from one animal to another by the agency of fleas. Having found that he was unable to transmit the disease by mere contact, when the animals were previously freed from any fleas they might have, he placed a rat dying from plague in a wide mouthed bottle, and, *as it had only a few fleas upon it,* he added 20 fleas from a cat (species not identified). A young rat, enclosed in an iron box with a grating on one side, was lowered into the bottle. The rat which was affected with plague died after 24 hours and its carcase was left in the bottle for 36 hours and then withdrawn. The other rat died of plague on the 5th day. Three further similar experiments were made by Simond, one of which gave a positive result. Simond considered that such a parasitic transmission of the plague bacillus explained most of the difficulties in the epidemiology of plague. He found it difficult to believe that transmission was occasioned by mere soiling of the proboscis of the flea with blood containing plague bacilli, as such a method would unduly limit the time during which the insect could remain infective, and suggested that most probably infection was conveyed by the faeces of the insect. In support of this view he recorded the observation that, whilst sucking, fleas were in the habit of discharging the contents of their intestine upon the skin in the neighbourhood of the puncture, and that in consequence infective material might subsequently be rubbed in during the relief of the irritation by scratching.

The German Plague Commission (1899) also found *B. pestis* in fleas taken from plague rats, but did not regard the bites of fleas as a probable means of transmission.

Hankin (1898), when discussing the epidemiology of plague from observations made in Bombay, pointed out that the incidence of plague bore definite relation to the accessibility of man for rats, and expressed the opinion that some intermediary insect appeared necessary to communicate the disease from rat to man. Nuttall (1899) in his monograph on the rôle of insects in the spread of bacterial diseases, which gives a full account of the literature of this subject up to 1898, mentions his unsuccessful attempts to transfer plague from one animal to another by means of bugs. Tidswell (1900) found virulent plague bacilli in the stomachs of fleas taken from plague-infected rats, but failed to successfully repeat Simond's experiments on transmission from rat to rat by

means of fleas. Thompson (1900), notwithstanding the negative results of Tidswell's experiments in his own laboratory, inclined, from purely epidemiological considerations, to Simond's view of the means of spread from rat to man. Galli-Valerio (1900) subjected Simond's views to criticism principally on the ground that the fleas commonly found on rats *in Europe* will not attack man. Kolle (1901) tried to convey infection from rat to rat by means of fleas. The experiments (number not stated) were negative. Zirolia (1902) found that *B. pestis* multiplied in the stomachs of fleas and retained its original virulence for 7—8 days, during which time it was passed in the faeces. He confirmed Simond's statement that fleas while sucking frequently discharge the contents of their intestine.

Gauthier and Raybaud (1902, 1903) repeated Simond's experiments in Marseilles. In their experiments they employed a cage divided in the middle by two grills 2 cm. apart. The cage was placed in a glass jar. In one compartment was placed an inoculated white rat on which had been placed a dozen fleas captured upon rats from ships in the harbour. When the inoculated rat died, a healthy rat was placed in the second compartment, and after some hours had elapsed, during which the fleas transferred themselves from the dead to the living animal, the cadaver was removed. In this way Gauthier and Raybaud succeeded five times in conveying the infection from one rat to another: the number of negative experiments is not stated. An examination of the fleas found upon the septicaemic animals showed the presence of *B. pestis*. They found, as was stated by Simond, that rats did not contract plague from one another by mere contact in the absence of fleas. The fleas used in their experiments were not identified, but from an examination made about the same time of 250 fleas caught upon rats from ships, the authors found

Pulex irritans	2
" Puces non-pectinées autre que *P. irritans*" corresponding to *P. pallidus* (Taschenberg)	64
Typhlopsylla musculi	178
Pulex fasciatus	6.

14 out of 16 fleas (probably, according to the authors, *P. pallidus* and *P. fasciatus*) taken from rats bit men; and some lived for several weeks upon an exclusively human diet[1].

[1] Specimens of these non-pectinated fleas were sent by Gauthier and Raybaud to Rothschild, who identified them as *P. cheopis*.

Simpson (1903) made two experiments with monkeys and flea-infested rats which had been inoculated with plague. The experiments were performed in a double cage permitting fleas to pass from one compartment to another, but not allowing the monkeys to come in contact with the rats. After the rats were dead they were removed. Both monkeys became seriously ill three or four days after, but recovered.

Tidswell (1903) made further attempts to convey plague from rat to rat by the agency of fleas, but was unable to do this. He also studied the ectoparasites of the rats of Sydney and other Australian ports and tabulated the number of fleas of different species and percentage frequency. In Sydney and Brisbane 80 per cent. of the fleas on rats were identified as *P. pallidus* (Taschenberg)[1]. He made the observation that rats during the epizootic of plague harboured more fleas than at other times. He found that *P. pallidus* readily bit man when hungry, and *P. fasciatus* on occasion. Ashburton Thompson (1903), from an analysis of the epidemiological facts which he had collected during the outbreaks of plague at Sydney, concludes that Simond's hypothesis of the flea as a transmitter from rat to man best explains the phenomena of epidemic plague as observed by him. This reasoning purely from the facts of epidemiology is of the greatest importance, for, as pointed out by this observer, after it had been shown that plague *could* be transmitted by these parasites, the proof that *epidemic* plague *was* thus caused could only be furnished by an epidemiological study of the field facts.

Galli-Valerio (1903) contributed a further critical review upon the question of plague transmission by the agency of fleas. This article deals more particularly with the work of Zirolia and of Gauthier and Raybaud mentioned above. Galli-Valerio considers Gauthier and Raybaud's statement that rats freed from fleas do not become infected by mere contact as astonishing. This has, however, also been the experience of Simond, Klein (1902), Kister and Schumacher (1905), and Liston (1905). Galli-Valerio's principal criticism of the conclusions of Simond and of Gauthier and Raybaud concerning the importance of fleas in the epidemic spread of plague is based upon a misunderstanding. He says "Il n'y a pas de doute que les puces les plus frequentes sur les animaux (rats) sont *Ceratophylus fasciatus* et *C. musculi*," which he

[1] Specimens of these fleas from Sydney have also been identified for us by Rothschild as *P. cheopis*.

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maintains do not bite man. This conviction is no doubt justified regarding the ectoparasites of rats examined by this author in Europe, but in India as shown by Liston and in Australia by Tidswell a totally different flea, *Pulex cheopis* or *pallidus*, is the one present in greatest proportion. This flea was also found by Gauthier and Raybaud on rats from ships in Marseilles and presumably used by them for their experiments.

Hill (1904) reports that fleas on rats at Maritzburg were very scarce during the time that the plague was absent. From some experiments made upon infection from rat to rat in miniature granaries, in which he presumed he had eliminated fleas by fumigation with SO_2 and "Paraform," he concludes that infection may take place without the agency of fleas. Herzog (1904) found *B. pestis* in three *Pediculus capitis* taken from a child which had died of plague in Manila. This patient had cervical buboes and Herzog suggests that infection might have been conveyed by the lice.

Liston (1905) in a lecture given before the Bombay Natural History Society in November, 1904, on "Plague, rats, and fleas," pointed out that the common flea infesting rats in India was not *C. fasciatus* or *Typhlopsylla musculi*, as in Europe, but a non-pectinated flea possessing considerable resemblance to *P. irritans*. This was identified by Rothschild as *P. cheopis* and is identical with the flea (*P. pallidus*) found by Tidswell to comprise 80 per cent. of the flea population of rats in Sydney and Brisbane. Liston records having observed multiplication of the plague bacillus in the stomach of this flea, and although his attempts to transfer plague from one animal to another by allowing fleas to bite first an animal suffering from plague and subsequently a healthy animal had not been successful, he brings forward much interesting and valuable circumstantial evidence in favour of the view that plague is so epidemically spread. The fact that *P. cheopis* takes readily to another host when rats are not available is shown by the following observation. In March 1903 an outbreak of plague occurred in the guinea-pig cages at the Zoological Gardens, Bombay. On visiting the gardens Liston was surprised to find the guinea-pigs, especially those which were sick, infested with rat fleas (*P. cheopis*). Guinea-pigs do not usually harbour fleas, but dead rats had been found in the neighbourhood of the guinea-pig cages and Liston imagined that the fleas on the guinea-pigs were derived from this source. Acting on this idea he subsequently made use of guinea-pigs as traps for rat fleas, and in this way was able to discover their

presence in plague-infected huts on several occasions. The following instance is sufficiently striking to quote:

On March 7th a servant (syce) was attacked by plague. Dead rats had been seen near his quarters a day or two previously. The man was removed to hospital and the servants' quarters evacuated. The man died on the 9th March. Nothing further occurred in the servants' quarters till the 16th when a dead rat was found in one of the empty rooms. The rat was examined bacteriologically and was found to have died of plague. Six guinea-pigs were brought to this house, and on the evening of the 16th two of these were placed in the room in which the rat had died. Two others were placed in a similar room in a neighbouring house, which was at the time occupied, and two others in an empty room of similar construction to the room in which the rat had died. Neither of these latter two rooms had been infected with plague.

On the morning of the 17th the guinea-pigs were chloroformed and examined in the usual manner. No fleas were found on the four guinea-pigs from the two non-infected rooms. Ten rat fleas were taken on the two guinea-pigs in the infected room. The guinea-pigs were marked and returned to the Laboratory, and the fleas reserved for dissection and examination. *Three of the ten showed numerous plague germs in their stomachs.*

One of the two guinea-pigs which were placed in the infected room was decidedly ill on the 21st March. It was worse on the 22nd and a large bubo could be made out in the right groin. The guinea-pig died on March 25th, 1905, *i.e.* nine days after exposure to infection. A pure culture of plague was obtained. None of the other guinea-pigs suffered in any way.

The important point of this experience was that rat fleas, which had apparently fed on a plague-sick rat, could be captured on an animal which was not a normal host for that flea.

After detailing further observations of the same kind, Liston says:—

To sum up, then, rat fleas can always be found in infected houses; these fleas will take to an animal which is not their normal host. Some of these fleas have been shown to be infected with large numbers of plague germs in their stomachs, and these germs, far from being destroyed by the digestive juices of the stomach, seemed to be multiplying and in a healthy state. Many of the guinea-pigs on which these rat fleas were found died of plague, while other animals placed in uninfected quarters were not attacked by rat fleas and did not suffer or die from plague.

That *P. cheopis* will also attack man, the following account by Liston shows undoubtedly:

About the 6th or 7th of April, rats began to die in large numbers in a chawl, or block of tenement houses. Suddenly the deaths amongst rats ceased, and on April 11th the people became troubled with fleas. The fleas became so numerous that they had to quit their rooms and sleep out in the verandah. While living in the verandah on April 17th one of the inhabitants of the particular room in which the fleas were taken became infected with plague. Another case occurred on the same day in a room adjoining. The people who inhabited the room where the

above case occurred were induced by Mr Lord to collect some of the fleas from their persons which they said troubled them, and he sent the collection to me on April 20th. An examination of this collection was most instructive. Now I must tell you that on previous occasions, of 246 fleas which were caught on man under normal conditions, I had only found one rat flea, *Pulex cheopis*. But of the collection of 30 fleas caught on man under the circumstances above recorded, no less than 14 were rat fleas.

Hunter (1905) reviewed the question of the rôle of insects in the spread of plague. He found that flies, fleas and bugs contained *B. pestis* in their alimentary canals when they had access to plague-infected material, but that in the case of the latter, the bacilli, as previously maintained by Nuttall, disappeared from the intestine in a few days. He concludes that the part played by suctorial insects is similar in all respects to that of non-suctorial, *i.e.* the mechanical conveyance of infection from place to place. Hankin (1905) reports the finding of *B. pestis* in the stomach of a flea at Agra in 1901. He draws attention to the disappearance of dog fleas in hot weather in Agra (India), and suggests that, if rat fleas similarly disappear, this may be a possible explanation of the seasonal decline of the epidemic. He further puts forth the suggestion that plague may also be a disease of fleas and that these parasites may only be able to transmit the infection after 10—20 days. Herzog (1905) reviewed the question of the rôle of insects in the spread of plague. He also examined the fleas upon rats (*Mus rattus* and *M. decumanus*) in Manila and found only one species which he regarded as new, and described under the name of *Pulex philippinensis*. From a consideration of the description given, Mr Rothschild has informed us that he is satisfied that this flea is *P. cheopis*. Noc (1905) also reviewed the present knowledge regarding the part played by fleas. Kister and Schumacher (1905) have recently repeated in Hamburg the experiments of Gauthier and Raybaud. Their method was similar to that of the Marseilles observers but they took additional precautions in order to prevent the possibility of the sick and healthy animals coming into contact. They take no note of the species of fleas upon the rats used, and the amount of infestation of their experimental animals was apparently slight. They made in all 31 experiments, 8 of which were with bugs (origin not mentioned). All experiments were negative, and they conclude that flea-transmission is neither usual nor important.

In view of its importance in plague epidemiology, the systematic study of the ectoparasites of the rat has been taken up by C. Tiraboschi (1903, 1904). In the former publication he deals briefly with the

literature concerning fleas as possible agents in the spread of plague, and gives a list and short description of fleas found upon rats and mice in Italy. His later work is a monograph upon the cutaneous parasites of rats and mice throughout the world. Tiraboschi found a common flea upon rats in Italy to be what he calls *P. murinus*: this appears to be identical with *P. cheopis* (Rothschild). The occurrence of this flea was particularly frequent upon ship-rats, and in Genoa he found it constituted 40 % of the fleas captured at the docks. Tiraboschi satisfied himself by numerous trials that this flea readily bites man. This contribution of Tiraboschi to the subject is extremely welcome, for fleas infesting rats are not the same under different conditions in different parts of the world, and, as is evident from the above short review of the literature, experimenters have in many cases taken no note of, or have not been able to identify, the fleas with which they have been concerned. This has given rise to confusion and may no doubt account to some extent for discrepancies in the results obtained.

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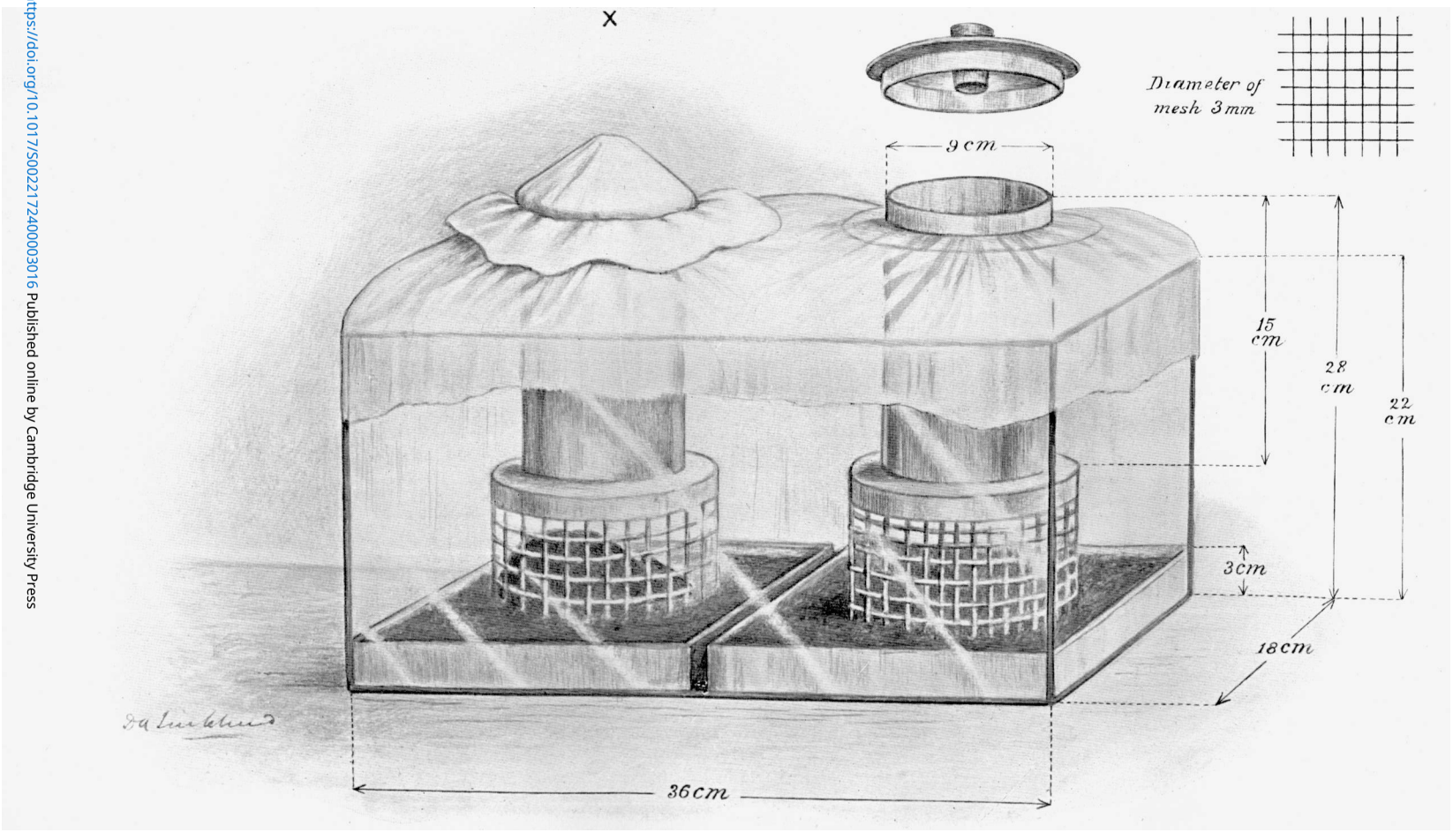

CAGE EMPLOYED IN REPEATING THE EXPERIMENTS OF GAUTHIER AND RAYBAUD.

The actual size of the mesh (3 mm.) is shown in the small figure. In the drawing it is shown much too large for the sake of clearness.

The arrangement employed for the second series of experiments consisted of one-half of that shown; i.e., only one cage was placed in a correspondingly small glass box.