# REPORT UPON THE POST-MORTEM EXAMINATION OF RATS AT IPSWICH<sup>1</sup>.

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#### INTRODUCTION.

On June 30th, 1911, we proceeded to Ipswich, with instructions from the Local Government Board to assist in an enquiry, the purpose of which was to determine the extent of the plague epizootic amongst rats in the surrounding districts. The share of this work allotted to us consisted in examination, at the Municipal Laboratory, of the animals received, and in selection, for further investigation by the Board's pathologists in London, of material which appeared suggestive of plague. For this purpose, rats presenting features in any degree consistent with the presence of plague were regarded by us as suspicious.

#### PRELIMINARIES.

The rats were delivered at the laboratory in boxes. These were opened, and the rats taken out and affixed to dissecting boards. Dissections were made so as thoroughly to expose the principal lymphatic glands, thoracic and abdominal viscera. After inspection, rats obviously free from plague and in other respects devoid of interest, were removed to suitable receptacles, pending transference to the destructor. Those of pathological interest, either with regard to the possibility of plague-infection or from other cause, were set apart for further scrutiny.

For purposes of identification and reference, all rats were numbered.

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Rats set aside on the strength of gross post-mortem appearances as possibly infected with plague were submitted to a complete microscopical examination. Films from heart-blood, liver, spleen and lymphatic glands, stained with carbol-thionin blue, were searched for the presence of organisms resembling plague bacilli. After this, the evidence, macroscopic and microscopic, was reviewed, and the rat was either rejected or reserved for cultural and inoculation tests. In the latter case, the liver, spleen and any other portions indicated by the post-mortem characters were packed and sent to London, accompanied by cards describing the pathological features presented by the animal from which they were taken. Cultivations were usually taken from the organs before despatch. Rats which had been so treated were then immersed in strong formalin, and removed separately in tins for destruction. A record was kept of other features of pathological interest.

# Number of Rats, &c. Examined.

# Summary of Results.

Sexes and Pregnancies:				
Males			 	7,490
Females			 	7,342
Pregnant Females			 	1,213
Average number of	Foe	tuses	 	9.9
Species:				
Mus decumanus			 	15,167
Mus rattus			 	$165^{1}$
Ferrets			 	<b>2</b>
Moles			 	3
Hares			 	3
Stoat			 	1
Weasel			 	1
Rabbit			 	1

# Plague infection.

	Killed	Found dead	Total
Rats examined	15,263	69	15,332
Sent up as suspicious, and proved negative	105	11	116
Proved plague infected by inoculation	21	14	35

<sup>&</sup>lt;sup>1</sup> This number includes 134 rats caught on board ships in the port of Ipswich, and 31 caught in and around the docks.

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The work was performed by us with the help of two attendants, and we wish to record our appreciation of the valuable and conscientious service rendered by J. Yerrell, our chief assistant.

#### POST-MORTEM APPEARANCES.

The accompanying tables show diagrammatically the characters of the selected rats, those found upon further enquiry in London to be infected with plague being placed in Table I, whilst particulars regarding those which proved to be negative are set forth in like manner in Table II. A certain number of rats which were sent up and found to be negative are excluded from Table II for reasons hereinafter stated. (See p. 321.) The following paragraphs contain some amplification of these tabular statements.

#### Plague-Infected Rats.

Lymphatic Glands.—Enlargement of glands was present in most infected rats; three only failing to exhibit this feature. It was confined to the submaxillary region in five instances, whilst four rats showed congestion of these glands with no increase in size. On eight occasions, the lymphatic glands showed general congestion, but no enlargement. In some of the rats the enlarged glands were associated with minute ecchymoses upon the surface or on section, and definite haemorrhages were observed in a few cases. These appearances were accompanied in some instances by a peripheral zone of congested tissues surrounding the gland, and paling off into a less-marked degree of general subcutaneous congestion (2876 and 3430). In one rat (2876) cross section of an enlarged and congested inguinal gland displayed a necrotic centre. In another (15,079) the left pelvic gland was necrotic. Involution forms, resembling those of B. pestis, were observed in some cases, upon microscopic examination of smears from enlarged glands (2876, 11,724, 12,013, Bipolar bacilli were demonstrated in 23 cases. and 13.663).

Subcutaneous Congestion. Congestion, distributed universally over the subcutaneous tissues, was seen in 24 cases. In two instances (2064 and 2522) it was described as being confined to the thoracic and axillary regions. In four cases only was it altogether absent. This feature was very generally present to a marked degree in the infected rats obtained during the concluding period of the investigation. In general, the congestion was manifested as a uniform subcutaneous blush due to distension

of the capillaries, but in a few cases venous engorgement was most prominent, dilation of individual venules being obvious.

Haemorrhages.—Small haemorrhages were found in 10 rats, but in no case was this feature conspicuous. Four instances of retroperitoneal haemorrhage, the pelvic glands being invaded in two cases, were observed. The lungs showed minute ecchymoses on two occasions. Effusions of blood into the bronchial glands and mesentery, and into the subcutaneous tissues of the axillary and submaxillary regions were also described.

Pleural Effusion.—In three plague-infected rats there was no effusion into the pleural cavity. In one putrid rat turbid fluid was found; four cases showed blood-stained effusion. In all the remaining cases a clear pleural effusion, usually considerable in amount, was observed.

Liver.—The pathological changes exhibited by the liver varied greatly in degree and in quality, variations in size, colour and consistency, surface and surface markings being observed. In two rats, both somewhat decomposed, the liver was not described as abnormal. Three rats (2064, 5381, and 13,817) presented livers which appeared at first sight to be normal, but scrutiny with a hand lens showed the presence of fine pitting distributed universally over the surface of the organ, indicative, possibly, of fibrotic change. In a fourth animal (13,663) this pitting was accompanied by signs of congestion. Enlargement, with congestion, was recorded on nine occasions. No register was kept of variations in the degree of consistency of the organ, as this depended to a large extent upon its state of preservation. In 17 cases, the liver is said to be mottled. The term "mottling," as applied to liver changes, is not intended to indicate any specific pathological conditions, but is used to indicate a mottled or marbled appearance of the organ associated with abnormal definition of the liver lobules. This condition was often shown by livers undergoing putrefactive change (e.g. 10,848).

Granular livers, in which were present necrotic foci appearing as scattered whitish points, were found in 18 cases. In two instances the liver is described as granular but no obvious areas of necrosis were observed. It was noticed in one rat (8086), which had been found dead, that although the liver showed advanced putrefactive changes, whitish points of necrosis stood out clearly from the discoloured surface. The manner in which these various features—congestion, mottling, and necrotic change—were combined in different cases, is shown in the table; but it may here be stated that the complex to which has been applied the name of "typical pest liver" (i.e. an enlarged, pale, mottled

liver covered with numerous necrotic points) was found only in three cases (2876, 5381, and 12,012).

In every animal except one (1264) microscopical examination showed the presence of bipolar bacilli in liver smears, well-marked involution forms being observed in a number of cases. In two livers (2522 and 11,407) bipolar bacilli were seen in relatively small numbers, together with a large variety of putrefactive forms. In Rat No. 8086 referred to above, very large involution forms of the swollen and globular types were observed.

Spleen.—In eight cases the spleen was macroscopically normal. Fourteen rats showed spleens which presented signs of congestion, being dark in colour and firm in texture. Fifteen exhibited various degrees of granular change. Enlarged spleens showing no distinctive pathological change were not regarded as abnormal. In two cases (2876 and 13,817) coarse punctate necrotic foci were observed. In one rat (1030) the spleen showed a white infarction.

Microscopical examination showed the presence of bipolar bacilli in 26 cases, enormous numbers being observed in seven of these. Well-marked involution forms were found in several instances (e.g. 8086). Spleen smears from seven rats did not show any organisms, although with one exception (1264) these were found in corresponding preparations from the liver. It appeared that there was little correlation between the degree of gross morbid change observed and the number of bacilli seen on microscopic examination. In some cases (3430 and 14,855) spleens which appeared normal to naked-eye inspection yielded films found to be crowded with organisms. This condition was met with in the case of the liver in two cases (5382 and 13,817).

Heart Blood.—Films prepared from the heart blood showed no organisms in six cases. The type of organism observed in the remainder was similar to that shown by the smears from liver and spleen. The number varied from very few (in 1264) to enormous quantities (in 1694). The small number which was found in 1264 afforded in that case the only microscopical evidence of plague infection, as the smears from liver and spleen showed no organisms.

Oedema, etc.—Pelvic oedema was seen in one case (1769). Another rat (10,848) showed the rare condition of general subcutaneous oedema. In Rat 13,817 the lungs were markedly engorged, and were found upon microscopical examination to contain large numbers of bipolar bacilli.

### Negative Rats.

Particulars are shown in Table II of 76 rats selected as possibly plague infected, which, however, were shown by cultural and inoculation experiments to be negative. Some of the salient features of these rats are summarised below. In addition to the negative rats included in Table II 35 rats were sent up for further investigation: 19 of these exhibited abundant pleural effusion containing numerous bipolar bacilli, and are more fully described below; the remaining 16 were found to harbour bipolar bacilli in their accessory sexual glands. In most rats, even those apparently healthy, smears from accessory sexual glands showed large numbers of organisms, which often exhibited bipolar staining and bore a close resemblance to the plague bacillus. Cultural investigation and inoculations carried out in these cases proved the absence of any such infection. As soon as it was ascertained that neither of the conditions was in any way associated with infection suggestive of plague, such animals were regarded as negative.

Lymphatic Glands.—Glandular enlargement was a very common feature, and was particularly well marked in two cases. Bipolar bacilli were found in gland smears from 21 rats, and in some cases organisms resembling plague involution forms were observed. Enlargement of lymphatic glands, particularly those in the submaxillary region, was observed in a great majority of the rats received for examination, but in most cases, when microscopic examination was made, no organisms were found. The pelvic glands also were as a rule conspicuous in the rats examined during the course of this enquiry, although it had previously been observed by one of us who had the opportunity of examining a series of rats in January, that these glands were not usually obvious at that season. In the majority of cases enlargement of the glands was not accompanied by congestion.

Subcutaneous congestion.—Intense and general subcutaneous congestion was only observed twice. Localised congestion was seen in a number of cases. In 22 rats no signs of congestion were observed.

Haemorrhages.—Haemorrhages were described as occurring in 11 cases. The majority of these were strictly localised and were probably traumatic in origin.

Pleural Effusion.—Clear pleural effusion was observed in 39 cases, the amount of fluid being scanty in the majority of these. Effusion described as blood-stained occurred in 39 instances. In several decomposed rats turbid fluid was found in the pleural cavity. These numbers

include 19 rats not included in Table II. In 12 of these the pleural effusion was blood-stained, and in seven instances it was clear or turbid. Microscopical examination of films prepared from such pleural effusions showed the presence of a great variety of organisms, some of which simulated very closely both typical and pleomorphic forms of plague bacilli. Further, the groupings of organisms on some films bore a most striking resemblance to those characteristic of *B. pestis*. These organisms were subsequently regarded as being putrefactive.

Liver.—The livers showed punctate foci of necrosis in 16 cases, in five of which the feature was well marked. In four such rats infection with the Gaertner bacillus was subsequently demonstrated. Microscopically no organisms were found in 26 cases; 50 showed the presence of bipolar bacilli.

Spleen.—Granular changes in the spleen were frequently observed. In three animals the spleen showed necrotic foci. Bipolar bacilli were found in 42 rats.

Heart Blood.—Films prepared from the heart blood showed coccobacilli or bipolar bacilli in 36 rats.

Minor changes in the viscera were observed in a great number of rats which were rejected at once, as well as in those reserved for microscopic examination. Mottling or marbling of the liver due to commencing putrefaction was very common. Minor granular changes in the spleen, overgrowth of submaxillary glands, and effusions of blood into the pleural cavity were noticed with great frequency. No statistical record of such changes was kept, but, in about 600 such rats, microscopic examinations were made. These gave negative results.

#### OTHER PATHOLOGICAL CONDITIONS.

#### Gaertner Infection.

In 14 of the cases, where infection with plague was, upon preliminary examination, considered possible, further investigation demonstrated the presence of bacilli of the Gaertner group. The allocation of these organisms was based upon cultural and fermentation reactions.

Five other rats were noticed, which demonstrated so clearly the post-mortem character associated with Gaertner infection, that they were not included among the plague-suspects. Nineteen rats altogether were, therefore, regarded as being infected with this organism. It is probable, however, as the investigation was not directed definitely to

the detection of such cases, that this number does not represent the degree of prevalence of this disease among the rats received.

The most prominent post-mortem features typically associated with Gaertner infection were displayed by the liver and spleen. The former was not as a rule granular, but thickly peppered with white points. It should be noted that although a typical plague-infected liver differs markedly from the appearances presented by the organ in a typical Gaertner infection, in certain cases the post-mortem appearances are of no great assistance in differential diagnosis, and further investigation is needed to determine the nature of the disease under consideration. The spleen, on the other hand, was much more markedly granular than that found in the majority of plague-infected rats. Microscopically the number of organisms seen was usually small, but these exhibited, not infrequently, bipolar staining. Some slight amount of subcutaneous congestion was shown by a number of Gaertner-infected rats.

# Trypanosomiasis.

Trypanosomiasis was very common, particularly during the first two months of the investigation. The most general and prominent indication of this infection was blood-stained pleural effusion consisting in many cases of pure blood. Rats exhibiting such a blood-stained effusion, whilst appearing fairly healthy in other respects, might with some degree of certainty be regarded as infected with trypanosomiasis. continuous series of 2000 rats received in August were investigated particularly with regard to this point. Of these, 145 showed pleural effusion which was decomposed and putrid in many cases, and clear in some others, while in 55 cases the fluid was blood-stained: 45 of these showed the presence of trypanosomes. These parasites were also found in five cases where the pleural effusion was turbid. Incidentally, three rats in this series of 2000 were found to be plague-infected. In these three (2522, 2876, 3346) the effusions were severally turbid, clear, and blood-stained. Other appearances, associated with trypanosomiasis, were congestion of the subcutaneous tissues and lymphatic glands, enlargement of glands, and congestion of the liver. In one case these features were particularly obvious, and the right inguinal gland, particularly, was enlarged and surrounded by a zone of deeply congested tissues. Microscopic examination of this gland showed the presence of many trypanosomes, the agglutination phenomenon being well demonstrated. Large numbers of trypanosomes were found also in the heart blood. This rat was interesting, as showing that the infection was introduced probably within the area drained by the right inguinal gland. It was also very important, in that the post-mortem appearances presented a picture very closely resembling that associated with plague. Agglutination of trypanosomes was, on another occasion, found in a film prepared from the turbid pleural effusion.

# Other Infections.

Suppurative conditions of the lungs occurred with great frequency. This phenomenon is extremely common amongst rats, and has been observed on every occasion when large numbers have been examined. In one series, all stages of the condition were seen, from the earliest, presenting a few small foci containing glairy material, to advanced stages in which the lung tissue is almost entirely replaced by caseous matter, the healthy lung which remains being thereby compressed and displaced and the bony wall of the thorax deformed. Suppurations, general and localised, in the abdominal cavity were not infrequent, and abscesses in lymphatic glands were very common. Osteomyelitis of the hind-limb bones was twice found.

Twenty-five cases of rat-leprosy were observed.

#### DISCUSSION.

Some facts, observed in the study of both negative and positive cases, may illustrate certain difficulties of preliminary diagnosis, which assume their greatest importance in the investigation of outbreaks of rat-plague occurring in this country.

Infected rats presenting atypical appearances were relatively common, particularly during the early part of the enquiry, at the commencement, that is, of the seasonal epizootic. On the other hand, those found during the last two months of the investigation showed features typical of plague. Broadly speaking, preliminary diagnosis during the first period of two months was usually tentative, while during the second period it was, in the great majority of instances, certain. It must not be assumed, however, that this statement implies that negative cases could always be diagnosed as such without resort to animal experiment. Even in regard to cases in which the diagnosis appeared certain, a caveat must be entered. A study of the characters

ABLE I. Positive Cases.

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TABLE II. Negative Cases.

9	Glands	Subcu-				Liver			Spleen			Microscopic appearances	ppearance	m
Enlarge- ment	Conges- tion	conges- tion	Haemor- rhages	Pleural effusion	Necrosis	Mottling	Congestion	Necrosis	Granu- lation	Conges- tion	Glands	Liver	Spleen	Heart
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shown by some rats (4843, 4886, and 10,150), in Table II, will illustrate the danger of making positive diagnoses upon the evidence afforded by post-mortem features, not confirmed by inoculation experiments. Reference, on the other hand, to three cases (1264, 2064, and 11,407), in Table I, will illustrate the necessity of care in the investigation of epizootics where rats presenting such slender evidence of infection may occur. Reports of similar investigations carried out at Hamburg and elsewhere indicate that such atypical plague rats may always be encountered in the investigation of European epizootics.

The individual features of greatest service for diagnosis were subcutaneous congestion, clear pleural effusion, and granular, necrotic changes in the liver. All three were present, usually to a marked degree, in most of the plague-infected rats, but only in 9 rats found to be negative. Pleural effusion, either clear or blood-stained, and congestion were observed in a considerable number of cases. No rat found positive failed to display obviously one or more of these characters. In order of relative value, subcutaneous congestion and pleural effusion would come first, the liver changes being less important, but their collective significance should be considered rather than the individual prominence of each single factor.

Enlargement of lymphatic glands possesses, generally speaking, little weight as primary evidence. At the season in which the enquiry was carried out, pelvic glands were conspicuous in most rats. Submaxillary glands were enlarged as a rule. Congestion in regions where this feature was generally not obvious was of some value as a secondary piece of evidence.

In general the facts observed agree with those which emerge from the great bulk of work which has been published upon the question of plague epizootics.

Reference has already been made to the misleading character of gross morbid changes associated in one case with trypanosomiasis. Enlarged and congested glands, subcutaneous congestion, pleural effusion, engorgement of liver and spleen, all features suggestive of plague, were shown, though microscopic examination demonstrated readily the real nature of the infection.

In one case a dual infection of pest and trypanosomiasis was present, and it is difficult to say how far each infection was responsible for the post-mortem appearances observed.

The peppery liver associated with Gaertner infections is a crisply defined pathological entity, but in many cases this organ presented

appearances which caused trouble in diagnosis. Concurrent microscopic and macroscopic evidence gave in most cases clear indication of the true nature of the infection, but atypical livers and spleens showing signs of congestion with minor necrotic and granular changes were in a number of instances reserved for inoculation purposes. The result of inoculations with such material showed the importance of microscopic examination, for negative results were obtained in every case where no bipolar bacilli were found in the films.

Microscopical examination presents, however, a number of fallacies. Bipolar staining is at times shown in intestinal and putrefactive organisms, as well as by certain bacteria, probably of intestinal origin, which are found in the accessory sexual glands of otherwise healthy rats. Putrefactive organisms may also present forms resembling very closely pleomorphic plague bacilli, and assume groupings usually regarded as characteristic of pest. These were best seen in decomposed pleural effusions. Inoculation of such material from 16 cases—not recorded in Table II—showed the fallacious nature of such appearances. As previously mentioned, many rats not infected with plague revealed organisms in the liver and spleen which could not be differentiated from plague bacilli on microscopical examination alone.

In the infected rats generally, plague bacilli were less numerous in blood films than in spleen smears, but in a few cases the reverse held true. In some rats received in October plague bacilli were present in enormous numbers in the blood. In one or two of these, the experiment was tried of cutting off an inch of tail and preparing a film from the cut surface of the stump. Films crowded with plague bacilli were thus obtained. This point has a practical application, indicating that the practice, prevalent amongst those who catch rats, of cutting off the tails is not without danger. The cut stump presents a sharp vertebral point which might readily inflict an inoculation scratch.

#### Conclusions.

- 1. Many plague-infected rats in the earlier period (July and August) of the epizootic presented atypical appearances.
- 2. The majority of those found in the later period were typical and could usually be diagnosed upon post-mortem examination with a con siderable degree of certainty. A number of the negative cases presented difficulty in diagnosis throughout the whole enquiry.

- 3. Features suggestive of plague infection may be simulated by rats infected with trypanosomiasis or with bacilli of the Gaertner group.
- 4. The most valuable diagnostic points are the presence of subcutaneous congestion, pleural effusion, and necrotic changes in the liver. These should be considered collectively.
- 5. Minor granular and necrotic changes in liver and spleen uncorroborated by other suggestive pathological characters, macroscopic and microscopic, are in general not indicative of plague.
- 6. Major granular and necrotic changes in liver and spleen are very suggestive, but not necessarily indicative, of pest infection.
- 7. Fallacies in direct microscopic diagnosis are presented by certain intestinal and putrefactive organisms.