

AN ACCOUNT OF A GLANDERS-LIKE DISEASE  
OCCURRING IN RANGOON.

By A. WHITMORE, M.D. (Cantab.).

(With Plate I and 2 Charts.)

THE opportunities of a pathologist at a large Eastern Hospital are many; but his time for research work is short, and his conveniences are few. I, therefore, feel that we, at the Laboratory of the Rangoon General Hospital, are more than usually fortunate to be able to give, within the first two years of the official existence of the Laboratory, an account of a strange disease. Doubtless it is to chance that we owe the first discrimination of the disease; but I hope that it has been by accurate observation and precise experiment that we have sought to fulfil our knowledge. The guidance and application of our observations have been my care, and upon me rests the responsibility for the accuracy of our work; but the work itself has been carried out entirely by my assistants, and to them belongs the credit for the zeal and patient perseverance with which the task has been performed.

About one and a half years ago we had occasion to report to the Health Authorities of Rangoon the discovery of a few cases of human glanders infection; the opportunity was then seized for a much-needed effort to lessen the prevalence of this infection among the "gharry" ponies of the town. The difficulties and opposition met with by the authorities in carrying out their sanitary measures so excited our sympathy, and stimulated our interest, that our zeal in the detection of the infection was not allowed to wane. In the course of these bacteriological investigations our eyes were opened to the presence among the ill-nourished and neglected inhabitants of the town of a strange infective disease somewhat resembling glanders.

In April, 1911, we performed a post-mortem examination upon the body of a Burman aged 40 years (Case 1). He had been admitted to the hospital for fever of seven days' duration and died three days after

admission; during these three days' stay in hospital his temperature had been high, ranging from 103° to 104° F.: he was a morphia injector; for his thighs were covered with the marks of injections, and in connection with these there were several superficial abscesses.

At the post-mortem examination the principal lesion discovered was a peculiar cheesy consolidation of the lungs. The distribution and appearance of this consolidation were those of neither lobar pneumonia nor tubercular infection, and upon examining smears from the diseased patches a large number of non-Gram staining bacilli, of the size and shape of *Bacillus mallei*, were seen to be present. As our minds were then intent upon the detection of glanders, it was not strange that we made a preliminary diagnosis of this infection. We notified the Medical Officer of Health of our suspicion, and he replied that a glanders infection appeared improbable; as, so far as he could discover, the man had been released from the jail only a short time previously and had had no close contact with horses. In the meantime we had made cultures from the diseased lung: these cultures upon ordinary peptone agar gave luxuriant growths, and, upon examining the growths after three days' incubation, we found that they consisted of pure cultures of what appeared to be non-motile bacilli of the size, and shape, of those which we had found in the lung smears. We were rather puzzled by the rapidity, and luxuriance, of the growth, otherwise we were quite satisfied that the bacillus would turn out to be *B. mallei*; and it was without any misgivings as to the results that we passed on to carry out the cultural and inoculation tests characteristic of this bacillus.

After 24 hours an inoculation of a potato slope gave a lightish yellow growth which, although rather rapid and luxuriant, was otherwise not unlike the growth to be expected from an inoculation with *B. mallei*. 20 minims of a 24 hours' broth culture were injected intraperitoneally into a male guinea-pig. To our disappointment, the guinea-pig died within 36 hours without any obvious inflammation of the testicles. The post-mortem examination disclosed no signs of very acute peritonitis, although a small amount of free fluid was present within the peritoneal cavity: the omentum was rolled up, and along the rolled up, matted omentum were deposits of acute inflammatory lymph; there was also acute peri-hepatitis, but the spleen appeared to be normal. Smears from the general peritoneal cavity showed a few bacilli, in the matted omentum these were very numerous, in the liver smears they were present in moderate numbers; while in the spleen smears one or two only could be seen. From the omentum, liver, and spleen, pure

growths of a very actively motile bacillus were obtained. As we were under the impression that the bacilli obtained from the diseased lung were non-motile, we were at first inclined to the opinion that the bacilli isolated from this guinea-pig were not of the species of those inoculated, but belonged to that of *B. coli*; an injury of the intestine at the time of operation having provided a possibility for this infection. We would, I think, have abandoned this experiment as a failure, had it not been that during the past few years we have seen much of the effects of an acutely fatal peritonitis, the result of bowel injury. For in considering the signs of peritonitis presented by the peritoneal cavity of this guinea-pig, we felt dissatisfied with the simple view that they were due to a "coli" infection, and adopted an alternative view, viz. that the bacillus isolated from the human lung, though at first motile, might lose its motility after a few days' cultivation upon artificial media. This view proved to be correct; for it was found, not only that bacilli in the cultures from the guinea-pig had almost completely lost their very active motility after a few days' cultivation, but also that the bacilli in young subcultures from our original lung cultures had become actively motile. It now seemed possible that the bacilli which had caused the death of the guinea-pig, and those which had been isolated from the diseased lung, were of one and the same species; but if so it was plain that we were dealing, not with *B. mallei*, but with some other organism with which we were up to that time unacquainted; and that therefore, if, as seemed probable, the disease in the lung was the result of an infection by this bacillus, it was a disease so far unfamiliar to us. Further experience alone could decide this question; nor had we long to wait for such experience. A Burman, aged 30 years, with a history of having suffered from fever for about a month, and from dysentery during the last week, was admitted in a moribund condition to hospital: he died after less than 24 hours' stay (Case 2).

Post-mortem notes:

"An emaciated body with numerous marks of morphia injections.

"Lungs: scattered throughout both lobes of the left lung were numerous patches of the peculiar and characteristic consolidation; while in the right lung there were a fair number of such patches in the upper lobe, and a few in the lower lobe.

"The spleen was soft, and twice the normal size.

"The large bowel was extensively ulcerated: the ulcers having the appearances usual in those due to amoebic dysentery.

"The other organs of the body were normal."

Cultures from both lungs and spleen of this case gave luxuriant growths, in pure culture, of the bacillus under investigation.

Animal inoculations with the bacilli isolated from these two cases were again undertaken. Male guinea-pigs were inoculated both intraperitoneally and subcutaneously with young broth cultures, and similar results were obtained with both strains of the bacillus. The guinea-pigs inoculated intraperitoneally died, or rather were moribund, within 48 hours; and in contrast with the effects of our first animal inoculation there was, in both these animals, an obvious inflammatory enlargement of the testicles; which at the post-mortem examination was seen to be due to an acute infection of the tunica vaginalis. The abdominal cavity and its contents presented similar changes to those noted in our first inoculation; and in addition, in these two cases, the spleen was enlarged and studded with numerous small white points of inflammatory deposits. Along the needle track of inoculation a sort of caseous infiltration with a haemorrhagic surrounding gave evidence of acute inflammation of the abdominal walls. The lungs were normal.

The animals inoculated subcutaneously died more slowly; in from three to four days. Within ten hours the tissues around the sites of inoculation became widely infiltrated, and inflamed; and after death the most important change noted was the extensive matting of the tissues around the inoculation sites. This matting was due to caseous, inflammatory material, and very little fluid pus was present. In both cases there was an obvious enlargement of the spleen; which organ contained numerous tiny, white, inflammatory deposits.

From the diseased organs and tissues of all these four animals pure cultures of the bacilli were obtained.

The similarity of these two cases in their pathological lesions and bacteriological findings compelled the supposition that we had to deal with a definite and unfamiliar infective disease; if this supposition were correct, it seemed reasonable to expect that cases of the infection must have been previously met with among the numerous post-mortem examinations, which we carry out here every year; and that the records of these examinations, if kept as carefully as we hoped, would afford us satisfactory evidence upon this point. We were not disappointed; for upon referring to the records of the previous six months we were able to find some four or five cases, in which lesions of the lungs similar to those present in the above two cases had been noted. In one of these cases we had at first actually returned the case as almost certainly one of glanders infection; but later upon bacteriological investigation we

had failed to confirm this provisional diagnosis: the body had been moderately decomposed at the time of examination, and consequently the motile bacillus isolated had been classed as a product of decomposition; and our failure to isolate the slow growing *B. mallei* explained by the difficulties caused by its association with this very rapidly growing putrefactive bacillus. However, in two other cases we had persevered with our bacteriological researches for some considerable time, and had carefully noted our findings; so that we were able now to resume these researches with a bacteriological knowledge already well founded.

The conviction, that we were justified in our hypothesis that we were dealing with a strange disease, brought us face to face with a problem very different from that in which we had been previously engaged. Until then we had accepted the lung lesions as those not unusual in glanders infection, and had been employed in the simple task of substantiating this diagnosis by bacteriological investigations upon well-known lines. Now, however, our first and most obvious business was to endeavour to ascertain, whether any such disease as this, though unfamiliar to us, had been discovered and described by others. The circumstances of our work are such that it has been impossible for us to refer to literature of wider scope than that of the ordinary current text-books; from these we could obtain no hint that an infective disease of this character had been hitherto described. Therefore, so far as we were concerned, we had now to elucidate an entirely new disease: it was for us, not only to single out the characteristic features of a new bacillus; but also to describe the symptoms set up by its infection of man, to discover their underlying lesions; and to discern the method and incidence of such infections.

During the past year the material, and time, at our disposal have permitted us to satisfactorily fulfil the first portion of the task; but of the second the probable results have been only dimly indicated. From 38 subjects we have isolated bacilli with similar characteristics: in the majority of instances these bacilli alone have been isolated; in the few examples where mixed cultures have been obtained there have been adequate reasons why such mixed infections could have been expected. With difference of origin, the characteristics of the bacilli have differed slightly; but these differences have been so slight, and the resemblances in all points so close, that there has been no doubt possible, but that from all these 38 cases we have isolated bacilli of one and the same species. It has been a laborious, but by no means a difficult task, to

pick out a few characteristics of the bacillus so peculiar, as to distinguish it from all other pathogenic bacteria; and so easily observed as to be ready guides to its speedy identification in the laboratory.

The bacilli as seen in smears from the lesions of an infected organ are rod-shaped bacilli, about the size and shape of the *B. mallei*: they stain readily with all the usual stains, but are not acid-fast; nor do they retain the stain when stained by Gram's method. Stained with Leishman's stain they show a well-marked bipolar staining; the poles being stained a dark purple, while the bodies are blue.

Growth upon all the usual culture media is rapid and luxuriant; and occurs under both aerobic and anaerobic conditions; though more luxuriantly under the former.

For the first 24 hours growth in broth is not very luxuriant; although as early as the end of the tenth hour of incubation it can be seen as a diffuse, faint haze: after 24 hours there is a general turbidity of the broth and a pellicle begins to form at the surface; this pellicle gradually thickens until at the end of the fourth or fifth day it is a tough, resistant, wrinkled skin.

Upon ordinary peptone agar the growth appears in from 8 to 10 hours, as moist, translucent, slightly raised colonies; in 48 hours these colonies have become opaque and thick, and are of a cream colour. In agar cultures of over a month's growth the colonies are dry, with the middle portions wrinkled, and their colour is brown with a tinge of pink.

Upon salted agar, the salt being  $1\frac{1}{2}$  to 2% in strength, growth is slow, and appears as a thin layer rather like a thin coating of white paint. A smear preparation from a salted agar culture shows that the bacilli are growing in dense felted masses, composed of very long sinuous filaments. If the strength of salt is over 2%, growth is so slow, that, in order to secure this curious change in the appearance of the bacilli, it is advisable to inoculate a large number of these, sufficient to form immediately after inoculation a thick, visible streak.

Upon glycerine agar, containing 3 to 5% of glycerine, the growth is rapid and luxuriant, but at the end of the second day the lowest third of the culture begins to acquire a wrinkled appearance; and this wrinkling rapidly extends to the whole growth, until after little more than a week's incubation the growth has become heaped up, and rugose, not unlike a thick growth of tubercle bacilli.

Upon gelatine at a temperature of 18° to 22° C. growth is rather slow, but at the end of the third day of incubation there is a white

streak of visible growth, and beneath this liquefaction of the gelatine slowly takes place. In stab cultures this growth produces very characteristic appearances: at the end of the third day there is a faint white streak of growth along the whole needle track, and at the surface the growth is spread out in the shape of a small white disc: by the fourth or fifth day the gelatine just below this surface disc is obviously liquefying; and by the end of the week, or a little later, the liquefaction has progressed to form a small cup of liquefied gelatine covered by a thick wrinkled pellicle; while along the rest of the inoculation stab is a white line of growth with extremely fine dots distributed in a radiating manner out into the surrounding clear gelatine.

Liquefaction of the gelatine has occurred in every case, but the actual rate of the liquefaction has varied considerably with the different strains of bacilli inoculated.

Upon potato a vigorous growth appears in 24 hours. As a rule at its first appearance the growth has been of a cream colour; but with bacilli from one or two cases the initial colour has been light yellow, not unlike that of young cultures of *B. mallei*, but this yellow colour is very quickly lost. The potato round the growth is not discoloured, nor is there much spread of the growth away from the line of inoculation.

In litmus milk growth readily occurs. For the first three days there is no marked change in reaction, but later the casein is precipitated, a thick white fluffy sediment collects at the bottom of the tube, the whey becomes pink, and a violet coloured scum dotted with white spots is formed on the surface.

The various sugar media have been inoculated with the bacilli, but, though growth is vigorous, there has never been the slightest gas formation in any of these media.

In young cultures upon all media the bacilli are actively motile, but this motility is almost entirely lost as the cultures age. In agar cultures the motility is often so diminished by the beginning of the third day that cultures examined then would be accepted as those of non-motile organisms. In broth cultures the bacilli retain their motility for a longer time, but after the tenth day of incubation they have become practically non-motile.

When present the motility is of a curious serpentine character.

We have no evidence of spore formation under any conditions, but our observations upon this point are meagre.

The cultural and other characteristics upon which we rely for distinguishing this bacillus from other pathogenic bacteria are, I think,



fairly obvious; those which we find of particular utility in the rapid identification of the bacillus are:

1. The rapid and luxuriant growth upon ordinary peptone agar.
2. The wrinkling which occurs so early in the growth upon glycerine agar.
3. The pellicle formation at the surface of broth cultures.
4. The appearance of gelatine stab cultures at the end of the third day, and after one week's growth.
5. The curious, tangled masses of long filamentous bacilli found in cultures upon salted agar.
6. The active serpentine motility of the bacilli in young cultures, and its early disappearance as the cultures age.

When a rough preliminary examination of smears from diseased organs is being made the bipolar nature of the staining with Leishman's stain is exceedingly useful in arousing an early suspicion of the nature of the infection.

For testing the pathogenic effects of the bacilli upon animals we have made use of guinea-pigs only.

Both subcutaneous and intraperitoneal inoculations into these animals have been made, and all strains of bacilli have been found markedly pathogenic. In all our experiments the animal has shown signs of very serious illness within a few days. At first the dosage of bacilli used was very large, 20 minims of a 24 hours' broth culture being injected as a dose, and in these cases the animals were either dead or moribund within 48 hours; but in the later experiments, made for diagnostic purposes, very much smaller doses have been given.

The results of the large inoculations have already been mentioned while describing the investigations into our first two recorded cases of the disease. The guinea-pigs die of a septicaemic disease with well-marked local lesions depending upon the site of infection. With the large intraperitoneal inoculations the animals die so rapidly that the inflammation of the testicles, which occurs in the male pig, may not have time to develop in any very obvious manner; the swelling and redness may be so slight as to be easily overlooked; this no doubt happened in our first experiment. Therefore, if the occurrence of these characteristic local inflammations is to be utilised for diagnostic purposes, a very small dosage is requisite: we have found that half to one minim of an 18 hours' broth culture given, either intraperitoneally, or subcutaneously, is an ample and useful dose. This dose given intraperitoneally to a



male pig causes a very well-marked, and characteristic, Strauss's reaction which is obvious within 36 hours of the injection.

Within the fourth or fifth day from the time of inoculation the guinea-pig is obviously seriously ill, and may die even within five days of injection; however, the exact dates of obvious serious illness and death have varied very considerably with the strains of bacilli used.

A small dose given subcutaneously gives rise to a rapid induration of the tissues around the site of injection, and this infiltration, or induration, is due to a matting of the tissues by a thick caseous exudate; in the caseous matter, which can be easily expressed, the bacilli are extremely numerous, and can be readily demonstrated. This rapid local increase of bacilli after inoculation, and the obvious, accompanying inflammatory exudate into the tissues, are extremely useful in demonstrating the presence of bacilli, when they exist in very small numbers in any infective material.

The onset of serious illness is of course later with a subcutaneous than with an intraperitoneal infection, but in all cases serious and fatal illness has occurred, and, as a rule, has developed within seven days of infection.

A few feeding experiments with contaminated food and drink have been carried out, and, so far as infection of the animals is concerned, have always given positive results. For purposes of clinical diagnosis such experiments are too protracted to be serviceable, yet they have proved of great value as a convincing proof that the bacillus isolated from the lung and other organs of man is the cause of the illness; for by food infection we have succeeded in setting up in guinea-pigs a fatal septicaemic disease characterised by lesions of the lungs, exactly similar to the human lung lesions. We have carried out four such experiments, and in all four cases have caused fatal illnesses; and have been able to demonstrate after death extensive lung consolidations due to this bacillary infection. These experiments will be referred to again when considering the method of infection in man.

For the bacillus whose cultural and pathogenic characters have just been described I propose the name *B. pseudomallei*.

In the first cases of the disease observed by us the lesions of the lungs were so obvious, and striking, that we were not unnaturally impelled to the view that we had to deal with a "lung disease," and that it was in the lungs alone that gross evidence of infection was to be expected. It is true that in Case 2, the recovery of bacilli from the spleen proved that, at any rate bacteriologically, the disease was more

widespread; but at that time we failed to appreciate the importance of this observation. However, the isolation of bacilli from the heart's blood in Case 3 afforded further proof of the general nature of the infection, and in subsequent cases we found that the presence of bacilli in the spleen could be generally demonstrated as easily as in the macroscopic lesions of the lungs. We therefore adopted the view that though the disease was essentially a "lung disease," yet, that just as in typhoid fever though the most obvious lesions are confined to the intestine, the infection is general; so also in this disease, with its gross and obvious lesions restricted to the lungs, the local nature of the lesions gave no clue to the possible extent of the infection throughout the body.

This recognition that infection had a distribution in the body beyond that of the usual local lesions led to our examining very carefully other organs of the body for macroscopic evidence of infection, and we were not greatly surprised when gross evidence of infection was discovered in the kidneys of Case 4. Subsequently such lesions were found in both liver and kidney of the subjects of infection; but it was not until the occurrence of Case 9 that we became alive to the truth, that the existence of lung lesions was not an essential feature of the disease. In this case the lungs were quite healthy, and at the post-mortem examination one or two very minute abscesses in the liver, and an enlarged soft spleen, were the only evidence of disease to be found. Such evidence pointed to some septicaemic disease as the cause of death, and in accordance with our ordinary routine we made cultures from the spleen to determine if possible the exact nature of the infection. We had no suspicion whatsoever that the infection might prove to be by this new bacillus, and it was not until the agar cultures had aged sufficiently to show the peculiar wrinkling, that we realised with what bacillus we were probably dealing; once our suspicions were aroused they were very rapidly confirmed by the results, both of subcultures upon suitable media, and of the animal inoculation tests.

By the detection of this case we were at last fully convinced that the disease we were investigating was a septicaemia, and that, although macroscopical lesions in the lungs were the usual, and most obvious, signs of infection, yet their presence was not invariable; so that to properly determine the existence of the infection in any suspected case we should be guided, not only by the presence of lung lesions, but also by the results of a bacteriological examination of the spleen. Our subsequent investigations have given results in full agreement with this

conviction. Cultures from the spleen have been attempted in 26 of the recorded cases: in 21 of these the cultures gave positive results: in the five cases, in which the results were negative so far as the isolation of this particular bacillus was concerned, it is important to note that in three the cultures gave luxuriant growths of a coliform organism, from which through want of experience and skill we may have been unable to separate this particular bacillus, even if present. In Case 12 no note has been made beyond the fact that we failed to isolate the bacillus under investigation; and, as in this case there was severe, and acute, dysenteric ulceration of the large bowel, it is quite possible that here also a growth of coliform organisms confused the issue. In Case 13 streptococci in pure culture were grown from the spleen, and as there would be no difficulty in separating the new, rapidly growing bacillus from an associated growth of slowly growing streptococci, it seems that this case must be accepted as proving that in exceptional cases of infection by this new bacillus a splenic culture may fail to reveal the infection; also it is perhaps possible that even with further experience this detection by splenic culture will prove difficult in cases where the cultures are contaminated with such an organism as *B. coli*. It may indeed happen that the presence of some other organism such as *B. coli* or streptococcus prevents the associated growth of these new bacilli: such a point though unlikely has to be yet investigated.

Up to the present time spleen cultures have succeeded in demonstrating in the absence of positive evidence from the lungs an infection by this new bacillus in four cases; viz. Nos. 14, 15, 16 and 29.

The *lung lesions* caused by this infection have been already described as peculiar. The commonest lesion is a patch of consolidation about the size of a hazel nut, the central portion of this consolidation is pale, and generally soft and cheesy, but not so soft as ordinary tubercular caseation; the outer zone is markedly congested, and the seat of minute haemorrhages. Upon the cut surface of an incised lung the patch stands up slightly above the surrounding healthy lung tissue; and is usually more sharply defined, and drier in appearance, than a patch of ordinary broncho-pneumonic consolidation due to pneumococcal infection. In a few cases there have been patches in which very small portions of the consolidated areas have liquefied, and minute abscesses have been formed; in two cases such suppuration has progressed so as to form quite large cavities; but such cavity formation is rare. Patches of this acute consolidation are distributed irregularly throughout the lungs, and the infection appears to have no predilection for any

particular lobe, or part of a lobe. The relatively small patches of consolidation may coalesce so as to form very large areas of consolidation extending over many square inches, in such cases the individual, small, coalescing areas can frequently be distinguished by their haemorrhagic borders; but in other cases the whole of the extensive consolidation presents a uniform, pale, cheesy appearance. It has seemed to us possible that these extensive areas of cheesy consolidation indicate that the disease has run a somewhat chronic course, and we have provisionally classed them in our records as "chronic" cases, and the other cases as "acute." In favour of such a view is the observation that frequently the bacilli are quite scarce in these large areas, while in the small areas with acute haemorrhagic borders the bacilli are always exceedingly numerous.

Where an area of consolidation lies close to the lung surface the pleura over it is acutely inflamed, and irregularly raised, so as to form an injected, corrugated surface, corresponding in extent with the size of the inflamed patch beneath. There is not as a rule much pleural exudate, and adhesions if present are ill-organised, being simply those due to an acute pleural inflammation. In no cases have we found adhesions so organised as to suggest a chronic inflammation comparable with that so usually due to tubercular infection; nor have we so far met with any pleural exudate sufficient in amount, or of such a character, as to warrant a suggestion of empyema: in Case 4 the exudate was considerable, but it consisted of thick, cheesy material without signs of liquefaction.

The *bronchial lymphatic glands* do not appear to be infected; at any rate, we have never found them obviously enlarged or necrotic; and in Case 26 in which we inoculated media with material from the bronchial glands the tubes remained sterile.

The macroscopic lesions sometimes present in the *liver*, and *kidney*, are very similar in their broad features to those found in the lungs; if due allowance is made for the different consistency of the organs. They consist of small areas of necrotic, caseous material, surrounded by injected haemorrhagic zones; these areas, though as a rule small and widely scattered, may become confluent, and lead to the complete disorganisation of the infected organ; the kidneys of Case 4 are examples of this. Liquefaction of the necrotic areas so as to form abscesses occurs more often in the infection of the liver, or kidney, than in that of the lung.

In the *spleen* minute miliary abscesses may occur; but more frequently enlargement and softening only are the signs of infection of this organ.

Such are the pathological lesions usually set up by this infection, but, as our present experience of the disease has been almost entirely acquired in the mortuary, we are as yet very ignorant of the clinical course of the illness during which such lesions appear. In one case only of the infection has the whole course of the illness been observed by a competent medical observer. The case is Case 27, reported to us by Captain Knapp of the Indian Medical Service, who, puzzled during the patient's lifetime by the clinical course of the illness, recognised at the post-mortem examination that the peculiar lesions present in the lungs were similar to those which he had heard me describe, as occasionally met with in our mortuary subjects. Captain Knapp brought the diseased lungs to me at once, and from the appearance of the lesions present in them I had no difficulty in diagnosing the disease; and later this diagnosis was confirmed by the isolation of the new bacillus in pure culture.

An examination of the notes of this case shows that clinically the illness bore a very close resemblance to acute glanders; in fact upon clinical signs alone a diagnosis of glanders would probably have been made; for this diagnosis was seriously considered by Captain Knapp during the patient's lifetime, and rejected only because of the apparent impossibility of a patient living in the jail having had contact with glanders infection. Pyaemia of unknown origin was the diagnosis made. When it is remembered, that a small dose of this new bacillus, injected intraperitoneally into a male guinea-pig, gives rise to an inflammation of the testicles, as marked as that described by Strauss as so typically a result of an injection of *B. mallei*, that its occurrence could be accepted as a test of the nature of the bacillary infection; then the interest in the clinical resemblance between the two diseases is much increased. Of course it may be objected that we have no proof that the subcutaneous, superficial abscesses so prominent a feature in this case of Captain Knapp's, were caused by this new bacillus; such an objection has weight, particularly in view of the occurrence in Cases Nos. 13, 28, 31 and 33 of superficial abscesses which were due to infections, not by the new bacillus, but by some of the ordinary pus-forming organisms. However, the importance of the presence of abscesses in these four cases is much diminished by the observation that such abscesses were very obviously due to infections through the use of dirty needles for the morphia injections, with the marks of which the patients' thighs were covered; that is to say, the abscesses were symptoms, not of the fatal illnesses, but of comparatively trivial, and obviously added, complaints.

Moreover in Case 28, the two abscesses in the neighbourhood of the ankle, far removed from the sites of morphia injection, were proved to be due to this new bacillus; and afford proof that these bacilli do occasionally cause such abscesses as occurred in this case of Captain Knapp's.

The appearance of the lung lesions in this jail case was that of the class we have provisionally called "chronic," and yet the duration of the patient's illness was only forty days. It is worthy of particular remark that at the time of infection the man was in apparent good health, he had never been addicted to morphia injection, or the taking of opium in any form, and was classed in the jail register as a prisoner in every way fit for full hard labour.

The course of the illness in this the only properly observed, and fully recorded, case of infection strikingly fulfilled the expectations based upon a knowledge of the disease acquired in the laboratory and mortuary; and I think that even with such knowledge only it should not be difficult to suspect the infection reasonably early in the course of the illness; once such suspicion is entertained bacteriological proof ought to be easy. At any rate Case 29 shows that such proof is possible. The patient was a morphia injector, and had been admitted for cellulitis of the scrotum. With adequate treatment of the local disease he did not improve; and shortly before the man's death it was reported to us that an infection with this new bacillus appeared to be possible. A bacteriological examination was at once attempted. Although from the clinical signs the existence of a lung infection appeared probable, yet the man, weak and dying, was coughing up very little sputum; as much as could be collected was sent to the laboratory, and examined, but afforded no evidence of the nature of the infection. A few hours before death blood was drawn from a superficial vein of the arm. This small operation was performed amid circumstances of much difficulty; a delirious patient, a midnight hour, absence of intelligent assistance, are not favourable for accurate bacteriological work; and it is not surprising that blood so drawn had become contaminated, and that in the inoculated culture media diverse organisms grew; amid these organisms we failed to detect this particular new bacillus. However, a small amount of the blood had been drawn into a tube of sodium citrate solution and kept as "citrate" blood. In the morning a few minims of this blood were injected subcutaneously into a guinea-pig. Upon the morning of the third day after inoculation the pig was ill, and at the site of inoculation was a small indurated swelling containing

caseous material; in this caseous matter we were able to demonstrate bacilli in large numbers, and by the inoculation of suitable media to obtain pure luxuriant growths of the new bacillus.

The patient died a few hours after examination, and though the fact that he was a Mahommedan prevented permission for a full post-mortem examination, yet we were able to open the body sufficiently to prove that both lungs were free from infection, but that in both liver and spleen macroscopic evidence of infection existed: from both these organs we obtained pure growths of the expected bacillus.

It is somewhat unfortunate that this, the only case up to the present bacteriologically examined during life, should have been so exceptional as to have no gross lesions in the lungs; for it is reasonable to suppose that, when there are lesions in the lungs, the sputum would be necessarily infected, and would be the material most convenient and profitable for furnishing bacteriological proof of the nature of the infection.

Although this case is satisfactory, in so far as it furnished an excellent example of the possibility of establishing the diagnosis of infection in a living patient, yet it helps but little towards the clear delineation of the clinical picture of the disease. The patient was a hospital inmate for the three concluding days only of his illness, he was delirious and desperately ill, quite unable to give any account of the nature or length of his illness; and his friends, negligent of his welfare, did not return to visit him in hospital. Clinically all that could be said of his illness was, that he, a morphia injector, was dying from the effects of some toxæmic disease; and it was the presence of the marks of morphia injections which alone directed suspicion towards the particular infection. It may be objected that in this case bacteriological examination of the blood furnished a positive result in the very last stage only of the illness, and that had such examination been undertaken earlier it would probably not have been helpful. It is impossible to meet this objection in the present state of our knowledge, but upon the whole it seems more probable that bacilli exist in the blood stream fairly early in the illness, than that such a phenomenon is limited to the terminal stages only: the septicaemic nature of the disease in guinea-pigs lends support to this view. Moreover, it has been already pointed out that in the majority of cases the sputum would be much more likely than a bacteriological examination of the blood to provide a convenient answer to the problem of diagnosis. In the case of Captain Knapp's first prisoner the presence of signs of lung infection upon the day of



admission indicates that such infection is probably a very early event in the course of the disease.

The utility of such a test as Widal's agglutination test for typhoid fever for the early detection of this disease is doubtful. In Case 30 blood serum, collected after death, showed no power whatsoever of agglutinating the bacilli from a young broth culture of the new bacillus; but of course this question cannot be decided by this one experiment.

If simple methods such as a sputum, or blood, examination do not prove fruitful except in the later stages of the illness; then a splenic puncture would, I think, be a useful means of diagnosis.

We have seen that we have had but scanty material from which to acquire a proper clinical understanding of the disease, but when we turn to consider the probable pathways of infection, the evidence at our disposal is still more meagre. At the best an experience drawn from the mortuary only can afford but little more than a suggestion as to the usual portal and method of infection; but more particularly is this true where the mortuary subjects are those of an Eastern hospital, where custom forbids post-mortem examination of any save the wastrels and vagabonds of society, who die in hospital deserted by their relatives and friends, or whose dead bodies are brought in from the streets, without a clue to their abode, or a note as to their illness. It is therefore difficult with our present knowledge to do more than discuss, very briefly, the possible ways in which infection may occur. When we looked upon the disease as primarily a lung infection, we were naturally imbued with the idea that experience would show infection to be by way of the respiratory track, and the disease to be spread by means of infected sputum. Although the later widening of our views by no means forbids the consideration of the possibility of such happenings, it does, I think, make them less exclusively probable. For the recognition of the lung disease as a part only of a widespread malady prevents the prejudice that such lesions probably represent the first footprints of invasion, or that the lungs provide the sole strongholds of attack.

It is a striking and suggestive fact that, of the 38 reported cases of infection, 31 bore marks of morphia injections; and of these 31 persons all save two, viz. Cases 28 and 33, were clearly still addicted to the habit at the time of their last illnesses. The question of a direct connection between these morphia injections and the disease naturally arises. The social status of these friendless wastrels is in itself a guarantee that the injections of morphia are given under the very worst

conditions; but still further proof that all the usual precautions of cleanliness are absent in these administrations of the drug is afforded by the reflection that in very many of the cases the sites of past injections are obviously, and grossly, septic. Yet dirty though the injecting syringes and needles may be it appears improbable that this particular infection is thus conveyed. In several of the infected subjects, whose thighs bore numerous injection marks, we have carefully examined the groin glands, and, though it is not unusual to be able to isolate ordinary pyogenic organisms from these glands, we have never succeeded in isolating this new bacillus; but it is to be borne in mind that this new bacillus does not seem to readily infect the lymphatic system, for in cases of severe lung infection in man, and in the artificial infection of guinea-pigs, the appropriate lymph glands are not obviously infected. Moreover, considering the local reaction which occurs after the subcutaneous injection of the bacilli into guinea-pigs, it is not unreasonable to suppose that in man also a very marked local induration would occur at the site of a cutaneous infection; yet, neither in the majority of morphia injectors, nor in any of the other cases of human infection, has there been any evidence whatsoever of an inflammatory induration, such as could indicate the site of infection through a skin injury. The real explanation of the frequency of this infection among morphia injectors appears to lie in the theory that this morphia habit is so disastrous to the well-being of its victims.

While it is unlikely that infection is by way of cutaneous injuries, we have direct experimental evidence that infection may take place by means of contaminated food and drink. We have already described how pathogenic the bacilli are to guinea-pigs. At first we determined this by inoculation experiments only, but later we fed four guinea-pigs with food or drink contaminated with bacilli; and all four animals quickly succumbed to the infection: in each of the animals after death we found lung lesions exactly similar in character to those so usual in the human infection; but in none were we able to demonstrate any intestinal lesion, nor were we able to recover the bacilli from the intestinal contents; it is therefore possible that infection of these animals occurred through the respiratory, and not through the intestinal tract, though the latter would appear to be the more probable route. However this may be, it will be admitted that, if a disease similar in all respects to that occurring naturally in man can be easily caused in susceptible animals by contamination of their food and drink, then in man also such a method of infection is probable.

One fact not already mentioned has a very important bearing upon the facilities for the occurrence of this contamination: in Cases 4 and 7 a small amount of turbid urine was present in the bladder after death, and when this urine was examined bacteriologically it was found that the turbidity was due to the presence in the urine of vast numbers of these new bacilli. Upon post-mortem evidence alone it is quite impossible to form any opinion as to the prevalence of this bacilluria among cases of the infection: but so far as such evidence goes it appears probable that bacilluria is a marked feature in those cases only in which some gross kidney lesion exists; for in Case 24, in which the post-mortem findings seem to indicate that the infection ran a rapid and acute course, the urine collected after death was free from infection. That only a comparatively slight lesion of the kidney can produce a marked bacilluria is shown by the nature of those lesions present in Case 7. The comparative frequency of kidney lesions in cases of the disease cannot really be estimated by the present series of cases, for in the earlier cases it is quite likely that small lesions were overlooked; however, obvious evidence of kidney infection is noted in seven out of the 38 cases recorded.

It might be reasonably expected that amongst an Eastern community, the habits of whose members are such that the ordinary laws of sanitation are more honoured in the breach than in the observance, an acute infectious disease endowed with those facilities to spread afforded by an infected sputum and urine, would be an exceedingly common and important item in the mortality returns. Yet so far as our experience goes the incidence of this particular disease is very narrow, and its victims comparatively few. Of the 38 cases here recorded 30 were morphia injectors, and four of the remaining eight had other serious debilitating diseases associated with this infection. Only three of the subjects of the disease examined by us were well nourished, and thus suggested that the infection had attacked persons previously in good health and strength. However, in considering the significance of the signs of wasting and debility so usually present, it must not be forgotten that one of the effects of the illness itself may be rapid wasting; such rapid wasting is a striking feature in the illnesses of the artificially infected guinea-pigs. Similarly the significance of the association of the infection with other diseases, such as occurred in 13 of our cases, must not be appreciated without paying due regard to the difficulty of determining in such cases the relative dates of onset of the new bacillary infection and the associated disease.

The probable nature of the effect of morphinism as an adjunct to infection has already been mentioned.

Upon the whole the facts at our disposal support the belief that the bacillus is but slightly virulent towards man, but in estimating the incidence of any disease it would be unwise to attach too great a value to facts collected from a public mortuary; and it may well happen that these first reassuring impressions of the low virulence of the bacillus may be early contradicted as experience ripens. Indeed, in Case 27, reported by Captain Knapp, we have very clear proof that a man enjoying certainly averagely good health, and living under better sanitary conditions than those affecting the majority of his free, but from a sanitary point of view less fortunate, fellows, may succumb to the infection.

It is true that in their practical application the results of these observations are of local interest only, yet the inquiry, from which they have been obtained, has had a scope so wide that our inferences, drawn from an experience so narrow and from facts so few, can do but little more than pave the way for further investigations; it is therefore particularly important that our results should be clearly displayed; for this purpose it is, not only convenient, but necessary that our report should end with a brief review of our present position.

#### SUMMARY.

Upon 38 separate occasions during the year we have isolated from diseased human organs a bacillus with constant characters, of which some are sufficiently peculiar to distinguish it from all pathogenic bacteria previously known to us.

The pathological lesions, from which such bacilli can be easily isolated in pure culture, are often so peculiar in appearance that this appearance alone would suggest doubts, as to the causation of the lesions by any of the usual pathogenic bacteria; and after a short experience would warrant an anticipatory diagnosis of this particular infection.

If guinea-pigs be fed with food or drink contaminated with pure cultures of this bacillus, the animals speedily die, and after death, not only can the bacilli be easily recovered from various organs, but also lesions are present in every way similar to those found in the human subject.

The human disease, characterised by the constant presence of these bacilli, and by the usual presence of these peculiar lesions, is a pyaemic

or septicaemic disease, attended by symptoms which may bear a very close clinical resemblance to glanders; but the distinction between the two diseases is easy if a proper bacteriological examination be carried out; though confusion would at once arise if Strauss's guinea-pig testicular reaction were allowed to decide the nature of infection.

So far as our present knowledge goes, this new disease is particularly prevalent among morphia injectors; but such prevalence is due rather to the general effects of the morphia habit than to any peculiar exposure of its devotees to infection. We expect that it will be found that, just as in guinea-pigs the infection can be conveyed by contaminated food and drink, so in man such contamination affords the usual method and means of infection.

Moreover the excretion of vast numbers of living bacilli in the urine, and probably in the sputum, of many of the infected persons living amid crowded, insanitary surroundings, makes contamination of food and water inevitable.

Finally, while our clinical knowledge of the disease is so scanty that upon clinical signs only no more than a suspicion of the infection can be entertained; yet our bacteriological knowledge is sufficiently exact, and its application sufficiently easy, to allow such suspicion to be readily confirmed, or denied, by a reference to the pathological laboratory.

Plate I illustrates cultures of the bacillus and the macroscopic appearance of the lung in Case 1. Brief notes of the 38 cases hitherto investigated are added.

*The brief records of the thirty-eight cases upon which this paper is based.*

**Case 1.** A Burman, aged 40, admitted to hospital for fever, said to have been of about seven days' duration.

A fairly nourished man, a morphia injector; a few superficial abscesses scattered over the body; temperature fairly high, ranging up to 104° F., moist sounds in both lungs, but no note of any signs of consolidation. He died after three days' stay in hospital. P. M. the lungs contained very numerous patches of the peculiar consolidated areas; smears from these areas showed the bacilli present in large numbers, and a pure culture was obtained with ease: no culture was taken from the spleen or other organ.

**Case 2.** A Burman, aged 30 years, admitted to hospital in a moribund condition with a history of fever of a month's duration and of lately passing blood in the motions. He died after less than 24 hours' stay in hospital.

P.M. An emaciated body with marks of morphia injection.

Lungs. Left lung, contained numerous patches of a typical appearance throughout both lobes.

Right lung contained numerous similar patches in the upper lobe, with a few patches in the lower lobe.

The spleen was twice the normal size.

The large bowel was covered with gangrenous ulcers of the usual amoebic dysentery type.

Other organs normal.

Culture from both lungs and spleen gave luxuriant growths of the bacillus in pure culture.

**Case 3.** A Madrassi, male, aged about 45, admitted to hospital for debility and cough; the illness said to have been of one month's duration. He died a few hours after admission.

An emaciated morphia injector.

P.M. performed very shortly after death while the body was still warm.

There were numerous typical consolidated areas in both lungs; also evidence of old tubercular infection, in the shape of a small fibrotic consolidation at the apex of the right lung, and a small thick-walled cavity at the apex of the left lung.

Upon the surface of the spleen were flakes of recent inflammatory lymph.

The groin glands were fairly markedly enlarged.

Cultures were taken from the lungs, spleen, heart's blood and groin glands: pure growths of the bacilli were obtained from the lungs, spleen, and heart's blood, but not from the groin glands.

**Case 4.** Hindu, male, admitted for pain in the chest and fever; the illness said to have been of one month's duration.

A moderately well-nourished man, very ill, temperature ranging from 99° F. Dulness at the base of the right lung, with increased vocal fremitus; while over both lungs were very numerous bronchitic rales. The patient died three days after admission. *Clinical diagnosis* 'Lobar Pneumonia' right lung.

P.M. No marks of morphia injection upon the body, which was fairly well nourished.

Lungs. Right, pleura covered with a thick layer of inflammatory lymph, middle lobe of the lung largely consolidated by fluent patches characteristic of this infection: lower lobe a few such patches.

Left lung: a few very small patches of typical consolidation present. Spleen about three times normal in size, and covered with flakes of recent inflammatory lymph. In the interior were one or two minute abscesses.

Kidneys both extensively infected, the kidney substance being riddled with caseous deposits.

In smears from the lungs, kidneys, and urine, were a very large number of bacilli; while a spleen smear showed a few bacilli.

Cultures from the lungs, spleen, and kidneys, gave a luxuriant growth of the bacilli; and from a plate culture of the urine very numerous colonies of the bacilli could be picked out.

**Case 5.** A Burman, aged about 38 years, found moribund in the street. P.M. An emaciated body with marks of morphia injections upon both thighs.

Lungs. Left lung, a small old cavity at the apex almost certainly tubercular in origin, otherwise lung normal.

In the right lung, there was puckering at the apex, due to old tubercular infection; in lower lobe a very small patch of acute broncho-pneumonia of characteristic appearance was present.

Spleen, old strong adhesions, otherwise normal.

Liver, recent acute adhesions.

Kidneys: in the left were two or three infiltrated patches of a typical character. The right was normal.

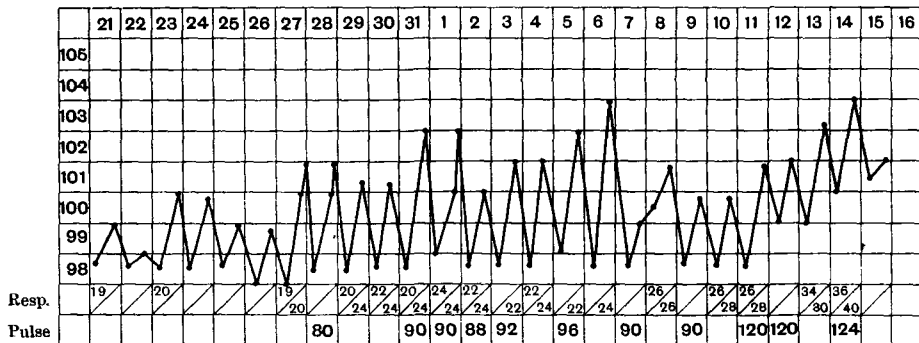
In smears from the lung there were a few acid-fast bacilli.

In smears from the kidney were a fair number of non acid-fast bacilli. Cultures from the kidney patches only were made, and gave pure growths of the bacilli.

**Case 6.** A Hindu, male, aged 30, admitted to the jail hospital upon arrival, for general debility thought to be the result of chronic "morphinism." The man had irregular fever ranging from normal to 104° F. but had no other very obvious symptoms. Malarial parasites were looked for but not found.

Seven days before death a blood count gave the following differential leucocyte count:

Polynuclears	49 0/0
Lymphocytes	8 0/0
Mononuclears	37 0/0
Eosinophiles	6 0/0



Temperature chart of Case 6.

The patient was admitted to the jail hospital upon the 21st of October, 1911, and died November 15th.

The man gradually grew worse, and died twenty-six days after admission to the jail hospital.

P.M. Typical patchy consolidation of the lungs was found, and there were also areas of inflammatory deposits in the liver; the appearance of many of these areas was very similar to that of inflammatory nodules in the lungs, but in one or two places actual suppuration had taken place.

Cultures from both lungs and liver gave pure growths of the bacilli under discussion.



**Case 7.** Burman, aged about 40 years, picked up in a dying condition, and died very shortly after being brought to hospital.

P.M. A poorly nourished body with fairly numerous marks of morphia injection.

Lungs. Both lungs oedematous, and in the middle lobe of the right lung was one patch of broncho-pneumonia about the size of a pea with the characters of the inflammation caused by this infection.

Spleen, large, and flaccid, covered with old organised adhesions. Kidneys, right healthy, the left contains two small areas of inflammation with characters usual in this disease.

Urine turbid, but no signs of bladder infection or inflammation. Intestine : lower, two-thirds of the large intestine contains fairly numerous old healing ulcers of dysenteric type.

*Cultures.* From the lung nodule gave a fair number of colonies of the bacillus.

From the kidneys a large number of colonies.

From the spleen about a dozen colonies of the bacillus.

From the urine a fair number of colonies of the bacillus were grown.

**Case 8.** A Burman, aged about 30 years, picked up dead. A moderately nourished man, with a fair number of morphia injection marks on the right thigh.

P.M. Lungs. Both lungs studded with very numerous nodules ranging in size from a millet seed to a bean, in appearance characteristic of the infection.

Liver surface mottled with small, minute, white dots, and small inflammatory deposits of a typical appearance.

Spleen, slightly enlarged, with fairly numerous, tiny, abscesses. In both kidneys were small deposits characteristic of the infection.

A small amount of turbid urine in the bladder.

In smears from the lung nodules bacilli in fair numbers were seen.

In smears from the spleen a few bacilli were present.

Cultures : liver, a fairly vigorous growth of the bacillus.

Gall-bladder, a coliform bacillus.

**Case 9.** Hindu, male, aged about 32 years ; dead body picked up in the street.

P.M. A poorly nourished body with slight oedema of the feet, but no marks of morphia injection.

Lungs. No obvious disease in either lung.

Spleen slightly enlarged, about  $1\frac{1}{2}$  times normal ; substance soft and friable.

Liver. One or two very minute abscesses, otherwise normal.

A few ankylostoma worms in the intestine.

No other evidence of disease ; death was returned as being probably due to a septicæmic infection of some sort. We did not suspect in any way that it might be this particular infection. However, cultures taken from the spleen gave a luxuriant growth of these bacilli in pure culture. These cultures were tested by animal inoculation.

**Case 10.** Burman, aged 35 years, admitted to hospital for anorexia and malaria fever of one and a half months' duration. Stay in hospital nine days ; his symptoms being diarrhoea with 6 to 18 stools in the 24 hours, irregular fever, the temperature ranging from 99° F. to 102° F. ; there were signs of acute bronchitis in the lungs, and

the clinical diagnosis was pulmonary tuberculosis, with diarrhoea due to tubercular ulceration of the bowel.

P.M. An emaciated man with the marks of numerous morphia injections.

Lungs. Left lung, one nodule of characteristic appearance in the lower portion of the upper lobe, with a larger nodule of similar appearance in the middle of the lower lobe.

Right lung, one or two characteristic nodules in the lower lobe; the rest of the lung being normal.

The large intestine was full of large acute ulcers of the amoebic dysentery type.

Spleen, normal.

From the lungs were isolated pure growths of the bacilli, but from the spleen these bacilli were not isolated; the spleen cultures growing bacilli of the colon type.

Cultures from the lung patches grew pneumococci and a large coliform bacillus; no new bacilli.

Spleen gave a pure growth of the new bacillus.

**Case 11.** Hindu, male, aged 25 years, admitted to hospital for looseness of bowels of three months' duration; temperature 101° F.; motions 10 in the twenty-four hours: he died after twenty-four hours in hospital.

P.M. An emaciated young man, not a morphia injector.

Lungs. Right lung normal.

Left lung, a few nodules in the lower lobe characteristic of the infection.

Intestines. The large intestine has numerous ulcers of an amoebic dysentery type chiefly confined to the caecum; the appendix is sloughing in its distal half.

The liver contains one large abscess in the lower part of the right lobe (the usual abscess due to tropical dysentery).

Spleen, normal.

Cultures from the lung gave a vigorous growth of the bacillus.

From the spleen a growth of a coliform bacillus was obtained, but no bacilli of the type under discussion.

**Case 12.** Dead body of an emaciated Madrassi, aged about 30 years, not a morphia injector, picked up in the street.

P.M. Lungs. Left, upper lobe normal; lower lobe consolidated, with a consolidation like that present in an acute lobar pneumonia, with areas of broncho-pneumonia typical of the new infection scattered through the consolidated portion.

In the right lung, a fair number of dark red consolidated areas probably secondary to a dysenteric infection present.

Spleen twice normal in size; culture negative.

In the kidneys were one or two nodules characteristic of the infection.

Large intestine very extensive, chronic, amoebic ulceration.

Cultures from the left lung gave pure growths of this bacillus, whereas cultures from the dark red consolidated portions of the right lung gave negative results.

A culture from the spleen was negative.

The kidney patches gave a fairly copious growth of the bacillus.

**Case 13.** A Burman, 26 years old, admitted to hospital with a large gluteal abscess. Temperature upon admission 103·8° F.

Died upon the third day after admission.

P.M. An emaciated morphia injector with a large abscess in the left gluteal region (opened before death); the subcutaneous tissues of the thigh below the abscess were infiltrated with pus.

Lungs. Both lungs contain typical deposits of the new bacillary infection; more numerous in the left lung than in the right.

Spleen, slightly enlarged, with a few small nodules not very characteristic of the infection.

Cultures :

	Lung,	pure growth of new bacillus.
	Spleen, ,, ,,	streptococci.
	Thigh abscess, ,, ,,	streptococci.

**Case 14.** Burmese, male, aged 30 years, admitted for tubercle of the lungs and diarrhoea; the history of the illness nil. There was impaired resonance at the right apex and moist rales all over; temperature 100° F. Bowels acted frequently; but no blood, only slime in the motions, which were offensive. Died two days after admission.

P.M. An ill-nourished morphia injector.

Pleura obliterated by well-organised adhesions.

Left lung, upper lobe normal, but in the lower lobe are a few small nodules of inflammatory consolidation.

Right lung, posterior portions engorged and oedematous, but no areas of consolidation.

Spleen, twice normal in size but no abscesses.

Large intestine, the mucous membrane largely destroyed by gangrenous ulcers of the amoebic dysentery type.

**Case 15.** Burman, aged 30 years, picked up in a dying condition in the streets: died soon after admission.

An emaciated morphia injector.

P.M. Lungs. Left lung, there are several small consolidated areas; one broken down into a cavity. The consolidation in appearance like that secondary to dysentery, and not like that due to an infection with this bacillus.

Right lung oedematous, otherwise normal.

Spleen, normal in size with well-organised adhesions around.

Heart, recent small vegetations on the mitral valves.

Large intestine covered with numerous large, gangrenous, amoebic dysenteric ulcers, which in the sigmoid are practically perforating.

Cultures. Lungs gave only a coliform organism.

Spleen, a pure growth of the bacillus under discussion.

**Case 16.** Burman, aged about 35 years, picked up in the street dead.

An emaciated morphia injector.

P.M. Lungs normal, but some old adhesions in the pleura.

A large amount of clear fluid in the abdominal cavity.

Liver shows well-marked multilobular cirrhosis.

Spleen, about four times normal in size, soft.

Large intestine covered with a large number of old, healed, and healing ulcers of the amoebic dysenteric type.

Smear from the spleen shows a few malaria parasites, and also a large amount of pigment.

A culture from the spleen gave half-a-dozen colonies of the new bacillus.

**Case 17.** A Burman, aged about 40 years, died in the out-patient department before examination: an emaciated morphia injector.

P.M. A few patches of the typical broncho-pneumonia were found in both lungs, particularly at their bases; there was a small fibrotic tuberculous induration at the right apex of the lung, otherwise the organs were apparently free from disease.

Pure growths of the bacilli were obtained from the consolidated areas of the lungs.

**Case 18.** A Hindu, aged about 30 years, picked up unconscious in the street, and died very shortly after being brought to hospital.

An emaciated morphia injector.

P.M. Posterior parts of both the upper and lower lobes of the left lung were extensively consolidated with what were then thought to be tubercular deposits: the right lung showed similar, but not quite such extensive, consolidation: the spleen was slightly enlarged.

Smears from the lungs showed non-acid-fast bacilli; cultures from the lungs, and from the spleen, gave copious growths of the bacilli in pure culture.

**Case 19.** A Burman, aged 33 years, admitted to hospital for general debility, and bronchitis, said to be of fifteen days' duration. The man was practically moribund upon admission, but when examined by a medical officer the suggestion was made that the infection was with this bacillus: unfortunately the patient died shortly after admission before any bacteriological examination could be made.

P.M. An ill-nourished body with numerous marks of morphia injection.

Lungs. Left lung, typical nodules on the lower lobe.

Right lung, numerous typical nodules scattered throughout.

At the apices of both lungs were old fibrotic patches, the remains of tubercular infection.

Spleen, twice the normal size with recent perisplenitis.

Other organs normal.

Cultures from both lungs and spleen gave copious pure growth of the bacilli.

**Case 20.** Burman, aged 40, admitted for fever, and cough of about twenty days' duration, in a weak, dying condition; there were signs of pneumonia upon the right side of the chest. A poorly nourished man with numerous marks of morphia injection; upon admission temperature 104° F., pulse 130, respirations 48. Died day after admission.

P.M. A moderately nourished Burman.

Lungs. Both lungs full of numerous typical nodules, the patches at the lower third of the upper lobe, right side, were coalescing so as to cause complete consolidation.

Spleen, slight enlargement, but no abscesses.

The lungs gave a pure luxuriant growth of the bacillus.

**Case 21.** A Burman picked up dead in 19th Street.

An emaciated morphia injector, aged about 28 years.

P.M. Lungs. Left upper lobe normal, lower lobe contains numerous patches of small areas of consolidation rather like miliary tubercular deposits.

Right lung, upper lobe one or two small suppurating cavities with a few greyish consolidated areas.

Middle lobe, oedematous, with large consolidated patches with purulent points.

Lower lobe, almost entirely consolidated with numerous very minute suppurating points.

Lung condition thought to be very likely tubercular.

Spleen,  $1\frac{1}{2}$  times normal in size, fairly recent perisplenitis.

Liver, scarred, with well-organised adhesions to the diaphragm.

Large intestine, numerous recent and several old healed amoebic dysenteric ulcers.

Lung smear. No acid-fast bacilli, only basic staining bacilli.

Spleen smear, a few bacilli and cocci.

Cultures. From the lung a copious growth of the bacillus in pure culture.

From the spleen growths of coliform bacillus and a staphylococcus.

From the liver, coliform bacilli were grown.

**Case 22.** A Burman, aged about 33 years, died in the outdoor department before examination.

P.M. An emaciated body with very numerous marks of morphia injection.

Lungs. Left lung normal.

Right lung, upper lobe consolidated with what, in appearance, were acute tubercular deposits undergoing suppurating, the pus being thick and tenacious and of a greenish colour.

Middle lobe, a few deposits of acute broncho-pneumonia.

Lower lobe normal.

Spleen normal. Other organs normal.

Smears from the lung showed very numerous bacilli, but none acid-fast.

Cultures from the various diseased parts of the lung gave pure growths of the bacilli under consideration.

**Case 23.** A Hindu, male, aged about 48 years, picked up dead in the street. A moderately nourished old man with marks of morphia injection upon thighs and arms.

P.M. Lungs. Left lung, numerous coalescing patches of the infection with a small cavity at the apex, not tubercular in appearance.

In the middle and lower lobes a few discrete patches characteristic of the infection were found.

Spleen, slightly enlarged, with one or two tiny abscesses.

Other organs normal.

Smears from the lung patches showed bacilli to be present in large numbers.

In those from the spleen no bacilli were seen.

Cultures from the spleen gave a pure and vigorous growth of the bacillus; culture from the lung not taken.

**Case 24.** A well-nourished Hindu, male, aged about 28-30 years; dead body picked up in the street. Not a morphia injector.

P.M. Right lung, upper lobe in the lower half contains a large purulent cavity about the size of a tangerine orange; so far as appearances went this cavity was due to a breaking down of confluent patches of broncho-pneumonia the result of infection with this bacillus.

In the middle and lower lobes were very numerous patches typical of the infection.

Left lung, upper lobe middle portion, consolidated with confluent broncho-pneumonic patches of the infection.

Spleen, about twice the normal size, surrounded by numerous old, and recent, adhesions. Spleen substance soft. Other organs normal.

Smears and cultures from the lung gave numerous bacilli of the type under discussion.

Spleen culture not taken.

Urine cultivated but no growth of this bacillus obtained.

**Case 25.** A Mohammedan, male, aged 40 years, picked up dead in the street; an emaciated morphia injector.

P.M. Lungs. Left lung, upper lobe, numerous tubercular-like nodules, with a few more acute in appearance.

Lower lobe, a few similar small nodules.

Right lung, upper lobe, a big gangrenous foul-smelling cavity; with the rest of the lobe consolidated with what looked like small coalescing tubercular deposits. Other lobes normal. Other organs normal.

Smears from the lung showed the presence of a few acid-fast bacilli together with a fair number of non-acid-fast bacilli.

Cultures from the lung grew four colonies of the bacilli.

From the spleen a copious and pure growth of the bacillus was obtained.

**Case 26.** Burman, aged about 35 years, picked up dead in the street.

P.M. A moderately well-nourished body, with morphia injection marks upon both thighs.

Lungs. Left lung, a very few, tiny, nodules of characteristic appearance in the lower lobe; in the upper lobe was a little scarring, probably due to tubercular infection.

Right lung. Both upper and lower lobes full of characteristic nodules; while in the middle lobe were a few such nodules.

Other organs normal.

Cultures from the lungs and spleen gave copious and pure growths of the bacillus.

From the heart's blood a couple of colonies were obtained; while cultures from the groin and bronchial glands were sterile.

**Case 27.** Patient a Punjabi, male, aged 35 years.

Admitted to jail as a prisoner upon three years' sentence in September, 1910, in good general health; not an opium smoker or morphia injector.

Admissions to hospital since coming to jail:

- (1) February, 1911, for a bad attack of *acne vulgaris*.
- (2) Suspicious symptoms of dysentery in February.
- (3) Fever on the 16th of June.

Nothing of note in personal or family history.





Admitted to hospital for final illness on 28th June, complaining of fever.

Conditions upon admission: temperature 101·2°, pulse 80, resp. 19, a few moist rales in the left chest, and pleuritic pain.

June 29th, a single malarial parasite found in the blood.

July 2nd, sputum examined and tubercle bacilli not found.

July 3rd, swelling over the thyroid cartilage. Upon the 8th this swelling was incised and a little pus found. Friction rubs were audible over the right and left bases of the lungs. Upon the 10th a swelling formed over the right clavicle which was incised on the 11th. Upon the 14th swelling over the right trochanter, which was incised on the 18th. Upon the 20th began to have marked dyspnoea, and dulness was detected at the base of the right lung. Upon the 22nd there were signs of consolidation at the left base. Upon the 30th a swelling appeared over the left malleolus: incised on the 1st August. Sputum examined and neither pneumococci nor tubercle bacilli found.

The patient died unconscious upon the 7th August.

P.M. The abscesses had all been superficial, there was a small acute abscess on the surface of the left lobe of the liver; from this pus a film was made and stained with methylene blue and a few rod-shaped bacilli were seen.

With the exception of the lungs the other organs were healthy. Both lungs were the seat of an extensive but patchy consolidation, the larger patches presenting a whitish cheesy appearance. The smaller patches were reddish and surrounded by a zone of hyperaemia. From the lungs a pure culture of the bacillus under investigation was obtained without difficulty, and films showed these bacilli present in great numbers.

**Case 28.** Burman, male, age about 35 years; dead body picked up in the street. A well-nourished muscular man with a very few, apparently old, marks of morphia injections.

P.M. Lungs. Left lung, both lobes contain very numerous, but rather small, broncho-pneumonic nodules of about the size of a marble, fairly characteristic of the infection but a little more moist than usual in appearance.

Right lung, a few scattered nodules in the upper lobe; the other lobes normal.

Spleen, twice normal in size.

In the left kidney were three or four deposits the size of a two anna piece.

An abscess of the groin; and two abscesses over the right ankle.

Smears from the groin abscess showed staphylococci and streptococci, no bacilli. From the ankle abscesses, a few possible bacilli.

Cultures from the lung, spleen, and kidney, gave colonies of the bacillus in pure growth.

Cultures from the ankle abscesses also grew the bacillus.

**Case 29.** A Mohammedan male, aged about 55 years, was admitted to hospital, suffering from cellulitis of the scrotum. He was in a very poor state of general nutrition; being a neglected morphia injector. Upon admission to hospital he was delirious, and obviously very ill: no history of his illness could be obtained. As he had not improved two days after efficient local treatment had been carried out, it was suspected that he was suffering from a septicaemia of which his scrotal condition was merely a symptom. When seen by a senior medical officer a suggestion

of this new infection was made, and the case reported to the laboratory for investigation.

He died three days after admission to hospital and although a full post-mortem examination was not carried out the lungs, liver and spleen were viewed. The lungs were found to be free from disease, but in both the liver and spleen were small inflammatory deposits in all respects similar to those, which had so frequently been seen in previous cases of this infection. Pure cultures of the bacilli were obtained from both the liver and spleen.

**Case 30.** A Burman, aged 38 years, admitted to hospital for general debility; duration of illness not stated.

A poorly nourished morphia injector, by trade a beggar; complains of cough with pain in the chest. Dulness was found over the apex and base of right lung, and rales and harsh breathing were heard over these areas: the clinical diagnosis was tubercular infection of the lungs. The sputum is described as frothy but not blood stained: no tubercle bacilli were detected upon examination. The patient had been in hospital for eight days when he died; during his stay in hospital his temperature was irregular, ranging from normal to 103° F.

P.M. There were numerous patches of acute broncho-pneumonia in both lungs; from these patches the bacilli were easily isolated in pure growth. Cultures from other organs were not attempted.

In addition to the disease of the lungs there were scars of old healed dysenteric ulcers in the large bowel, and a few, very small, open ulcers in the lowest few inches of the small bowel.

Blood serum from this case was taken, and its agglutinating power upon the bacilli isolated from other cases was tried; but no such power was found in any dilution of the serum.

**Case 31.** A Burman, about 40 years of age, admitted to hospital for general debility, and ulcers of both legs due to morphia injections; duration of illness said to have been of one month.

During his stay in hospital his temperature was irregular, ranging up to 101° F. He died after nine days in hospital.

P.M. An emaciated body.

Lungs. Both lungs contained very numerous nodules of acute broncho-pneumonia with the characteristic appearance of the infection.

Spleen of normal size, but covered with old, well-organised, adhesions.

In the lower portion of the large intestine were a few chronic ulcers.

The groin glands were fairly markedly enlarged.

Pure growths of the bacilli were obtained from the lungs and the spleen; but from the groin glands staphylococci only were isolated.

**Case 32.** Burman, male, picked up dead in the street, age about 28 years.

P.M. A poorly nourished body, with numerous marks of morphia injections.

Lungs. Left lung, upper portion of the lower lobe consolidated with coalescing patches of a typical appearance.

Right lung. Upper lobe practically solid, with similar patches, a few small scattered patches in the lower lobe.

Spleen  $2\frac{1}{2}$  normal in size, with minute points of inflammatory deposits.

Liver contained very numerous, scattered, white points without any definite abscess formation.

Large intestine showed numerous scars of old dysenteric ulcers. Inguinal glands enlarged and upon the cut surface of the glands were areas of suppuration.

Cultures from the lungs and spleen gave a luxuriant growth of the bacillus.

From the liver and inguinal glands the bacilli were not isolated; but the inguinal glands gave a growth of staphylococcus.

**Case 33.** A poorly nourished Burman, of about 40 years of age, found in a dying condition in the street. Died shortly after admission to hospital. Duration of illness (fever and cough) said to have been two months.

A poorly nourished man with a few marks of morphia injection.

Numerous abscesses in the groin.

P.M. Lungs. Left, about a dozen small areas of broncho-pneumonic consolidation scattered throughout the lung.

Right lung. In upper and middle lobes, about five or six small nodules present.

Lower lobe almost completely solid with confluent patches of a typical appearance.

Spleen of normal size; a little recent deposit of inflammatory lymph on the surface.

Kidneys. Both kidneys contain five or six fairly typical small and large patches of this infection.

Smears from the lung and kidney show very numerous bacilli.

Culture from the spleen grew a pure growth (about half-a-dozen colonies) of the bacilli.

From the groin abscesses the bacillus was not isolated.

**Case 34.** Burman, aged 21 years, admitted to hospital with the symptoms of acute dysentery; which was the clinical diagnosis. The man died ten days after admission: his temperature during his stay in hospital had been normal until the last day.

P.M. An emaciated body with numerous marks of morphia injections.

Lungs. Both lungs contained very numerous deposits of a typical appearance.

The large bowel was extensively ulcerated, the ulcers being those of the ordinary amoebic dysentery.

Cultures from the lungs alone were taken and gave luxuriant growths of the bacilli.

**Case 35.** A Hindu, male, aged about 33 years, picked up in a dying condition in the street.

P.M. A well-nourished man, no evidence of morphia injections present.

Lungs. Right lung, normal.

Left lung, acute pleurisy over the lower half of the lung, with a few haemorrhagic patches of consolidation in the lower lobe, more like those due to a terminal dysenteric infection than to the infection under discussion; but in the upper lobe was one patch with the characteristics of this infection.

Large bowel in a condition of acute dysenteric ulceration.

Cultures from the haemorrhagic patches in the lower lobe gave growths of a coliform organism; while a culture from the patch of different appearance in the upper

lobe gave a pure growth of the new bacillus. This culture was proved, both by sub-culture, and by animal inoculation.

**Case 36.** A Chinaman, about 27 years old, admitted to hospital for general debility, and diarrhoea, of one month's duration.

Died after seventeen days' stay in hospital; during this time he was suffering from diarrhoea, general loss of appetite, and rapid wasting. His temperature was irregular and he had a cough, of which no very serious notice was taken; his lung condition was attributed to the terminal broncho-pneumonia not uncommon in wasted dysenterics; his history was unknown to us, as he spoke only an incomprehensible Chinese dialect, and had no friends. He was not a morphia injector.

P.M. An emaciated body.

Lungs. Left lung was full of very numerous nodules of acute broncho-pneumonia of a very characteristic appearance.

The right lung was free from any obvious disease.

The spleen was normal in appearance.

In the large intestine were fairly numerous, very tiny, acute, shallow ulcers, such are not uncommon in diarrhoea cases apart from true dysentery.

Cultures were taken from the lung and spleen and from both sources pure growths of the bacillus were obtained.

**Case 37.** Hindu, male, aged about 22 years; the dead body was picked up in the street.

P.M. An emaciated body, with numerous marks of morphia injections.

Lungs. Several small nodules scattered throughout both lungs, more numerous in the left than in the right lung, of a character typical of the infection.

Spleen, normal in size, but soft.

Intestine showed chronic inflammation of the bacillary dysentery type, both small and large intestines being infected.

Other organs were normal.

Cultures from the lung nodules gave pure and vigorous growths of the bacillus.

Those from the spleen gave only a few colonies.

**Case 38.** A Burman, about 25 years of age, admitted for looseness of bowels with pain in the abdomen and back, of about four months' duration.

Temperature irregular, ranging from 99° F. to 102° F.: the patient remained in hospital for eighteen days; then died.

P.M. An emaciated Burman with a few marks of morphia injections.

Lungs. Both lungs contain numerous typical nodules of the infection.

Peritoneum, acute peritonitis present.

Large intestine covered with large gangrenous ulcers of amoebic dysentery, which have penetrated to the peritoneal coat, and caused the peritonitis. Amoebae present in the ulcers.

Spleen, normal in appearance.

Cultures from the lung nodules gave very vigorous growths of the bacilli.

From the spleen a fair number of colonies of the bacillus grew.

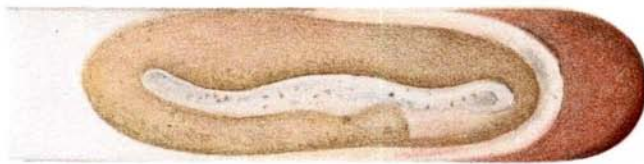
## DESCRIPTION OF PLATE I.

Fig. 1. Section of the lung of Case I, showing single and confluent areas of consolidation.

This illustration was painted by a Native artist, quite ignorant of the particular points which the specimen intended to represent; therefore, though these points may not be as plain as could be wished, yet the painting has the merit of representing the specimen as seen by an unbiassed observer.

Fig. 2. Agar culture, one month old.

Fig. 3. Agar culture, cultivated for 48 hours.



E. Wilson, Cambridge