Third interim report of the Royal Commission appointed to inquire into the relations of human and animal tuberculosis. Report and Appendix.

ROYAL COMMISSION ON TUBERCULOSIS (HUMAN AND BOVINE).

THIRD INTERIM REPORT

OF THE

ROYAL COMMISSION

APPOINTED TO INQUIRE INTO THE RELATIONS OF

HUMAN AND ANIMAL TUBERCULOSIS.

REPORT AND APPENDIX.

Presented to both Houses of Parliament by Command of His Majesty.

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By DARLING & SON, Ltd., 34-40, Bacon Street, E.

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NEW ROYAL COMMISSION ON TUBERCULOSIS.

EDWARD R.

EDWARD THE SEVENTH, by the Grace of God of the United Kingdom of Great Britain and Ireland, King, Defender of the Faith, To

Our Trusty and Well-beloved Sir MICHAEL FOSTER, Knight Commander of Our most Honourable Order of the Bath, Doctor of Medicine, Fellow of the Royal Society, Professor of Physiology in Our University of Cambridge ;

Our Trusty and Well-beloved GERMAN SIMS WOODHEAD, Esquire, Doctor of Medicine, Professor of Pathology in Our University of Cambridge ;

Our Trusty and Well-beloved SIDNEY HARRIS COX MARTIN, Esquire, Doctor of Medicine, Fellow of the Royal Society, Professor of Pathology at University College, London ;

Our Trusty and Well-beloved JOHN MCFADYEAN, Esquire, Principal and Professor of Comparative Pathology and Bacteriology at the Royal Veterinary College ; And

Our Trusty and Well-beloved RUBERT WILLIAM BOYCE, Esquire, Professor of Pathology at University College, Liverpool.

GREETING :

Whereas We have deemed it expedient that a Commission should forthwith issue to inquire and report with respect to Tuberculosis :—

1. Whether the disease in animals and man is one and the same ;

2. Whether animals and man can be reciprocally infected with it ;

3. Under what conditions, if at all, the transmission of the disease from animals to man takes place, and what are the circumstances favourable or unfavourable to such transmission.

Now know ye, that We, reposing great trust and confidence in your knowledge and ability, have authorised and appointed, and do by these Presents authorise and appoint you, the said Sir Michael Foster, German Sims Woodhead, Sidney Harris Cox Martin, John McFadyean, and Rubert William Boyce, to be Our Commissioners for the purposes of the said inquiry.

And for the better effecting the purposes of this Our Commission We do by these Presents give and grant unto you, or any three or more of you, full power to call before you such persons as you shall judge likely to afford you any information upon the subject of this Our Commission ; and also to call for, have access to, and examine all such books, documents, registers, and records as may afford you the fullest information on the subject, and to inquire of and concerning the premises by all other lawful ways and means whatsoever.

And We do by these Presents authorise and empower you, or any three or more of you, to visit and personally inspect such places as you may deem it expedient so to inspect for the more effectual carrying out of the purposes aforesaid.

And We do further by these Presents will and ordain that this Our Commission shall continue in full force and virtue, and that you, Our said Commissioners, or any three or more of you, may from time to time proceed in the execution thereof, and of every matter and thing therein contained, although the same be not continued from time to time by adjournment.

And We do further ordain that you, or any three or more of you, have liberty

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to report your proceedings under this Our Commission from time to time if you shall judge it expedient so to do.

And Our further Will and Pleasure is that you do, with as little delay a possible, report to Us under your hands and seals, or under the hands and seals of any three or more of you, your opinion upon the matters herein submitted for your consideration.

Given at Our Court at St. James's the Thirty-first day of August, 1901 ; in the first Year of Our Reign.

By His Majesty's Command.

CHARLES RITCHIE.

EDWARD R. & I.

EDWARD THE SEVENTH, by the Grace of God, of the United Kingdom of Great Britain and Ireland and of the British Dominions beyond the Seas King, Defender of the Faith, To

Our Trusty and Well-beloved WILLIAM HENRY POWER, Esquire, Companion of Our most Honourable Order of the Bath, Fellow of the Royal Society, Medical Officer of the Local Government Board,

GREETING :

Whereas by Warrant under Our Royal Sign Manual, bearing date the Thirty-first day of August, one thousand nine hundred and one, We were pleased to appoint Commissioners to inquire and report with respect to Tuberculosis, and to authorize the late Sir Michael Foster to act as Chairman of the Commission :

And whereas the Chairmanship of the Commission is at this present void.

Now know ye that We, reposing great trust and confidence in your knowledge and ability, have authorized and appointed, and by these Presents authorize and appoint you, the said William Henry Power, to be Chairman of the said Commission in the room of the said Sir Michael Foster, deceased.

Given at Our Court at Saint James's the Eighteenth day of March, 1907 ; in the seventh Year of Our Reign.

By His Majesty's Command.

H. J. GLADSTONE.

TO THE KING'S MOST EXCELLENT MAJESTY.

May it please your Majesty,

We, your Majesty's Commissioners, appointed to inquire and report with respect to Tuberculosis :—

1. Whether the disease in animals and man is one and the same ;

2. Whether animals and man can be reciprocally infected with it ;

3. Under what conditions, if at all, the transmission of the disease from animals to man takes place, and what are the circumstances favourable or unfavourable to such transmission ;

humbly submit the following Further Report containing an account of certain experiments we have carried out regarding the Infectivity of the Milk and Faeces of Naturally Infected Tuberculous Cows, that is, Cows that had contracted the disease in the ordinary way.

We wish to take this opportunity of expressing our deep sense of the great loss caused not only to ourselves but also to the whole country by the lamented death of Sir Michael Foster, the late Chairman of this Commission.

Since the date of our Second Interim Report the work of the Commission has been mainly directed to determining the special characters of the bacilli which are the cause of tuberculosis in animals other than the cow, and the relationships of the different types of tubercle bacilli which we have encountered in man and certain of the lower animals. The investigations bearing on these and other matters referred to in that Report as engaging our attention are not yet complete and the publication of the results obtained must therefore be postponed.

In the meantime we have thought it advisable to describe the results of a series of experiments which have been carried out by us with a view of obtaining information regarding the excretion or discharge of tubercle bacilli in the Milk and Faeces of tuberculous cattle.

In our Second Interim Report we expressed the opinion, as a result of our investigations, that a very considerable amount of disease and loss of life, especially among infants and children, must be attributed to the consumption of cow's milk containing tubercle baciili.

Tuberculosis involving the udder is comparatively common in cows, and in such cases their milk always contains tubercle bacilli and is therefore dangerous for human beings consuming it. It was, however, undecided what is the danger, if any, attaching to the milk of tuberculous cows in which the udder presents no evidence of disease. We therefore took the opportunity of making a number of observations and experiments bearing on this point. The experiments were made with the milk of cows which had contracted the disease in the natural way.

In natural tuberculosis in the cow, cases which show such obvious symptoms of the disease as emaciation and cough should be considered separately from the cases in which there are no such signs and in which the disease is to be recognised during life only by means of the injection of tuberculin.

None of the cows investigated showed any sign of disease of the udder during life, and in all, after slaughtering, the udder was carefully examined for tuberculous lesions and tubercle bacilli. No tuberculosis was found except in one case (Cow F) in which one quarter of the udder showed four small nodules. These could not possibly have been detected during life.

We found that the milk of the cows obviously suffering from tuberculosis (*see* Appendix ; Cows B, C, and F) contained tubercle bacilli whether the milk was obtained in the ordinary way or was withdrawn from the teat by means of a sterilised

catheter. The presence of tubercle bacilli in the milk of cows clinically recognisable as tuberculous confirms the opinion we expressed in our Second Interim Report that the milk of such cows must be considered dangerous for human beings.

The experiments which we have carried out with regard to the infectivity of the faeces of tuberculous cows were dictated by knowledge of the fact that dirt of various kinds from cows and the cow-shed is almost constantly present in milk as it reaches the consumer. Cows suffering from extensive tuberculosis of the lungs must discharge considerable numbers of bacilli from the air passages in the act of coughing, and some of the bacilli thus expelled may find their way into the milk. But our experiments indicate that the excrement of cows obviously suffering from tuberculosis of the lungs or alimentary canal must be regarded as much more dangerous than the matter discharged from the mouth or nostrils. We have found that even in the case of cows with slight tuberculous lesions tubercle bacilli in small numbers are discharged in the faeces, while as regards cows clinically tuberculous our experiments show that the faeces contain large numbers of living and virulent tubercle bacilli.

The presence of tuberculous cows such as B, C, and F in company with healthy cows in the cow-shed is therefore distinctly dangerous, as some of the tubercle bacilli which escape from their bodies in the excrement are almost certain to find their way into the milk.

The experiments are described in detail in the Appendix attached to this Report. They were carried out by Dr. F. Griffith under our supervision, and we desire to express our high appreciation of the skill and care devoted by him to the work.

(Signed) W. H. POWER, *Chairman.*

G. SIMS WOODHEAD.

SIDNEY MARTIN.

J. McFADYEAN.

RUBERT BOYCE.

EDWARD J. STEEGMANN, *Secretary.*

January, 1909.

APPENDIX

BY

DR. F. GRIFFITH.

INTRODUCTION.

This Appendix gives the results of inoculation and feeding experiments made with the faeces and milk of naturally tuberculous cattle. Observations have been made on six milch cows. Three of the animals, B, C, and F, showed clinical evidence of tuberculosis but in none during life could any tuberculous disease of the udder be detected. The object of this investigation was to ascertain if tubercle bacilli were present in the faeces and milk of these animals.

Description of Methods Used.

For the purposes of the experiments a considerable quantity of faecal matter was required, and in order to avoid risk of contamination from the genito-urinary passages the following method of collection was employed. The action of the rectum was stimulated by the injection into it of air through a sterile glass tube and the faeces were received directly into a pail which was applied to the margin of the anal orifice. These precautions were necessary as in one case, B, there was a purulent discharge from the vagina and the post-mortem examination in three cases, B, C, and F, revealed extensive tuberculous disease of the uterus. A portion of the faeces was rubbed up in a mortar with sufficient salt solution to moisten it and pressed through muslin to form an emulsion. This emulsion was used for the feeding and inoculation of guinea-pigs. The inoculation of fresh faeces into guinea-pigs frequently causes death within a few days and it was possible to estimate roughly a minimal fatal dose of the emulsion which was prepared each day in the same way. It was found that 0·5 cubic centimetre of the emulsion almost invariably caused death from acute peritonitis while after the inoculation of 0·05 cubic centimetre all the animals survived. The intraperitoneal method of inoculation was almost exclusively used.

The infectivity of the faeces was also tested by feeding guinea-pigs and swine. The swine were young animals about 11 weeks old, belonging to three litters and all obtained from the same farm. They were all tested with tuberculin before being used for experiment and gave negative results in each case. Two animals were kept as controls, one from each of two litters, and when killed were found to be free from tuberculosis. No control to the third litter was kept, but all the eight pigs belonging to it though used for experiment were quite healthy when killed.

The milk of five of the cows, B, C, D, E, and F, was tested for the presence of tubercle bacilli and strict precautions were taken to ensure absence of contamination during its collection. A metal catheter, connected by pressure tubing to a flask, was inserted into the milk sinus of the udder, a separate apparatus being used for each quarter, and the milk was withdrawn from the udder by the exhaustion of the air in the flask. Before the insertion of the catheter each teat was washed with a solution of perchloride of mercury and with methylated spirit, and the opening was inspected to ensure that no faecal matter was pushed in with the catheter.

The milk thus obtained was tested as to the presence in it of tubercle bacilli by the inoculation of guinea-pigs and occasionally of rabbits. Two guinea-pigs were inoculated intraperitoneally from each quarter and each animal received, when sufficient milk was obtained, a dose of 10·0 cc. of uncentrifuged milk plus the deposit of 20·0 cc. of centrifuged milk, or sometimes 6·0 cc. plus the deposit of 24·0 cc.

In the case of three cows young swine were fed in each instance with the milk from the different quarters mixed together.

DETAILS OF THE EXPERIMENTS.

1. Animals showing clinical signs of disease.

2. Animals in which the only evidence of disease during life was a positive reaction to tuberculin.

1.

COW B.

This cow was a shorthorn and had calved four weeks previously. It was in poor condition and had a short infrequent cough; it reacted positively to the tuberculin test.

When killed it was found to have severe general tuberculosis. The lungs contained caseous masses which had broken down and had become partly emptied with the formation of cavities. There were numerous tubercles along the whole length of the trachea and the tonsils were infiltrated with breaking down caseous tissue. In the small intestine there were about 60 ulcers varying up to 1·5 cubic centimetre in diameter and scattered caseous nodules not yet ulcerated. The bronchial, mediastinal, mesenteric and portal glands were greatly enlarged and replaced by firm caseo-necrotic tissue. The posterior pharyngeal, and the cervical glands were large and extensively caseated. The walls of the uterus were thick, firm, and infiltrated with tuberculous tissue, while the cavities were filled with muco-purulent discharge such as issued from the vagina during life. The udder was free from tuberculous lesions.

The calf from this animal was in good condition and apparently healthy, but the post-mortem examination revealed disseminated tuberculosis. It was evident from the distribution of the disease (see post-mortem), and its extent in relation to the age of the calf, that the tuberculosis had been acquired in utero. That the cow had been able to bear a calf is remarkable considering the advanced tuberculous disease of the uterus, though probably the pregnancy itself had hastened the progress of the disease.

Inoculation and Feeding Experiments with Faeces.

The faeces of Cow B passed on the 1st, 3rd, 4th, 5th, 8th, and 9th of October, 1907, were tested for the presence of tubercle bacilli by the inoculation of guinea-pigs.

In all 25 guinea-pigs were inoculated intraperitoneally, of which 8 succumbed to acute infection in from one to two days. One, killed after 27 days, was free from tuberculosis. The remaining 16 were killed after about four weeks and were found to be tuberculous — that is, all the guinea-pigs with one exception inoculated with faeces which lived for a sufficient period for tuberculosis to develop became tuberculous. The doses in relation to the amount of faeces passed were exceedingly small, consisting in the majority of cases of ·05 cc. of a thick filtered emulsion.

Guinea-pigs were also fed with the faeces. Six were fed from October 1st to October 9th inclusive with faeces mixed with sterilized milk, receiving no other food, and when killed were healthy.

Two guinea-pigs were fed each day from October 1st to October 9th, sixteen in all, with a single dose of faeces administered by means of a pipette, each receiving 1·0 cc. of the emulsion used for the intraperitoneal inoculations. They were killed after 14 weeks and were free from tuberculosis in spite of the fact that they received 50 times the amount of faecal emulsion which invariably caused tuberculosis when inoculated intraperitoneally.

Four young swine were fed with faeces mixed with sterilized milk from October 1st to October 9th, 1907, the total amount shared between the four from the same trough being 19·1 kilogrammes. They were tested with tuberculin 58 days after the experiment began and all gave positive reactions, the rise of temperature varying in the individual cases from 1·3° C. to 3·0° C. They were killed after periods varying from 63 to 100 days since the first feeding, and all showed generalized tuberculosis (see post-mortem records).

Inoculation and Feeding Experiments with Milk.

The milk of Cow B, collected in the manner previously described, was inoculated into guinea-pigs on the 11th, 14th, 15th, 16th, 17th, 18th, and 19th of October, 1907. The inoculations were all made intraperitoneally, and two guinea-pigs were used for the milk of each quarter, each animal receiving a dose consisting of the deposit of 20·0 cubic centimetres of centrifuged milk plus 10·0 cubic centimetres of uncentrifuged milk (except on the first day when each received the deposit of 15·0 cubic centimetres).

In all 56 guinea-pigs were inoculated. One was killed in 79 days and had general tuberculosis without disease of the omentum. In these experiments I have not accepted tuberculosis in a guinea-pig as giving positive evidence of the presence of tubercle bacilli in the material inoculated unless there were lesions in the omentum, muscle, or skin at the seat of inoculation containing tubercle bacilli, and therefore this guinea-pig was rejected. The remaining 55 guinea-pigs were killed, the majority after 11 weeks, and all were healthy with the exception of one which had tuberculosis obviously due to the inoculation.

On November 5th, 1907, the cow was inoculated with 20·0 cubic centimetres of tuberculin under the skin of the neck after which she became ill, with laboured breathing. The next day, 19 hours later, the milk was inoculated as before into eight guinea-pigs of which four subsequently became tuberculous. The milk collected on November 7th, 43 hours after the inoculation of tuberculin, caused tuberculosis in seven out of the eight guinea-pigs inoculated.

Two young pigs were fed from October 14th to October 20th inclusive, receiving between them 18·4 litres of milk. They were killed 86 days after the first feeding and showed no tuberculosis. A third pig, which received on November 1st a single feed of 2·8 litres of milk, when killed 69 days later was healthy.

The following experiments were performed in order to gain information as to the likelihood of the milk becoming infected during the ordinary process of milking.

On November 4th, the cow was milked in the ordinary way, though with special precautions as to cleanliness, into an open pail; two out of four guinea-pigs inoculated with the mixed milk became tuberculous.

On November 5th, before the tuberculin inoculation, the cow was milked without being cleansed in any way: two out of four guinea-pigs inoculated with the mixed milk became tuberculous.

The experiments are not conclusive since it is possible that the tubercle bacilli were excreted in the milk, although use of it on seven separate occasions two or three weeks previously had caused tuberculosis in one guinea-pig only. In an animal so severely infected as this cow an invasion of the blood stream by tubercle bacilli is always liable to occur and these may be eliminated in the milk.

This natural distribution of tubercle bacilli in the course of the disease may account for the presence of tubercle bacilli in the milk after the inoculation of tuberculin, this inoculation being coincident with and not the cause of the dissemination.

COW C.

This cow was a Jersey with obvious clinical signs of tuberculosis. She was emaciated and feeble, breathed hard, and had a frequent cough. Her temperature was febrile and there was no rise sufficient to constitute a positive reaction after the inoculation of tuberculin. After death she was found to have severe thoracic tuberculosis: the lungs were closely beset with caseous nodules and large bright yellow caseo-necrotic masses, many of which were softening and breaking down. In several cases caseo-purulent substance was seen protruding from a necrotic mass into a bronchus and the trachea was filled with a cast of inspissated muco-pus. The bronchial and mediastinal glands were greatly enlarged and caseo-necrotic throughout. The Peyer's patches of the small intestine all contained a few caseous nodules up to a hemp-seed in size, and there were several small ulcers up to 5·0 millimetres in diameter. One mesenteric gland was greatly enlarged and caseous. The uterus was extensively tuberculous and the cavities were filled with purulent fluid and caseous flocculi. The udder was normal.

Inoculation and Feeding Experiments with Faeces.

The faeces of Cow C were tested for the presence of tubercle bacilli on the 24th, 25th, 28th, 29th, and 30th of October, 1907, by the inoculation of 30 guinea-pigs. Of these 17 became tuberculous: the rest died too soon for tuberculosis to develop.

Four guinea-pigs were fed continuously for six days with faeces mixed with sterilized milk: one became tuberculous, the rest remained healthy.

Each of ten guinea-pigs received by the mouth from a pipette 1·0 cubic centimetre of the faecal emulsion used for the inoculation experiments, and when killed after about 90 days all were found to be free from tuberculosis.

The following experiment gives some idea of the large numbers of tubercle bacilli in the faeces of this cow. One gramme of faeces was added to two litres of sterilized water, and two guinea-pigs were inoculated intraperitoneally, one with one cubic centimetre, the other with two cubic centimetres of the mixture. Both developed severe general tuberculosis, the former dying in 63 days.

A young pig was fed with the faeces from October 23rd to October 30th inclusive, receiving 5·56 kilogrammes mixed with sterilized milk. It was killed 48 days after the first feeding and showed enlargement and caseation of the submaxillary and mesenteric glands and disseminated tuberculosis.

Inoculation Experiments with Milk.

The milk was collected by catheter on each of three days and was inoculated intraperitoneally into guinea-pigs and rabbits. Each guinea-pig received 10·0 cubic centimetres of uncentrifuged milk added to the deposit of 40·0 cubic centimetres of centrifuged milk.

None of the animals inoculated on October 25th became tuberculous. The milk of October 29th caused tuberculosis in two guinea-pigs and that of October 30th caused tuberculosis in three rabbits and four guinea-pigs. The infectivity of the milk with reference to the individual quarters was irregular, but each quarter at some time gave tuberculous milk.

The explanation of this fact may be that the quantity of milk inoculated was not sufficient to be representative rather than that the elimination of tubercle bacilli was irregular, since in several of the animals the slight amount of disease produced showed that only a few bacilli had been inoculated.

COW F.

This animal was very ill: she was emaciated and feeble, and was kept under observation only for a few days, after which she was killed.

The post-mortem examination revealed severe general tuberculosis apparently originating in the alimentary tract. In the left hind quarter of the udder, in the tissue forming the wall of the main sinus near the teat, there were four reddish grey caseating nodules up to a pea in size. The rest of this quarter and the other three quarters were normal in appearance.

Inoculation Experiments with Faeces and Milk.

From the faeces of Cow F, excreted January 29th, 1908, seven guinea-pigs were inoculated intraperitoneally: of these four died too early for tuberculosis to have developed, and the remaining three, when killed after 33 days, had general tuberculosis.

The milk was collected on each of four days and inoculated into 32 guinea-pigs of which 11 died prematurely. The remaining 21 developed general tuberculosis. Many of the guinea-pigs died in from 18 to 24 days with tuberculosis resembling that following the intraperitoneal inoculation of 0·1 mg. of culture.

2.

COW A.

This animal was a shorthorn heifer in good condition and the diagnosis of tuberculosis depended entirely on the positive result of the tuberculin test.

When killed it was found to have on the right side an enlarged retro-pharyngeal gland which was cystic, with thick fibrous walls and filled with breaking down caseo-necrotic substance. In the Peyer's patches of the small intestine there were three grey nodules containing caseous foci, two soft caseous nodules and a small ulcer in which no tubercle bacilli could be demonstrated. There was also a caseous nodule in a mesenteric gland, caseation of a gluteal gland, and four tubercles in the lungs. All other organs and glands were healthy.

The faeces were collected for 9 days from September 30th, 1907, to October 9th, 1907, and were used to inoculate and feed 41 guinea-pigs of which only one died prematurely.

None of the guinea-pigs developed tuberculosis.

Four young swine were fed for the same length of time with the faecal matter mixed with sterilized milk, the total amount shared between the four from the same trough being 25·6 kilogrammes of faeces. They were tested with tuberculin 59 days after the experiment began and one alone reacted, giving a rise of temperature of 2·6° C. This animal was killed a week later and the post-mortem examination showed tuberculosis of the submaxillary glands on the left side, a caseous focus in one mesenteric gland, four caseating tubercles in the liver and about thirty on the surface beneath the pleura of each lung. The remaining three swine were killed after 90 days and were found to be free from tuberculosis.

COW D.

This animal was fat and in good condition, and the diagnosis of tuberculosis rested entirely upon the positive result of the tuberculin test. At the post-mortem examination the lungs were found to contain discrete tuberculous nodules several of which measured about 10·0 by 6·0 by 5·0 cm. On section, these were composed of softening yellow caseo-necrotic substance surrounded by fibrous walls. A few of the nodules had ulcerated into the bronchi in which soft caseous substance was seen, and muco-pus could be squeezed out of many of the bronchioles. The bronchial and mediastinal glands were enlarged and were to a large extent replaced by bright yellow caseo-necrotic gritty masses.

There was no tuberculosis of any other organ or gland in the body.

Inoculation and Feeding Experiments with Faeces.

The faeces of Cow D were tested on February 20th and 21st and March 24th, 1908, by the inoculation of guinea-pigs and rabbits. Eleven guinea-pigs were inoculated intraperitoneally, of which two became tuberculous; two showed a few tubercles in the omentum containing moderately numerous acid fast bacilli and the remaining seven were free from tuberculosis. Two out of three rabbits inoculated developed tuberculosis. Two swine were fed for 14 days with the faeces and when killed after 79 and 99 days were found to be healthy.

Inoculation and Feeding Experiments with Milk.

The milk was collected by catheter on each of 8 days and was inoculated intraperitoneally into guinea-pigs; in all 60 guinea-pigs were used. None developed tuberculosis.

In several guinea-pigs the omentum contained a few translucent, sometimes whitish, foci, in which a few acid fast bacilli were demonstrated in smear preparations. These bacilli were evidently dead, since guinea-pigs inoculated with the omentums did not develop tuberculosis, and only streptococci were isolated in cultures made from the foci.

COW E.

The condition of this cow was very good: she gave a positive reaction to the tuberculin test. After death there were found in the lungs three small tuberculous nodules and in the caudal mediastinal gland 30 to 40 caseo-calcareous nodules up to

a pea in size. In a suprarenal body there was a tubercle the size of a rape-seed in which tubercle bacilli were demonstrated. There was no tuberculosis elsewhere.

Inoculation and Feeding Experiments with Faeces.

From the faeces passed on four days 18 guinea-pigs were inoculated intraperitoneally. Of these five died (three prematurely) and the rest were killed after 50 days. All were free from tuberculosis.

Two swine fed for 14 days with the faeces remained healthy.

Inoculation and Feeding Experiments with Milk.

The milk was collected by catheter on each of six days and 36 guinea-pigs and four rabbits were inoculated intraperitoneally. None developed tuberculosis.

Two swine were fed, each with 650·0 cc., and both remained healthy.

SUMMARY OF RESULTS.

The faeces of five naturally tuberculous cows, out of the total number of six so far investigated, have been found to contain living and virulent tubercle bacilli.

Three of these animals, Cows B, C, and F, were severely diseased and were eliminating large numbers of tubercle bacilli: this is shown by the occurrence of tuberculosis after the inoculation of very small doses of faecal matter in all but one of the guinea-pigs which survived a sufficient length of time, and by the fact that all the swine fed became tuberculous.

Two of the cows, A and D, were in apparently excellent condition of health. One, Cow A, showed after death a caseous and cystic posterior pharyngeal gland, a few small nodules in the intestine, and slight disseminated tuberculosis. The faeces of this animal caused tuberculosis in one out of four swine fed: the other three swine and all the guinea-pigs inoculated remained healthy. The other cow, D, had tuberculosis of the lungs, bronchial and mediastinal glands, without any disease elsewhere. The faeces of this animal caused tuberculosis in three guinea-pigs and two rabbits; two swine fed remained healthy.

The faeces of the sixth cow, E, which had slight tuberculosis of the lungs and a mediastinal gland, did not give rise to tuberculosis in any of the animals inoculated. Four, Cows A, B, C, and F, out of the five cows which gave positive results showed some tuberculosis of the alimentary tract, but in at least one case, Cow C, it was not sufficient to account for the large numbers of tubercle bacilli in the faeces. These bacilli must have been coughed up from the lungs and swallowed.

Tuberculosis was present in the uterus of each of the severely infected cows and the uterine discharge contained numerous tubercle bacilli. Such a condition constitutes another source of infection.

The milk of two of the cows, B and C, caused, though not invariably, tuberculosis in guinea-pigs inoculated with relatively small doses. The milk was withdrawn from the udder by catheterization, and post-mortem examination of the udders revealed no macroscopic evidence of tuberculosis. Small pieces were examined histologically by Dr. Eastwood and were found to be normal, but it is of course impossible positively to exclude microscopical lesions. The milk of a third cow, F, caused severe tuberculosis in every guinea-pig which lived a sufficient period of time after inoculation. The udder, except for four small nodules in the left hind quarter, was normal to the naked eye: the animal was very ill at the time the milk was collected.

The milk of the remaining two cows, D and E, tested did not give rise to tuberculosis in any of the animals inoculated.

The results of the post-mortem examinations of the naturally infected cows and the details of the inoculation and feeding experiments with guinea-pigs and swine are included in the following pages.

COW B.

COW C.

COW F.

COW A.

COW D.

COW E.

SHORTHORN COW B.

POST-MORTEM EXAMINATION.

General Condition.—Poor.

Tongue.—Normal.

Tonsils.—The tonsils on both sides were enlarged and firm and were infiltrated with tuberculous tissue, in parts breaking down forming ragged walled cavities.

Pharynx.—Normal.

The Right Submaxillary and Right Superior Cervical Glands.—Each showed an early caseous nodule.

The Left Submaxillary Gland was normal.

The Left Retro-pharyngeal Gland was more than half caseous. The right retro-pharyngeal gland was twice the size of the left and almost caseous throughout.

Cervical Glands.—The left superior cervical, and the middle and lower cervical glands on both sides contained firm caseous nodules, replacing the greater part of the gland substance.

Abdomen.

In the Omentum.—There were a few scattered grey nodules.

On the Peritoneal Surface of the Diaphragm there were loosely attached fibro-caseous nodules occurring singly and in clusters.

Intestines.—In each of the Peyer's patches of the first two-thirds of the small intestine there were from one to eight ulcers varying up to 1·5 cm., they were circular and had slightly raised undermined edges with injected vessels around. In some the floors were clean, in others covered with a little caseous substance; the bases and sides were infiltrated with caseous tubercles. In several places the ulcers coalesced becoming serpiginous. The Peyer's patches in the last third of the small intestine were not affected. Altogether about sixty ulcers were counted and there were also scattered small caseous nodules not yet ulcerated.

Large Intestine.—Normal.

Two Gastric Glands were partly caseous.

Mesenteric Glands.—The mesenteric glands were greatly enlarged and all were replaced by caseo-necrotic tissue which was pinkish in parts and bright yellow in others.

Colic Glands.—Similarly affected.

Spleen.—In the centre of the spleen there was a bright yellow softening caseous gritty nodule 5 mm. in diameter.

Liver.—The surface of the liver showed numerous depressions varying up to 1·0 and 1·5 cm., they were dark red in colour and on section were composed of soft tissue, from which blood welled readily; when all the blood was squeezed out a spongy tissue was left, quite different from the parenchyma. These areas were scattered thoughout the liver substance. No tubercles could be seen on the surface and on section through the substance, one miliary nodule was found.

Portal Glands.—In the portal glands there was an occasional caseous gritty nodule up to a hemp seed in size.

Kidneys.—The cortices of the kidneys were speckled with grey nodules varying up to a millet seed in size. On section they were irregular, many elongated, and the majority showed minute white centres.

Suprarenal Bodies.—In the right suprarenal there was a nodule nearly 1·0 cm. in diameter waxy and caseous with a more opaque yellowish centre.

Left Suprarenal Body.—Normal.

Iliac Glands.—Five iliac glands were greatly enlarged and practically replaced by waxy caseated tissue.

Lumbar Glands.—One lumbar gland contained a caseating nodule; the other glands appeared normal.

Coeliac Glands.—Enlarged and caseous throughout.

Uterus.—The cotyledons of the uterus were large and firm and on section the walls were found to be composed throughout of tuberculous tissue. The internal surfaces were roughened and covered with yellow muco-purulent discharge, such as constantly issued during life from the vagina.

Thorax.

Pleura.—Along the ribs on the parietal pleura there were numerous flattened tuberculous nodules, in places forming thickened areas and in others clusters.

Lungs.—The right anterior lobe was adherent to the pericardium and to the pleura by means of thickened caseous growths. On the surfaces of the lungs there were scattered fibro-caseous nodules and fairly numerous fibrous nodules in the fringes along the margins. About one third of the left caudal lobe and half of the right, at their posterior extremities, were in a condition of caseous pneumonia. On section the masses were soft and caseo-purulent and many had become partly emptied leaving cavities. The rest of the lung tissue was crepitant containing a few pneumonic lobules and was beset with numerous caseating miliary tubercles.

Caudal Mediastinal Gland.—Measured 27·0 by 12·0 cm. and weighed 2lbs. 4ozs. On section it consisted entirely of waxy caseating tissue in which were embedded bright yellow necrotic nodules. The other mediastinal and bronchial glands were enlarged and resembled the caudal mediastinal gland.

Trachea.—Along the whole length of the trachea were numerous small flattened congested tubercles and there was a caseous nodule on the larynx.

Heart.—Normal.

The Right Axillary and Right Gluteal Glands.—Each showed a small caseous nodule.

Parotid, Prescapular, Prepectoral, Left Axilliary, Left Gluteal, Precrural, Popliteal, and Ischiatic Glands.—Normal.

Microscopical Examination.

(Smear preparations.)

Liver (hæmorrhagic area).—No tubercle bacilli.

Kidney (nodule).—No tubercle bacilli.

CALF OF COW B.

POST-MORTEM EXAMINATION.

Condition.—Good.

Abdomen.

Liver.—In the liver just beneath the capsule there were thirteen grey tubercles with minute opaque centres about the size of rape seed. Similar tubercles were seen scattered throughout the substance, one attaining the size of a millet seed; they were grey with yellowish slightly gritty centres.

Portal Glands.—The portal glands were enlarged and on section they showed their cortices fairly closely filled with yellow gritty caseous nodules up to 3 mm. in diameter; in places becoming confluent they formed caseous patches.

Spleen.—In the spleen there were five grey nodules,

with a fine yellowish caseous gritty central network, varying up to a wheat grain in size.

Peritoneum and Omentum.—Normal.

Intestines.—Normal.

Mesenteric Glands.—In one mesenteric gland there was a single caseous tubercle.

Kidneys.—Normal.

Suprarenal Bodies.—Normal.

Renal, Coeliac, Lumbar, and Iliac Glands.—Normal.

Thorax.

Pleura.—Normal.

Lungs.—The lungs were crepitant and pink except for some congestion of the dorsal surfaces of the caudal lobes; they showed on the surface a few scattered reddish nodules, some with definite caseous foci.

Mediastinal and Bronchial Glands.—The caudal mediastinal gland showed part of its cortex filled with a coarse yellowish caseous network gritty from calcification, the rest of the gland containing discrete nodules. The other mediastinal and bronchial glands showed discrete yellowish caseous gritty nodules up to 5·0 mm. in diameter.

Heart.—Normal.

Tongue, Larynx, Pharynx, and Tonsils.—Normal.

The Right Precrural Gland showed one yellowish caseous nodule about 2 mm. in diameter

Various Lymphatic Glands.

Parotid, Submaxillary, Cervical, Pharyngeal, Prescapular, Axillary, Left Precrural, Pedic, Popliteal, Gluteal, and Ischiatic Glands.—Normal.

Testes.—Normal.

Microscopical Examinations.

(Smear preparations.)

Liver (nodule).—Three tubercle bacilli seen.

Portal Gland.—Showed a few tubercle bacilli.

Lung (nodule).—One tubercle bacillus seen.

Mesenteric Gland.—Showed a few tubercle bacilli.

GUINEA-PIGS INOCULATED INTRAPERITONEALLY WITH FAECES OF COW B.

Number.	Date of Inoculation.	Dose.	Duration of Life.	Result.
2648	October 1, 1907	2·0 cc.	Died 1 day	Acute infection. No T.
2649		1·5 cc.	Died 1 day	Acute infection. No T.
2650		·5 cc.	Killed 31 days	Early G.T.
2651		1·0 cc.	Died 1 day	Acute infection. No T.
2652		1·0 cc.	Died 2 days	Acute infection. No T.
2669	October 3, 1907	·5 cc.	Died 1 day	Acute infection. No T.
2670		·5 cc.	Died 1 day	Acute infection. No T.
2671		·5 cc.	Killed 28 days	G.T.
2672		·05 cc.	Killed 29 days	Early G.T.
2685	October 4, 1907	·05 cc.	Killed 28 days	Omentum contained 8 nodules and spleen 5. Caseation of portal gland.
2686		·05 cc.	Killed 28 days	A few tubercles in omentum and on peritoneum: opaque foci in spleen and pyloric gland.
2687		·05 cc.	Killed 28 days	Several tubercles in omentum, and caseation of pyloric, portal, and lumbar glands.
2692	October 5, 1907	·05 cc.	Killed 30 days	Early G.T.
2693		·05 cc.	Killed 30 days	Early G.T.
2694		·05 cc.	Died 1 day	Acute infection. No T.
2695		·05 cc.	Killed 30 days	Early G.T.
2710	October 8, 1907	·05 cc.	Killed 27 days	No tuberculosis. ? inoculation intra-cæcal.
2711		·05 cc.	Killed 27 days	G.T.
2712		·05 cc.	Killed 27 days	G.T.
2713		·05 cc.	Killed 27 days	G.T.
2720	October 9, 1907	·1 cc.	Died 2 days	Acute infection. No T.
2721		·05 cc.	Killed 27 days	Omentum thickened; pyloric gland caseous.
2722		·05 cc.	Killed 27 days	Similar to above.
2723		·05 cc.	Killed 27 days	Similar plus caseation of lumbar and portal glands.
2724		·05 cc.	Killed 27 days	Early G.T.

GUINEA-PIGS FED WITH FAECES OF COW B.

DOSE IN EACH CASE 1·0 CC. OF FAECAL EMULSION.

Number	Date of Feeding.	Duration of Life.	Result.
2653	October 1, 1907	Killed 98 days	No tuberculosis.
2654		Killed 98 days	No tuberculosis.
2665	October 2, 1907	Killed 98 days	No tuberculosis
2666		Killed 98 days	No tuberculosis.
2673	October 3, 1907	Killed 26 days	No tuberculosis.
2674		Killed 98 days	No tuberculosis.
2688	October 4, 1907	Killed 98 days	No tuberculosis.
2689		Died 81 days	No tuberculosis.
2696	October 5, 1907	Killed 98 days	No tuberculosis.
2697		Killed 98 days	No tuberculosis.
2704	October 7, 1907	Killed 98 days	No tuberculosis.
2705		Killed 98 days	No tuberculosis
2708	October 8, 1907	Killed 98 days	No tuberculosis.
2709		Killed 98 days	No tuberculosis.
2718	October 9, 1907	Killed 98 days	No tuberculosis.
2719		Killed 98 days	No tuberculosis.

GUINEA-PIGS FED CONTINUOUSLY WITH FAECES OF COW B MIXED WITH STERILIZED MILK.

Number.	Date of Feeding.	Duration of Life.	Result.
2642	From October 1, 1907, to October 9, 1907.	Killed 56 days	No tuberculosis.
2643		Killed 97 days	No tuberculosis.
2644		Killed 97 days	No tuberculosis.
2645		Killed 105 days	No tuberculosis.
2646		Killed 105 days	No tuberculosis.
2647		Died 7 days	No tuberculosis.

GUINEA-PIGS INOCULATED INTRAPERITONEALLY WITH THE MILK OF COW B.

Number.	Date of Inoculation.	Dose.	Quarter of Udder.	Duration of Life.	Result.
2734	October 11, 1907	5·0 cc. of milk plus deposit of 20·0 cc. obtained by the centrifuge.	R.F.	Killed 83 days	No tuberculosis.
2735			R.F.	Killed 83 days	No tuberculosis.
2736			R.H.	Killed 83 days	No tuberculosis.
2737			R.H.	Killed 83 days	No tuberculosis.
2738			L.F.	Killed 83 days	No tuberculosis.
2739			L.F.	Killed 83 days	No tuberculosis.
2740			L.H.	Killed 83 days	No tuberculosis.
2741			L.H.	Killed 83 days	No tuberculosis.

GUINEA-PIGS INOCULATED INTRAPERITONEALLY WITH THE MILK OF COW B—*continued.*

Number.	Date of Inoculation.	Dose.	Quarter of Udder.	Duration of Life.	Result.
2742	October 14, 1907	100 cc. of milk plus the deposit of 200 cc. obtained by the centrifuge.	R.F.	Killed 80 days	No tuberculosis.
2743			R.F.	Killed 80 days	No tuberculosis.
2744			R.H.	Killed 80 days	No tuberculosis.
2745			R.H.	Killed 80 days	No tuberculosis.
2746			L.F.	Killed 80 days	No tuberculosis.
2747			L.F.	Died 74 days	No tuberculosis.
2748			L.H.	Killed 80 days	No tuberculosis.
2749			L.H.	Killed 80 days	No tuberculosis.
2752	October 15, 1907	do.	R.F.	Killed 79 days	No tuberculosis.
2753			R.F.	Killed 79 days	No tuberculosis.
2754			R.H.	Killed 79 days	No tuberculosis.
2755			R.H.	Killed 79 days	No tuberculosis.
2756			L.F.	Killed 79 days	No tuberculosis.
2757			L.F.	Killed 79 days	No tuberculosis.
2758			L.H.	Killed 79 days	No tuberculosis.
2759			L.H.	Killed 79 days	No tuberculosis.
2760	October 16, 1907	do.	R.F.	Killed 79 days	No tuberculosis.
2761			R.F.	Killed 79 days	No tuberculosis.
2762			R.H.	Killed 79 days	No tuberculosis.
2763			R.H.	Killed 79 days	No tuberculosis.
2764			L.F.	Killed 79 days	No tuberculosis.
2765			L.F.	Killed 79 days	G.T. No disease of omentum. ? spontaneous tuberculosis.
2766			L.H.	Killed 79 days	No tuberculosis.
2767			L.H.	Killed 79 days	No tuberculosis.
2768	October 17, 1907	do.	R.F.	Killed 79 days	No tuberculosis.
2769			R.F.	Died 77 days	No tuberculosis.
2770			R.H.	Killed 79 days	No tuberculosis.
2771			R.H.	Killed 79 days	No tuberculosis.
2772			L.F.	Killed 79 days	No tuberculosis.
2773			L.F.	Killed 79 days	No tuberculosis.
2774			L.H.	Killed 79 days	No tuberculosis.
2775			L.H.	Killed 79 days	No tuberculosis.
2776	October 18, 1907	do.	R.F.	Killed 78 days	No tuberculosis.
2777			R.F.	Killed 78 days	No tuberculosis.
2778			R.H.	Killed 78 days	No tuberculosis.
2779			R.H.	Killed 78 days	No tuberculosis.
2780			L.F.	Killed 78 days	No tuberculosis.
2781			L.F.	Killed 78 days	No tuberculosis.
2782			L.H.	Killed 78 days	No tuberculosis.
2783			L.H.	Killed 78 days	No tuberculosis.
2787	October 19, 1907	do.	R.F.	Killed 47 days	No tuberculosis.
2788			R.F.	Died 46 days	G.T. Omentum thickened.
2789			R.H.	Killed 79 days	No tuberculosis.
2790			R.H.	Killed 47 days	No tuberculosis.

GUINEA-PIGS INOCULATED INTRAPERITONEALLY WITH THE MILK OF COW B—*continued.*

Number.	Date of Inoculation.	Dose.	Quarter of Udder.	Duration of Life.	Result.
2791	October 19, 1907	10·0 cc. of milk plus the deposit of 20·0 cc. obtained by the centrifuge.	L.F.	Killed 79 days	No tuberculosis.
2792			L.F.	Killed 47 days	No tuberculosis.
2793			L.H.	Killed 79 days	No tuberculosis.
2794			L.H.	Killed 47 days	No tuberculosis.
	MILK WITHDRAWN AFTER THE INOCULATION OF COW WITH TUBERCULIN.				
2882	November 6, 1907	do.	R.F.	Killed 63 days	No tuberculosis.
2883			R.F.	Killed 63 days	No tuberculosis.
2884			R.H.	Died 39 days	G.T. Omentum thickened by fibro-caseous nodules.
2885			R.H.	Killed 63 days	No tuberculosis.
2886			L.F.	Killed 63 days	No tuberculosis.
2887			L.F.	Killed 63 days	G.T.
2888			L.H.	Killed 63 days	G.T.
2889			L.H.	Killed 63 days	G.T.
2890	November 7, 1907	do.	R.F.	Killed 62 days	Early G.T.
2891			R.F.	Killed 62 days	Early G.T.
2892			R.H.	Killed 62 days	No tuberculosis.
2893			R.H.	Died 19 days	A few tubercles in omentum containing tubercle bacilli.
2894			L.F.	Killed 62 days	G.T.
2895			L.F.	Killed 62 days	G.T.
2896			L.H.	Killed 62 days	Caseation of inguinal gland with T.B. No local lesion seen.
2897			L.H.	Killed 62 days	Early G.T.

MILK OF COW B WITHDRAWN IN THE ORDINARY WAY: UDDER CLEANSED.

Number.	Date of Inoculation.	Dose in each case.	—	Duration of Life.	Result.
2874	November 4, 1907	10·0 cc. of milk plus the deposit of 48·0 cc. obtained by the centrifuge.	Mixed milk	Killed 65 days	G.T. severe.
2875				Killed 65 days	G.T. severe.
2876				Killed 65 days	No tuberculosis.
2877				Died 10 days	No tuberculosis.

MILK OF COW B WITHDRAWN IN THE ORDINARY WAY: UDDER UNCLEANSED.

Number.	Date of Inoculation.	Dose in each case.	—	Duration of Life.	Result.
2878	November 5, 1907	10·0 cc. of milk plus the deposit of 48·0 cc. obtained by the centrifuge.	Mixed milk	Killed 64 days	Early G.T.
2879				Killed 64 days	Early G.T.
2880				Killed 64 days	No tuberculosis.
2881				Killed 64 days	No tuberculosis.

PIG 212.

Fed with the faeces of Cow B from October 1, 1907, to October 9, 1907.

Dose—One-fourth part of 19·11 kilogrammes of faeces.

Age—11 weeks.

Killed in good health—January 3, 1908. [94 days after feeding began.]

Weights.

	qrs.	lbs.
October 1, 1907	1	4
January 3, 1908	2	23

Gain in weight.—1 qr. 19 lbs.

Tuberculin Tests.—September 16, 1907. [15 days before the experiment began.] Reaction: Negative.
November 28, 1907. [58 days after the experiment began.] Reaction: Positive. Rise of temperature 2·6° Centigrade.

POST-MORTEM EXAMINATION.

General Condition.—Good.

Tongue, Pharynx, and Larynx.—Normal.

Tonsils.—Each tonsil contained two or three firm congested patches up to 1 cm. in area beset with caseous foci.

On the Left Side of the Neck extending from the angle of the jaw to the root of the ear there was a chain of glands, the most anterior of which was the largest and measured 5·0 by 4·0 by 2·5 cm. On section it consisted of firm grey tissue with a close network of yellowish caseated tissue. At one extremity there was a caseous gritty nodule which easily shelled out. The next gland measuring 4·0 by 2·0 cm. was firm and grey with an early caseous network. Of the rest of the glands, one was filled with a caseous network, another contained caseous foci and several small glands were normal. On the right side of the neck the most anterior gland measured 6·0 by 4·0 by 2·5 cm.; on section it consisted of firm grey tissue extensively replaced by a caseous gritty network. Of the other lymphatic glands two were moderately enlarged and closely beset with small caseous patches.

The Left Prescapular Gland showed a minute opaque focus.

The Right Prescapular Gland and Cervical Glands were normal.

Abdomen.

Omentum.—Normal.

Peritoneum.—On the peritoneal surface of the diaphragm on the right side there were some flattened grey nodules where the liver had been in contact with it.

Stomach and Intestines.—Normal.

Mesenteric Glands.—Several of the mesenteric glands were a little enlarged and contained softening caseous nodules which easily shelled out; in the rest of the mesenteric glands there were occasionally found small collections of caseous tubercles.

Spleen.—The spleen contained about a dozen grey nodules, caseous in the centre, varying from a millet seed up to a large pea in size.

Liver.—On the surface of the liver beneath the capsule there were moderately numerous irregular grey nodules, with opaque caseous centres, varying from about 0·5 mm. to 2·0 mm. in diameter, those nearest to the surface had attached to them fibrinous fringes. On section similar nodules were evenly distributed throughout the substance.

Portal Glands.—The portal glands were enlarged and consisted of firm grey tissue beset with caseating streaks and foci.

Kidneys.—Normal.

Suprarenal Bodies.—Normal.

Coeliac Glands.—The coeliac glands were firm and beset with irregular caseous patches and foci.

Lumbar and Iliac Glands.—Normal.

Thorax.

Pleura.—On the pleural surface of the diaphragm there were two loosely attached fibrous growths.

Lungs.—In the lungs were scattered grey translucent nodules, with opaque caseous centres, the majority varying between a rape seed and a hemp seed in size; in the anterior lobes of each lung, however, there were several congested nodules beset with caseous foci up to 6·0 mm. in diameter: the nodules were situated mainly just beneath the pleura.

Dorsal Mediastinal Glands.—Normal.

The Bronchial Glands on each side although very little enlarged were beset with caseous foci.

Inguinal and Precrural Glands normal.

PIG 214.

Fed with the faeces of Cow B from October 1, 1907, to October 9, 1907.

Dose—One-fourth part of 19·11 kilogrammes of faeces.

Age—11 weeks.

Killed in good health—December 3, 1907. [63 days after the experiment began.]

Weights.

	qrs.	lbs.
October 1, 1907	1	8
December 3, 1907	2	0

Gain in weight.—20 lbs.

Tuberculin Tests.—September 16, 1907. [15 days before the experiment began.] No reaction.
November 28, 1907. [58 days after the experiment began.] Positive reaction. Rise of temperature 3·0° Centigrade.

POST-MORTEM EXAMINATION.

Carcass in good condition.

Tongue, Larynx, and Pharynx.—Normal.

Right Tonsil.—Normal.

In the Left Tonsil there was an ulcer 5·0 mm. in diameter with thin irregular undermined edges and base covered with a little whitish substance.

On the Left Side of the Neck, four of the glands below and posterior to the angle of the jaw, were

enlarged varying in size from a sparrow's egg up to a pheasant's egg. On section they were composed throughout of firm pinkish caseo-necrotic tissue with fine yellowish gritty streaks. Three small glands were not affected.

Cervical Glands.—The left cervical glands were slightly enlarged and showed discrete irregular caseous tubercles.

The right cervical glands were normal.

Prescapular Glands.—The left prescapular gland was about twice the normal and was firm, grey and beset with irregular caseous tubercles.

The right prescapular gland was normal.

Abdomen.

Peritoneum and Omentum.—Normal.

Intestines.—Normal.

Mesenteric Glands.—The mesenteric glands were not obviously enlarged. One gland in the centre had part of its substance a little prominent and firm, showing early caseous patches in the cortex.

Colic Glands.—Normal.

Spleen.—In the spleen there were two caseating nodules the size of hemp seeds and three minute opaque tubercles.

Liver.—On the convex surface of the liver there were ten tubercles and six on the concave, varying in size up to a millet seed. On section they consisted of grey translucent tissue with caseous centres. Similar tubercles were sparsely scattered throughout the substance.

Portal Glands.—In the cortices of the portal glands there were scattered irregular early caseous patches.

Kidneys.—One kidney showed a few minute grey points. The other was normal.

Suprarenal Bodies.—Normal.

Coeliac, Lumbar, and Iliac Glands.—Normal.

Thorax.

Lungs.—The lungs were pink and crepitant. In the anterior and middle lobes of the right there were 18 nodules varying from a rape seed up to 5·0 mm. in diameter. On section they consisted of grey tissue caseated in the centre. There were similar nodules scattered throughout the left anterior and the caudal lobes, one of which attained the size of a pea.

Bronchial Glands.—They were beset with small discrete early caseous patches.

Inguinal and Precrural Glands.—Normal.

Testes.—Normal.

Microscopical Examination.

(Smear preparation.)

Left Tonsil.—No tubercle bacilli. Moderately numerous blue stained organisms.

PIG 216.

Fed with the faeces of Cow B from October 1, 1907, to October 9, 1907.

Dose—One-fourth part of 19·11 kilogrammes of faeces.

Age—11 weeks.

Killed in good health—January 9, 1908. [100 days after feeding began.]

Weights.

	qrs.	lbs.
October 1, 1907	1	8
January 9, 1908	3	7

Gain in weight.—1 qr. 27 lbs.

Tuberculin Tests.—September 16, 1907. [15 days before the experiment began.] Reaction: Negative. November 28, 1907. [58 days after the experiment began.] Reaction: Positive. Rise of temperature 2·1° Centigrade.

POST-MORTEM EXAMINATION.

General Condition.—Good.

Tongue.—Normal.

Tonsils.—Normal.

Pharynx.—Normal.

Submaxillary Glands.—On the left side of the neck beneath the jaw, the gland situated most anteriorly was the size of a pigeon's egg, and on section was about three quarters replaced by caseous gritty tissue. All the other glands about the jaw on each side of the neck were normal.

Pharyngeal, Cervical, and Prescapular Glands.—Normal.

Abdomen.

Peritoneum.—Normal.

Omentum.—In the omentum there were about four dozen discrete spherical nodules from a rape seed up to 4·0 mm. in diameter. On section they were translucent with yellow caseous centres.

Stomach.—Normal.

Intestines.—Normal.

Mesenteric Glands.—Several of the mesenteric glands at each extremity and three glands in the middle of the mesentery were enlarged and the cortices extensively replaced by yellowish caseous substance, just perceptibly gritty. One gland at one extremity measured 3·0 by 1·5 cm. and was entirely replaced by a pinkish yellow caseo-necrotic substance. Many glands appeared normal; the remainder showing discrete yellow nodules and foci.

Ileo-Colic Glands.—The ileo-colic glands were extensively affected containing numerous yellow caseous nodules.

Colic Glands.—Several showed foci and small nodules.

Spleen.—The spleen showed a dozen nodules up to 5·0 mm. in diameter, two of them being on the surface; the rest could be seen beneath the capsule slightly projecting from the surface. All of them were grey and translucent with irregular yellow caseous centres.

Liver.—There could be seen just beneath the surface of the liver about two hundred and seventy nodules ranging from a point up to 5·0 mm. in diameter; the smallest were grey and translucent throughout, the larger ones were grey with caseous centres or beset with caseous foci. On section the substance contained numerous similar nodules chiefly about 2·5 mm. in diameter.

Portal Glands.—The portal glands were enlarged and they showed their cortices closely beset with large irregular yellow caseous nodules.

Kidneys.—Normal.

Suprarenal Bodies.—Normal.

The Renal and Lumbar Glands were enlarged (the largest and most severely affected being on the left side of the spine), and showed numerous irregular yellow caseous foci, which in places had run together forming large nodules with a caseous network, just perceptibly gritty.

Iliac Glands.—Two left iliac glands showed a few minute caseous foci.

Right Iliac Glands.—Normal.

Coeliac Glands.—(Seven in number), four were enlarged and showed fairly numerous yellow irregular caseous nodules up to 3 and 4 mm. in diameter; the rest appeared normal.

Thorax.

Diaphragm. — On the peritoneal surface of the central tendon of the diaphragm, mainly on the right side, there were two dozen nodules up to about 6·0 mm. in diameter, many of which extended through the diaphragm and formed nodules on the pleural surface; they were grey and translucent and beset with yellow caseous foci. There were two similar nodules on the right pleura.

Lungs.—The lungs were pink and crepitant, they showed on the surface about one hundred and fifty nodules up to 5·0 and 6·0 mm. in diameter; the smallest were grey with opaque centres; the largest were considerably caseated and gritty. In each of the anterior and middle lobes there was a single nodule, from 0·8 to 1·0 cm. in diameter, they were grey and translucent with a fine caseous network. On section the lung parenchyma showed moderately numerous similar nodules.

Thoracic Lymphatic Glands.

The Bronchial and Mediastinal Glands were enlarged and showed their cortices closely beset with yellow caseating nodules in places forming a coarse network.

Pericardium.—Normal.

Heart.—Normal.

Inguinal Glands.—One on the left side contained a small irregular yellow caseous nodule; other inguinal and precrural glands normal.

PIG 218.

Fed with the faeces of Cow B from October 1, 1907, to October 9, 1907.

Dose—One-fourth part of 19·11 kilogrammes of faeces.

Age—11 weeks.

Killed in good health—December 11, 1907. [71 days after the experiment began.]

Weights.

	qrs.	lbs.
October 1, 1907	1	7
December 11, 1907	2	7

Gain in weight.—1 qr. 0 lbs.

Tuberculin Tests.—September 16, 1907. [15 days before the experiment began.] No reaction.

November 28, 1907. [58 days after the experiment began.] Positive reaction. Rise of temperature 1·3° Centigrade.

POST-MORTEM EXAMINATION.

Carcass in good condition.

Tongue, Tonsils, Larynx, and Pharynx.—Normal.

On the Right Side beneath the Jaw anterior to the submaxillary salivary gland there was a gland measuring 3·3 by 2·5 by 1·3 cm. On section the substance was firm, translucent and more than half replaced by a pinkish caseous gritty nodule and with discrete tubercles in the remaining part.

A second smaller gland contained a caseous network.

The glands posterior to the salivary gland were normal.

Left Submaxillary Gland.—Normal.

Cervical and Prescapular Glands.—Normal.

Abdomen.

Stomach.—Normal.

Intestines.—Normal.

Omentum.—Normal.

Peritoneum.—Normal.

Mesenteric Glands.—In one mesenteric gland there was a caseating nodule 3·0 mm. in diameter, there was a slightly larger irregular nodule in a second. A third gland showed part of its substance replaced by a caseous network and a fourth gland was slightly enlarged at one extremity and contained an irregular waxy caseating nodule 1·0 cm. in diameter.

Spleen.—Normal.

Liver.—On the surface beneath the capsule of the liver there were eight grey tubercles with opaque centres up to a rape seed in size. On section through the substance an occasional grey tubercle was seen.

Portal Glands.—In the portal glands there were a few caseous foci.

Kidneys.—Normal.

Suprarenal Bodies.—Normal.

Renal, Coeliac, Lumbar and Iliac Glands.—Normal.

Thorax.

Lungs.—The left lung showed on the surface beneath the pleura, two grey submiliary tubercles with opaque centres. In the right there were three similar tubercles.

Bronchial Glands.—There was a caseous focus in a left bronchial gland. The right bronchial gland was normal.

Mediastinal Glands.—Normal.

Inguinal and Precrural Glands.—Normal.

PIG 222.

Fed once with the milk from Cow B.

Date—November 1, 1907.

Dose—2,870 cubic centimetres.

Age—11 weeks.

Killed in good health—January 9, 1908. [69 days after the experiment began.]

Weights.

	qrs.	lbs.
November 1, 1907	1	14
January 9, 1908	2	26

Gain in weight.—1 qr. 12 lbs.

Tuberculin Tests.—October 11, 1907. [20 days before the experiment began.] No reaction.

November 28, 1907. [27 days after the experiment began.] No reaction.

POST-MORTEM EXAMINATION.

General Condition.—Good.

There was no sign of tuberculosis.

PIG 224.

Fed with the milk of Cow B from October 14, 1907, to October 20, 1907.

Dose one-half part of 18,490 cubic centimetres.

Age—9 weeks.

Killed in good health—January 8, 1908. [86 days after the experiment began.]

Weights.

	qrs.	lbs.
October 14, 1907	1	0
January 8, 1908	2	6

Gain in weight.—1 qr. 6 lbs.

Tuberculin Tests.—October 11, 1907. [3 days before experiment began.] Reaction : Negative.

November 28, 1907. [45 days after the experiment began.] Reaction : Negative.

POST-MORTEM EXAMINATION.

General Condition.—Good.

There was no sign of tuberculosis.

PIG 226.

Fed with the milk of Cow B from October 14, 1907, to October 20, 1907.

Dose—One-half part of 18,490 cubic centimetres.

Age—9 weeks.

Killed in good health—January 8, 1908. [86 days after the experiment began.]

Weights.

	qrs.	lbs.
October 14, 1907	1	5
January 8, 1908	2	0

Gain in weight.—23 lbs.

Tuberculin Tests—October 11, 1907. [3 days before the experiment began.] No reaction.

November 28, 1907. [45 days after the experiment began.] No reaction.

POST-MORTEM EXAMINATION

General Condition.—Good.

There was no sign of tuberculosis.

JERSEY COW C.

POST-MORTEM EXAMINATION.

Body emaciated.

Thorax.

Pleura.—On the pleura along the ribs there were numerous flattened fibro-caseous nodules up to 2·0 cm., some loosely attached. There were numerous similar nodules on the pleura over the dorsal mediastinal glands. On the pleural surface of diaphragm there were a few small loosely attached fibro-caseous nodules.

Lungs.—The lungs were very heavy and voluminous. On the pleural surfaces there were numerous flattened perlsucht growths similar to but larger than those on the parietal pleura varying up to 4·0 cm. in diameter. In both anterior lobes there were large caseo-necrotic masses replacing a third of the substance, the rest of the anterior lobes was closely beset with nodules and masses varying in size. The posterior lobes were similarly severely affected. On section the masses were bright yellow, caseo-necrotic and in many parts becoming soft and caseo-purulent around the margins. The bronchi were filled with muco-pus and in several places caseous substance could be seen protruding into the cavity of a bronchus.

There was a cast of the trachea formed of inspissated muco-pus.

Mediastinal Glands.—The long mediastinal gland weighed 2 lbs. and measured 26·0 by 10·0 by 6·0 cm. On section it consisted almost throughout of bright yellow caseo-necrotic substance.

Bronchial Glands.—The bronchial glands were similarly greatly enlarged and caseo-necrotic throughout.

Other mediastinal and supra-bronchial glands were similar.

Heart and Great vessels.—Normal.

Abdomen.

Omentum and Peritoneum.—Normal.

Intestines.—All the Peyer's patches of the small intestine contained a few caseous nodules varying from a millet seed up to a hemp seed, many of them ulcerated on the surface. In addition there were several small ulcers 5·0 mm. in diameter from which the caseous substance had almost disappeared.

Mesenteric Glands.—The majority of the mesenteric glands appeared normal ; several contained discrete caseous nodules and a few at one extremity showed the cortices diffusely caseous. One mesenteric gland about the centre of the mesentery was greatly enlarged measuring 8·0 by 4·0 by 5·5 cm., on section it consisted practically throughout of an orange yellow caseo-necrotic slightly gritty substance.

Spleen.—Weighed 1 lb. 6 ozs. On section it contained ten caseous gritty tubercles varying from a rape seed up to a millet seed in size.

Liver.—Anterior surface normal. On the postero-inferior surface there was a single caseous tubercle. On section through the substance three caseous foci were met with, of which one was gritty.

Gall Bladder.—Normal.

Portal Glands.—The portal glands contained a few discrete caseous nodules, the size of hemp seed.

Kidneys.—Both kidneys showed in the cortices just beneath the surface scattered tubercles varying from a rape seed up to a hemp seed in size ; they were all caseous and the largest slightly gritty. On section similar nodules were found scattered throughout the deeper parts of the cortices.

Suprarenal Bodies.—The left suprarenal body contained ten, and the right five, caseo-calcareous nodules from a rape seed up to 3·5 mm. in diameter.

Lumbar and Iliac Glands.—Normal.

Tongue, Tonsils, Larynx, Pharynx, and Trachea.—Normal.

Uterus.—The walls of both cornua of the uterus and also the common portion were thickened and infiltrated with a network of grey nodules with bright

yellow caseous centres. The cavity was filled with purulent fluid and caseous flocculi.

Supramammary Glands. — Each supramammary gland showed a minute caseous focus; one contained also a grey nodule the size of a hemp seed, diffusely caseous.

The Udder.—Normal.

Retro-Pharyngeal Glands.—The left was congested and showed a number of caseo-calcareous masses arranged around the cortex. The right contained two caseous miliary tubercles.

Cervical Glands.—The right inferior cervical gland was enlarged and about three-quarters of the cortex was replaced by yellow caseo-calcareous masses; other cervical glands were normal.

Parotid, Prepectoral, Prescapular, Precrural, Axillary, Popliteal, and Gluteal Glands.—Normal.

Microscopical Examination.

(Smear preparations.)

Supramammary Gland (focus).—(1) Three tubercle bacilli.

Supramammary Gland (focus).—(2) Two tubercle bacilli.

Intestine (ulcer).—A moderate number of tubercle bacilli.

Bronchial Gland.—No tubercle bacilli.

GUINEA-PIGS INOCULATED WITH THE FAECES OF COW C.

Number.	Date of Inoculation.	Dose.	Method of Inoculation.	Duration of Life.	Result.
2805	October 24, 1907	·05 cc.	Ip.	Killed 22 days	G.T.
2806		·1 cc.	Ip.	Killed 18 days	G.T.
2807		·1 cc.	Sub.	Killed 16 days	No tuberculosis; discharging ulcers in the skin.
2808		·05 cc.	Ip.	Died 4 days	No tuberculosis.
2809		·05 cc.	Sub.	Killed 32 days	Early G.T.
2810		·05 cc.	Sub. & Ip.	Killed 32 days	G.T. severe.
2813	October 25, 1907	·05 cc.	Ip.	Killed 21 days	G.T.
2814		·1 cc.	Ip.	Killed 20 days	G.T. severe.
2815		·2 cc.	Ip.	Killed 17 days	Single nodule in omentum; two nodules in spleen; portal gland caseous.
2816		·1 cc.	Sub.	Killed 34 days	G.T. severe.
2817		·1 cc.	Sub.	Killed 34 days	G.T.
2818		·2 cc.	Sub.	Killed 20 days	No tuberculosis; ulcer in skin; no T.B.
2829	October 28, 1907	1·0 cc.	Sub.	Killed 17 days	No tuberculosis. Large ulcer in skin.
2830		·3 cc.	Ip.	Killed 29 days	G.T. severe.
2831		·1 cc.	Sub.	Killed 66 days	G.T. severe.
2832		·2 cc.	Sub.	Died 66 days	G.T. severe.
2833		·2 cc.	Ip.	Died 1 day	Acute infection. No T.
2834		·1 cc.	Ip.	Killed 18 days	Early G.T.
2837	October 29, 1907	·1 cc.	Ip.	Killed 28 days	G.T.
2838		·2 cc.	Ip.	Killed 28 days	G.T.
2839		·3 cc.	Ip.	Died 1 day	Acute infection. No. T.
2840		·1 cc.	Sub.	Killed 30 days	G.T.
2841		·3 cc.	Sub.	Died 3 days	No tuberculosis.
2842		1·0 cc.	Sub.	Died 2 days	No tuberculosis.
2853	October 30, 1907	·2 cc.	Ip.	Died 1 day	Acute infection. No T.
2854		·2 cc.	Ip.	Died 1 day	Acute infection. No. T.
2855		·2 cc.	Ip.	Killed 27 days	G.T.
2856		1·0 cc.	Sub.	Died 5 days	No tuberculosis.
2857		1·0 cc.	Sub.	Died 2 days	No tuberculosis.
2858		1·0 cc.	Sub.	Died 2 days	No tuberculosis.

Ip. = intraperitoneal. Sub. = subcutaneous.

GUINEA-PIGS INOCULATED WITH FAECES OF COW C.

DILUTED WITH SALT SOLUTION; 1 GRAMME OF FAECES IN 2,000 CUBIC CENTIMETRES OF STERILE SALT SOLUTION.

Number.	Date of Inoculation.	Dose.	Method of Inoculation.	Duration of Life.	Result.
2872	October 31, 1907	1·0 cc.	Ip.	Died 63 days	Severe G.T.
2873		2·0 cc.	Ip.	Killed 63 days	Severe G.T.

GUINEA-PIGS FED WITH FAECES OF COW C.

DOSE IN EACH CASE 1·0 CC. OF FAECAL EMULSION.

Number.	Date of Feeding.	Duration of Life.	Result.
2803	October 24, 1907	Killed 90 days	No tuberculosis.
2804			
2811	October 25, 1907	Killed 89 days	No tuberculosis.
2812			
2827	October 28, 1907	Died 44 days	No tuberculosis.
2828		Killed 86 days	No tuberculosis.
2835	October 29, 1907	Killed 85 days	No tuberculosis.
2836			
2851	October 30, 1907	Killed 84 days	No tuberculosis.
2852			

GUINEA-PIGS FED CONTINUOUSLY WITH FAECES OF COW C MIXED WITH STERILIZED MILK.

Number.	Date of Feeding.	Duration of Life.	Result.
2799	From October 24, 1907, to October 30, 1907.	Killed 74 days	No tuberculosis.
2800		Killed 90 days	Caseous ulcers in intestine, and caseation of mesenteric glands. G.T.
2801		Died 48 days	No tuberculosis.
2802		Killed 90 days	No tuberculosis.

ANIMALS INOCULATED INTRAPERITONEALLY WITH THE MILK OF COW C.

Number of Animal.	Date of Inoculation.	Dose.	Quarter of Udder.	Duration of Life.	Result.
Rabbit 1524	October 25, 1907.	3·0 cc.	R.F.	Died 13 days	No tuberculosis.
Rabbit 1525			R.H.	Killed 76 days	No tuberculosis.
Rabbit 1526			L.F.	Died 18 days	No tuberculosis.
Rabbit 1527			L.H.	Killed 76 days	No tuberculosis.
Guineapig 2819	October 25, 1907.	10·0 cc. of milk plus the deposit of 40·0 cc. obtained by centrifuging.	R.F.	Died 50 days	No tuberculosis.
Guineapig 2820			R.F.	Killed 73 days	No tuberculosis.
Guineapig 2821			R.H.	Killed 73 days	No tuberculosis.
Guineapig 2822			R.H.	Killed 73 days	No tuberculosis.
Guineapig 2823			L.F.	Killed 73 days	No tuberculosis.
Guineapig 2824			L.F.	Killed 73 days	No tuberculosis.
Guineapig 2825			L.H.	Killed 73 days	No tuberculosis.
Guineapig 2826			L.H.	Died 63 days	No tuberculosis.

ANIMALS INOCULATED INTRAPERITONEALLY WITH THE MILK OF COW C—*continued.*

Number of Animal.	Date of Inoculation.	Dose.	Quarter of Udder.	Duration of Life.	Result.
Rabbit 1531	October 29, 1907.	50·0 cc.	R.F.	Killed 72 days	No tuberculosis.
Rabbit 1532			L.F.	Died 3 days	No tuberculosis.
Rabbit 1533			L.H.	Killed 72 days	No tuberculosis.
Guineapig 2843	October 29, 1907	As on Oct. 25.	R.F.	Died 18 days	Three transparent tubercles in omentum containing tubercle bacilli.
Guineapig 2844			R.F.	Killed 71 days	No tuberculosis.
Guineapig 2845			R.H.	Killed 69 days	No tuberculosis.
Guineapig 2846			R.H.	Killed 71 days	No tuberculosis.
Guineapig 2847			L.F.	Died 24 days	Three transparent tubercles in omentum containing moderately numerous tubercle bacilli.
Guineapig 2848			L.F.	Killed 71 days	No tuberculosis.
Guineapig 2849			L.H.	Killed 69 days	No tuberculosis.
Guineapig 2850			L.H.	Killed 71 days	No tuberculosis.
Rabbit 1534	October 30, 1907.	30·0 cc.	R.F.	Died 25 days	Six transparent tubercles in omentum containing moderately numerous T.B.
Rabbit 1535			R.H.	Died 27 days	Several tubercles in omentum, one caseating, containing T.B.
Rabbit 1536			L.F.	Killed 71 days	No tuberculosis.
Rabbit 1537			L.H.	Killed 71 days	Three miliary tubercles and one caseating nodule (6·0 mm.) in omentum. Caseation of portal glands. Four caseating nodules in the lungs.
Guineapig 2859	October 30, 1907.	As on Oct. 25.	R.F.	Killed 71 days	G.T. Omentum contained about fifty nodules.
Guineapig 2860			R.F.	Killed 71 days	Severe G.T.
Guineapig 2861			R.H.	Killed 68 days	Early G.T.
Guineapig 2862			R.H.	Killed 71 days	Severe G.T.
Guineapig 2863			L.F.	Killed 68 days	No tuberculosis.
Guineapig 2864			L.F.	Killed 71 days	No tuberculosis.
Guineapig 2865			L.H.	Killed 68 days	No tuberculosis.
Guineapig 2866			L.H.	Killed 71 days	No tuberculosis.

PIG 230.

Fed with the faeces of Cow C from October 23, 1907, to October 30, 1907.

Dose—5·56 kilogrammes of faeces.

Age—10 weeks.

Killed when in good health—December 11, 1907. [48 days after the experiment began.]

Weights.

	qrs.	lbs.
October 23, 1907	1	11
December 11, 1907	2	7

Gain in weight.—24 lbs.

Tuberculin Tests. — October 11, 1907. [12 days before the experiment began.] No reaction.

November 28, 1907. [36 days after the experiment began.] Positive reaction. Rise of temperature 1·5° Centigrade.

POST-MORTEM EXAMINATION.

General Condition.—Good.

Tongue, Pharynx, and Larynx.—Normal.

Tonsils.—In the tonsils there were a few soft yellowish foci.

On the Left Side of the Neck, beneath the angle of the jaw, anterior to the submaxillary salivary gland, there was a gland measuring 5·0 by 3·0 by 2·2 cm. On section it was composed of firm translucent tissue

with a close yellowish network; attached to it was a small gland containing a few opaque foci.

Four glands posterior to the first were normal.

On the Right Side of the Neck, in front of the submaxillary salivary gland, there were two glands forming a mass 5·0 by 3·3 by 2·0 cm. On section it resembled that on the opposite side; the other glands about the jaw were normal.

Cervical Glands.—Normal.

Prescapular Glands.—Normal.

Abdomen.

Stomach.—Normal.

Intestines.—Normal.

Mesenteric Glands.—The majority of the mesenteric glands were normal. About six glands on each side of the mesentery in the centre were moderately enlarged, consisting of firm translucent tissue with a firm yellowish waxy caseous network.

Spleen.—Normal.

Liver.—On the convex surface of the liver there were visible beneath the capsule twenty slightly irregular grey caseating tubercles the size of rape seeds; they were sparsely scattered on the other surfaces and in the substance.

Portal Glands.—One portal gland was a little firm at one extremity and showed early caseous patches. A second small gland was similar.

Kidneys.—Normal.

Suprarenal Bodies.—Normal.

Coeliac, Lumbar, and Iliac Lymphatic Glands.—Normal.

Thorax.

Lungs.—In the left lung on the surface beneath the pleura there were fourteen grey caseating tubercles up to a millet seed in size. The right lung showed rather fewer. On section no more could be seen.

Bronchial Glands.—Normal.

Precrural and Inguinal Glands.—Normal.

Microscopical Examination.

(Smear preparation.)

Tonsil (focus).—Four tubercle bacilli seen.

COW F.

POST-MORTEM EXAMINATION.

General Condition.—Poor.

Tongue.—Normal.

Tonsils.—The tonsils were firm and on section contained caseous nodules.

Submaxillary Glands.—Normal.

Pharyngeal Glands.—The left posterior pharyngeal gland measured 9·5 by 5·5 by 3·0 cm. and on section was caseous throughout.

The right posterior pharyngeal gland measured 7 by 3·5 cm. On section the superficial part of the cortex was caseous.

Cervical Glands.—Several of the cervical glands contained large nodules, some caseous throughout.

Abdomen.

Intestines.—In the small intestine there were counted nineteen ulcers, varying up to 4·0 cm. in diameter; the bases and the raised margins were firm and caseating. There were also scattered nodules in both intestines.

Mesenteric Glands.—The mesenteric glands were enormously enlarged and replaced by a brownish yellow necrotic substance, in many parts softening. In points of size and appearance the lesions were older than those in the bronchial glands; also the tuberculosis of the lungs was fairly acute.

Spleen.—The spleen appeared normal.

Liver.—On the surface of the liver there was a single small tubercle; the parenchyma was beset throughout with small ill-defined yellowish grey necrotic patches.

Portal Glands.—The cortices of the portal glands were a little firm, but showed no caseation.

Kidneys.—In the medulla of the right kidney there were two caseating miliary tubercles. Left kidney normal.

Suprarenal Bodies.—The left suprarenal body contained three caseous nodules up to a pea in size.

Right suprarenal body showed three similar nodules up to the size of a millet seed.

There was an opaque focus in one renal lymphatic gland.

Lumbar Glands.—Five lumbar glands, up to a pigeon's egg in size, caseous throughout.

Iliac Glands.—Caseo-calcareous nodules in two iliac glands.

Thorax.

Lungs.—The lungs were voluminous, the anterior lobes were congested. The substance was closely beset throughout with irregular and for the most part small caseous nodules and patches. On the left lung there was a number of perlsucht nodules and also numerous similar nodules and masses on the parietal pleura.

Prescapular Glands were not tuberculous. The right gland was enlarged from the tuberculin inoculation.

Prepectoral and Axillary Glands.—Normal.

Supramammary Lymphatic Glands.—Both supramammary glands were enlarged and contained dirty yellow caseo-necrotic masses.

Udder.—In the tissue of the udder of the left hind quarter forming the wall of the main sinus close to the teat, there were four firm reddish grey nodules varying from a millet seed up to a pea; they resembled the tissue around, being distinguished by a central caseous streak and firmness from the tissue in that part of the udder which is mainly composed of ducts. The other quarters of the udder were normal.

Uterus.—In the horns of the uterus there were rounded yellow caseo-necrotic nodules, not unlike unopened mushrooms, projecting into the cavities and loosely attached by pedicles, composed of reddish grey tissue of which the centres of the nodules were also formed; the largest was the size of a robin's egg. There was a muco-purulent exudation in the uterus and vagina.

Microscopical Examination.

(Smear preparations.)

Udder (nodule I and II).—Showed moderately numerous tubercle bacilli.

GUINEA-PIGS WITH FAECES OF COW F.

ALL INTRAPERITONEAL.

Number.	Date of Inoculation.	Dose.	Duration of Life.	Result.
2979	January 29, 1908	1·0 cc.	Died 1 day	Acute infection.
2980		1·0 cc.	Died 1 day	Acute infection.
2981		·5 cc.	Died 11 days	Sub-acute infection.
2982		·5 cc.	Killed 33 days	General tuberculosis.
2983		·5 cc.	Died 8 days	No tuberculosis.
2984		·5 cc.	Killed 33 days	General tuberculosis.
2985		·5 cc.	Killed 33 days	General tuberculosis.

GUINEA-PIGS INOCULATED INTRAPERITONEALLY WITH THE MILK OF COW F.

Number.	Date of Inoculation.	Dose.	Quarter of Udder.	Duration of Life.	Result.
2971	January 29, 1908	6·0 cc. of milk plus the deposit of 24·0 cc. obtained by the centrifuge.	R.F.	Died 35 days	Caseo-purulent nodule in muscle at site of inoculation; caseation of sternal gland. Numerous T.B. in both.
2972			R.F.	Died 11 days	No tuberculosis.
2973			R.H.	Died 18 days	General tuberculosis.
2974			R.H.	Died 24 days	General tuberculosis.
2975			L.F.	Died 27 days	General tuberculosis.
2976			L.F.	Died 35 days	General tuberculosis.
2977			L.H.	Died 18 days	General tuberculosis.
2978			L.H.	Died 18 days	General tuberculosis.
2986	January 30, 1908	5·0 cc. plus the deposit of 10 cc.	R.F.	Killed 34 days	General tuberculosis.
2987			R.F.	Killed 34 days	General tuberculosis.
2988		As in the first series.	R.H.	Died 17 days	General tuberculosis.
2989			R.H.	Died 7 days	No tuberculosis.
2990			L.F.	Died 10 days	No tuberculosis.
2991			L.F.	Killed 34 days	General tuberculosis.
2992			L.H.	Died 17 days	General tuberculosis.
2993			L.H.	Died 4 days	No tuberculosis.
2994	January 31, 1908	7·0 cc.	R.F.	Killed 33 days	General tuberculosis.
2995		7·0 cc.	R.F.	Killed 33 days	General tuberculosis.
2996		As in the first series.	R.H.	Died 23 days	General tuberculosis.
2997			R.H.	Died 9 days	One minute tubercle in omentum. Tubercle bacilli found.
2998			L.F.	Died 6 days	No tuberculosis.
2999			L.F.	Killed 33 days	General tuberculosis.
3000			L.H.	Died 18 days	General tuberculosis.
3001			L.H.	Died 8 days	No tuberculosis.
3002	February 1, 1908	4·0 cc.	R.F.	Killed 32 days	General tuberculosis.
3003		10·0 cc.	R.H.	Died 8 days	No tuberculosis.
3004			R.H.	Died 7 days	No tuberculosis.
3005			L.F.	Killed 32 days	General tuberculosis.
3006			L.F.	Died 8 days	No tuberculosis.
3007			L.H.	Died 3 days	No tuberculosis.
3008			L.H.	Died 22 days	General tuberculosis.

SHORTHORN HEIFER A.

POST-MORTEM EXAMINATION.

General Condition.—Good.

Tongue.—Normal.

Tonsils.—Normal.

Pharynx.—Normal.

Submaxillary Glands.—Normal.

Pharyngeal Glands.—The right retro-pharyngeal gland measured 10·5 by 6·5 by 5·0 cm. On section it was a cyst with thick fibrous walls, filled with caseo-necrotic substance which was partly broken down into a brownish yellow purulent fluid with caseous flakes and partly adherent as congested caseo-necrotic masses to the internal walls.

The left retro-pharyngeal gland measured 4·1 by 3·0 by 1·5 cm. On section it was normal.

Cervical Glands.—Normal.

Abdomen.

Peritoneum and Omentum.—Normal.

Intestines.—In the Peyer's patches of the small intestine there were five nodules, two grey with opaque foci, and three soft yellow and caseous, varying up to about a millet seed in size.

There was also a small ulcer with a fibrous slightly opaque thickened base in which no tubercle bacilli could be demonstrated microscopically.

Large Intestine.—Normal.

Mesenteric Glands.—One mesenteric gland showed a yellow caseo-calcareous nodule nearly 1·0 cm. in diameter.

Spleen.—Normal.

Liver.—Normal.

Portal Glands.—Normal.

Kidneys.—Normal.

Suprarenal Bodies.—Normal.

Renal, Coeliac, Lumbar, and Iliac Lymphatic Glands.—Normal.

Thorax.

Pleura.—Normal.

Lungs.—In the lungs just beneath the pleura there were three translucent foci and a soft grey nodule the size of a hemp seed.

Bronchial and Mediastinal Glands.—Normal.

Heart and Pericardium.—Normal.

Gluteal Glands.—The right was larger than the left, measuring 2·5 by 2·0 cm. On section the substance was firm and infiltrated almost throughout, with a bright yellow caseo-necrotic network mottled with patches of hæmorrhage. The left gluteal gland was normal.

Various Lymphatic Glands.

Parotid, Prescapular, Prepectoral, Precrural, and Popliteal Glands.—Normal.

Udder.—Normal.

Supramammary Glands.—Normal.

Microscopical Examinations.

(Smear preparations.)

Intestine (grey nodule).—One tubercle bacillus.

Intestine (caseous nodule).—No tubercle bacilli.

Intestine (ulcer).—No tubercle bacilli.

Retro-pharyngeal Gland.—Four tubercle bacilli, also short blue stained bacilli.

Lung (grey nodule).—No tubercle bacilli.

Gluteal Gland.—No tubercle bacilli.

GUINEA-PIGS INOCULATED INTRAPERITONEALLY WITH FAECES OF COW A.

Number.	Date of Inoculation.	Dose.	Duration of Life.	Result.
2635	September 30, 1907	Small doses varying up to 0·1 cc.	Killed 92 days	No tuberculosis.
2636			Killed 92 days	No tuberculosis.
2637			Killed 92 days	No tuberculosis.
2638			Killed 56 days	No tuberculosis
2639			Killed 42 days	No tuberculosis.
2659	October 2, 1907	·05 cc.	Killed 30 days	No tuberculosis.
2660		·05 cc.	Killed 40 days	No tuberculosis.
2661		·05 cc.	Killed 55 days	No tuberculosis.
2662		·05 cc.	Killed 36 days	No tuberculosis.
2681	October 4, 1907	·05 cc.	Killed 88 days	No tuberculosis.
2682		·05 cc.	Killed 88 days	No tuberculosis.
2683		·5 cc.	Killed 88 days	No tuberculosis.
2684		·5 cc.	Killed 38 days	No tuberculosis.
2700	October 7, 1907	·05 cc	Killed 85 days	No tuberculosis.
2701		·05 cc	Killed 85 days	No tuberculosis.
2702		·05 cc.	Killed 85 days	No tuberculosis.
2703		·05 cc.	Killed 85 days	No tuberculosis.

GUINEA-PIGS FED WITH FAECES OF COW A.

DOSE IN EACH CASE 1·0 CUBIC CENTIMETRE OF FAECAL EMULSION.

Number.	Date of Feeding.	Duration of Life.	Result.
2640	September 30, 1907	Killed 99 days	No tuberculosis.
2641		Killed 99 days	No tuberculosis.
2655	October 1, 1907	Killed 98 days	No tuberculosis.
2656		Killed 98 days	No tuberculosis.
2663	October 2, 1907	Killed 99 days	No tuberculosis.
2664		Killed 99 days	No tuberculosis.
2675	October 3, 1907	Killed 98 days	No tuberculosis.
2676		Killed 98 days	No tuberculosis.
2679	October 4, 1907	Died 60 days	No tuberculosis.
2680		Killed 98 days	No tuberculosis.
2690	October 5, 1907	Killed 98 days	No tuberculosis.
2691		Killed 98 days	No tuberculosis.
2698	October 7, 1907	Killed 98 days	No tuberculosis.
2699		Killed 98 days	No tuberculosis.
2706	October 8, 1907	Killed 98 days	No tuberculosis.
2707		Killed 98 days.	No tuberculosis.
2716	October 9, 1907	Killed 98 days	No tuberculosis.
2717		Killed 98 days	No tuberculosis.

GUINEA-PIGS FED CONTINUOUSLY WITH FAECES OF COW A MIXED WITH STERILIZED MILK.

Number.	Date of Feeding.	Duration of Life.	Result.
2629	From September 30, 1907, to October 9, 1907.	Killed 57 days	No tuberculosis.
2630		Killed 98 days	No tuberculosis.
2631		Killed 98 days	No tuberculosis.
2632		Died 5 days	No tuberculosis.
2633		Killed 106 days	No tuberculosis.
2634		Died 100 days	No tuberculosis.

PIG 204.

Fed with the faeces of Cow A from September 30, 1907, to October 9, 1907.

Dose—One-fourth part of 25·65 kilogrammes of faeces.

Age—11 weeks.

Killed in good health—December 30, 1907. [91 days after the experiment began.]

Weights.

	qrs.	lbs.
September 30, 1907	1	5
December 30, 1907	2	19

Gain in weight.—1 qr. 14 lb.

Tuberculin Tests.—September 16, 1907. [14 days before experiment began.] No reaction.

November 28, 1907. [59 days after the experiment began.] No reaction.

POST-MORTEM EXAMINATION.

General Condition.—Good. There was no tuberculosis of any organ or gland in the body.

PIG 206.

Fed with the faeces of Cow A from September 30, 1907, to October 9, 1907.

Dose—One-fourth part of 25·65 kilogrammes of faeces.

Age—11 weeks.

Killed in good health—January 7, 1908. [99 days after the experiment began.]

Weights.

	qrs.	lbs.
September 30, 1907	1	2
January 7, 1908	2	16

Gain in weight.—1 qr. 14 lbs.

Tuberculin Tests.—September 16, 1907. [14 days before the experiment began.] No reaction.

November 28, 1907. [59 days after the experiment began.] No reaction.

POST-MORTEM EXAMINATION.

Carcass in good condition. There was no sign of tuberculosis anywhere.

PIG 208.

Fed with the faeces of Cow A from September 30, 1907, to October 9, 1907.

Dose—One-fourth part of 25·65 kilogrammes of faeces.

Age—11 weeks.

Killed in good health—January 7, 1908. [99 days after the experiment began.]

Weights.

	qrs.	lbs.
September 30, 1907	1	3
January 7, 1908	2	20

Gain in weight.—1 qr. 17 lbs.

Tuberculin Tests.—September 16, 1907. [14 days before the experiment began.] No reaction.

November 28, 1907. [59 days after the experiment began.] No reaction.

POST-MORTEM EXAMINATION.

Carcass in good condition.

There was no sign of tuberculosis anywhere.

PIG 210.

Fed with the faeces of Cow A from September 30, 1907, to October 9, 1907.

Dose—One-fourth part of 25·65 kilogrammes of faeces.

Age—11 weeks.

Killed in good health—December 5, 1907. [66 days after feeding began.]

Weights.

	lbs.
September 30, 1907	28
December 5, 1907	57

Total gain in weight.—29 lbs.

Tuberculin Tests.—September 16, 1907. [14 days before experiment began.] Reaction: Negative.

November 28, 1907. [59 days after the experiment began.] Reaction: Positive.

Rise of temperature—2·3° Centigrade.

POST-MORTEM EXAMINATION.

General Condition.—Good.

Tongue, Tonsils, Larynx, and Pharynx.—Normal.

On the Left Side of the Neck extending from below the angle of the jaw to the root of the ear, there was a chain of six glands the largest measuring 2·0 by 3·5 cm.; the smallest 1·6 by 1·2 cm. On section the largest consisted of a yellowish caseo-necrotic network in firm pinkish grey tissue. The other glands consisted of firm grey tissue with a fine yellowish network.

Right Submaxillary Glands.—Normal.

Cervical and Prescapular Glands.—Normal.

Abdomen.

Omentum and Peritoneum.—Normal.

Intestines.—Normal.

Mesenteric Glands.—The mesenteric glands were not enlarged and in one a single caseous focus was seen.

Spleen.—Normal.

Liver.—On the convex surface of the liver there were four grey tubercles with opaque centres up to a rape seed in size. On the concave surface there were two. On section through the substance no more were seen.

Portal Glands appeared normal.

Kidneys.—In the cortices of the kidneys there were scattered grey points.

Suprarenal Bodies.—Normal.

Renal, Coeliac, Lumbar, and Iliac Lymphatic Glands.—Normal.

Thorax.

Lungs.—In the left lung on the surface just beneath the pleura there were thirty caseating tubercles varying up to a hemp seed in size; there was about the same number on the right side; they were sparsely scattered throughout the parenchyma.

Bronchial Glands.—An occasional irregular caseous focus could be seen in the bronchial glands.

Precrural and Inguinal Glands.—Normal.

Microscopical Examination.

(Smear preparations.)

Kidney (grey foci).—Moderately numerous tubercle bacilli seen.

Mesenteric Gland (focus).—Eleven tubercle bacilli seen.

Bronchial Gland (focus).—No tubercle bacilli seen.

COW D.

POST-MORTEM EXAMINATION.

Animal fat and in good condition.

Thorax.

On opening the Thoracic Cavity there were numerous firm fibrous adhesions connecting the visceral and parietal pleurae. On the visceral side of these adhesions there were, in a majority of cases, nodules in the lung substance.

Lungs. Left Lung.—There was an adhesion between the anterior and the posterior lobes. The lung substance was pink and crepitant. The anterior lobe contained three nodules, the two largest the size of a sparrow's eggs; they consisted of yellow caseo-necrotic substance enclosed within fibrous capsules. In the posterior lobe there were eight large nodules varying from a large pea up to a mass 10·0 by 6·0 by 5·0 cm.; there were three nearly equal to the latter in size. On section they were composed of masses of yellow softening necrotic substance surrounded by fibrous walls. In the lung parenchyma, there were also seen scattered translucent tubercles with caseous centres varying up to a hemp seed in size.

Right Lung.—The anterior lobe contained five nodules up to a large pea in size and scattered translucent tubercles. The middle lobe contained a few nodules the largest the size of a pigeon's egg. The caudal lobe contained scattered nodules, about sixteen counted, varying in size up to a pigeon's egg, they all consisted of yellow caseo-necrotic substance in many cases becoming soft and purulent; there were also scattered minute translucent tubercles and nodules varying from a hemp seed up to a wheat grain in the substance. Several of the nodules were surrounded by pneumonic patches beset with caseous foci. A few of the softening nodules communicated with the smaller bronchi. Muco-pus could be squeezed from many of the bronchioles and soft caseous substance was seen in several of the larger bronchi.

Thoracic Lymphatic Glands.—The caudal mediastinal gland measured 24·0 by 7·0 by 5·0 cm. One half of it was much larger than the other and was firm and nodular. On section, the whole gland was replaced by bright yellow caseo-necrotic gritty masses, softening in many parts, disposed in a matrix of fibrous translucent tissue; the other mediastinal glands were a little enlarged and firm, and on section were more than half replaced by similar masses.

The bronchial glands were very slightly enlarged and resembled the mediastinal glands.

Abdomen.

Omentum.—Normal.

Intestines.—Normal.

Mesenteric and Colic Glands.—Normal.

Spleen.—Normal.

Liver.—In the centre of the liver there was a nodule of yellow caseo-purulent substance containing gritty foci lying in a bile duct with thickened walls.

Portal Glands.—Normal.

Kidneys.—Normal.

Suprarenal Bodies.—Normal.

Renal, Coeliac, Lumbar, and Iliac Glands.—Normal.

Ovaries and Uterus.—Normal.

Supramammary Lymphatic Glands.—Normal.

Udder.—Normal.

Tongue, Tonsils, Larynx, and Pharynx.—Normal.

Various Lymphatic Glands.

Parotid, Submaxillary, Pharyngeal, Cervical, Prescapular, Prepectoral, Axillary, Precrural, Gluteal, Ischiatic, and Popliteal Glands.—Normal.

Microscopical Examination.

(Smear preparation.)

Liver (pus).—No tubercle bacilli seen.

GUINEA-PIGS INOCULATED INTRAPERITONEALLY WITH A THICK EMULSION OF THE FAECES OF COW D.

Number.	Date of Inoculation.	Dose.	Duration of Life.	Result.
3017	February 20, 1908	·05 cc.	Killed 62 days	No tuberculosis.
3018		·05 cc.	Died 10 days	In the omentum there were several minute translucent tubercles containing moderately numerous tubercle bacilli.
3019		·05 cc.	Died 61 days	No tuberculosis.
3027	February 21, 1908	·05 cc.	Killed 61 days	No tuberculosis.
3028		·1 cc.	Killed 39 days	Three translucent foci and a small grey tubercle in omentum. No tuberculosis elsewhere. Smear from omentum showed moderately numerous acid fast bacilli.

GUINEA-PIGS INOCULATED INTRAPERITONEALLY WITH A THICK EMULSION OF THE FAECES OF COW D—*continued.*

Number.	Date of Inoculation.	Dose.	Duration of Life.	Result.
3133	March 24, 1908	·05 cc.	Died 14 days	No tuberculosis.
3134		·05 cc.	Died 3 days	No tuberculosis.
3135		·05 cc.	Killed 45 days	Early general tuberculosis. Culture isolated.
3136		·05 cc.	Died 4 days	No tuberculosis.
3137		·05 cc.	Killed 45 days	Caseation of pyloric and portal glands. Smear showed moderately numerous tubercle bacilli. Culture isolated.
3138		·05 cc.	Killed 45 days	No tuberculosis.

RABBITS INOCULATED INTRAPERITONEALLY WITH A THICK EMULSION OF THE FAECES OF COW D.

Number.	Date of Inoculation.	Dose.	Duration of Life.	Result.
1692	February 21, 1908	·05 cc.	Killed 82 days	Omentum contained caseating miliary tubercles. Caseous tubercles on diaphragm and in lungs. Caseation of pyloric and portal glands.
1693	February 21, 1908	·1 cc.	Killed 82 days	Omentum greatly thickened and caseated. Caseous nodules on caecum, mesentery, and diaphragm. Lungs closely filled with caseating tubercles. Tubercles in spleen and kidneys.
1694	February 21, 1908	·2 cc.	Killed 74 days	No tuberculosis.

GUINEA-PIGS INOCULATED INTRAPERITONEALLY WITH THE MILK OF COW D.

Number.	Date of Inoculation.	Dose.	Quarter of Udder.	Duration of Life.	Result.
3013	February 20, 1908	6·0 cc. plus the deposit 24·0 cc. obtained by the centrifuge.	R.F.	Died 26 days	Whitish tubercle in omentum containing moderately numerous acid fast bacilli. No tuberculosis elsewhere.
3014			R.H.	Died 21 days	No tuberculosis.
3015			L.F.	Killed 62 days	No tuberculosis.
3016			L.H.	Killed 62 days	No tuberculosis.
3037	February 24, 1908	do.	R.F.	Killed 35 days	No tuberculosis.
3038			R.F.	Killed 67 days	No tuberculosis.
3039			R.H.	Killed 35 days	No tuberculosis.
3040			R.H.	Killed 67 days	No tuberculosis.
3041			L.F.	Killed 58 days	No tuberculosis.
3042			L.F.	Killed 67 days	No tuberculosis.
3043			L.H.	Killed 58 days	No tuberculosis.
3044			L.H.	Killed 67 days	No tuberculosis.
3045	February 25, 1908	do.	R.F.	Died 2 days	No tuberculosis.
3046			R.F.	Died 62 days	Two translucent foci in omentum. No tuberculosis elsewhere.
3047			R.H.	Died 1 day	No tuberculosis.
3048			R.H.	Killed 66 days	No tuberculosis.
3049			L.F.	Killed 58 days	One translucent miliary nodule in the ligament of liver. No tuberculosis else.
3050			L.F.	Killed 66 days	No tuberculosis.
3051			L.H.	Died 58 days	Three tubercles in omentum; no T.B. No tuberculosis elsewhere.
3052			L.H.	Died 42 days	No tuberculosis.

GUINEA-PIGS INOCULATED INTRAPERITONEALLY WITH THE MILK OF COW D—*continued.*

Number.	Date of Inoculation.	Dose.	Quarter of Udder.	Duration of Life.	Result.
3087	March 13, 1908	60·0 cc. plus the deposit 24·0 cc. obtained by the centrifuge.	R.F.	Killed 50 days	No tuberculosis.
3088			R.F.	Died 6 days	No tuberculosis.
3089			R.H.	Killed 42 days	Two tubercles in omentum and two on peritoneum containing acid fast bacilli. No tuberculosis elsewhere.
3090			R.H.	Killed 50 days	No tuberculosis.
3091			L.F.	Killed 42 days	One yellowish nodule in omentum and one on liver containing acid fast bacilli. No tuberculosis elsewhere.
3092			L.F.	Killed 50 days	No tuberculosis.
3093			L.H.	Killed 43 days	No tuberculosis.
3094			L.H.	Killed 50 days	No tuberculosis.
3095	March 14, 1908	do.	R.F.	Killed 55 days	No tuberculosis.
3096			R.F.	Killed 55 days	No tuberculosis.
3097			R.H.	Died 29 days	Three translucent foci in the omentum. No tuberculosis elsewhere.
3098			R.H.	Killed 55 days	No tuberculosis.
3099			L.F.	Killed 55 days	No tuberculosis.
3100			L.F.	Killed 55 days	In omentum there was a yellowish miliary nodule containing soft caseous substance. Smear showed a few acid fast bacilli.
3101			L.H.	Killed 55 days	In omentum two similar but smaller nodules. Smear showed small acid fast bacilli.
3102			L.H.	Killed 55 days	Four similar bodies in omentum. Smear showed doubtful acid fast bacilli.
3103	March 16, 1908	do.	R.F.	Died 39 days	No tuberculosis.
3104			R.F.	Killed 47 days	No tuberculosis.
3105			R.H.	Killed 39 days	No tuberculosis.
3106			R.H.	Killed 47 days	No tuberculosis.
3107			L.F.	Killed 47 days	No tuberculosis.
3108			L.F.	Died 10 days	Three minute whitish tubercles in omentum containing acid fast bacilli. No tuberculosis elsewhere.
3109			L.H.	Died 39 days	No tuberculosis.
3110			L.H.	Killed 47 days	No tuberculosis.
3111	March 17, 1908	do.	R.F.	Killed 38 days	Purulent nodule in subcutaneous tissue showed no acid fast bacilli. No tuberculosis elsewhere.
3112			R.F.	Killed 42 days	No tuberculosis.
3113			R.H.	Killed 38 days	Purulent nodule in subcutaneous tissue containing numerous acid fast bacilli. No tuberculosis elsewhere.
3114			R.H.	Killed 42 days	No tuberculosis.
3115			L.F.	Killed 38 days	No tuberculosis.
3116			L.F.	Killed 42 days	No tuberculosis.
3117			L.H.	Killed 38 days	No tuberculosis.
3118			L.H.	Killed 42 days	In omentum three minute grey tubercles. No acid fast bacilli.
3125	March 23, 1908	do.	R.F.	Killed 43 days	No tuberculosis.
3126			R.F.	Died 6 days	No tuberculosis.
3127			R.H.	Died 1 day	No tuberculosis.
3128			R.H.	Killed 43 days	No tuberculosis.
3129			L.F.	Killed 32 days	No tuberculosis.
3130			L.F.	Killed 43 days	No tuberculosis.
3131			L.H.	Killed 43 days	No tuberculosis.
3132			L.H.	Died 27 days	No tuberculosis.

COW E.

POST-MORTEM EXAMINATION.

General Condition.—Good.

Thorax.

Pleura.—Normal.

Lungs.—In the right lung in close proximity to each other there were three loculated cystic nodules, the largest the size of a robin's egg; they were lined by reddish grey granulation tissue, and several of the small spaces in them contained a little muco-pus.

Thoracic Lymphatic Glands.—A left bronchial gland contained a soft grey nodule the size of a millet seed.

The long mediastinal gland contained 30 to 40 nodules varying up to a pea in size; they were yellowish caseo-calcareous and easily shelled out of the gland substance, leaving smooth walled cavities.

Abdomen.

Intestines.—Normal.

Gastric, Mesenteric, and Colic Glands.—Normal.

Spleen.—Normal.

Liver.—In the liver were sparsely scattered, irregular yellowish grey submiliary nodules situated just beneath the surface only; they were different from tuberculous nodules in appearance.

Portal Glands.—Normal.

Kidneys.—In the kidneys there were visible on the surface several pale grey patches of tissue which on section extended through the pyramids.

Suprarenal Bodies.—In a suprarenal body just beneath the cortex there was a yellowish grey nodule the size of a rape seed.

Abdominal Lymphatic Glands.

Renal, Lumbar, Coeliac, and Iliac Glands appeared normal.

Tongue, Tonsils, Larynx, and Pharynx.—Normal.

Uterus.—The uterus was pregnant and contained a foetus of about six months; the uterus, placenta, and foetus were normal.

Various Lymphatic Glands.

Submaxillary, Pharyngeal, Cervical, Prescapular, Axillary, Precrural, Gluteal, Ischiatic, and Popliteal Glands.—Normal.

Udder and Supramammary Lymphatic Glands.—Normal.

Microscopical Examinations.

(Smear preparations.)

Suprarenal (nodule).—Two tubercle bacilli.
Bronchial Gland (nodule).—No tubercle bacilli.
Lung (Cyst I and II).—No tubercle bacilli.
Liver (nodule).—No tubercle bacilli.
Kidney (grey patch).—No tubercle bacilli.
Mediastinal Gland (I and II).—No tubercle bacilli.

GUINEA-PIGS INOCULATED INTRAPERITONEALLY WITH THE FAECES OF COW E.

Number.	Date of Inoculation.	Dose.	Duration of Life.	Result.
3020	February 20, 1908	·05 cc.	Killed 62 days	No tuberculosis.
3021		·05 cc.	Killed 62 days	No tuberculosis.
3022		·05 cc.	Died 18 days	No tuberculosis.
3065	February 26, 1908	·05 cc.	Killed 57 days	No tuberculosis.
3066		·05 cc.	Died 2 days	No tuberculosis.
3067		·05 cc.	Died 1 day	No tuberculosis.
3068		·05 cc.	Died 1 day	No tuberculosis.
3081	March 13, 1908	·05 cc.	Killed 50 days	No tuberculosis.
3082		·05 cc.	Died 39 days	No tuberculosis.
3083		·05 cc.	Killed 50 days	No tuberculosis.
3084		·05 cc.	Killed 50 days	No tuberculosis.
3085		·05 cc.	Killed 53 days	No tuberculosis.
3086		·05 cc.	Killed 53 days	No tuberculosis.
3119	March 18, 1908	·05 cc.	Killed 51 days	No tuberculosis.
3120		·05 cc.	Killed 51 days	No tuberculosis.
3121		·05 cc.	Killed 51 days	No tuberculosis.
3122		·05 cc.	Killed 56 days	No tuberculosis.
3123		·05 cc.	Killed 56 days	No tuberculosis.

GUINEA-PIGS INOCULATED INTRAPERITONEALLY WITH THE MILK OF COW E.

Number.	Date of Inoculation.	Dose of Milk.	Quarter of Udder.	Duration of Life.	Result.
3023	February 21, 1908	6·0 cc. plus the deposit of 24·0 cc. obtained by the centrifuge.	R.F.	Died 59 days	No tuberculosis.
3024			R.H.	Killed 61 days	A translucent focus in omentum which contained acid-fast bacilli. No tuberculosis elsewhere.
3025			L.F.	Died 40 days	No tuberculosis.
3026			L.H.	Killed 61 days	No tuberculosis.
3029	February 24, 1908	do.	R.F.	Died 32 days	No tuberculosis.
3030			R.F.	Killed 67 days	No tuberculosis.
3031			R.H.	Died 35 days	No tuberculosis.
3032			R.H.	Died 62 days	No tuberculosis.
3033			L.F.	Died 41 days	No tuberculosis.
3034			L.F.	Died 63 days	No tuberculosis.
3035			L.H.	Killed 58 days	No tuberculosis.
3036			L.H.	Killed 67 days	No tuberculosis.
3053	February 25, 1908	5·0 cc. plus the deposit of 10·0 cc.	R.F.	Killed 58 days	No tuberculosis.
3054			R.F.	Killed 66 days	No tuberculosis.
3055		12·0 cc. plus the deposit of 12·0 cc.	R.H.	Died 18 days	No tuberculosis.
3056			R.H.	Died 21 days	No tuberculosis.
3057		10·0 cc.	L.F.	Killed 58 days	No tuberculosis.
3058			L.F.	Killed 66 days	No tuberculosis.
3059		5·0 cc. plus the deposit of 10·0 cc.	L.H.	Died 23 days	No tuberculosis.
3060			L.H.	Died 11 days	Two minute whitish foci in the omentum; smear showed acid-fast bacilli. No tuberculosis elsewhere.
3061	February 26, 1908	6·0 cc.	R.F.	Died 29 days	No tuberculosis.
3062		10·0 cc.	R.H.	Killed 57 days	No tuberculosis.
3063		6·0 cc.	L.F.	Died 16 days	Opaque yellowish nodule in subcutaneous tissue (no A.F.B.). No tuberculosis elsewhere.
3064		9·0 cc.	L.H.	Died 33 days	No tuberculosis.
3069	February 27, 1908	4·0 cc.	R.F.	Killed 61 days	No tuberculosis.
3070		4·0 cc.	R.F.	Died 16 days	No tuberculosis.
3071		7·0 cc.	R.H.	Killed 56 days	No tuberculosis.
3072		7·0 cc.	R.H.	Killed 61 days	No tuberculosis.
3073		3·0 cc.	L.F.	Killed 56 days	No tuberculosis.
3074		3·0 cc.	L.F.	Killed 64 days	No tuberculosis.
3075		3·0 cc.	L.H.	Killed 56 days	No tuberculosis.
3076		3·0 cc.	L.H.	Killed 64 days	No tuberculosis.
3077	March 3, 1908	6·0 cc.	R.F.	Killed 60 days	No tuberculosis.
3078		10·0 cc.	R.H.	Killed 60 days	No tuberculosis.
3079		8·0 cc.	L.F.	Killed 60 days	No tuberculosis.
3080		4·0 cc.	L.H.	Killed 60 days	No tuberculosis.

RABBITS INOCULATED INTRAPERITONEALLY WITH THE MILK OF COW E.

Number.	Date of Inoculation.	Dose of Milk.	Quarter of Udder.	Duration of Life.	Result.
1683	February 21, 1908	6·0 cc. plus the deposit of 24·0 cc. obtained by the centrifuge.	R.F.	Killed 85 days	No tuberculosis.
1684			R.H.	Killed 85 days	No tuberculosis.
1685			L.F.	Killed 85 days	No tuberculosis.
1686			L.H.	Killed 85 days	No tuberculosis.

SWINE FED CONTINUOUSLY WITH THE MILK OF COW D AND COW E.

Number.	Cow.	Duration of Feeding and Dose.	Duration of Life.	Result.
254	D	9 days, 7 litres each	Killed 88 days	No tuberculosis.
256	D		Killed 88 days	No tuberculosis.
250	E	4 days, 65·0 cc. each	Killed 88 days	No tuberculosis.
252	E		Killed 88 days	No tuberculosis.

SWINE FED CONTINUOUSLY WITH THE FAECES OF COW D AND COW E.

Number.	Cow.	Duration of Feeding and Dose.	Duration of Life.	Result.
238	D	14 days, 27 kilogrammes to each.	Killed 79 days	No tuberculosis.
240	D		Killed 99 days	No tuberculosis.
242	E	14 days, 21 kilogrammes to each.	Killed 79 days	No tuberculosis.
244	E		Killed 101 days	No tuberculosis.

CONTROL ANIMALS TO EXPERIMENTS ON SWINE.

PIG 220.

Reserved as a control to the litter to which belonged Pigs 204, 206, 208, 210, 212, 214, 216 and 218. The length of life of the experimental animals in this litter after the commencement of the experiment varied from 63 to 100 days.

Tuberculin test: September 16th, 1907. Result: Negative.

Killed: December 30th, 1907. Four months under observation.

Post-mortem examination: The animal was found to be healthy, and showed no sign of tuberculosis.

PIG 232.

Reserved as a control to the litter to which belonged Pigs 222, 224, 226 and 230. The experimental animals in this litter lived from 48 to 86 days after the commencement of the experiment.

Tuberculin test: October 11th, 1907. Result: Negative.

Killed: December 30th, 1907. After three months under observation.

Post-mortem examination: The animal was found to be healthy and showed no sign of tuberculosis.

The third litter contained Pigs 238, 240, 242, 244, 250, 252, 254 and 256. No control was kept, but all the experimental animals were found to be quite healthy when killed.

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APPOINTED TO INQUIRE INTO THE RELATIONS OF

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REPORT AND APPENDIX.

Presented to both Houses of Parliament by Command of His Majesty.

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NEW ROYAL COMMISSION ON TUBERCULOSIS.

EDWARD R.

EDWARD THE SEVENTH, by the Grace of God of the United Kingdom of Great Britain and Ireland, King, Defender of the Faith, To

Our Trusty and Well-beloved Sir MICHAEL FOSTER, Knight Commander of Our most Honourable Order of the Bath, Doctor of Medicine, Fellow of the Royal Society, Professor of Physiology in Our University of Cambridge ;

Our Trusty and Well-beloved GERMAN SIMS WOODHEAD, Esquire, Doctor of Medicine, Professor of Pathology in Our University of Cambridge ;

Our Trusty and Well-beloved SIDNEY HARRIS COX MARTIN, Esquire, Doctor of Medicine, Fellow of the Royal Society, Professor of Pathology at University College, London ;

Our Trusty and Well-beloved JOHN MCFADYEAN, Esquire, Principal and Professor of Comparative Pathology and Bacteriology at the Royal Veterinary College ; And

Our Trusty and Well-beloved RUBERT WILLIAM BOYCE, Esquire, Professor of Pathology at University College, Liverpool.

GREETING :

Whereas We have deemed it expedient that a Commission should forthwith issue to inquire and report with respect to Tuberculosis :—

1. Whether the disease in animals and man is one and the same ;

2. Whether animals and man can be reciprocally infected with it ;

3. Under what conditions, if at all, the transmission of the disease from animals to man takes place, and what are the circumstances favourable or unfavourable to such transmission.

Now know ye, that We, reposing great trust and confidence in your knowledge and ability, have authorised and appointed, and do by these Presents authorise and appoint you, the said Sir Michael Foster, German Sims Woodhead, Sidney Harris Cox Martin, John McFadyean, and Rubert William Boyce, to be Our Commissioners for the purposes of the said inquiry.

And for the better effecting the purposes of this Our Commission We do by these Presents give and grant unto you, or any three or more of you, full power to call before you such persons as you shall judge likely to afford you any information upon the subject of this Our Commission ; and also to call for, have access to, and examine all such books, documents, registers, and records as may afford you the fullest information on the subject, and to inquire of and concerning the premises by all other lawful ways and means whatsoever.

And We do by these Presents authorise and empower you, or any three or more of you, to visit and personally inspect such places as you may deem it expedient so to inspect for the more effectual carrying out of the purposes aforesaid.

And We do further by these Presents will and ordain that this Our Commission shall continue in full force and virtue, and that you, Our said Commissioners, or any three or more of you, may from time to time proceed in the execution thereof, and of every matter and thing therein contained, although the same be not continued from time to time by adjournment.

And We do further ordain that you, or any three or more of you, have liberty

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to report your proceedings under this Our Commission from time to time if you shall judge it expedient so to do.

And Our further Will and Pleasure is that you do, with as little delay as possible, report to Us under your hands and seals, or under the hands and seals of any three or more of you, your opinion upon the matters herein submitted for your consideration.

Given at Our Court at St. James's the Thirty-first day of August, 1901 ; in the first Year of Our Reign.

By His Majesty's Command.

CHARLES RITCHIE.

EDWARD R. & I.

EDWARD THE SEVENTH, by the Grace of God, of the United Kingdom of Great Britain and Ireland and of the British Dominions beyond the Seas King, Defender of the Faith, To

Our Trusty and Well-beloved WILLIAM HENRY POWER, Esquire, Companion of Our most Honourable Order of the Bath, Fellow of the Royal Society, Medical Officer of the Local Government Board,

GREETING :

Whereas by Warrant under Our Royal Sign Manual, bearing date the Thirty-first day of August, one thousand nine hundred and one, We were pleased to appoint Commissioners to inquire and report with respect to Tuberculosis, and to authorize the late Sir Michael Foster to act as Chairman of the Commission :

And whereas the Chairmanship of the Commission is at this present void.

Now know ye that We, reposing great trust and confidence in your knowledge and ability, have authorized and appointed, and by these Presents authorize and appoint you, the said William Henry Power, to be Chairman of the said Commission in the room of the said Sir Michael Foster, deceased.

Given at Our Court at Saint James's the Eighteenth day of March, 1907 ; in the seventh Year of Our Reign.

By His Majesty's Command.

H. J. GLADSTONE.

GEORGE, R.I.

GEORGE THE FIFTH, by the Grace of God, of the United Kingdom of Great Britain and Ireland and of the British Dominions beyond the Seas King, Defender of the Faith, to all to whom these Presents shall come,

Greeting :

Whereas it pleased His late Majesty from time to time to issue Royal Commissions of Enquiry for various purposes therein specified :

And whereas, in the case of certain of these Commissions, namely, those known as—

* * * * *

The Tuberculosis Commission,

* * * * *

the Commissioners appointed by His late Majesty, or such of them as were then acting as Commissioners, were at the late Demise of the Crown still engaged upon the business entrusted to them :

And whereas We deem it expedient that the said Commissioners should continue their labours in connection with the said enquiries notwithstanding the late Demise of the Crown :

Now know ye that We, reposing great trust and confidence in the zeal, discretion and ability of the present members of each of the said Commissions, do by these Presents authorise them to continue their labours, and do hereby in every essential particular ratify and confirm the terms of the said several Commissions.

And We do further ordain that the said Commissioners do report to Us under their hands and seals, or under the hands and seals of such of their number as may be specified in the said Commissions respectively, their opinion upon the matters presented for their consideration ; and that any proceedings which they or any of them may have taken under and in pursuance of the said Commissioners since the late Demise of the Crown and before the issue of these Presents shall be deemed and adjudged to have been taken under and in virtue of this our Commission.

Given at Our Court at *Saint James's*, the twenty-sixth day of *May*, one thousand nine hundred and ten, in the first year of our Reign.

By His Majesty's Command.

R. B. HALDANE.

CONTENTS.

REPORT.

To the King's Most Excellent Majesty.

May it please your Majesty,

We, your Majesty's Commissioners, appointed to inquire and report with respect to Tuberculosis :—

1. Whether the disease in animals and man is one and the same ;

2. Whether animals and man can be reciprocally infected with it ;

3. Under what conditions, if at all, the transmission of the disease from animals to man takes place, and what are the circumstances favourable or unfavourable to such transmission ;

humbly submit the following Final Report containing an account of the investigation we have carried out in accordance with the terms of our Reference and setting forth certain conclusions we have based on the results of our researches.

1. Three previous Reports have been issued by us. In the first (1904) the results of our preliminary investigations were discussed, and it was shown that the bacilli found in the lesions of certain cases of human tuberculosis produced in cattle a disease indistinguishable from bovine tuberculosis.

In our Second Interim Report (1907) we dealt at some length with bovine and human tuberculosis and embodied in it the results obtained up to that date in the investigation of the characters of the bacillus of bovine tuberculosis and of the bacilli found in cases of human tuberculosis.

In the Third Interim Report (1909) we dealt with certain conditions of the tuberculous cow which rendered her milk infective.

Since the second Report was presented we have continued our investigations into tuberculous disease of man and of the ox, and have also studied the tuberculosis which occurs in pigs, horses, some other mammals and birds. In this our final Report we propose to deal with the whole of our inquiry into the tuberculosis of all these various animals.

2. Our investigation has included the isolation of the bacilli from the lesions of the natural disease, the investigation of the cultural characters of the bacilli isolated and the study of their effects when introduced into different animals in varying doses and by several methods.

The species of animals used in this study have been cattle, rabbits, guinea-pigs, pigs, goats, chimpanzees, monkeys, horses, rats, mice, dogs, cats and birds. The experimental methods of infection employed have been subcutaneous, intravenous and intraperitoneal inoculation, and feeding. We have not attempted to infect by means of inhalation.

The experimental method of investigation we have adopted was essential in order to compare the characters of the bacilli isolated from the tuberculous lesions in different species of animals ; without it we should not have been able to give any answer to the questions referred to us.

We have necessarily made ourselves acquainted with the results published from time to time by others engaged in the study and experimental investigation of tuberculosis, but the conclusions arrived at in this Report are based solely on our own researches.

SECTION I.

Three Types of Tubercle Bacilli.

3. For purposes of description it is advantageous to distinguish three types of tubercle bacilli, recognisable by their individual characters. These are the human, bovine and avian types. The human type, although so named, is not the only one found in cases of tuberculosis in man. It is the organism present in the majority of such cases, but in some cases of the human disease the bacilli present are of the bovine type, and in others the bacilli have special characters distinguishing them from each of the three principal types. In natural cases of

tuberculosis in cattle the only type of bacillus present is the bovine type.* Similarly, in cases of natural tuberculosis occurring in poultry the bacillus belongs to the avian type.

The relationship between these three types of tubercle bacilli will be the subject of discussion in Section IX. At present only the individual characters of the three types will be described.

A.—The Bovine Tubercle Bacillus.

4. It will be convenient to take the bacillus of bovine tuberculosis as a standard for comparison with the bacilli found in the tuberculosis of other animals. The characters and properties of this bacillus have already been discussed in the Second Interim Report (2nd Int. Rep., page 6 *et seq.*) and it is unnecessary here to repeat many of the facts there recorded. But a summary of its behaviour will facilitate comparisons to be instituted between it and the bacilli of the tuberculous lesions of animals other than the bovine.

(a) *Cultural Characters.*—The bovine tubercle bacillus grows slowly on serum and at the end of two to three weeks shows on the surface of the medium a thin greyish uniform growth, not wrinkled and not pigmented.

2nd Int. Rep. p. 24.

In our Second Interim Report we divided the bovine tubercle bacillus into three grades or classes (I, II and III) according to the rate and luxuriance of its growth on glycerin media, Grade I growing the least and Grade III growing the most luxuriantly. We see no reason to alter this classification, but would insist from our further observations that this rate and kind of growth should not be taken as the sole basis of identification of the bacillus of bovine tuberculosis. The characters of the growth have to be considered in relation with the results of the inoculation of the bacillus before it can be stated that a particular tubercle bacillus is or is not a bovine tubercle bacillus.

2nd Int. Rep. Appendix, Vol. I.

(b) *Effects on Animals.*—The bovine tubercle bacillus produces characteristic effects when inoculated in certain doses into calves and rabbits, and it is these effects, taken with its mode of growth in artificial cultivation, that enable it to be recognised as such.

In calves the subcutaneous injection under the skin of the neck of 50 milligrammes of a culture of bovine tubercle bacilli not older than three weeks produces generalised tuberculosis starting from the point of inoculation and ending fatally usually within eight weeks. The nature of the acute disease produced has already been described in our Second Interim Report, and this statement may now be repeated (2nd Int. Rep., p. 7) :—

> "The local lesion is a mass of caseous tubercle, infiltrating the adjoining skin and muscle, and sometimes forming an abscess. The prescapular gland is a mass of caseous tubercle as is also the prepectoral gland, and as are also to a less but variable extent the thoracic and mediastinal glands. Tubercles more or less caseous are found in very many, sometimes in all, the other lymphatic glands. The lungs, spleen, liver, and also the kidneys are studded with tubercles, many of them caseous. Tubercles are found in the pleura, on the omentum, on the peritoneal surface, and in the intestinal walls."

The injection of this dose of the bovine tubercle bacillus causes severe general tuberculosis in the calf, and it is the result in this sense which we have taken as a standard of virulence for comparison with that of the other bacilli investigated.

It is true, as stated in our Second Interim Report (2nd Int. Rep., pp. 7 and 8), that definite tuberculosis may be produced in the calf by a much smaller dose than 50 milligrammes of culture of bovine tubercle bacilli. Some degree of tuberculosis has resulted in this animal from injection of so small an amount as 0·02 milligramme, while a dose no larger than 5 milligrammes has sufficed to cause generalised tuberculosis. This however, does not affect the statement already made as to the result produced by 50 milligrammes of culture.

In rabbits generalised tuberculosis ending in death within five weeks resulted from the intravenous inoculation of 0·01 or 0·1 of a milligramme of culture of bovine tubercle bacilli. With intraperitoneal injection in doses of 0·1 and 1 milligramme the duration of life was from 13 to 48 days, and 10 to 38 days, according to the dose, but with subcutaneous inoculation of doses of 10 milligrammes and

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* In a calf inoculated subcutaneously with bacilli of the human type (H 79 JN), the avian bacillus was found in a nodule in a mesenteric gland. (Appendix Vol. I Calf *1225*, p. 375.)

1 milligramme the duration of life was longer—28 to 101 days, and 29 to 165 days, according to the dose.

The disease caused in rabbits by intravenous injection is characterised by extensive miliary tuberculosis of the lungs, liver, spleen and kidneys, and other parts of the body. Intraperitoneal inoculation causes extensive tuberculosis of the peritoneum and abdominal lymphatic glands, extending afterwards into the internal organs. From subcutaneous inoculation there results a local lesion with tuberculosis of the neighbouring lymphatic glands, the lymphatic glands of the body, and the internal organs, especially the lungs and kidneys.

The results produced by injecting the bovine tubercle bacillus into calves and rabbits in the above doses are thus very striking and definite, and taken with the cultural characters of the bacillus afford a trustworthy means of recognising the bovine tubercle bacillus. Indeed, as our investigation progressed we found that it was sufficient to inoculate rabbits for differential diagnosis; for if an undetermined culture produces severe generalised disease in the rabbit within the period mentioned and by the doses referred to, administered in the various manners described, the same culture should produce an acute tuberculosis in the calf in doses of 50 milligrammes of culture subcutaneously inoculated. (*See* page 6.)

Other properties of the bovine tubercle bacillus may be mentioned. It invariably produces acute tuberculosis in the chimpanzee, monkey and guinea-pig, by subcutaneous inoculation in very small doses. In the goat, pig and cat generalised tuberculosis is also readily induced by it. Indeed, the results of an adequate dose in the goat, pig and cat have an equal value with those obtained in calves and rabbits in differentiating the bovine tubercle bacillus from the tubercle bacillus found in other kinds of tuberculosis. The rat and mouse are highly resistant to the subcutaneous inoculation of the bovine tubercle bacillus, but after intraperitoneal inoculation the tendency is for the bacillus to multiply in the body and to be present in large numbers in the organs, even in the blood, without causing the formation of tuberculous lesions such as are produced in animals susceptible to the bovine tubercle bacillus. The dog is highly resistant to the subcutaneous inoculation of the bovine tubercle bacillus but may succumb to general tuberculosis when large doses are inoculated intravenously or intraperitoneally.

In the fowl, the bovine tubercle bacillus injected intravenously causes death in about half the number of cases, usually with wasting of the bird, oedema of the lungs and pallor of the liver. In some cases the lungs show definite tubercles and the liver shows minute necrotic areas. Death is apparently caused by the toxic effect of the bacilli, as dead tubercle bacilli intravenously injected will produce the same effects as living. When injected intraperitoneally or intramuscularly, even in large doses, bovine bacilli produce in fowls only a local lesion, without dissemination of the disease.

In our experiments with horses the bovine tubercle bacillus in moderate doses did not produce progressive tuberculosis by subcutaneous inoculation or by feeding; given intravenously in a dose of 10 milligrammes, it caused the death of the animal from acute tuberculosis in 20 days.

Stability in Culture.—We have not found that the bovine tubercle bacillus diminishes in virulence to any great extent when subcultured for long periods—in one instance for as long as 1487 days. Appendix, Vol. IV., pp. 391 & 434.

B.—Bacillus from certain cases of Tuberculosis in the Human Body.

The Human Tubercle Bacillus.

5. In our Second Interim Report (2nd Int. Rep., p. 14) we described the tubercle bacilli which we had found in cases of human tuberculosis and divided them into Groups (I, II, and III). Those belonging to Group I were proved to be identical with the bovine tubercle bacillus. The features of the bacilli of Group III were discussed, but final conclusions were not drawn by us regarding the significance of the somewhat anomalous results obtained. The bacilli of Group II had, however, definite characters and were obtained from the larger number of cases of human tuberculosis. This is the type of bacillus we have agreed to call the *human tubercle bacillus*, as it is the bacillus found in the majority of cases of human tuberculosis. What we stated in our Second Interim Report regarding this bacillus is confirmed by our further investigations. The chief characters of the bacillus are as follows:— Appendix, Vol. I. Appendix, 2nd Int. Rep. Vol. II.

(a) *Cultural Characters.*—The human tubercle bacillus grows more rapidly 2nd Int. Rep., page 26

than the bovine tubercle bacillus on serum, hence we have called it eugonic in contrast to the bovine bacillus, which is dysgonic. The growth tends to become wrinkled on glycerinated media, and becomes pigmented to a greater or less extent on all media.

(b) *Effects on Animals.*—It is in still greater contrast with the bovine tubercle bacillus when it is subjected to inoculation tests under the same conditions.

In calves, a subcutaneous inoculation of 50 milligrammes of a culture under three weeks old does not produce progressive tuberculosis in the animal, nor does it kill it. In the majority of instances the inoculation results in the formation of a local lesion, a larger or smaller mass, which may become a cyst, surrounded by a fibrous capsule: the lesion is thus retrogressive and localised. Lesions in the internal organs may occur, but these consist mainly of caseous or calcareous nodules in the lymphatic glands nearest the seat of inoculation, or of a few calcareous tubercles in various internal organs. In about half the number of experiments performed with this bacillus in 50 milligramme doses on calves, tuberculous lesions did not extend beyond the nearest glands, no lesions being found in the spleen, liver, or kidneys. It is quite clear therefore that the human tubercle bacillus possesses a much lower virulence for the calf than the bovine tubercle bacillus.

When inoculated into rabbits the contrast is also as a rule well-marked, so that, as previously stated, subject to certain precautions the rabbit test can be taken as a measure of virulence for calves; that is, if a bacillus is found slightly virulent for the rabbit it will be found slightly virulent also for the calf.

When the bovine tubercle bacillus is intravenously inoculated into rabbits in doses of 0·01 milligramme or 0·1 milligramme death occurs from acute and generalised tuberculosis within five weeks. With the human tubercle bacillus intravenously inoculated in doses of 0·1 to 1 milligramme, although the animals sometimes died in under 20 days, the majority lived for three months. Some died of tuberculosis of a chronic kind. The lungs may be free from lesions or may show only scattered grey fibrous or calcareous tubercles, or there may be fibrous nodules containing a little caseous matter. The kidneys usually show a few grey or caseous miliary tubercles. Besides the lungs and the kidneys, one or two glands are the only other parts usually affected. The liver and spleen are rarely tuberculous, but the eyes, genital organs, bones and joints, are sometimes diseased. This slowly progressive disease with limited lesions induced by intravenous injection of the human bacillus is in strong contrast with the acute generalised tuberculosis ending fatally within five weeks which results in the rabbit from the injection of similar doses of the bovine tubercle bacillus. When the bovine tubercle bacillus is injected into the peritoneal cavity of the rabbit the duration of life with a dose of 1 milligramme was 10 to 38 days; in the case of the human tubercle bacillus injected in doses of 1 milligramme the animals had survived for over three months before they were killed. After subcutaneous inoculation of the bovine bacillus in doses of 1 to 10 milligrammes the duration of life of the rabbit was from 28 to 65 days; with the human tubercle bacillus in doses of 1 to 100 milligrammes inoculated in the same way the animals survived or were killed in 94 to 725 days. Intraperitoneally and subcutaneously injected into rabbits the human tubercle bacillus produces lesions which are scattered, or localised and retrogressive.

Appendix, Vol. I, p. 38.

The above statement may be taken as generally correct. It has however been noted by Dr. A. Stanley Griffith that in certain cases intravenous inoculation of 1 milligramme or 0·1 milligramme of a culture of the human tubercle bacillus produced in rabbits an acute and rapidly fatal tuberculosis indistinguishable from that which was caused by the bovine tubercle bacillus, but that death from tuberculosis never occurred within three months when 0·01 milligramme was used as a dose, whereas such a dose of the bovine tubercle bacillus invariably produced a rapidly fatal tuberculosis in the rabbit. Dr. Griffith would therefore conclude that for the purposes of distinguishing between the bovine tubercle bacillus and the human tubercle bacillus by means of intravenous inoculation in the rabbit a dose of 0·01 milligramme should be used. With subcutaneous inoculation it was found that a dose of 10 milligrammes or more was a suitable one for the purposes of differential diagnosis. Such a dose of the bovine tubercle bacillus causes the death of the rabbit from acute generalised tuberculosis in 28 to 101 days, whereas with the human tubercle bacillus death does not occur from tuberculosis, and the animals have been killed in periods varying from 94 to 725 days.

The goat and the pig are not to any great extent affected by the human tubercle bacillus. In both animals the inoculation of this bacillus leads only to a slight retrogressive tuberculosis. Pigs perhaps are slightly more susceptible than calves. Acute tuberculosis is produced in the chimpanzee, monkey and guinea-pig by the human tubercle bacillus. The effect in the chimpanzee and monkey is similar to that which follows inoculation of like doses of the bovine tubercle bacillus. In the guinea-pig, however, the average duration of life is longer when the human tubercle bacillus is inoculated than after inoculation with the bovine tubercle bacillus. In the rat and mouse injected intraperitoneally with large doses of the human tubercle bacillus the bacilli become disseminated over the body, multiply in the tissues and cause death without producing characteristic tuberculous lesions. In the dog the human tubercle bacillus behaves like the bovine tubercle bacillus, that is, the animal is highly resistant to subcutaneous inoculation, but may die of generalised tuberculosis after intravenous or intraperitoneal inoculation of large doses.

The cat is resistant to the human tubercle bacillus when this is given subcutaneously, intraperitoneally, intramuscularly or by feeding. A few tuberculous lesions have been produced by intraperitoneal inoculation, but these were not widely distributed and did not affect the health of the animal.

In the fowl the effect of the human tubercle bacillus is similar to that of the bovine bacillus. In one experiment in a horse, the subcutaneous injection of 50 milligrammes produced only local disease.

Thus the human tubercle bacillus is distinguished from the bovine tubercle bacillus by its more ready growth on artificial media and by the results of its inoculation into rabbits, calves, cats, pigs and goats.

But both the bovine tubercle bacillus and the human tubercle bacillus are alike in that they readily produce tuberculosis in chimpanzees, monkeys and guinea-pigs, and in the circumstance that the lesions produced in these animals are the same in distribution and structure.

Stability in Culture.—The human tubercle bacillus has not shown any alteration in cultural characters on prolonged subcultivation.

C.—The Bacillus of Avian Tuberculosis.

6. Avian tuberculosis, as it occurs naturally in birds, is discussed in a separate section (VII). In this place an account is given of the characters and properties of the avian tubercle bacillus as exhibited under experimental conditions for comparison with those of the bovine tubercle bacillus and the human tubercle bacillus.

Appendix, Vol. IV, p. 167.

(a) *Cultural Characters.*—The avian tubercle bacillus forms a slimy whitish growth, which is easily emulsified, thus contrasting with the growth of bovine and human tubercle bacilli. It grows especially well on glycerinated media.

(b) *Effects on Animals.*—The results of the inoculation of the avian tubercle bacillus into animals are in marked contrast with those obtained from inoculation of the bovine and the human tubercle bacillus.

Fowls are very susceptible to the action of the avian tubercle bacillus by intravenous, subcutaneous, and intramuscular inoculation, and by feeding. After inoculation there are tuberculous lesions in the spleen and liver, and frequently in the lungs, cervical glands, muscles, and bones. After feeding, the distribution of the lesions is the same, with the exception that characteristic tuberculous lesions are produced in the mucous membrane of the intestines.

The lesions produced by the avian tubercle bacillus in parrots do not differ from those produced in fowls ; but the avian bacillus, when introduced by feeding, does not cause lesions in the intestines of parrots so constantly as in fowls. Parrots are susceptible to the action of both the bovine and human tubercle bacillus, and when either of these is given by inoculation or by feeding the lesions set up are similar to those produced by the avian bacillus, the bovine tubercle bacillus being apparently more virulent for these birds than either the human or the avian tubercle bacillus.

The rabbit and mouse are the only two mammals in which the avian tubercle bacillus causes progressive tuberculosis.

In certain respects the results produced in the rabbit by the avian tubercle bacillus differ from those induced by bovine and by human tubercle bacilli. Moderately large doses of the avian bacillus, though fatal by inoculation to the rabbit, are less virulent than the bovine, but more virulent than the human tubercle bacillus.

It is, however, in the distribution of the lesions that the disease induced in the rabbit by the avian tubercle bacillus differs most markedly from the disease set up in this animal by either of the other two types of tubercle bacilli.

Intravenous inoculation of moderately large doses (1–10 milligrammes) leads to speedy death, with great multiplication of the bacilli in the organs, the only visible changes in which are general pallor with slight oedema of the lungs, and slight enlargement, with tubercles, of the spleen. If, however, the animal lives four or five weeks, the spleen is greatly enlarged owing to the formation of tubercles ; and these are seen also in the liver and to a less extent in the lungs. With a very small dose (·001 milligramme) the disease is very chronic and resembles the disease following subcutaneous inoculation, the joints being affected.

The disease set up in rabbits by subcutaneous inoculation of the avian bacillus in doses ranging from 50 milligrammes to a fraction of a milligramme is very chronic, and the distribution of the lesions is practically the same, irrespective of size of dose. Besides the local lesion the nearest lymphatic glands are implicated ; the liver and spleen are but rarely affected, while the amount of disease in the kidneys varies. The lungs are slightly oedematous and a few nodules may be seen on the surface. Caseating tubercles are seen in the areolar tissues and in a few of the lymphatic glands and in the testes. But the most characteristic and most commonly occurring lesion is a tuberculosis of the joints of the limbs which runs a chronic course. Joint tuberculosis may occasionally occur in the rabbit after intravenous inoculation with the human tubercle bacillus, but has not been observed after subcutaneous inoculation. It may, however, follow subcutaneous inoculation of the bovine bacillus, when the animal survives for a long period.

The distribution of the lesions in the chronic form of the disease in the rabbit therefore differs strikingly from that produced by the bovine and human tubercle bacillus.

Rabbits infected by feeding with the avian bacillus exhibit, besides the local lesion in the intestinal tract, a distribution of the lesions similar to that following subcutaneous inoculation. Intraperitoneal inoculation produces a tuberculosis similar to that following intravenous inoculation, the disease, however, being less acute.

In the mouse, a generalised tuberculosis is produced by the avian bacillus, whether this is inoculated subcutaneously or intraperitoneally or is given by feeding.

The calf, pig, monkey, guinea-pig, horse, cat, and rat behave alike to the avian bacillus, which in them never produces a progressive tuberculosis, though it sometimes multiplies in the body and becomes disseminated in the tissues and may kill if a large dose is given intravenously. The adult goat reacts similarly, resisting subcutaneous inoculation and feeding, although it succumbs to the effects of intravenous injection of the bacilli. Young goats are rather more susceptible than adults. The chimpanzee, in the single experiment performed, was found to resist a large dose (50 milligrammes of culture) of the bacillus injected subcutaneously and no tuberculous lesion was found when the animal died three years afterwards. In the dog, large doses injected intravenously produce no effects.

Appendix, Vol. IV., p. 178.

Vitality in Culture.—The bacillus was found alive in culture after 1067 days.

Chemical Properties of the Three Types of Tubercle Bacilli.

Appendix, Vol. VI.

7. With a view to obtaining further data for differentiating tubercle bacilli of the several types, Dr. Harden undertook, as stated in our Second Interim Report, an investigation with the object of ascertaining what differences, if any, existed between them that could be detected by chemical means. This investigation, carried out by him with the assistance of Mr. Stanley Walpole at the Lister Institute, occupied a considerable time ; the results are set out in Dr. Harden's Report, containing full details of his experiments, which forms a separate volume of our Appendix.

For the purpose of this Section it is sufficient for us to state that although certain minor points in which tubercle bacilli of one type differed slightly but not always uniformly from those of another were noted, such differences appeared to be due rather to the amount and rapidity of growth in artificial culture than to any fundamental differences in the chemical properties of the bacilli themselves.

Dr. Harden was unable to detect any definite and constant bio-chemical character by which tubercle bacilli of one type can be differentiated from those of another.

SECTION II.

Bovine Tuberculosis.

8. In our Second Interim Report the investigation of 30 cases of bovine tuberculosis was recorded. No further special investigation of cases of bovine tuberculosis has been made as the results already obtained were definite. Only one form or type of tubercle bacillus was found in these cases, the bacillus having the cultural and pathogenic characters repeated in detail in our present Report.

SECTION III.

Human Tuberculosis.

9. In our Second Interim Report the results obtained in the investigation of the bacilli isolated from 56 cases of human tuberculosis were recorded, as also the results of the investigation of the infectivity of mixed sputum. Other cases have since been investigated, and these will now be discussed together with those previously recorded in our Second Interim Report. It will be convenient, for reasons which will presently appear, to discuss these cases under two headings : (a) Cases of Human Tuberculosis other than Lupus ; (b) Cases of Lupus.

Appendix, Vols. I & II.

2nd Int. Rep., Appendix. Vol. II.

Cases of Human Tuberculosis other than Lupus.

10. These cases, 108 in number, are arranged as regards the primary seat of disease as far as this could be ascertained. The results obtained are shown in the table on the following pages. The arrangement of the table differs from that used in our Second Interim Report, inasmuch as the viruses obtained from these different cases are now classified according as they are bovine, human, or mixed (bovine and human). The classification here given must be considered as embodying the final results of our investigation of the cases under consideration.

Appendix, Vol. I.

2nd Int. Rep., Appendix, Vol. II.

On comparing this Table with the details given in the Appendix an apparent discrepancy in the relative numbers will be found, and a brief explanation is therefore necessary. The total 108 is the number of individual cases of tuberculosis (other than Lupus) occurring in the human subject on which we have based our final conclusions, but it is not the total number of separate "viruses" of human tuberculosis examined by us and reported in the Appendix. Viruses H 2 and H 17 are not included in the Table because they did not represent individual cases but were viruses consisting of mixed sputum from a varying number of cases of human pulmonary tuberculosis ; they are, however, separately considered later in this Report. In the preface to Volume II of the Appendix to our Second Interim Report it was stated that a virus provisionally numbered H 60 had not been included in that Report as there appeared to be a possibility that the material might have been accidentally contaminated. Subsequent experience proved that this misgiving was without foundation, and the case is now included amongst the 108 in this Table. A few viruses included in the Appendix to the Second Interim Report are altogether omitted from further consideration. Of these, H 1, H 4, and H 6 were early experiments which appear now to have been incomplete. H 62 and H 147, viruses consisting of sputum from separate patients are omitted because precautions afterwards adopted in collecting sputum had not been taken. Another virus, H 150, is left out as no cultures were isolated. One case numbered Virus H 24 in the Appendix to our Second Interim Report, and certain others the details of which are summarised on page 18 of Volume I of our Appendix to this Report, are omitted from further consideration and not included in this Table because the material yielded no culture and failed to give rise to tuberculosis when injected into guinea-pigs.

CASES OF HUMAN TUBERCULOSIS OTHER THAN LUPUS.

(108 Cases.)

TABULAR SUMMARY OF RESULTS.

Nature of Case.	Part from which Experimental Material was obtained.	Bovine Viruses (Group I).	Human Viruses (Group II).	Mixed Viruses (Bovine and Human).
I.—(A) Primary Pulmonary Tuberculosis (14 Cases).	Lung ... ... / Thoracic Gland ...	—	H 22. "F.W."	
	Lung	—	H 23. "J.P."	
	"	—	H 25. "A.T."	
	Bronchial Gland ...	—	H 45. "F.M."	
	Lung	—	H 48. "W.P."	
	"	—	H 50. "P.H."	
	"	—	H 51. "H.M."	
	"	—	H 52. "T.F."	
	"	—	H 56. "F.T."	
	Lung ... ... / Cervical Gland ...	—	H 58. "F.G."	
	Lung	—	H 79. "J.N."	
	"	—	H 80. "D.M."	
	Lung ... .. / Spleen	—	H 81. "P.W."	
	Lung .. ... / Mesenteric Gland ...	—	H 104. "E.R."	
(B) Sputum from Individual Cases of Pulmonary Tuberculosis (28 Cases).	Culture from Sputum	H 127. "R.R." H 128. "D.D."	H 118–126 (9 Cases). H 129–145 (17 Cases).	
II.—General Tuberculosis (3 Cases).	Bronchial Glands...	—	H 35. "C.B."	
	Lung ... ... / Acne Spots... ...	—	H 93. "C.D."	
	Lung ... ... / Meninges ... ... / Bronchial Gland ...	—	H 78. "O.D."	
III.—Tuberculous Meningitis (3 Cases).	Meninges	—	H 86. "C.P."	
	Cerebro-spinal Fluid	—	H 98. "B.R."	
	" "	—	H 115. "N.G."	
IV.—Bronchial Gland Tuberculosis (5 Cases).	Bronchial Gland ...	—	H 21. "G.B."	
	Spleen	—	H 54. "C.W."	
	Mesenteric Glands / Meninges	—	H 61. "E.C."	
	Bronchial Glands and Spleen.	—	—	H 13. "A.D."
	Bronchial Gland ... / Meninges ... ... / Lung ... ... / Mesenteric Gland...	—	—	H 60. "W.B."
V.—Cervical Gland Tuberculosis (9 Cases).	Cervical Glands ...	H 28. "C.L." H 29. "M.F." H 31. "L.F."	H 27. "B.D." H 34. "C.U." H 37. "O.J." H 39. "M.B." H 44. "D.C."	
	Axillary Glands ...	—	H 33. "R.T."	

CASES OF HUMAN TUBERCULOSIS OTHER THAN LUPUS—*continued.*

Nature of Case.	Part from which Experimental Material was obtained.	Bovine Viruses (Group I).	Human Viruses (Group II).	Mixed Viruses (Bovine and Human).
VI.—Primary Abdominal Tuberculosis (29 Cases).	Mesenteric Glands	H 7. "C.M."	H 8. "S.C."	H 49. "T.C."
		H 10. "B.S."	H 12. "H.N."	
		H 14. "F.S."	H 18. "T.T."	
		H 19. "S.W."	H 55. "R.D."	
		H 20. "F.L."		
		H 65. "K.B."		
		H 88. "E.L."		
	Mesenteric and Bronchial Glands.	—	H 30. "E.M."	
	Mesenteric Glands Bronchial Glands ...	—	H 36. "M.D."	
	Cervical Gland ...	H 38. "J.M."		
	Mesenteric Glands Lung	—	H 57. "B.J."	
	Mesenteric Gland... Cervical Gland ... Brain	—	H 63. "G.R."	
	Mesenteric Gland... Lung ... ... Bronchial Gland ...	H 32. "Y.W."		
	Mesenteric Gland... Lung ... ... Cervical Gland ... Brain	H 59. "L.B."		
	Mesenteric Gland... Retro-peritoneal Gland.	—	—	H 90. "I.P."
	Mesenteric Gland... Meninges	H 64. "M.G."		
	Mesenteric Gland ... Meninges	H 69. "F.K."		
	Cervical Gland ... Mesenteric Gland ... Lung ... ... Bronchial Gland ...	—	H 70. "N.W."	
	Mesenteric Gland... Bronchial Gland ... Lung ... ... Spleen	—	H 74. "D.S."	
	Peritoneal Fluid ... Lung	—	H 75. "A.H."	
	Mesenteric Gland... Liver	H 77. "R.L."		
	Mesenteric Gland... Lung	—	H 82. "G.F."	
	Mesenteric Gland... Bronchial Gland ...	—	H 83. "G.C."	
	Mesenteric Gland... Lung	H 89. "W.I."		
VII.—Joint and Bone Tuberculosis (14 Cases).	Scrapings from Joints	—	H 9. "C.T."	*H 16. "J.H."
			H 11. "E.D."	
			H 15. "I.W."	
			H 41. "A.S."	
			H 42. "M.R."	
			H 43. "F.F."	
			H 46. "H.W."	
			H 47. "S.B."	
			H 76. "G.M."	
	Lumbar Abscess ...	—	H 66. "W.C."	
	Scapular Abscess ...	—	H 67. "E.P."	
	Sacral Abscess ...	—	H 68. "R.B."	
	Rib Abscess ...	—	H 72. "H.C."	
VIII.—Tuberculosis of Testicle. of Kidney. of Suprarenal. (1 case of each.)	Testicle	—	H 40. "J.G."	
	Kidney	—	H 26. "K.M."	
	Suprarenal	—	H 87. "W.D."	

* H 16. "J.H." is discussed in the text (p. 15).

11. *Cases of Pulmonary Tuberculosis.*—These fall into two series. In the first series (14 cases) a portion of the tuberculous lesion obtained at the post-mortem examination was used for investigation. In 13 of the cases this was the lung, in the other a bronchial gland only was used. In addition to the lung, a thoracic gland in one case, a cervical gland in a second case, a mesenteric gland in a third, and the spleen in a fourth, were investigated. These were clinically all cases of primary pulmonary tuberculosis, the disease which is commonly called consumption, in which the main and seemingly primary tuberculous lesion was in the lung, and in which death resulted from the pulmonary disease. In all these 14 cases the bacillus found was the human tubercle bacillus, and no evidence of the presence of the bovine tubercle bacillus was obtained.

Appendix, Vol. I, p. 8.

The second series of cases included those in which sputum alone was examined. The sputum from 28 cases was used. The patients were usually young adults, and each case was investigated separately. To meet the possibility of the sputum being mixed with bovine bacilli derived from milk or butter the following precautions were taken :—Twenty-four hours before the collection of the samples of sputum the teeth and gums of the patient were carefully cleansed, and the mouth washed out repeatedly. Subsequently the patient was not allowed to take any milk or milk product until after the sputum had been collected. It was received directly into sterilised wide-mouthed bottles, and was then sent for investigation. Guinea-pigs were inoculated with the sputum and cultures obtained from them. In two cases cultures were also obtained direct from the sputum.

As regards the patients themselves, nineteen were aged 16 to 25, eight were aged 26 to 33, and one was 50 years old. Twenty-six were males, and two females. In 8 cases the disease had lasted 12 months or less ; in 16 cases, from 1 to 3 years ; in one case, 4 years, in one 5, and in another 7, and one was of doubtful duration. The stage of the disease at which the sputum was collected was noted as far as could be detected by physical signs. In 12 cases there were signs of excavation of the lungs, or cavity formation, and in 16 cases there were signs of consolidation of the lungs on one or both sides, but with no signs of cavity formation. In no case could any evidence be found of disease except in the lungs.

The results of the investigation of these cases showed that the living tubercle bacilli present in the sputum in 26 cases were human, and in 2 cases were bovine. In none of the cases was there a mixture of bovine and human tubercle bacilli.

Appendix, Vol. I, p. 9.

The two cases which showed only bovine bacilli in the sputum deserve special notice. The cultures in these two cases grew like bovine bacilli on artificial media and gave rise to fatal generalised tuberculosis in both calves and rabbits. There was no evidence of the presence of eugonic human bacilli in the sputum. One examination in these cases was not considered sufficient. From one of the patients, H 127. "R.R." additional specimens of sputum were collected on three separate occasions at intervals of 76, 117, and 118 days after the collection of the first specimen. Cultures were obtained direct from the sputum. The investigation of these three specimens gave the same results as the first. The sputum yielded only bovine tubercle bacilli. From the other patient, H 128. "D.D." one additional specimen was obtained 118 days after the first. This, like the first, yielded only bovine tubercle bacilli, which were isolated from the sputum direct and produced fatal tuberculosis in calves and rabbits. These two cases were therefore definite cases of pulmonary tuberculosis caused by bovine tubercle bacilli, and as far as could be ascertained during life they were cases of primary pulmonary tuberculosis. In neither of the patients was there any evidence of tuberculous disease elsewhere, such as disease of the cervical glands or of the intestinal tract when the sputum was collected.*

12. In three cases of *general tuberculosis*, the primary lesion of which could not be determined, and in three cases of *tuberculous meningitis*, in which the meninges and cerebro-spinal fluid were used for investigation, the lesions yielded human tubercle bacilli only.

13. *Bronchial gland tuberculosis* :—Five cases were examined. Three of these yielded human tubercle bacilli. Two others, H 13. "A.D." and H 60. "W.B.", contained each a mixture of bovine tubercle bacilli and human tubercle bacilli. These two kinds of bacilli were separated and their characters investigated. (*See* page 15.)

14. Nine cases of *cervical gland tuberculosis* in which the tubercle bacilli were

* Both these patients subsequently died ; the cause of death in one case was stated to have been phthisis, and in the other was apparently general tuberculosis with intestinal ulceration. No post-mortem examination could be obtained in either case.

obtained from specimens removed by operation were examined. Of these six yielded human tubercle bacilli and three bovine tubercle bacilli.

15. *Primary abdominal tuberculosis*, twenty-nine cases in all. Of these, 14 yielded bovine tubercle bacilli, 13 human tubercle bacilli, and two cases were proved each to contain a mixture of bovine tubercle bacilli and human tubercle bacilli. The ages of the patients were as follows : In the bovine cases, ten were aged 1 to 3 years ; three, from 4 to 5 years ; and one, 8 years ; in the human cases, eight were aged 1 to 3 years ; three, from 3 to 5 years ; one, 7 years and one 15 years. The causes of death in the bovine cases were as follows : 11 died of tuberculosis, either of the generalised disease (6), of tuberculous peritonitis (2), or of meningitis (3) ; 2 died of intestinal obstruction following cicatrization of the gut, and one died of non-tuberculous pneumonia. The causes of death in the human cases were as follows : 12 died of tuberculosis, and one of streptococcal pericarditis and pleurisy.

Of the 14 cases found to be bovine the mesenteric glands in seven instances and the cervical glands in one instance were alone investigated. In the remaining six of these 14 other lesions besides the mesenteric glands were in each instance subjected to scrutiny, as follows :—Mesenteric glands and meninges, two cases ; mesenteric glands, lung and bronchial glands, one case ; mesenteric glands and liver, one case ; mesenteric glands and lung, one case ; and mesenteric glands, cervical glands, lung and meninges, one case. In such cases as these there can be little doubt that the tubercle bacillus entered the system through the intestinal tract, affecting first the mesenteric glands and subsequently other parts of the body ; and inasmuch as in the six cases in this category which supplied each a plurality of lesions for examination only one type of tubercle bacillus was found, whether in lesions near or in lesions remote from the point of entry, it is to be inferred that the persons, all of them children, died as a result of infection with bovine tubercle bacilli.

All cases of abdominal tuberculosis are not however caused by infection with the bovine type of tubercle bacillus. Of the 15 such cases in which a plurality of lesions was in each instance tested on exactly parallel lines, nine yielded none but human tubercle bacilli. In the remaining 12 cases of abdominal tuberculosis in regard of which a single lesion in each instance (mesenteric gland or cervical gland) was alone examined, four yielded human and no less than eight yielded bovine bacilli.

The two remaining cases in this group showed a mixture of bovine and human tubercle bacilli. In one case, a youth aged 18 years who died of pulmonary tuberculosis, the mesenteric glands alone were investigated. In another, an old man aged 70 years who died of pneumonia, the mesenteric glands and the retro-peritoneal glands were investigated (*See* page 15).

16. *Joint and bone tuberculosis.*—Fourteen cases. The cases illustrate very fairly the different forms of "primary" bone and joint tuberculosis occurring in man. The material used from ten consisted of scrapings from joints ; in four pus from bone abscesses was used. Thirteen of these cases yielded the human tubercle bacillus only. The circumstances relating to one case, H 16. "J.H.", were peculiar and are discussed later (page 15).

17. One case of tuberculosis of the *testicle*, one of the *kidney* and one of the *supra-renal capsule* were investigated. They each yielded human tubercle bacilli only.

18. Of the total of 108 cases of human tuberculosis investigated 84 yielded human tubercle bacilli only, 19 yielded bovine tubercle bacilli only, and five both bovine and human tubercle bacilli. Although the bovine tubercle bacillus may, as it appears, be solely responsible for certain cases of pulmonary tuberculosis (consumption) and though it may be present with the human tubercle bacillus in the bronchial glands, it is evident from the data recorded that the majority of cases in which the bovine tubercle bacillus is the infective agent in the human being are cases of alimentary tuberculosis. Such are cases of cervical gland and primary abdominal tuberculosis. In the latter class of cases at least the tubercle bacillus has unquestionably been swallowed. Received in this way the tubercle bacillus, whether human or bovine, may pass through the pharyngeal or buccal mucous membrane and infect the cervical glands, or getting into the small intestine it may produce several different lesions such as ulceration of the gut, tuberculosis of the mesenteric glands attached and of the peritoneal covering. The percentage of these cases of alimentary tuberculosis due to the bovine tubercle bacillus is very large. Taking both classes of cases (cervical gland and abdominal) together, numbering 38, there are 17 in which the bovine bacillus alone was found, 19 in which the human bacillus alone was found, and two in which both were found. Taking the

primary abdominal cases alone it is seen that in 16 out of 29 the bovine bacillus was found ; in 14 of these it was the sole infective agent present.

*Mixed Viruses in Human Tuberculosis.**

19. In our Second Interim Report we recorded the results of feeding two sets of bovine animals with large quantities of mixed sputum, the experiments being designated respectively Virus H 2. "Sp. A." and Virus H 17. "Sp. B."

In the experiments with H 2 "Sp. A." one of two heifers which had been fed with the sputum for 209 days was killed at the end of that period and found to have only a few calcareo-caseous tuberculous lesions in the mesenteric and hepatic glands. The bacilli from these glands, which had been passed on into calves and guinea-pigs in an emulsion of the tissues, were found to possess the cultural characters of the bovine tubercle bacillus and the high virulence of that bacillus for the calf and rabbit. In the other heifer, fed with mixed sputum for 300 days, retrogressive calcareous tubercles were found in the mesenteric glands ; and emulsion of these glands produced in one calf limited retrogressive tuberculosis, but the same emulsion passed through a guinea-pig produced in another calf fatal progressive generalised tuberculosis.

Re-investigation of two of the cultures of this virus which still existed has not added more to our knowledge than was available at the time of the issue of the Second Interim Report, but in the light of more extended observations on other viruses and of new facts acquired during their investigation we are now of the opinion that the results obtained are to be accounted for by the presence in the human sputum as used for feeding of a small number of bovine tubercle bacilli.

With regard to the second sputum experiment (H 17. "Sp. B."), the virus, which we placed in Group III., was slightly virulent at first and became virulent afterwards, but only in one of the four series of animals through which the virus was passed. The tuberculous material consisting of mesenteric glands from one of the four calves with which the several series began, after passing through two guinea-pigs in succession, was injected subcutaneously in the form of an emulsion into a calf (Calf *339*). It produced a limited retrogressive tuberculosis and a culture from the tuberculous organs of this calf (through a guinea-pig) was eugonic and exhibited low virulence for calves and rabbits. Clearly the virus up to this point possessed the characters of the human tubercle bacillus. Tuberculous material from Calf *339* was injected intravenously in the form of an emulsion into a second calf, and from this animal also intravenously and in the form of an emulsion successively into a third, fourth, and fifth calf. A culture derived from the last calf of the series was dysgonic and highly virulent. But a culture isolated from a rabbit which had been inoculated with material from one of the intermediate calves was eugonic and at first virulent ; after 16 months cultivation it was found to have no higher virulence than the human tubercle bacillus. This strain was tested again after a still longer period of subcultivation and was proved to be composed of slightly virulent eugonic bacilli only.

The result obtained with this virus is not so readily explained as in the case of H 2. "Sp. A.", on the assumption that the original material (the sputum) contained bovine as well as human tubercle bacilli, and the appearance of bovine tubercle bacilli might possibly have been the consequence of an accidental contamination of one of the calves during the course of the experiment. On the other hand it might be suggested that the bovine bacilli were present in the sputum in such small numbers that they became lodged in one only of the four calves fed with it and needed several passages through animals before they became so increased in numbers as to be able to produce their characteristic pathogenic effects.

Though in mixed sputum from many cases of pulmonary tuberculosis the majority of bacilli present are doubtless human tubercle bacilli, it is always possible that one or more of a group of phthisical patients may contribute sputum containing besides the human bacillus bacilli of the bovine type. We have shown indeed that cases of pulmonary tuberculosis (H 127 and H 128) can supply sputum yielding no other tubercle bacillus than the bovine.

* For the details of the original investigation of certain of these viruses *see* Vol. II. of the Appendix to the 2nd Interim Report. The results of those investigations are discussed by Dr. Cobbett in a Report submitted by him to the Commission in 1906 and now included in the Appendix to this Report (Vol. III). Recent work by Dr. A. Stanley Griffith on these and other similar viruses will be found in Vol. III of the Appendix, p. 5.

20. Five other viruses which presented anomalous features remain for special consideration ; three of these were discussed in our Second Interim Report (H 13. "A.D.", H 49. "T.C.", H 16. "J.H.") ; two others (H 60. "W.B." and H 90. "I.P.") were investigated after that Report was published. Those previously described in our Second Interim Report and placed in a group (Group III) by themselves were viruses which, after animal passage, became more virulent for calves and rabbits. We came, in that Report, to no definite conclusion as to the interpretation of the experiments recorded, but suggested two possible explanations. The first was that the results were due to a mixture of bacilli, the bovine tubercle bacillus and the human tubercle bacillus, and that during the passage through the series of calves the human bacillus was lost owing to the fact that the tissues of the calf are hostile to the growth of this bacillus, the bovine bacillus persisting meanwhile in the tissues of the calf and finally, in appropriate doses, setting up fatal generalised tuberculosis in that animal. The second possible explanation discussed by us was that the cases might be examples of modification, that the eugonic human bacillus, introduced successively into a series of calves, might have become modified into the dysgonic bovine bacillus.

2nd Int. Rep., p. 30.

The subject appeared one of such great importance that special investigations were undertaken by Dr. A. Stanley Griffith to determine whether the cultures used were mixtures of the two kinds of bacillus, and the procedure adopted may be shortly described.

Appendix, Vol. III.

In a mixture of bovine and human tubercle bacilli separation of the two types of bacillus may be effected in one or other or all of three ways :—(1) By passing the culture through the bodies of animals, for example calves and rabbits, which permit the multiplication of the bovine bacillus and resist that of the human bacillus ; (2) by sub-culturing on a glycerin medium which is more favourable to the growth of the human bacillus than to that of the bovine bacillus ; (3) by sowing the culture to be tested on the flat surface of a medium on a plate, on which any individual colonies that develop can be seen and separated for investigation.

These experiments were successful in showing that in viruses H 13. "A.D.", H 60. "W.B.", H 49. "T.C.", and H 90. "I.P.", two cases of bronchial gland tuberculosis and two cases of abdominal tuberculosis, the tested cultures were a mixture of the bovine bacillus and the human bacillus. Thus Virus H 13. "A.D.", which in culture was eugonic though virulent, after inoculation into calves and rabbits, grew like a bovine bacillus, the eugonic element or human bacillus having been in this way eliminated. By plate cultivation of the eugonic tubercle bacillus from a passage Calf (*301*) in this series two sorts of colonies were obtained, one like the bovine bacillus, the other like the human bacillus. In the case of Virus H 60. "W.B." the bovine bacillus was separated by animal inoculation from the human bacillus ; by plate culture both the human bacillus and the bovine bacillus were isolated. A similar result was obtained with Virus H 49. "T.C." and with Virus H 90. "I.P."

Viruses H 13. "A.D." and H 49. "T.C.", therefore, are not to be regarded as instances in which the slightly virulent human bacillus became transformed in the body of the calf into the dysgonic virulent bovine bacillus. On the contrary the anomalous results recorded in our Second Interim Report are to be explained by the fact that the viruses each contained two elements, the bovine tubercle bacillus and the human tubercle bacillus.

There remains one virus for consideration, viz., Virus H 16. "J.H." This was obtained from the knee-joint and was one of those which, as stated in our Second Interim Report, was at first only slightly virulent but became on passage highly virulent. When slightly virulent the cultures were eugonic, that is, were like the human tubercle bacillus, but in the later stages of the passage when the cultures were virulent they were dysgonic and like the bovine tubercle bacillus. The cultures of this series which were available for re-investigation after a lapse of $2\frac{1}{2}$ to 3 years did not yield results different from those obtained in the first investigation ; that is, one culture from the earlier calf in the passage was eugonic and non-virulent, whilst two cultures from animals later in the series were dysgonic and virulent. It is quite clear therefore that in the case of H 16 we were dealing with two different kinds of cultures, the human tubercle bacillus and the bovine tubercle bacillus ; and so far it may be concluded that the virus was a mixed one. As an original culture of the virus was not available for investigation we were unable to determine by experiment whether this particular virus was a mixture or not.

Cases of Lupus.

Appendix, Vol. II.

21. Cases of lupus are considered separately from the other cases of human tuberculosis for the reason that they present certain divergent features of particular interest.

The cases of tuberculosis which have already been considered are those in which the disease affected the internal parts of the body : the internal organs, glands, joints or bone. In lupus the tuberculosis is usually limited to the skin. It runs as a rule a very chronic course and is not commonly associated with internal tuberculosis. It may persist for many years without any sign of disease in the lungs or other parts of the body, and indeed even the lymphatic glands near the area of skin affected by lupus are not usually tuberculous.

22. The investigation was conducted with great care and completeness by Dr. A. Stanley Griffith. Twenty* cases of lupus were examined, one of which (H. 53) was referred to in our Second Interim Report. Of these cases fourteen were females and six were males. The ages of the patients when they first came under our observation were as follows : from 4 to 10 years of age, three females and four males ; from 10 to 20 years, five females and two males ; from 20 to 40 years, four females ; and two females were aged 53 and 68 respectively. The site of the lupus varied considerably. In two cases the disease was on the hip and leg, and in the remainder one or other part of the upper half of the body was affected : the face, arm, hand, elbow and neck ; and in one of these cases the buttock in addition. The duration of the disease varied considerably in the different cases, from 3 months to 36 years. None of the cases had undergone light or X-ray treatment, whereby the character of the bacilli might have been altered. Some had been treated by scraping or curetting, others had not been treated at all.

23. Our investigations of cases of human tuberculosis other than lupus have shown that from internal lesions there was obtainable one or other type of tubercle bacillus, either the bovine tubercle bacillus or the human tubercle bacillus ; that, from a few cases only, both bovine bacilli and human tubercle bacilli were obtained. The identification of these bacilli from internal tuberculosis of the human subject was based on certain experimental data : viz., the cultural characters of the bacillus and its pathogenic effects when injected into animals. It is not necessary to repeat here what has already been said on this point. For the present purpose the following considerations may be emphasized : the bovine bacillus on the one hand possesses characteristic cultural features and when subcutaneously injected is highly virulent for the calf and the rabbit in certain defined doses, and for the monkey and guinea-pig in very small doses. On the other hand the human tubercle bacillus grows more luxuriantly on artificial media than the bovine bacillus and when subcutaneously administered is only slightly virulent for the calf and rabbit, but is, like the bovine bacillus, highly virulent for the monkey and guinea-pig in very small doses. These facts need to be borne in mind when considering the results of our investigation of lupus cases. For it has been found that the bacilli isolated from certain cases of lupus exhibit a pathogenicity or degree of virulence differing from that which would have been anticipated from a study of their cultural characters alone. The following table shows the general results obtained :—

Classification of Lupus Viruses according to Cultural Characters and Virulence.

Virus.	Cultural Characters.	Virulence for the Calf, Rabbit, Monkey and Guinea-pig.
(1.) H 110. "J.B." ...	Bovine (Class I.)*	Like the bovine bacillus virulent for the calf, rabbit, monkey and guinea-pig.

* *See* 2nd Interim Report Appendix, Vol. III., page 5.

* Material from one other case of lupus (H 113. "O.S.") was obtained, but guinea-pigs inoculated with it did not develop tuberculosis. No tubercle bacilli were seen in a smear preparation made from the material.

Classification of Lupus Viruses according to Cultural Characters and Virulence—continued.

Virus.	Cultural Characters.	Virulence for the Calf, Rabbit, Monkey and Guinea-pig.
(2.)		
H 100. "R.S." ...	Bovine (Class II.)	All these had lower virulence for the calf than the bovine bacillus. In rabbits although generalised tuberculosis was produced the duration of life was longer than with the bovine bacillus. In guinea-pigs and monkeys the disease was less severe than with a similar dose of the bovine bacillus or of the human bacillus.
H 105. "G.S." ...	Bovine (Class I.)	
H 53 "D.H." ...	Bovine (Class III.)	
H 107. "H.H." ...	Bovine (Class II.)	
H 108. "H.R." ...	Bovine (Class II.)	
H 85. "H.B." ...	Bovine (Class II.)	
(3.)		
H 111. "S.E." ...	Bovine (Class III.)	For the calf this had low virulence, not higher than that of the human tubercle bacillus. Intravenously in rabbits fatal tuberculosis was produced; subcutaneously, chronic tuberculosis. Virulence for the monkey and guinea-pig was lower than that of either the bovine or the human tubercle bacillus.
(4.)		
H 91. "H.S." ...	Bovine (Class III.) Slightly pigmented growth on serum.	This had low virulence for the calf, no greater than that of the human tubercle bacillus, and for the rabbit lower than that of the human tubercle bacillus. For the guinea-pig lower and for the monkey much lower virulence than either the human or bovine tubercle bacillus.
(5.)		
H 99. "L.K."	Human	These resembled the human tubercle bacillus in virulence for the calf, rabbit, monkey and guinea-pig.
H 92. "D.N."		
(6.)		
H 109. "M.W."	Human	These resembled the human tubercle bacillus in virulence for the calf and rabbit. They were less virulent for the monkey and guinea-pig than the human bacillus.
H 112. "B.B."		
H 71. "L.V."		
H 101. "E.G."		
H 114. "A.U."		
(7.)		
H 103. "N.S."	Human	These had very low virulence for the calf and rabbit, and lower virulence for the monkey and guinea-pig than the human tubercle bacillus. H 102. "N.H." was the least virulent of all the lupus cultures.
H 106. "K.R."		
H 84. "M.S."		
H 102. "N.H."		

24. The bacilli isolated from these several lupus cases retained their cultural characters after repeated subcultivation and also after residence in the animal body. Numerous cultures were made from lesions in the calves and other animals inoculated and the cultures thus obtained preserved the cultural characters of the bacilli isolated from the original material. Despite this cultural constancy, it is evident from a consideration of the results shown in the Table that only three of the viruses behaved pathogenically like the types of the bacilli (the bovine bacillus and the human bacillus) which are found in the internal lesions of human tuberculosis. These viruses are H 110. "J.B.", which is identical with the bovine bacillus in cultural characters and in virulence, and H 99. "L.K." and H 92. "D.N.", which are

in cultural characters and in virulence identical with the human tubercle bacillus.

25. Of the remaining seventeen lupus viruses we found eight showing the characters of the bovine tubercle bacillus in culture, but differing from the bovine bacillus in their effects when injected into calves and rabbits, monkeys and guinea-pigs. As regards certain of these eight viruses, some of those included in (2) of the Table showed a very wide range in their virulence for the calf. For instance, in the case of virus H 100. "R.S.", one calf (*1523*) developed fatal generalised tuberculosis from a dose of 50 milligrammes; three other calves, one of which (*1419*) received a dose of 50 milligrammes and two (*1409* and *1547*) a dose of 100 milligrammes each, were killed in 95 to 122 days and showed generalised tuberculosis of a not very severe type, progressive in one, retrogressive in the other two. With another virus (H 53 "D.H. b.") fatal generalised tuberculosis followed in 52 and 63 days respectively from a dose of 50 milligrammes in two (*1507* and *1545*) out of three calves; whereas the third calf (*1535*) receiving a similar dose showed slight generalised but retrogressive tuberculosis.

With none of the other of these dysgonic lupus viruses was fatal tuberculosis produced in the calf by doses of from 48 to 96 milligrammes within 90 days. Certain of these animals showed only retrogressive and limited tuberculosis not fatal within the 90 days; while in other calves again there were intermediate effects, *i.e.*, the disease was widespread but not fatal within 90 days. A minimal result was obtained in one calf (*1331*) injected with 96 milligrammes (H 85. "H.B."); the animal killed 90 days after inoculation showed disease limited to the site of inoculation and the nearest gland. Another calf (*1289*) injected with a dose of 50 milligrammes of culture of the same virus showed slight retrogressive generalised tuberculosis in 94 days. Slight effects such as these are not obtained in calves with these doses of the bovine tubercle bacillus when derived from the lesions of bovine tuberculosis, and there can be no question therefore as to the feeble virulence of many of these dysgonic lupus viruses. In this respect the experiments performed on rabbits confirm the results obtained in calves, *i.e.*, as regards the wide and lower range of virulence of the viruses.

Moreover, feeble virulence was especially well seen when certain of these viruses were injected into guinea-pigs and monkeys; for instance, with viruses H 111. "S.E." and H 91. "H.S.", both of which viruses were in culture bovine in character. The first (H 111) had virulence for the calf and for the rabbit lower than that of the bovine and for the calf not higher than that of the human bacillus, but its virulence for the monkey and guinea-pig was less than that of the human bacillus. The second (H 91) had low virulence for the calf and rabbit, *i.e.*, not greater than that of the human bacillus, while for the guinea-pig and monkey it had lower virulence than the human bacillus.

26. In view of the above facts and on a working assumption that the dysgonic tubercle bacilli found in lupus might be degraded bovine bacilli, it was sought to increase their virulence by passage through animals. Certain of the viruses were accordingly thus tested, the tissues of calves and rabbits being regarded as most likely to induce intensification of their virulence. These viruses were the six which are shown in the Table (2). One experiment with Virus H 100. "R.S." may be quoted to illustrate the result obtained. The culture derived from the original material through a guinea-pig was injected subcutaneously into a calf (*1409*) in a dose of 100 milligrammes. The animal was killed in 119 days and only a limited tuberculosis was found: a cyst at the seat of inoculation, a few tuberculous lesions in the nearest glands and in the lungs, and in a few lymphatic glands of the body—a result very different from that which follows inoculation with 100 milligrammes of a culture of bovine tubercle bacilli. A culture obtained from the mediastinal gland of this calf was inoculated into another calf (*1543*) in a dose of 50 milligrammes. This second calf was killed, when dying, in 34 days and showed general miliary tuberculosis. Two other experiments with the same virus on similar lines lasting respectively 73 and 122 days gave like results. The cultures obtained from the passage animals in each series were also fully virulent for rabbits. In another experiment the virulence of Virus H 100 was found increased for the rabbit by residence for 337 days in the body of the rabbit. Apparently, therefore, residences in a calf for 73, 119 and 122 days of the bacilli obtained from the lupus lesion was sufficient to raise the virulence of the bacillus to that of the bovine tubercle bacillus, and residence in the rabbit for 337 days had like effect.

Similar results were obtained with Virus H 108. "H.R."

But in the cases of Viruses H 105. "G.S.", H 53. "D.H.", H 107. "H.H." and H 85. "H.B.", the result was different; neither a single residence in the calf or rabbit, nor passage through a series of calves, led in these cases to an increase of virulence up to the standard of the bovine tubercle bacillus. In one case, however (H 105. "G.S."), the virulence for the rabbit was slightly increased by passage through the calf, and in another (H 53. "D.H.a"), for the monkey by passage through the monkey.

To sum up the results obtained in these nine cases of lupus in which a bacillus was obtained presenting the cultural characters of the bovine tubercle bacillus, in only one case did the bacillus obtained from the original material possess the high virulence as well as the cultural characters of the bovine tubercle bacillus. The other eight viruses, though their bacilli exhibited and retained the cultural characters of the bovine tubercle bacillus, proved less virulent than that bacillus not only for the calf and rabbit but also for the monkey and guinea-pig. It was found possible in two cases to increase the virulence of the culture from the original material by residence in the tissues of the calf and rabbit so as to bring it up to the high virulence of the bovine tubercle bacillus.

27. There remain for consideration eleven lupus viruses the original cultures from which manifested the cultural characters of the human tubercle bacillus. All these showed low virulence for the calf and rabbit, agreeing in this respect with the human type of the bacillus, though some of them exhibited for these animals much less virulence than that bacillus. They differed, too, from the human tubercle bacillus in that generally they had a lower, some of them a much lower (the four viruses in 7 of the Table), virulence for the monkey and guinea-pig.

The effects of the lupus viruses on rhesus monkeys are of especial interest. With the exception of the three (H 110, H 99, and H 92) which produced fatal general tuberculosis in these animals in no wise differing from that set up by human or bovine tubercle bacilli, none of the viruses, 17 in number, was equal in virulence to the human or to the bovine tubercle bacillus. Progressive generalised tuberculosis was, it is true, produced by each of these viruses, but this led to a fatal result only after longer, and in some cases much longer, periods than the tuberculosis caused by the typical bovine or typical human tubercle bacillus. Eight of these 17 viruses had the cultural characters of the bovine tubercle bacillus and nine had those of the human tubercle bacillus. These effects on monkeys supply further evidence that viruses may possess a virulence differing from that which was to have been anticipated from the cultural characters of the bacillus.

It may be noted that the bacillus of one virus, H 84. "M.S.", after residence in a monkey (*145*) for 139 days was found to be increased in virulence, the virulence being then raised to that of the human tubercle bacillus for the monkey and guinea-pig.

SECTION IV.

Swine Tuberculosis.

28. Tuberculosis is not an uncommon disease in swine, and the lesions from 63 individual cases were investigated. Four of these have to be excluded from consideration owing to the fact that cultures were not obtained. There remain 59 cases which were completely examined as regards the type of bacillus isolated from the lesions. Appendix, Vol. III. p. 145.

In swine the commonest method of infection is by ingestion of tuberculous material, and the parts first affected are the lymphatic glands in close relation to the alimentary tract (submaxillary, pharyngeal, and mesenteric). The abdominal organs, especially the spleen, are not infrequently involved, and in many cases the organs of the thorax as well.

29. The specimens investigated were obtained in all cases from the slaughter-house, and were taken from the carcases of animals sent there for the purpose of being slaughtered for food. It was found impossible to obtain a complete post-mortem record of each pig the lesions of which were used for investigation. In a certain number of the cases the disease was stated to have been localised in the glands of the neck and in certain others it was stated to have been generalised.

In some of the former, the internal organs having been removed before examination of the carcass was made, lesions may possibly have been present elsewhere in the body. The investigation of these local lesions can therefore be held to concern only the disease which had affected the glands in question. In the generalised cases on the other hand, that is where the material was obtained from lesions of the internal organs, the investigation must be considered as dealing with the generalised disease as it occurs in the pig.

In 26 cases the disease was stated to have been localised; in 25 of these the lesions submitted for examination were in the submaxillary glands and in one in the mesenteric glands only. In 33 cases the disease was generalised; in the majority of these it was of moderate severity, although in a few instances there were only scattered lesions throughout the body.

30. The material used in the investigation of the 59 cases was obtained from the following parts:—Submaxillary glands, 44 cases; bronchial glands, 4 cases; spleen, 2 cases; mesenteric glands, 2 cases; submaxillary and bronchial lymphatic glands, 1 case; skin, bone, joint, lung, udder, and inguinal gland, 1 case each. Cultures were obtained direct from the original material in all but four instances; in these four cases they were obtained after the inoculation of the original material into guinea-pigs. In securing cultures in swine tuberculosis it is of importance to obtain them direct from the original material if practicable, for the reason that the pig is capable of harbouring more than one type of tubercle bacillus, and one of the types of bacillus (namely the avian) might escape detection if guinea-pigs were inoculated for the purpose of cultures being grown from the lesions produced in them. In the guinea-pig the avian bacillus does not induce progressive tuberculosis and the lesions produced may be minimal.

The cultures which were obtained from these lesions were observed as to their mode of growth and were used for inoculation into guinea-pigs, rabbits, calves, fowls and other animals in order to determine the characters of the bacilli present, whether bovine, human, avian, or a mixture of these.

31. The results thus obtained are shown in the following table:—

Degree of Tuberculosis in the Pig.	Bovine Virus.	Human Virus.	Avian Virus.	Mixed Avian and Bovine.	—
Local Tuberculosis	18 cases	3 cases	5 cases	—	26
Generalised Tuberculosis ...	32 „	—	—	1 case	33
	50 cases	3 cases	5 cases	1 case	59

From this Table it is evident that all three types of bacillus are capable of infecting the pig—the bovine tubercle bacillus, the human tubercle bacillus, and the avian tubercle bacillus.

32. The cases of infection by the bovine tubercle bacillus were by far the most numerous: 50 cases out of 59. Though in many of these 50 cases the only tuberculous lesion detected at the time of slaughter was in the submaxillary lymphatic glands, in many others of the 50 this bacillus had produced generalised tuberculosis, and in our experience the bovine bacillus only has been found to be the cause of natural generalised tuberculosis in pigs.

The cultures obtained from all these 50 cases were identical in mode of growth with the bovine tubercle bacillus. They were also identical in virulence with the bovine tubercle bacillus, with one exception, Virus P. XIV. The original culture of this virus in doses of 50 milligrammes produced in four calves generalised tuberculosis but the disease was less severe and of longer duration than that set up in this animal by a similar dose of the bovine tubercle bacillus. A culture from one of the inoculated calves when injected into two other calves caused fatal generalised tuberculosis similar to that caused by a like amount of culture of the bovine bacillus.

33. In three cases of local swine tuberculosis, the human tubercle bacillus alone was found. The bacilli isolated from these cases had the cultural characters of the human type and a low degree of virulence for the calf and rabbit. One of these viruses (P. XLI) though it showed, like the other two, a slight degree of virulence for the

calf and rabbit, produced in the pig after subcutaneous inoculation a severe tuberculous pneumonia in three different instances, a result which has not occurred in our experiments from inoculation into pigs of the human bacillus obtained from human tuberculosis. The culture from the last pig of the series was non-virulent for rabbits like the human tubercle bacillus and resembled that bacillus in cultural characters. One of the three viruses (P. IV) produced rather more severe results in calves and rabbits than had usually occurred in our other experiments with the human tubercle bacillus, but the difference was not great.

34. From five cases of local swine tuberculosis a bacillus was obtained, which, in mode of growth and virulence for animals, was identical with the avian bacillus, as described in this Report on page 7.

35. There remains for consideration one case of swine tuberculosis (P. XLII) in which both avian and bovine bacilli were obtained as a mixed culture from the submaxillary lymphatic glands. This occurred in a pig about eight months old, in which the lungs and liver were stated to have been also very slightly affected with tuberculosis. The original culture on serum was bovine in appearance (the avian element growing badly on this medium), and caused in rabbits and guinea-pigs effects like those produced by the bovine bacillus. The avian element in the culture was separated in a pure form by subculture on glycerin agar incubated at 42° C. It produced characteristic effects in fowls and guinea-pigs, and from one of these guinea-pigs a pure culture of the avian bacillus was isolated.

This result is of some importance in connection with the instances of mixed viruses already described in discussing Human Tuberculosis, and it illustrates the difficulty of deciding the nature of the virus in certain cases without special and, it may be, prolonged investigation, as the following considerations show.

When a culture isolated from a tuberculous lesion is found to grow on repeated subcultivation like a bovine tubercle bacillus, it might be concluded that the avian tubercle bacillus is not present. But this conclusion might not be correct, for as the avian tubercle bacillus grows badly on serum it would not be recognisable in a culture on that medium if present only in a small proportion, as in the original culture of Virus P. XLII. Similarly, when the culture isolated grows like the human tubercle bacillus, the eugonic and luxuriant growth of the culture may hide the presence of the bovine or of the avian tubercle bacillus.

Thus it is not always safe to infer from the mere appearance of a culture that a bovine or an avian element is not present in it; in a case of doubt the only means of determining this is to test the virulence of the culture in calves, fowls, and rabbits, or to separate the two elements by one or other of the methods already described.

36. The results of our investigation of Swine Tuberculosis are clear, and may be summarised as follows:—

All three types of tubercle bacilli are capable of infecting the pig, but the human bacillus and the avian bacillus are less frequently found in this animal than the bovine bacillus. The bovine tubercle bacillus, though in many pigs it may have caused no more than a localised lesion in the submaxillary lymphatic glands at the time of slaughtering the animal, nevertheless in many instances produces a severe and generalised disease. One case of mixed infection with bovine and avian tubercle bacilli was met with and a mixed infection with human and bovine tubercle bacilli must be considered possible in the pig, although it was not found in any of the cases investigated by us.

SECTION V.

Equine Tuberculosis.

37. In horses tuberculosis is in most cases primarily an affection of the glands and organs in connection with the alimentary tract, the abdominal organs being chiefly affected. Five cases of equine tuberculosis were investigated (E I to E V). In one there were tuberculous lesions in the mesenteric glands and spleen; in a second case the mesenteric glands alone were affected; in a third case the spleen was the only tuberculous organ; and in two cases the mesenteric glands, spleen and lungs were affected, the disease having become generalised. Appendix, Vol. IV, p. 5.

In three cases the material investigated was from the tuberculous mesenteric glands, in one case from the spleen, and in another case from the lungs, spleen, and mesenteric gland.

38. In four cases the material was first injected into guinea-pigs and cultures were obtained from these animals ; in one instance, Virus E V, the culture was obtained direct from the original material. In all cases the cultures obtained grew like those of the bovine tubercle bacillus. Two of the viruses (E II and E III) belonged culturally to Class I of the bovine series, which comprises cultures that grow the least easily ; one (E I) belonged to Class II and two (E IV and E V) belonged to Class III, in that they behaved like the most readily growing bovine bacilli. In all cases the bacilli obtained from the experimental animals retained their cultural characters after prolonged subculturing, and none showed variation in their mode of growth even in prolonged passage experiments such as were carried out with Viruses E II and E IV.

39. The results of the experiments performed in testing the potency of the bacilli of these equine viruses show that notwithstanding the similarity of their cultural behaviour their virulence is not in all cases parallel with that of the bovine bacillus.

The bacilli isolated from Viruses E I, E III, and E V were exactly similar to the bovine tubercle bacillus in their virulence for rabbits and guinea-pigs. Viruses E I and E III were also tested on calves and pigs, and in these animals caused, like the bovine bacillus, a fatal generalised tuberculosis. Virus E V was not tested on pigs and calves, but the acute tuberculosis which was produced by it in rabbits was so definite in type as to suffice for identifying it with the bovine bacillus. Virus E I was also tested on a pony which received 10 milligrammes of culture intravenously. This pony died in 17 days of acute tuberculosis, an effect similar to that which was produced in this way in the horse by the bovine tubercle bacillus. Virus E III, in a dose of 1 milligramme subcutaneously injected, produced acute tuberculosis in a lemur, death occurring in 28 days.

40. Viruses E II and E IV did not behave like the three viruses above mentioned, nor like the bovine tubercle bacillus, when injected into animals ; and they must be considered separately.

Virus E II, which in culture was found to belong to the class of most dysgonic bovine bacilli, was inoculated into seven calves. Two of these calves (*404* and *406*) inoculated subcutaneously with 10 milligrammes of culture, showed when killed in about 90 days only a very slight amount of disease. Five other calves, of which three received 50 milligrammes each, one 20 milligrammes and one 100 milligrammes subcutaneously, remained in good health after their inoculation, and showed, when killed in from 90 to 100 days, only a slight amount of disease which was apparently retrogressive ; an effect similar to that produced in calves by the subcutaneous injection of an equal dose of the human tubercle bacillus. This result, namely, that a culture typically bovine in appearance should have uniformly produced only slight disease when injected into calves, is a notable circumstance.

For rabbits Virus E II was only moderately virulent, for although it caused fatal generalised tuberculosis by intravenous and intraperitoneal inoculation, the duration of life was longer and the extent of the disease less than in the case of rabbits inoculated with the bovine tubercle bacillus. After subcutaneous inoculation the amount of disease produced by E II varied very greatly being sometimes acute, but usually chronic.

For monkeys also this virus was less virulent than the bovine bacillus. After subcutaneous inoculation the course of the disease was less acute than after inoculation with the bovine bacillus, but it was invariably fatal in the end. The disease set up by feeding was still more chronic in its course.

Although in pigs and guinea-pigs subcutaneous inoculation of this virus produced in every case fatal generalised tuberculosis, the disease ran a chronic course.

It may be said, therefore, that the virus of E II, although growing like the bovine tubercle bacillus, produced much less severe effects than that bacillus when inoculated into animals, its slighter virulence for the calf being especially well marked.

41. Similar experiments were performed with the virus of E IV. Six calves were inoculated subcutaneously, two with doses of 10 milligrammes, and four with doses of 50 milligrammes. Five of these remained well, and when killed, in about three months, showed slight non-progressive tuberculosis. The sixth calf died in 89 days of a severe tuberculous pneumonia, but with very little disease elsewhere. This result is possibly to be explained on the assumption that the injection was

accidentally intravenous as well as subcutaneous. It is clear that the virus of E IV, like that of E II, was not as virulent for the calf as the bovine tubercle bacillus.

For rabbits this virus was only moderately virulent, the results in that animal being similar to those obtained with the virus of E II.

The baboon and rhesus monkey were less susceptible to this virus than to the bovine bacillus. For example, a baboon (*74*) fed with a dose of 1 milligramme of culture was killed in 448 days when still apparently in good health ; post mortem there was found very slight and non-progressive tuberculosis. The culture obtained from lesions in this animal was unchanged in character as compared with the original culture, and was not increased in virulence for the calf or rabbit.

Virus E IV, like Virus E II, produced generalised tuberculosis in pigs and guinea-pigs. It also produced generalised tuberculosis in horses both by intravenous inoculation (10 milligrammes) and by subcutaneous inoculation (50 milligrammes), while E II produced a similar effect by intravenous inoculation. Both E II and E IV were found non-virulent for fowls.

42. Viruses E II and E IV therefore closely resembled each other in the following points. The bacilli isolated from them, although they had the characters in culture of the bovine tubercle bacillus, differed from that bacillus in that they did not produce an acute disease in calves with doses of 50 milligrammes and more of culture given subcutaneously. Less severe disease too was produced by these two viruses than by the bovine bacillus in rabbits and monkeys ; and though they, like the bovine bacillus, were capable of producing acute disease in pigs and guinea-pigs, these animals survived longer after inoculation with E II and E IV than after inoculation with the bovine tubercle bacillus.

On the whole the properties of these viruses more closely resembled those of bovine tubercle bacilli than those of the other two types of tubercle bacilli—the human and the avian. Accordingly, experiments were undertaken to ascertain whether by passage of culture of the original material of these viruses through calves and, to a less extent, through rabbits and monkeys, their virulence could be enhanced and brought parallel to that of the bovine bacillus.

43. *Passage Experiments with Virus E II.*—Four separate passage experiments on calves were undertaken. (*See* Chart, Appendix, Vol. IV, page 105.) The first passage experiment was through calves, two series of these animals being tested concurrently, and lasted 2½ years. Cultures were used, the dose for the first animal being 10 mgs. while the succeeding calves received 50 mgs. each. As a result of the passage the virulence for the calf was perhaps increased slightly, but for rabbits it was definitely increased.

The second passage experiment was carried out, like the first, through a double series of calves and lasted 2 years and 7 months. In one branch of the experiment the virulence of E II for the calf became increased up to the standard of the bovine bacillus. In the other branch the virulence was not increased.

The third and fourth passage experiments each included 4 calves and lasted 1 year and 4 months and 1 year and 7 months respectively. In both experiments there was an increase of virulence of E II up to the standard of the bovine tubercle bacillus.

In parallel experiments on rabbits performed with each of the cultures isolated during the passage through calves, it was found that the results obtained with the rabbits coincided with those obtained with the calves. The cultures which produced slight tuberculosis in calves had not the virulence for rabbits of the bovine bacillus, whereas those which killed the calves with acute tuberculosis killed the rabbits with acute disease. In one instance the culture obtained from one of the calves which died of generalised tuberculosis was found fully virulent for the monkey, whilst in another instance in which at the end of the passage the calf had only slight tuberculosis the culture obtained from it was found not to be increased in virulence for the monkey. Throughout all the passage experiments the cultural characters of the bacillus remained unaltered. In one experiment a culture derived from a rabbit which had been inoculated with a culture from the original material of E II was found to have increased virulence for the calf, in which it produced severe generalised tuberculosis.

44. *Passage Experiments with Virus E IV.*—Three passage experiments were performed, two of which were negative and one positive. (*See* Chart, Appendix, Vol. IV, page 123.) The first passage lasted 2 years and 4 months and began with a dose of 10 mgs. injected subcutaneously into a calf. A culture

from this calf, passed on in doses of 50 mgs. into other two calves, produced only slight disease. Cultures from each of these two calves passed on in a similar dose into each of two other calves also produced but slight disease.

The second passage experiment lasted 1 year and 7 months : a dose of 50 mgs. was injected in the first instance and the experiment was performed in the same way and with the same number of calves as before ; it was also negative.

The third E IV passage experiment lasted 1 year and 7½ months, and began with a calf (*502*) which received 50 milligrammes subcutaneously ; only slight disseminated tuberculosis was produced in this animal. The culture isolated from the lung of this calf was passed on into two calves (*630* and *614*) in similar doses. One died in 31 days of generalised tuberculosis, the other in 33 days of pneumonia with some tuberculous lesions. Another calf (*602*) inoculated with a culture from the suprarenal body of Calf *502* was killed in 90 days, and showed progressive but not severe generalised tuberculosis. The culture from this calf, injected in a 50 milligramme dose into another calf, killed the animal in 39 days of generalised tuberculosis. The virulence of E IV for the monkey was also increased at the end of the passage.

SECTION VI.

Cases of Natural Tuberculosis in Mammals other than Man, Ox, Pig, and Horse.

Appendix, Vol. IV, p. 150.

45. From time to time during the course of our investigation opportunity occurred for examining some cases of natural tuberculosis in mammals other than man, the ox, the horse, and the pig. Five such cases were studied in the following animals : a gnu, an antelope, a rhesus monkey, a chimpanzee, and a cat.

46. The gnu (*connochætes taurinus*) died at the Zoological Gardens from generalised tuberculosis, the parts affected being the lungs, liver, and a few glands in the thorax and abdomen. Cultures were obtained direct from the lung, a mediastinal gland, and a portal gland. The bacillus from each of these parts showed in culture the characters of the human tubercle bacillus. One of these cultures was tested on calves and rabbits, and was found to produce the same effects as the human tubercle bacillus.

47. The antelope (*oryx beisa*) was killed when ill at the Zoological Gardens, where it had been in captivity for many years. There was extensive tuberculosis, with cavities in the lungs, which were the parts used for investigation. Cultures were obtained direct from the lung, and showed the characters of the human tubercle bacillus. The virulence of these cultures was tested on calves, pigs, and rabbits, as well as on guinea-pigs. In the three former animals it produced only localised disease similar to that caused by the human tubercle bacillus. A series of passage experiments was performed on rabbits. There was no evidence of the presence in the virus of the bovine tubercle bacillus, nor was the original virulence of the bacillus altered by the passage.

The presence of the human tubercle bacillus in these two animals, the gnu and the antelope, and the fact that they suffered from severe tuberculosis is of some interest as both these animals are ruminants. The human tubercle bacillus has not been isolated by us from any case of natural tuberculosis in a bovine animal.

48. The rhesus monkey was killed at the quarantine station at Isleworth on account of illness and was found to have tuberculosis of the lungs, bronchial glands, spleen, liver and kidney, the disease not being very extensive in any part except the lungs. A culture isolated from the lung grew like the human tubercle bacillus and had only slight virulence for rabbits.

49. A chimpanzee which had been purchased by the Commission as apparently a healthy animal died shortly afterwards during its period of quarantine at Isleworth of acute miliary tuberculosis, starting from the intestinal tract. A culture isolated from its mesenteric gland grew like the human tubercle bacillus and behaved like this bacillus when inoculated into rabbits and guinea-pigs.

In all the four cases described above the human tubercle bacillus was the cause of the naturally acquired disease.

50. The mesenteric gland of a cat suffering from naturally acquired tuberculosis was investigated. The culture isolated direct from the gland grew like the bovine tubercle bacillus (Class II). Like this bacillus it produced fatal generalised tuberculosis in rabbits.

The only comment which it is necessary to make on these cases is that the tuberculosis developed by mammals kept in captivity may be due either to the human tubercle bacillus or to the bovine tubercle bacillus. Owing to the small number of cases investigated, no conclusions can be drawn as to the relative frequency of infection of such animals by the one or the other type of bacillus.

SECTION VII.

Avian Tuberculosis.

51. The characters and properties of the avian tubercle bacillus have already been discussed by us on pages 7 and 8 of this Report. There remain to be noted our observations of avian tuberculosis as it occurs naturally in birds and pigs. Appendix. Vol. IV. p. 167.

The cases of tuberculosis in birds which were investigated by us occurred in three fowls, three pheasants, a pigeon, a demoiselle crane, and a Senegal touracon*. In these cases the disease revealed by the post-mortem examination showed the well known features of tuberculosis in birds, viz., the presence of tuberculous nodules in the intestine, spleen, and liver. In some cases the lungs, joints, and bones were affected.

52. The material used for investigation in the different cases was : the spleen, four cases ; spleen and liver, one case ; liver, one case ; lung, two cases, and an intestinal nodule, one case. Cultures were obtained from the original material directly except in one case in which the culture was obtained from a rabbit which had been inoculated with the lesions of a fowl.

In all cases the bacilli isolated proved to be identical with and had the characters and properties of the avian tubercle bacillus as already described.

The avian bacillus was also found in the submaxillary lymphatic glands in six cases of tuberculosis in pigs ; in five alone and in the sixth case in association with the bovine tubercle bacillus (page 21).

SECTION VIII.

Behaviour of Bacilli and Fate of Bacilli in the Tissues of Animals Inoculated and Lesions Produced.

53. During the course of our investigation concerning the virulence of the three types of tubercle bacilli in various animals numerous observations were made on the inter-action of the bacilli and the tissues of the inoculated animals as regards the distribution of the bacilli, their fate in the tissues and the lesions produced by them.

These observations were made by the investigators conducting the experiments, Drs. Cobbett, A. Stanley Griffith and F. Griffith ; the histological and some of the bacteriological observations being made by Dr. Arthur Eastwood. The results of these observations, which will now be discussed, have an important bearing on the relation of the three types of bacilli to each other, in that they enable comparison to be made of the effects in animals of each of the several types. Moreover, the results of the observations on the lesions produced by the different methods of inoculation and by feeding, and on the sequence of the lesions, have a bearing on the question of the seat of primary tuberculosis as it occurs in man and animals.

54. In previous sections of this Report the results of introducing each of the three types of bacilli into various animals have been discussed without entering into any detail as to the histology of the lesions produced, or as to the fate of the bacilli in cases where no lesions resulted. The successful infection of an animal with tuberculosis usually leads to the formation of well-defined lesions which have a definite anatomical structure and undergo certain changes. In some cases the disease rapidly involves numerous parts of the body ; this we call acute or miliary tuberculosis. In other cases, though not so acute, the disease is progressive and consists in the gradual formation and development of lesions in various organs, but some of such cases may become retrogressive. In

* We have not investigated cases of natural tuberculosis in parrots, but we are aware that other observers have isolated the human tubercle bacillus from the lesions occurring in such cases.

other cases the disease remains localised at the site of inoculation without any apparent effect on the general health of the animal, and such cases may end in complete recovery. We have recognised, however, that other events may happen when tubercle bacilli are introduced into the animal body. In some cases the bacilli die and disappear without leaving any lesions ; in other cases the bacilli become dispersed throughout the body where they may even multiply, sometimes to an enormous extent, but without producing any lesion.

55. In our Second Interim Report we recorded experiments performed by Dr. Cobbett, Dr. A. Stanley Griffith and Dr. F. Griffith, in which the distribution of bacilli in the animal body was investigated at an early date after their introduction beneath the skin. Other experiments have since been performed by Dr. A. Stanley Griffith on the same subject.

2nd Int. Rep., Appendix, Vol. III, p. 219.

Experiments on calves with the human tubercle bacillus by Dr. Cobbett (Viruses H 46 and H 26) showed that after subcutaneous injection of the calf with a dose of 50 milligrammes of culture tubercle bacilli could be demonstrated, by means of inoculation of the calf tissues into guinea-pigs, after 25 days in the liver, lung, spleen and rib marrow of one calf, and that in another calf, after a lapse of 90 days from the injection, the lung was found (by like means) to contain tubercle bacilli, though these were absent from the spleen, liver and rib-marrow. In neither of these cases were there visible tuberculous lesions in the organs of the calf. In another experiment on a calf the human tubercle bacillus was subcutaneously injected in a dose of 50 milligrammes of culture. This animal was killed in three days and the presence of tubercle bacilli in the spleen, liver and lung, bone marrow and popliteal gland was detected by the production of tuberculosis which followed the injection of an emulsion of these parts into guinea-pigs. A similar result was obtained eight days after subcutaneous injection in another calf and after 14 days in a third calf ; after three months in a fourth calf tubercle bacilli were still present in the lungs, liver and spleen. After three months in a fifth calf also the results were positive in the lung, the popliteal gland, the thoracic, bronchial and hepatic glands, but the other organs were free from tubercle bacilli. In Dr. Cobbett's words, "Tubercle bacilli are frequently present in the organs and glands of bovine animals several months after they have been injected subcutaneously with human tubercle bacilli." It is clear indeed that in the early stages of invasion these bacilli produce no visible lesions in the organs, but that after some months their presence may result in the formation of minute fibrous or calcareous tubercles which are non-progressive. Such lesions have been found on post-mortem examination in about 50 per cent. of the calves injected subcutaneously with large doses of the human tubercle bacillus.

2nd Int. Rep., Appendix, Vol. III, p. 235.

Dr. A. Stanley Griffith and Dr. F. Griffith, investigating the same subject, employed a variety of animals : the calf, monkey, pig, cat, rabbit, guinea-pig, rat and fowl. Cultures of the bovine bacillus were injected by them subcutaneously into a monkey (20 milligrammes), a calf (44 milligrammes), and five pigs (each 20 milligrammes), two rats (each 10 milligrammes), one fowl (10 milligrammes), one guinea-pig (10 milligrammes), and one rabbit (10 milligrammes). Cultures of the human tubercle bacillus were injected subcutaneously into a cat (10 milligrammes), two rabbits (20 and 10 milligrammes), one pig (20 milligrammes), and two guinea-pigs (10 milligrammes). Most of the above animals were killed in 24 and 48 hours ; the remainder, four pigs, in 3, 5, 8 and 14 days respectively. It was found that in all cases, that is both with the bovine tubercle bacillus and the human tubercle bacillus, there was evidence of dissemination when the animals were killed ; the bacilli being found in the blood, lungs, and the other organs of the body. Bacilli were present in the blood even when the human tubercle bacillus was used for injection.

From the above experiments it is obvious that after subcutaneous inoculation rapid and abundant distribution of bacilli over the body takes place, provided the infective dose has been large and the tissue conditions of the animal such as to allow it to take full effect. Essentially this is a mechanical dispersion, by means of the blood vessels and lymph channels, of a considerable proportion of the injected bacilli occurring speedily on their insertion into the body ; and the acute tuberculosis resulting from such doses of virulent tubercle bacilli is in its inception in strong contrast to the similar but more slowly developing generalised disease induced by smaller experimental doses or such as occurs, it would seem, most commonly in nature.

This more slowly developing, though acute, tuberculosis is due also to dispersion of bacilli by means of blood vessels and lymphatics, but the bacilli thus dispersed are not necessarily those primarily invading the animal : rather they are their progeny which, protracted conflict between invading bacteria and resisting tissue of the local lesion having been decided in favour of the invaders, have multiplied greatly at the site of primary infection. Both these possible processes of invasion are to be taken into account in considering the method of infection that has probably operated in any case of naturally occurring tuberculosis.

In the case of speedy dispersion of a multitude of inoculated bacilli such as no doubt occurred in the experiments above referred to, the result to the animal, if the bacilli are virulent, is that they produce almost at once and in many different parts of the body lesions of greater or less size, no doubt in proportion to the number of bacilli present. This occurs with the bovine bacillus. In the case of the human bacillus, injected, say, into a resistant animal like the calf, although the bacilli are distributed like the bovine bacillus, they do not produce progressive lesions, though they may induce the indolent, non-progressive tuberculous foci seen in the internal organs of so many of the calves subcutaneously inoculated with the human bacillus.

56. It is important in this matter of distribution and fate of tubercle bacilli in the tissues of the invaded animal, to compare with results such as follow subcutaneous inoculation, the effects obtained by administration of tubercle bacilli along with food ; the latter process of experimental infection having been adopted by us as most nearly parallel with conditions under which in nature a large amount of tuberculous infective material may get opportunity of suddenly invading the animal body. In our Second Interim Report feeding experiments with large doses of the bovine bacillus administered to dogs and pigs were recorded, and it was shown conclusively that after ingestion the bovine bacillus can pass through the mucous membrane of the intestine within a comparatively short space of time, and become lodged in the adjoining lymphatic glands. 2nd Int. Rep., Appendix, Vol. I, pp. 499–706.

Further study of the subject has been made by Dr. A. Stanley Griffith in the pig, goat and cat. Two pigs were fed with large doses of bovine tubercle bacilli and seven with similar doses of human tubercle bacilli. In the case of the two pigs fed with the bovine bacillus, the presence of bacilli was demonstrated, by means of inoculation into guinea-pigs, in the submaxillary and mesenteric glands and lungs in seven and thirteen days after the ingestion of the bacillus, but not in the other organs of the body. In five of the seven pigs fed with human tubercle bacilli in from two to twelve days these bacilli were present in the mesenteric and submaxillary glands alone, while in the other two pigs they were present in the lungs as well. In a goat the human tubercle bacillus after ingestion was found in eight days in the submaxillary glands, mesenteric glands and lung ; and in a cat, fed with the same bacillus, bacilli were found in nine days in the submaxillary and mesenteric glands, lung, liver and spleen. Three rhesus monkeys were fed each with 50 milligrammes of human tubercle bacilli ; one killed in two days showed no bacilli in the glands or internal organs ; the second killed in four days showed bacilli in the mesenteric glands, liver, spleen, and lungs ; while the third killed in six days showed bacilli in the submaxillary and mesenteric glands and spleen, the experiment with the lungs failing, owing to premature death of the guinea-pigs. Appendix, Vol. I, pp. 48–52.

After ingestion the distribution in the organs of the body, therefore, of the bovine and human tubercle bacillus is much slower than after subcutaneous inoculation. In these experiments the bacilli which had passed through the mucous membrane of the intestine were arrested in the adjacent glands ; some, however, appeared to have passed into the lungs and other organs of the body.

57. Certain experiments which were performed by Dr. A. Stanley Griffith in investigation of the question as to excretion of the tubercle bacilli into the milk of healthy cows and goats after subcutaneous or intravenous inoculation of these animals with cultures deserve mention. A large dose (100 milligrammes) of bovine culture was injected subcutaneously into a healthy milch cow (Cow *300*),with the result that her milk caused tuberculosis in guinea-pigs by the end of the first week and on every subsequent occasion. This cow died in thirty days of general tuberculosis but her udder was normal both to the naked eye and on microscopical examination. In two other experiments on cows with the human tubercle bacillus it was shown not only that these tubercle bacilli, when subcutaneously inoculated, were excreted in the cow's milk, but that in some cases the excretion of them lasted Appendix, Vol. III, p. 81.

for a considerable time, and in addition there was evidence of some multiplication of tubercle bacilli in the milk sinuses. In one cow (Cow 77) which received 100 milligrammes of culture of the human tubercle bacillus subcutaneously, tubercle bacilli were present in her milk 24 hours later, and the milk, in small doses, also caused tuberculosis in guinea-pigs 155 days later as well as at intermediate periods, the udder being found normal when the cow was eventually killed. Of one cow (Cow *565*) which received 10 milligrammes of similar culture intravenously the milk was found to contain these tubercle bacilli 24 hours after inoculation and up to 14 days, but not subsequently. This cow was killed in 182 days and showed no tuberculous lesions. Similar experiments performed on milch goats (six in number), with both bovine and human tubercle bacilli, were confirmatory of the results obtained in cows. It would appear, therefore, from the results of these experiments that the inoculation of large doses, whether of bovine or of human tubercle bacilli, may result in the excretion of tubercle bacilli in the milk of the cow and of the goat without any disease of the udder being produced, and that in the case of the human tubercle bacillus, these bacilli may, when large doses are employed, be present in their milk for a long time after inoculation.

Appendix, Vol. III, p. 94.

58. Other experiments were performed to determine whether after subcutaneous inoculation of large doses of culture tubercle bacilli could be found in the undeveloped udders of heifers, 6–18 months old. Of the 12 experiments performed, two were carried out with human tubercle bacilli in doses of 68 and 100 milligrammes, eight with lupus viruses in doses of 50 to 100 milligrammes, and two with the bovine tubercle bacillus, the doses being emulsion estimated to contain 4½ million tubercle bacilli and 50 milligrammes of culture respectively. The heifers were killed in 62 to 127 days and in all but four of them tubercle bacilli were found in the milk sinuses of the undeveloped udder; in four cases they were present in such numbers as to suggest that they had multiplied in these sinuses.

59. We proceed now to consider the formation of tuberculous lesions which have been produced in different animals by the injection of each of the three types of bacilli. It is true that in some animals the intravenous inoculation of any one of the three types of bacilli will, in an appropriate dose, lead to the death of the animal. But in some of these cases such inoculation does not, as has been said, lead to the formation of tuberculous lesions in the organs of the body, and the condition produced is so acute as not to afford a correct idea of the pathological process usually occurring in the spread of tuberculosis in the animal body. More clearly interpretable results are obtained when bacilli are inoculated subcutaneously or intraperitoneally, or when administered by feeding.

Tuberculosis is a disease produced by the tubercle bacillus and characterized by the formation of definite lesions or tubercles. These lesions are a manifestation of the resistance of the body to invasion by the bacillus. Histologically, the tuberculous lesion is composed of leucocytes, "plasma" and other cells, of some tissue elements and of fibrin. The lesion varies somewhat in structure, and as the disease progresses it tends to undergo caseation and in some cases calcification.

A chronic lesion is characterised by the formation of a fibrous capsule round the lesion, by the limitation or absence of caseation, or by the extension of calcification.

Appendix, Vol. V.

2nd Int. Rep., Appendix, Vol. IV.

60. It may be said as a result of the work of Dr. Arthur Eastwood that there is no essential difference in the structure of the tuberculous lesion produced experimentally in animals by the bovine tubercle bacillus and the human tubercle bacillus. Lesions that are produced by the avian tubercle bacillus are generally distinguishable from those caused by mammalian tubercle bacilli, but in the case of lesions of a chronic type it may be impossible to decide by microscopic examination alone whether the tubercles were caused by avian or by mammalian bacilli. Accordingly, a comparison of the general results obtained with the three types of bacilli can only be made by considering, in addition to the histological details of the lesions, (1) the comparative effects in different animals as regards the lesions produced and their distribution, progress and extent, and (2) to a less degree the cultural characters of the type of bacillus involved. But it cannot be too clearly laid down that it is the diverse effect in different animals which constitutes the chief difference between the three types of bacilli.

61. The tubercle bacillus may, as has been said, be present in the tissues of certain animals without producing marked or characteristic lesions. An example of this occurs when the bovine or the human tubercle bacillus is introduced into the body of the rat or mouse. Under certain conditions, in

these resistant animals, the bacillus is present in large numbers in the organs, and even in the blood, without forming tuberculous lesions, although there is no doubt from the large number of bacilli found present that they have actually multiplied in the body. In some of the bovine animals injected with the bovine tubercle bacillus, Dr. Eastwood found, in addition to the lesions of the disease, that the bacilli were present in large numbers in some of the tissues without the formation there of lesions, so that this notable multiplication of bacilli in the tissues of the rat and mouse is only, so to speak, parallel with what may occur in animals which show a progressive tuberculosis. With the avian bacillus this condition, viz., the presence of bacilli in the tissues without the production of definitely tuberculous lesions, is perhaps more frequently observed after intravenous inoculation. In the acute infection produced in fowls by intravenous injection of the avian bacillus, the bacilli are present in enormous numbers in the tissues, and even in the blood stream, although no tuberculous lesions are found after death. In monkeys, rabbits and calves the intravenous injection of the avian bacillus may lead to great multiplication of the bacilli in the body without the formation of lesions characteristic of tuberculosis, and similar results may be produced in swine after subcutaneous and intraperitoneal inoculation of this bacillus, and to a less extent after feeding. In goats and ponies intravenous injection of avian bacilli leads to great multiplication of this bacillus, and in the cat and rat injected intraperitoneally these bacilli become disseminated and multiply and survive for a long period with very little tubercle formation. These results are of interest as showing that in the case of highly resistant animals tubercle bacilli even when introduced in large numbers, though producing none but temporary and minimal tuberculous lesions, may multiply in the body of the animal and persist there for a long period. This result is not always obtained, however, for in certain of our experiments mammalian tubercle bacilli, when introduced intravenously, produced but little effect on the resistant animal and soon died.

SECTION IX.

Question of Modification of Bacilli.

62. In Section I of this Report we have set out the special characters of the tubercle bacilli commonly found in bovine animals, man, and birds, and for convenience in describing the results of our investigations we have termed them respectively the bovine, the human, and the avian type of tubercle bacillus. The three types are to be distinguished from each other by their cultural characters and by the effects of their inoculation into various animals. Distinction cannot accurately be made between these types on the basis of microscopic character alone. Morphologically mammalian tubercle bacilli from whatever source derived, are uniform in character when grown on serum. The microscopical characters of mammalian bacilli were described in our Second Interim Report, pages 25 and 26.

Avian tubercle bacilli when grown on glycerin-serum are generally very short (·5 to 1μ) and rather thick, often looking like cocci. Other media commonly yield longer and more irregular forms; and such forms are also sometimes found on glycerin-serum. Amongst these irregularities is found every counterpart to the irregularities observed amongst mammalian bacilli; and, in addition, large club-shaped thickenings are common and branching occurs more frequently than with the mammalian bacillus. In films obtained from emulsions of cultures it is noticeable that avian bacilli are generally distributed; they do not present the solid clumps of closely adherent bacilli which are characteristic of mammalian tubercle bacilli. When growing freely in the tissues the avian bacillus is short, straight, and uniformly stained; when growing under difficulties it is longer and more irregularly stained and is indistinguishable from mammalian bacilli growing under similar adverse conditions.

Appendix, Vol. V, p. 286, and Plate XVI.

63. To the difficult question of fixity of type of bovine, of human and of avian bacilli, we have given much time and attention. There is here involved a problem of much complexity, the facts bearing on it being not only voluminous but in certain senses conflicting, and we have had to regard the problem broadly from two points of view.

First we have had to inquire:—

Whether *as regards naturally acquired tuberculosis* evidence is forthcoming of

modification, in any sense great or small, in the ordinary animal body, of any particular type of tubercle bacillus—bovine, human or avian ?

And *secondly* we have had to ask ourselves whether *under experimental conditions* any, and, if so what, modification can be induced, and in this connection we have experimented as follows :—

We have—

(*a*) Submitted the several types of bacillus to a series of cultural processes ;

(*b*) Submitted them to long sustained influence of the living tissues of the animal body.

Before proceeding to discuss matters from these points of view it is necessary to restate certain considerations which it is essential should be borne in mind in dealing with the question of fixity of type.

64. We have already noted that by the application of appropriate tests three types of bacilli can be recognised, these tests being an examination of the cultural characters of the bacillus on various media, together with a study of the results of its injection into animals. We have shown in our Second Interim Report that the bacilli cultivated from natural cases of bovine tuberculosis and called the bovine type of tubercle bacillus are not absolutely uniform in cultural characters. As compared with the bacilli of the human type they all grow with difficulty upon artificial media, *i.e.*, they are dysgonic. Bovine bacilli from different bovine cases of tuberculosis exhibit diversities in their degree of growth, diversities that are, however, mostly constant ; that is, a given bacillus when subcultured for many generations commonly affords in the final cultures a type of growth precisely similar to that which it exhibited when isolated from the original material.

The human type of tubercle bacillus grows more luxuriantly than any bovine bacillus, and this luxuriance of growth has been maintained on repeated subculture and even after passage through animals.

The avian type differs from the other two types in forming a slimy whitish growth which is easily emulsified, and it maintains these characters after repeated subculture.

65. All important in the present connection is consideration of the types of bacilli found in the cases of natural tuberculosis which we have investigated. From all the cases of bovine tuberculosis only one type of bacillus was isolated by us : the bovine type of tubercle bacillus. From all birds suffering from natural avian tuberculosis we have only isolated one form of bacillus : the avian type of tubercle bacillus. From the cases of natural tuberculosis in human beings, other than lupus, bacilli of two types were isolated, the bovine tubercle bacillus and the human tubercle bacillus, and in a few of the cases both types were obtained from the same individual. From pigs, bacilli of all three types have been isolated from natural lesions, the bovine, the human, and the avian. And from certain other animals sometimes the human and sometimes the bovine tubercle bacillus was isolated (Section VI).

Our investigation of cases of lupus, as of human tuberculosis affecting other tissues than the skin, resulted in the isolation of bacilli which culturally were either of the bovine type or of the human type. But in most cases of lupus the bacilli isolated did not correspond in pathogenic effects with the bovine, human, or avian type, and from tuberculosis naturally occurring in horses some of the bacilli isolated also did not correspond in pathogenic effects with any of these three types of bacilli.

66. In most of the cases of natural tuberculosis in mammals investigated by us, the lesions were proved to contain only bacilli which could be definitely referred to either the bovine or human type, this statement being based upon a study of the bacillus by repeated subculturing, and a study of the effect of the bacillus on a series of animals. Wherefore the exceptional results obtained in the cases of lupus and in the cases of equine tuberculosis come to be of great importance in that they demonstrate the occurrence in natural tuberculosis of bacilli which depart widely from the types of bacillus which have been described. These results, therefore, demand restatement.

Appendix, Vol. II, p. 28.

There were isolated from six lupus cases bacilli which, although they had the cultural characters of the bovine tubercle bacillus and retained these characters throughout the subsequent investigation, showed a lower virulence for the calf, rabbit, monkey and guinea-pig than the bovine bacillus, and in the case of the two last animals, lower virulence than that of the human bacillus. From two other lupus cases cultures were obtained like those of the bovine bacillus but which were of

even lower virulence for the animals mentioned (Section III). In nine other cases of lupus the bacillus isolated had the cultural characters of the human type but was remarkable in that it showed lower virulence for the monkey and guinea-pig than the human bacillus. The cultures obtained in these 17 cases were not mixtures of different types of tubercle bacilli. The repeated investigation of the cultures from each case and the results of their injection into animals showed this. Here, however, we have eight cases in which the culture was bovine in character but had a virulence for animals below that of the bovine bacillus, and nine cases in which the culture was human in character but had virulence below that of the human type of bacillus. These facts are very striking inasmuch as no such divergencies from the recognized types were encountered among the numerous strains of bovine tubercle bacilli isolated from bovine tuberculosis or among human tubercle bacilli isolated from internal human tuberculosis.

67. In the case of equine tuberculosis (Section V) the bacilli isolated from two horses, although growing like the bovine tubercle bacillus, did not in animals behave like that bacillus, in that they were proved by inoculation to be much less virulent for the calf and other animals (guinea-pig, rabbit and monkey). Here again there is a conspicuous divergence from the three types of bacilli previously recognized, the results being similar to those produced by certain dysgonic lupus bacilli. Appendix, Vol. IV, p. 7.

68. The question accordingly arises: Whether we are to regard these bacilli isolated from cases of lupus and of equine tuberculosis which present exceptional characters and vary, some of them widely, from the three types of bacilli described, as (1) independent fixed types, or (2) modifications on the one hand of the bovine tubercle bacillus and, on the other, of the human tubercle bacillus.

As bearing on this question the results of experiments with some of the lupus viruses and with two equine viruses must be again referred to (*see* pages 16 and 21). As regards the cases of lupus yielding bacilli which, culturally, were of the bovine type but which did not correspond pathogenically with the bovine type when injected into animals, if it proved possible by experiment to increase the virulence of these bacilli to that of the bovine type, such bacilli might be considered as modified forms of the bovine type. In two cases (H. 100. "R.S." and H. 108. "H.R.") it was found that after the lupus culture had been injected into a calf, and carried on from this calf into a second calf it exhibited a virulence fully equal to that of a bacillus of bovine type. A similar result, however, in the calf was not obtained with four of the viruses (H. 105. "G.S.", H. 53. "D.H.", H. 107. "H.H.", and H. 85. "H.B."). In one of these (H. 105. "G.S.") the virulence for rabbits was, however, slightly increased by passage through the calf, and in another, (H. 53. "D.H.a") for the monkey by passage through the monkey. In one of the cases of lupus in which the bacillus isolated had the cultural characters of the human type but a feeble virulence for the monkey, it was found that by a single residence in the monkey for 139 days its virulence was increased to that of the human tubercle bacillus. In other instances the results of the passage were negative. Appendix, Vol. II, pp. 21 & 22.

With the two equine viruses (p. 23) the passage experiments resulted in an increase of virulence of the bacillus up to that of the bovine type. Appendix, Vol. IV, p. 8.

It can hardly be contended that the cases of lupus in which bacilli with these special characters were found had no etiological connection with ordinary cases of human or bovine tuberculosis, or even with the other cases of lupus in which the bacilli present were of the usual bovine or human type. The virulence of the bacilli in these exceptional cases showed a great divergence from the bovine and from the human type, and if it were to be held that virulence is a fixed quality it would be necessary, in order to classify the lupus viruses, to recognize several new types of tubercle bacilli amongst those which grew like the bovine bacillus but differed from this bacillus in virulence, and several new types amongst those which grew like the human bacillus and differed from it in the same way in virulence. If the proposition were entertained that lupus bacilli are all different types of bacilli, each of which is stable when cultivated and when injected into animals, it would follow that infection in these cases of lupus could not be thought of as having been brought about by tubercle bacilli from cases of ordinary tuberculosis in man or animals; that instead, each of the lupus patients had been infected from an antecedent like case of lupus or by some acid-fast saprophyte resembling the tubercle bacillus. Clearly this proposition is one which cannot be accepted; the less so since by experiments performed with the lupus and equine viruses it has been found

possible in some of the cases to enable the bacillus to acquire the full virulence of the bovine tubercle bacillus by residence in the animal body.

The results of our investigation of lupus do not induce us to add a plurality of new types of tubercle bacilli to the three already described. Further investigation of natural tuberculosis in man and animals may possibly disclose other additional variations in the types of bacilli ; since not only in human tuberculosis does this disease when affecting the skin furnish types diverging from the human and from the bovine tubercle bacillus, but the internal organs of the tuberculous horse likewise yield divergent types.

69. We pass now to the consideration of artificial conditions specially contrived for inducing modification of type.

We have already stated that we have failed to modify by means of artificial cultivation the pathogenic properties of any one of the three types of bacillus, though for this purpose we have employed many and various media on some of which the bacilli grow more and on others less readily.

We have also investigated the question as to whether by experiment an example of a given type of tubercle bacillus can be modified by prolonged relation with the tissues of the animal body, either during continuous residence in a single animal or repeated passage through a succession of animals. The animals used have been as a rule such as were specially resistant to the growth of the given bacillus, it being considered that in this way modification of type was the more likely to be obtained. It will be borne in mind that in our Second Interim Report we published the results of experiments with human viruses which were relegated by us to a provisional Group—Group III. In certain of those experiments the virus, growing originally like a human tubercle bacillus, was at the end of passage through calves found to be virulent for this animal and to present the cultural characters of the bovine tubercle bacillus. We came to no definite conclusion as regards the explanation of these facts at that time ; but in this Report (page 14), as a result of our further investigation, we have shown that these Group III results were due, certainly in most if not in all cases, to the presence of two types of bacilli, the human and the bovine, in the original material, and that during the course of the passage the human type, not developing in the calf, had died out, leaving the bovine type which multiplied and exerted its virulence on that animal.

Appendix, Vol. III, p. 5.

70. In further experiments with other viruses designed to effect modification of the type of bacillus, whether human or bovine, we satisfied ourselves that the material used in those experiments contained only one type of bacillus.

In one group of experiments, the investigation was carried out by means of collodion capsules, containing cultures of mammalian tubercle bacilli, which were inserted in the peritoneal cavities of birds.

Appendix, Vol. IV, p. 388.

With 10 mammalian viruses, from various sources, 8 of which were bovine, 16 collodion capsule experiments on fowls and 20 on pigeons were performed, lasting from 55 to 186 days. In certain of the cases cultures which were obtained from the capsules on removal from the bird's peritoneal cavity, were placed, again in capsules, in the peritoneal cavities of other birds, the total duration of residence being in one series as much as 475 days. In 20 of these experiments cultures were obtained from the capsules and found to be unchanged in character. In 16 cases no culture could be obtained, the bacilli in the capsules being apparently dead.

Appendix, Vol. I, p. 59.

Similar experiments were performed with human tubercle bacilli, obtained from 12 different sources. In nine cases there was only a single residence in the peritoneal cavity of the fowl or pigeon ; in three cases the capsules were transferred in series to other fowls. These experiments lasted from 59 to 685 days. In many of the capsules the bacilli were dead, but in the others, the bacilli were alive and showed no change in cultural characters or in virulence.

Appendix, Vol. IV, p. 388.

With cultures of five avian viruses 25 collodion capsule experiments were performed on guinea-pigs. The duration of residence in individual guinea-pigs ranged up to 253 days and the total periods during which the cultures were in the peritoneal cavities of series of guinea-pigs varied up to 424 days. In two instances only was there failure to obtain growth of culture from the capsules ; from all the other capsules cultures were obtained and were found to be unchanged.

Appendix, Vol. IV, p. 389.

As regards further experiments with bovine tubercle bacilli directly introduced into the tissues, two passage experiments on fowls with Virus B. XXVI deserve mention. One of these lasted 2½ years, and included a long series of birds, but no change in the characters of the bacillus was observed. The second lasted the same

time with a like result. One of the fowls in the first passage (one of four inoculated at the same time) showed, when killed, avian tuberculosis which was regarded as naturally contracted. It was the only fowl in the two series which was so affected, but this occurrence during the passage shows the danger of drawing conclusions from the result of experiments on fowls unless they are sufficiently controlled.

Among experiments with bovine tubercle bacilli, some on dogs, both by inoculation and by feeding, were recorded in our Second Interim Report. In two of the dogs referred to in that Report residence in this animal appeared to have altered the bovine tubercle bacillus, inasmuch as cultures obtained from these two animals resembled the human tubercle bacillus. In the remainder of the experiments on dogs no change in the bovine tubercle bacillus occurred. In certain further experiments eight dogs were fed with doses varying from 40 to 100 milligrammes of culture of bovine tubercle bacilli and were killed in from 103 to 302 days. From five it was impracticable to secure cultures, but from the remaining animals cultures were obtained which were not changed either in character or virulence. From nine other dogs which had been inoculated by various methods eight cultures were obtained which showed no alteration.

2nd Int. Rep., Appendix, Vol. III, p. 91.

Appendix, Vol. IV, p. 389.

A chimpanzee passage experiment was performed, five chimpanzees being used in series; three of the animals were fed and two were inoculated. The experiment lasted 542 days and no change in the bovine bacillus was found at the end of the experiment. A similar result was obtained by passage in baboons.

Appendix, Vol. IV, p. 390.

In further experiments with the human tubercle bacillus nine separate viruses were used. With six of the viruses passage experiments were carried out on calves, the number of animals included in each experiment varying from two to seven and the total duration of the residence of the bacilli in the calf's body varying from 247 to 512 days. There was no alteration in the characters of the bacillus at the end of the passage in any of the cases. After continued residence in one case for 484 days in the bodies of three rabbits consecutively, and in another after 725 days single residence in the body of one rabbit the human cultures were found unchanged. Similar results were obtained in two experiments on the rat after residence in the one case for 454 days in the body of one rat, and in the other for 1614 days in the bodies of eight rats consecutively. Single residences in a cow for 529 days, in a pig 378 days, a guinea-pig 320 days, a dog 413 days, produced no change in the characters or virulence of the cultures of the human bacillus.

Appendix, Vol. I, p. 55.

These particular experiments, therefore, failed to effect any modification in the bovine or human tubercle bacillus.

71. As regards experiments directed to modify the virulence of the avian tubercle bacillus similar negative results were obtained. Single residence in the horse, calf, goat, pig, monkey, cat, dog, rat, mouse, rabbit, and guinea-pig showed no change in the cultural characters nor in the virulence of the avian bacillus originally inoculated. Passage experiments were performed on calves with the culture of Virus A. X, which was obtained from the lung of a rabbit inoculated from natural tuberculosis in a fowl. From one of the calves of this series a culture obtained from the bronchial gland was bovine in character, while in the same animal a typical avian culture was obtained near the seat of inoculation. There can be little doubt that this was not a case of modification, but one of accidental infection of the calf by the bovine bacillus. Other experiments were performed with avian bacilli obtained from pig tuberculosis, and in some of these experiments the bovine tubercle bacillus, and in one case the human tubercle bacillus, was obtained from some of the lesions of the animals into which the culture derived from the pig lesion had been introduced. These results, which are set forth in the Appendix, were obtained in only a few experiments and were so discordant that we cannot draw any conclusions from them.

Appendix, Vol. IV, p. 385.

72. In cases of internal human tuberculosis we found a certain number which showed a mixture of human and bovine tubercle bacilli, and in the pig there was one case in which there was a mixture of bovine and avian tubercle bacilli. When separated, the bacilli from these cases were found to correspond in their characters to the bovine, human and avian types. Although it might be urged that the mere finding of the two types in a lesion indicated the occurrence of a process of modification in one or other type, yet we found no transitional types in the lesions

Appendix, Vol. III, pp. 12 18, and 151.

of internal tuberculosis in the human being, nor in the pig any but doubtful suggestion of such transition. The only variation from the three types which we have found in our extended investigations have occurred in cases of lupus and in equine tuberculosis.

SECTION X.

Consideration of the Results in relation to the Terms of Reference.

73. The questions that were referred to us for investigation and report are as follows :—

1. " Whether the disease in animals and man is one and the same ;
2. Whether animals and man can be reciprocally infected with it ;
3. Under what conditions, if at all, the transmission of the disease from animals to man takes place, and what are the circumstances favourable or unfavourable to such transmission."

We have attempted to answer these questions by investigating cases of natural tuberculosis in man, and by studying the disease in animals as it occurs naturally in them as well as when produced by experimental means. Our investigation has dealt not only with the naked-eye and microscopical appearances of the diseased tissues, but also with the tubercle bacillus itself—the essential cause of the disease. Separating the bacillus from the lesion, we have obtained it in pure culture and studied the variations of its growth under artificial conditions and the results produced by it when injected into animals of various species. Tuberculosis being a disease affecting not only man but also domestic animals such as cattle, horses, pigs and poultry, and certain other animals when kept in captivity, our investigation has covered a wide range of tuberculous disease, and enabled us to make a careful comparison of the conditions of tuberculosis as it occurs naturally in man and in animals. In three Interim Reports presented during the progress of our investigation we set out certain results as they were arrived at, expressing opinion on the facts before us ; and we have already, in the preceding Sections of this our Final Report, summarized those earlier results together with others not previously recorded. It is now necessary to consider how far the total results of our investigation afford material for definite reply to the questions put to us.

First Term of the Reference.

74. The first question is :—Whether tuberculosis in animals and man is one and the same.

The morbid conditions in man and animals which are embraced under the term tuberculosis are all bacterial in their origin, and the question of the identity or non-identity of a case of tuberculosis in one animal with a case in another animal of the same or of a different species depends upon the identity or non-identity of the bacilli responsible for the lesions in each case. It therefore becomes necessary to inquire whether it is possible to arrange bacteria in sharply defined groups corresponding with what are called species in the case of the higher plants and animals, or to affirm of any two bacteria that they are identical in the sense that all members of the canine species are identical. The characters which are generally relied upon to fix the species of bacteria are their morphology (including size and form), their appearances in artificial culture, and their pathogenic properties or capacity for causing disease in various species of animals. As in the classification of the higher plants and animals, so also in the classification of bacteria, morphological characters have the greatest value, and no two organisms which constantly differed in form and size could be considered identical or belonging to the same species, even though they were indistinguishable in every other respect. In spite of their minuteness and the simplicity of their structure some bacteria present well-marked morphological differences as compared with others, and in such a case non-identity is obvious, and classification presents no difficulty. Classification is still easy in spite of morphological identity when bacteria differ markedly in cultural and pathogenic characters, but it becomes difficult when bacteria that are morphologically indis-

tinguishable exhibit only minor differences in respect of their cultural and pathogenic characters.

The particular case which we are now considering is exactly of that nature.

Leaving aside for the moment the question of the relationships of the bacilli of avian tuberculosis, it has to be admitted that the human and bovine types of bacilli are morphologically indistinguishable, but appreciably different in respect of their cultural characters and their capacity for causing disease in various species of animals. The question of the identity or non-identity of these two types therefore clearly depends upon the importance which it is permissible to attach to their cultural and pathogenic differences, and this in turn on the fixity or variability of the differences in question. If these differences are not constant they cease to be of value for classification, but if according to all the available evidence they are constant, the human and bovine types of tubercle bacilli must be considered distinct, and the diseases which they cause as not identical, that is to say not one and the same.

At an earlier part of this Report we have discussed the question whether the human and the bovine types are stable in respect of their cultural characters and pathogenic properties. With regard to the first of these we need only repeat here that the only difference in respect of cultural characters between the two types is that the human type exhibits a greater luxuriance of growth on all the different media which we have employed in making comparisons, and that although this difference is not maintained with absolute constancy, we have not in our cultural experiments observed any case in which the mode of growth of the one type became so far modified as to be indistinguishable from the mode of growth usually exhibited by the other. But the point must be emphasised that the bacilli which we have referred to the bovine type vary considerably among themselves in respect of luxuriance of growth, and that the gap which separates those of them that grow most abundantly from bacilli of the human type is not a wide one.

The bovine tubercle bacillus produces a fatal tuberculosis in cattle, rabbits, guinea-pigs, chimpanzees, monkeys, goats and pigs.

The human tubercle bacillus readily produces a fatal tuberculosis in guinea-pigs, chimpanzees and monkeys, but causes, even when administered in large doses, only slight and non-progressive lesions in cattle, goats and pigs. Its effect on rabbits is not uniform, for whilst in the majority of cases these animals are only slightly affected, in others extensive and fatal tuberculosis results in them from the inoculation of the human tubercle bacillus.

In other words, we have always found that guinea-pigs, chimpanzees and monkeys are all highly susceptible to the effects of either the human or the bovine tubercle bacillus and that the disease produced in these animals by both types is histologically and anatomically identical.

Obviously it has not been permissible to induce tuberculous disease experimentally in the human subject by the injection of bovine tubercle bacilli, and no opportunity presented itself to us of examining any case of accidental infection in which the bovine tubercle bacillus entered the human body through the skin and set up a generalised disease. But we have investigated many instances of fatal tuberculosis in the human subject in which the disease was undoubtedly caused by a bacillus of the bovine type and by nothing else. We have compared the lesions from such cases with those obtained from parallel cases of fatal tuberculosis in which the human tubercle bacillus alone was discovered. Except for the difference in the type of bacillus found in them, these two groups of cases presented similar features ; the clinical histories of the patients were alike, the cases all terminated fatally, and the lesions examined after death were found to be anatomically indistinguishable. Man must therefore be added to the list of animals notably susceptible to bovine tubercle bacilli.

Chief among the differences between bovine and human tubercle bacilli is, of course, difference of virulence towards certain animals. Why, it may be asked, is the human bacillus, though as virulent for the monkey and the guinea-pig as is the bovine, far less virulent than that bacillus for the calf, goat, and pig. Is the human bacillus a bovine bacillus which, through some cause or combination of causes, has become modified, and, if so, is its degradation in this sense permanent ?

We have recorded (paragraphs 69 and 70) our repeated attempts to transmute

the bovine bacillus into the human bacillus and *vice versâ*. Most of these attempts failed altogether, a few only were equivocal ; we found indeed that under the conditions contrived by us both types of bacilli remained remarkably stable, alike as regards their growth on artificial media and their virulence for animals. Thus, we are inclined to regard transmutation of bacillary type as exceedingly difficult if not impracticable of accomplishment by laboratory procedure, though in view of certain instances in which we obtained from one and the same human body both types of bacillus, we are not prepared to deny that the transmutation of one type into another may occur in nature.

With respect to the question of the stability of the pathogenic properties which distinguish the two types, we must again refer to the exceptional characters possessed by certain of the bacilli which were isolated from cases of lupus and equine tuberculosis. In some of these cases the bacilli had the ordinary cultural characters of the bovine type, associated with a degree of virulence for the calf and rabbit no greater than is usually exhibited by the human type. We have already given reasons for declining to accept these exceptional bacilli as distinct fixed types, and if that view of them is excluded they must be regarded as either modified human or modified bovine bacilli. On the former assumption they had acquired the character of growth ordinarily exhibited by the bovine type, and on the latter assumption they had lost the higher degree of virulence for certain animals which is characteristic of the bovine type. The latter appears to be the more probable explanation, and if that view be accepted the discovery of these exceptional bacilli makes it impossible to regard difference of virulence for the calf and rabbit as sufficient to establish the non-identity of the human and the bovine types.

There would therefore remain only slight cultural differences on which to found the conclusion that the human and the bovine types represent two distinct organisms. We prefer to regard these two types as varieties of the same bacillus, and the lesions which they produce, whether in man or in other mammals, as manifestations of the same disease.

But while we regard the point which we have just considered as one concerning which there is room for difference of opinion, there is an aspect in which tuberculosis in men and in cattle must unquestionably be pronounced one and the same disease. Whether one prefers to regard bovine tuberculosis and the cases of tuberculosis in man which are caused by the human type of bacilli as varieties of the same disease or as independent diseases, there can be no question that human tuberculosis is in part identical with bovine tuberculosis. Our researches have proved that in a considerable proportion of cases of the human disease the lesions contain, and are caused by, bacilli which are in every respect indistinguishable from the bacilli which are the cause of tuberculosis in cattle. In all such cases the disease therefore is the same disease as bovine tuberculosis.

There remains the question whether avian tuberculosis and bovine tuberculosis, or avian tuberculosis and the tuberculosis caused by the human type of bacillus, are one and the same disease. In this matter there does not appear to us to be in the present sufficient ground for answering the question in the affirmative.

Second Term of the Reference.

75. In the second term of our Reference we were asked :—Whether animals and man can be reciprocally infected with tuberculosis ; that is, whether the disease known as tuberculosis can be communicated direct from man to animals and from animals to man. The question thus presented to us was one of exceptional difficulty. For though the liability of animals to infection from man could be tested in detail by direct experiment, man's liability to infection from animals remained of necessity matter only of inference. Certain instances have, it is true, been reported in which suspicion had arisen that man had become infected through contact with tuberculous cattle, but the evidence afforded by these cases, notwithstanding that they had been carefully investigated, could not be accepted as unequivocally positive in character. Accordingly the transmissibility of tuberculosis of the three several types has had to be judged of by the behaviour of the bacilli representing them when introduced, each in separate series, into the bodies of a variety of animals.

By subcutaneous inoculation the human type has been found transmissible in some degree to many different species of animals, but for most of them transmission has been effected only by the employment of large doses. And moreover in some species of animals the lesions thus induced were either local or sparsely distributed and non-progressive in character. The animals that we have found to be especially refractory to the human tubercle bacillus administered by subcutaneous inoculation are cattle, pigs, and fowls, and these animals are often even more refractory, or are indeed practically immune, when the bacilli are administered, even in large amounts, with their food. Corroboration of this high degree of resistance to human tubercle bacilli on the part of cattle, pigs and fowls is afforded by the circumstance that so far as our investigation of tuberculosis naturally occurring in the lower animals has gone we have not in a single instance detected the human type of tubercle bacillus in cattle or in fowls, and but rarely in pigs. Rabbits are not so resistant to the human tubercle bacillus, which is capable of producing in them progressive and fatal tuberculosis (page 6).

In strong contrast to this small liability of certain of the lower animals to tuberculosis of the human type is the susceptibility of animals generally to infection by the bacillus of the bovine type (whatever the source, lower animal or man, of such bacillus). Over a very wide field of experiment in this connection, the only animals that we have found at all uniformly resistant to this type of bacillus are the common fowl, the rat and (to a less extent or at least less uniformly) the dog. And similarly our investigations of tuberculosis naturally occurring in lower animals indicate the great preponderance of the bovine type among them.

In cattle suffering from tuberculous disease acquired other than by experimental means, we have in no single instance detected any but the bovine bacillus.* This is also the type of bacillus found in progressive tuberculosis in the pig, though this animal is capable of harbouring (while perhaps not encouraging) the human and avian types of tubercle bacillus. So far as our experiments show, the chimpanzee, an animal closely related to man, is equally susceptible to the bovine and human tubercle bacillus, the effects produced by them in this animal both by feeding and inoculation with parallel doses being closely alike.

As regards the avian type of tubercle bacillus, reciprocity among animals to this infection hardly calls for notice. Though the fowl and other birds are highly susceptible to tuberculosis of this type, mammals generally, with the exception of the rabbit and mouse, and, perhaps to a less extent, the pig and goat, would appear almost absolutely resistant to it. The monkey and the guinea-pig, both of them highly susceptible to bovine and human tubercle bacilli, are notable instances of this.

Taking these facts into consideration together with those others already discussed in relation to the first term of our Reference, and for the above reason excluding the fowl and other birds from further consideration in this connection, we must conclude that mammals and man can be reciprocally infected with the disease (tuberculosis). The possible danger to man through reciprocity in this sense was, of course, the more important question presented to us, and as we have conclusively shown that many cases of fatal tuberculosis in the human subject have been produced by the bacillus known to cause the disease in cattle, the possibility of such infection cannot be denied.

And the importance of this conclusion is not diminished by the fact that the majority of such cases examined by us occurred in young children, or by the merely local results following the administration of the human type of bacillus to bovine animals. Bovine animals are not completely immune to the human tubercle bacillus, and adult human beings can be infected with the bovine type, even the pulmonary form of the disease in man being sometimes caused by the bovine tubercle bacillus.

Third Term of the Reference.

76. The third question with which we are called upon to deal is :—

Under what conditions, if at all, the transmission of tuberculosis from animals to man takes place, and what are the circumstances favourable or unfavourable to such transmission.

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* *See* footnote on page 4.

Transmission of tuberculosis from animals to man must obviously be mainly dependent on the susceptibility of any given animal to this disease and on the opportunities afforded such animal for transferring its acquired and developed infection to the human subject. From what we have already said, man must clearly be regarded as being liable to risk of infection from at least two of the three types of tubercle bacilli, the human and the bovine. In this connection it will be convenient to discuss each type separately.

Avian Tuberculosis.—Prima facie, man might be regarded as at some risk from this form of tuberculosis owing to his food relations with fowls and certain other birds, and the fact that we have in more than one instance discovered the avian tubercle bacillus in the bodies of pigs might also be considered a matter of importance. But in no single instance have we found the avian tubercle bacillus in the lesions of tuberculosis in the human being, whilst man's comparatively near relative, the monkey, would appear from our experiments to be highly resistant to tubercle bacilli of this type. The pig is the only mammal in which we have found the avian bacillus in the lesions of naturally acquired tuberculosis, but possible danger to man from this source would appear to depend on an ability not yet demonstrated of this animal to bring about modification or alteration of this type of tubercle bacillus in the direction of greatly enhancing its virulence for man. We must conclude, as the result of our investigations, that the unmodified avian tubercle bacillus is a negligible factor in the production of human tuberculosis.

Human Tuberculosis.—In so far as tuberculosis of this type in animals lower than man has resulted from infection contributed to them by man himself, man has been multiplying in bodies other than his own that type of tubercle bacillus to which he is seemingly most prone, and thus increasing his chances of death by tuberculosis. But, as has been shown, animals, domestic and other, which have been found capable of suffering from severe generalised tuberculosis of the human type are comparatively few; and further, none of these active multipliers of human tubercle are common food animals. The bovine animal for instance is not an active multiplier of the human tubercle bacillus, being highly refractory to this infection; and the cow herself, however prone she may be when the subject of bovine tuberculosis to excrete bovine bacilli in her milk, has never under natural conditions been convicted of eliminating in this way the human tubercle bacillus. Experimentally, it is true, the human bacillus has been made to appear in the milk of the cow and goat, but for securing this end very large doses of culture have been requisite. Probably only when the cow or goat has received a large dose of tuberculous material derived from man does the human tubercle bacillus escape into the blood stream of the animal, reach her milk sinuses, and become eliminated with her milk.

Nevertheless, it is not to be affirmed with confidence that man is wholly free from risk through animal food of infection with that type of tubercle bacillus to which he appears most prone, though the degree of danger to him in this sense must remain for the present undetermined. The pig, though not capable in our experimental experience of fostering tubercle bacilli of the human type except in a minor degree, may have to be regarded as a possible source of the disease caused in man by that type of bacillus; for the reason that particular glands of the pig's body, which are likely to enter into certain prepared foods, do on occasion yield tubercle bacilli of the human type.

Bovine Tuberculosis.—Before dealing with the conditions affecting the direct transmission of tuberculosis from bovine animals to man, one other potential source of infection of man with the bovine type of the tubercle bacillus must be referred to. The pig is, besides the bovine, the only animal commonly used for food by man in which during our investigation we have found the bovine tubercle bacillus producing the progressive lesions of the natural disease. We found this bacillus in a number of cases of swine tuberculosis sufficient to justify us in calling attention to the danger without entering into a discussion as to its extent. Bovine tubercle bacilli are infective to human beings, and we have no reason to suppose that they can be rendered less so by previous residence in the bodies of pigs.

During the course of our inquiry we investigated material obtained either post-mortem or by operation from 146 individual cases of persons suffering from tuberculosis; a total which does not include the two viruses consisting of sputum collected

daily from a varying number of patients. But some of those 146 have been excluded from our final conclusions for reasons already set out on page 9, and certain others of them, though dealt with in detail in our Appendix, are not considered in this Report, the investigations in which material from them was employed having but an indirect bearing on the terms of our Reference. Thus the actual number of cases, representing the various clinical manifestations of tuberculosis commonly found in man, that have passed under strict observation and on which our conclusions are based, is 128.

So far as these 128 cases have been examples of tuberculosis in the adult, and especially when they have been cases of pulmonary tuberculosis, the lesions of the disease when fatal have been referable with few exceptions to human bacilli. Only rarely has a pulmonary lesion in adult man yielded the bovine bacillus. Our experience of abdominal tuberculosis in the human subject has been very different, especially as regards children. Of young children dying from primary abdominal tuberculosis, the fatal lesions could in nearly one half of the cases be referred to the bovine bacillus, and to that type alone. In children, too, and often also in adolescents, suffering from cervical gland tuberculosis, a large proportion of the cases examined by us could be referred to the bovine tubercle bacillus. We have already in an earlier portion of this Report referred to the importance of infection by the bovine type of tubercle bacillus in cases of lupus occurring in adolescents and children.

Whatever, therefore, may be the animal source of tuberculosis in adolescents and in adult man, there can be no doubt that a considerable proportion of the tuberculosis affecting children is of bovine origin, more particularly that which affects primarily the abdominal organs and the cervical glands. And further, there can be no doubt that primary abdominal tuberculosis as well as tuberculosis of the cervical glands is commonly due to ingestion of tuberculous infective material.

Judging by our feeding experiments there would appear to be strong presumption that as regards most animals comparatively large doses given either singly or by frequent repetition are necessary to produce by ingestion acute progressive generalised tuberculosis, though we have recorded instances in which a very small dose administered but once has produced this result. Applying a like presumption to man (and our observations on the monkey and chimpanzee in this connection afford warrant for so doing) it may be asked in what way are children, the members of the human family who are especially liable to exhibit acute fatal tuberculosis commencing as an abdominal affection, most likely to obtain a large and fatally infective dose of tubercle bacilli?

As already indicated by us, to this question there can be but one answer:—namely that the evidence which we have accumulated goes to demonstrate that a considerable amount of the tuberculosis of childhood is to be ascribed to infection with bacilli of the bovine type transmitted to children in meals consisting largely of the milk of the cow.

In many cases of abdominal tuberculosis and in tuberculosis of the cervical glands, however, it must be recollected that the child may be injured by the ingestion of bovine tubercle bacilli in milk without a fatal result occurring. The cases of abdominal tuberculosis examined by us had all been fatal, that is death occurred from a generalised tuberculosis or from some local condition resulting, with possibly two exceptions, from tuberculosis of the abdomen. But many cases of abdominal tuberculosis in children recover, though what proportion of these is due to the bovine bacillus and what to the human, we have no means of knowing at present. The cases of cervical gland tuberculosis investigated by us were all cases that recovered or were recovering after operation, and a large proportion of them were bovine in origin.

Although the potency of tuberculous cow's milk in the causation of the tuberculosis of infancy and childhood is clearly demonstrated, in our examination of material from 55 cases of tuberculosis in adolescents and adults we have found rarely in the former and extremely seldom in the latter the bovine bacillus colonising the fatal lesions.*

Instead we found abundantly in these lesions none but the human bacillus, a circumstance, which, if considered alone, might tend to discount the extent of the danger to the adult human subject not only of the milk of tuberculous cows but also of the flesh of that and other animals capable of fostering the bovine tubercle bacillus. But it must be remembered that we have found cases of tuberculosis in adult man,

* *See* footnote next page.

sufficiently extensive to incapacitate the patient for the ordinary duties of life and in two instances ending fatally, in which we were able to attribute the disease solely to the effects of the bovine tubercle bacillus. Though of the 55 cases of adolescent and adult tuberculosis which came under scrutiny no more than 5 yielded bacilli of the bovine type, we cannot say that this figure adequately represents the proportion of like cases obtaining among the tuberculous population generally.*

77. Meanwhile we, in view of the evidence adduced by us, regard ourselves as called upon to pronounce on administrative measures required in the present for obtaining security against transmission of bovine tubercle bacilli by means of food. In the interests therefore of infants and children, the members of the population whom we have proved to be especially endangered, and for the reasonable safeguarding of the public health generally, we would urge that existing regulations and supervision of milk production and meat preparation be not relaxed ; that on the contrary Government should cause to be enforced throughout the kingdom food regulations planned to afford better security against the infection of human beings through the medium of articles of diet derived from tuberculous animals.

More particularly we would urge action in this sense in order to avert or minimise the present danger arising from the consumption of infected milk. And in this connection it may be convenient for us to repeat certain facts observed by us in reference to the conditions tending to the elimination by the cow of bovine tubercle bacilli in her milk ; facts in our opinion of such importance that they formed the subject of our Third Interim Report.

Bovine tubercle bacilli are apt to be abundantly present in milk as sold to the public when there is tuberculous disease of the udder of the cow from which it was obtained. This fact is, we believe, generally recognised though not adequately guarded against. But these bacilli may also be present in the milk of tuberculous cows presenting no evidence whatever of disease of the udder, even when examined post-mortem. Further, the milk of tuberculous cows not containing bacilli as it leaves the udder may, and frequently does, become infective by being contaminated with the faeces or uterine discharges of such diseased animal. We are convinced that measures for securing the prevention of ingestion of living bovine tubercle bacilli with milk would greatly reduce the number of cases of abdominal and cervical gland tuberculosis in children, and that such measures should include the exclusion from the food supply of the milk of the recognisably tuberculous cow, irrespective of the site of the disease, whether in the udder or in the internal organs.

We desire to express our sense of the great value of the services rendered to the Commission by our officers, professional and other.

To our Secretary, Dr. E. J. Steegmann, we are indebted not only for further unwearied diligence in our behalf during additional years, but also for exercise by him throughout the whole period of this Commission of administrative capacity of the highest order.

The work of our several investigators is summarised by each (above his signature) in those volumes of the Appendix to this Report in which details of his particular research are recorded. The volumes in question are sufficient testimony to the painstaking accuracy and intelligent resourcefulness of these experts. In this place, however, we would express our special appreciation of Dr. A. Stanley Griffith's original and highly important researches on Lupus and his admirably effective scrutiny of anomalous viruses ; Dr. Frederick Griffith's investigation of Equine tuberculosis ; Dr. Arthur Eastwood's histological researches ; and also of the importance of the work carried out jointly by Dr. A. Stanley Griffith and Dr. Frederick Griffith in connection with the tuberculosis of swine.

The duties undertaken by Dr. Hammond-Smith are referred to in detail in the Memorandum accompanying this Report. We wish here to record our sense of the great value of his services.

Our non-professional administrative officers and our laboratory assistants have each and all of them rendered throughout admirable and faithful service. Among

* The 55 cases referred to include only those of tuberculosis other than lupus. Cases of lupus coming under observation in adolescent and adult patients numbered 10, 3 of which yielded tubercle bacilli presenting the cultural characters of the bovine type though possessing less virulence for the calf and rabbit than the bovine tubercle bacillus.

the former we are on these grounds particularly indebted to Mr. C. F. Fox and Mr. J. Keddie ; among the latter to Mr. C. Attoe.

Finally we again record our grateful recognition of the keen interest in and never failing generosity towards our researches which have ever been conspicuously manifested by Lord Blyth. By his ungrudging hospitality, during a decade of years, in placing at our disposal his Stansted Farms he has enabled our investigations to be carried on untrammelled by outside interference or objection, and (a matter of great practical importance) absolutely without risk of transferring infection to animals the property of neighbours.

(Signed) W. H. POWER, *Chairman.*

G. SIMS WOODHEAD.

SIDNEY MARTIN.

J. McFADYEAN.

RUBERT BOYCE.

EDWARD J. STEEGMANN, *Secretary.*

June, 1911.

MEMORANDUM.

In the Introduction to the Second Interim Report the procedure adopted by the Commissioners for carrying out their investigation was explained, and the Farms and Laboratories at Stansted were described. An account was also given of the methods of experiment, of the precautions taken to obtain healthy animals for experimental purposes and of the means used for procuring the material required for research. Though not necessary to repeat all that was there said, no alteration having been made in any important particular in the period that has elapsed since that Report was issued, it may be convenient to re-state briefly certain essential facts connected with the practical administration of the inquiry.

During the whole of the time occupied by the Commission in investigating the questions contained in the several terms of their Reference, all the experimental work on which conclusions have been based was carried out in the Stansted Laboratories and Farms by resident investigators working under the direct supervision and control of the Members of the Commission. A few independent investigations were, it is true, entrusted to other observers, but these affected matters in the nature of side-issues, and no additional positive facts bearing on the main points of the investigation having been thus established the results obtained were not taken into account by the Commission.

At Stansted, three widely separate places were used by the Commission for research work; each was in charge of an investigator, with an adequate staff of assistants under him, and no communication was permitted between those where experimental animals were kept except under strict rule and supervision.

The whole of the land occupied by the Commission at Stansted, the house known as Royalcot, used for administrative purposes as well as for the accommodation of Members of the Commission when visiting Stansted, and the farm buildings, were lent by Lord Blyth, without any expense to the Government for rent, rates, or taxes. In addition, he allowed the Commissioners to erect laboratories and animal houses, and to alter in any way they pleased the existing buildings. But at Blythwood the buildings that had been previously erected by Lord Blyth for his own stock proved so eminently suitable for the purposes of the investigation that very little modification was required; indeed it would have been difficult to find, even apart from the question of cost, any places so well adapted for the practical experimental work as those provided by the far-sighted generosity of Lord Blyth.

Animal experiments were only carried out at two of these places, Walpole and Blythwood Farms.

Walpole Farm was at first used solely for the investigation of the tuberculosis of bovine animals, and no other work carried out at this farm was considered in the Second Interim Report of the Commission. But before the issue of that Report the practical inquiry in connection with Swine Tuberculosis had been commenced at Walpole, and the preliminary experiments relating to the subject of Immunity had been completed there.

In the present and final Report, four separate investigations that were carried out at Walpole are dealt with, namely, those on Swine, on Equine, and on Avian Tuberculosis, and an investigation of a limited number of viruses obtained from natural tuberculosis in various animals. In addition, some of the practical work on which the views of the Commission on modification are based was performed at Walpole. No viruses of known human origin were at any time received there.

In course, however, of the researches into Swine Tuberculosis, three pigs, material from which had been sent to Walpole Farm for examination, were found to have been the subjects of tuberculosis of the human type; and in the course of the immunity investigations a number of experimental calves, which had previously been vaccinated with human viruses at Blythwood, were transferred to Walpole for the subsequent test inoculation with bovine tubercle bacilli. But, with one exception, none of these animals was taken to Walpole before 1906, and in the case of each of them stringent precautions were adopted to prevent possible contamination of other viruses. These immunity calves were kept apart from all other animals. After the termination of the investigations particularly connected with Bovine Tuberculosis, four viruses, received from the Zoological Gardens and other

sources, were found to contain tubercle bacilli of human type (Appendix, Vol. IV., p. 149). The experimental work at Walpole farm, which had commenced in May, 1902, was brought to an end in March, 1909.

At Blythwood there was carried out during eight years the whole of the experimental work in connection with human tuberculosis. Practical work commenced there in April, 1902, and was brought to an end in September, 1910, though by the kindness of Lord Blyth the Commission remained in occupation of the laboratory at Blythwood for some months longer.

The third place occupied by the Commission at Stansted was known as Royalcot, and, so far as the scientific work was concerned, consisted of laboratories only, without any accommodation for experimental animals. The Royalcot laboratories were used only for the histological examinations of tissues and for the comparative investigation of cultures sown in the first instance at Blythwood or at Walpole, or which were grown at Royalcot from material supplied from one or other of these places. The work at Royalcot commenced early in January, 1903, and lasted till nearly the end of the year 1909, a total period of about seven years.

Walpole and Blythwood farms being licensed for the performance of experiments on living animals were repeatedly visited by the Inspector appointed by the Home Office. All the investigators, with the exception of Dr. Eastwood, were fully licensed to perform animal experiments, and Dr. Steegmann also held a licence for each place, as such necessary inoculations that had to be done during any temporary absence of one or other of the resident investigators were performed by him.

At the time of the issue of the Second Interim Report, as stated therein in the Introduction, Blythwood Farm was in charge of Dr. A. Stanley Griffith,* and Walpole Farm of Dr. F. Griffith, Dr. Eastwood being at that date responsible for the work carried out at Royalcot. The Commission have been so fortunate as to retain until practically the end of their labours the services of all these resident investigators. Dr. Eastwood, having finished the inquiries entrusted to him, resigned his appointment with the Commission at the end of December, 1909. Dr. F. Griffith, after the termination of the practical work he had carried out at Walpole, was engaged for a further period of three months finishing his written reports. Dr. A. Stanley Griffith, although not occupied at Blythwood after the end of July, 1910, gave up much of his time to the service of the Commission during many months subsequently, and his assistance in the deliberations of the Commission and in the preparation of the Report proved of very great value.

For a long time, in fact during the whole of the period during which material for experimental investigation was being received at Stansted, Dr. Hammond-Smith acted as clinical observer and collector. Hardly ever was any material obtained from a post-mortem examination or an operation at which he had not been present, and the fact that nearly all the specimens were received at the laboratories in a condition rendering them suitable for experimental use and free from accidental contamination was in large measure due to his skill and careful precaution. The operation patients, frequently kept under observation for months and in some cases for over two years, were visited by him, and, whenever possible, the family histories of the patients were verified by personal interviews with relations or with parents of children. Dr. Hammond-Smith's tact and patience overcame many difficulties that otherwise might have proved of great disadvantage.

Mr. C. F. Fox, appointed at an early stage of the work at Stansted to carry out the clerical work at Blythwood Farm, acquired a knowledge of scientific methods that rendered his assistance in many other ways of great advantage. After the cessation of the practical investigation at Stansted he was transferred to London, and co-operated with the Secretary in the preparation for the press of the various volumes of the Appendix.

Mr. Keddie, throughout the whole of the time that the Commission was in occupation at Stansted, was in charge of the non-scientific administrative work. His wide knowledge and experience in the management of cattle was of the utmost value in obtaining and keeping healthy the stock required for experimental purposes.

No alteration had to be made in the several staffs of skilled assistants employed in the laboratories, and the fact that all the laboratory workers were

* Previously Dr. Cobbett had carried out the work at Blythwood.

experienced and trained in the special methods of the Commission has been an important element in ensuring uniform accuracy of the investigations. Mr. Attoe, the head assistant at Blythwood, engaged by the Commission from the beginning, remained till the whole of the work there was finished ; and after Dr. A. Stanley Griffith left Stansted until it was finally decided that no further investigations were to be undertaken, he was in sole charge of the laboratory and such viruses as it was still desired to keep alive in culture.

The methods adopted for collecting material to be used for investigating bovine and human tuberculosis have already been described (Second Interim Report, page 47). As regards tuberculosis naturally occurring in other animals the sources of material subjected to experiment were as follows :—

Swine Tuberculosis.

All the specimens of natural tuberculosis in pigs that were utilised for this investigation were obtained by Dr. Hammond-Smith, who personally examined every carcass from which lesions were taken. Of the 63 cases detailed in the table of Origins (Appendix Vol. III, page 153), 58 came from the Metropolitan Meat Market in London and 5 from the Corporation Slaughter House in Birmingham. The first specimen was received at Stansted on March 5th, 1905, and the last on July 19th, 1907.

At both these places special facilities were afforded the Commission for collecting the material required. At the Metropolitan Meat Market a room was set aside in which bottles and boxes could be stored and where the specimens could be isolated and packed. Dr. Hammond-Smith visited the Market from time to time at uncertain intervals, and accompanied the Chief Veterinary Inspector on his examination of the carcasses already slaughtered and partially dressed. The pigs came to the Market alive and a preliminary official veterinary inspection of the living animal prevented any pig that did not appear to be in good health and condition being admitted to the slaughter-house. On no occasion was tuberculous disease suspected in any pig before it was killed. As a rule not every carcass was systematically examined by the Veterinary Inspector, but mainly those in which the butchers, men of great experience, had reason to suspect some abnormal condition. In the majority of instances the viscera had been removed from the carcasses and put aside in groups for the veterinary inspection ; thus, in the event of disease being detected in any of the organs, it was not always possible for Dr. Hammond-Smith to identify with certainty the particular carcass from which such tuberculous organ had been taken. It is, therefore, important to note that in many of the cases where the single tuberculous organ found, such as a submaxillary or bronchial gland, was used as the material for investigation, it cannot be stated confidently that no tuberculous disease was present elsewhere in the same animal, even though none had been detected in the routine market examination ; it was obviously impossible to carry out in the slaughter-house a detailed and careful post-mortem examination of every pig killed there such as was always made at Stansted.

Comparatively few cases of generalised tuberculosis in swine being met with at the Metropolitan Meat Market, arrangements were made by Dr. Hammond-Smith by which he could be informed of any that occurred at the Corporation Slaughter House in Birmingham. By this means five cases of generalised tuberculosis were obtained, information concerning them being sent by telegram. On receipt of the notice Dr. Hammond-Smith went to Birmingham and despatched the specimens direct to Stansted. In all the five cases the animal had been slaughtered before his arrival, but the carcasses, together with all their viscera had been set aside in each instance for his examination.

The thanks of the Commission are due to the Authorities of both these slaughter-houses for their assistance.

One other point in connection with the investigation of swine tuberculosis deserves particular notice. Many hundred carcasses of pigs were examined by Dr. Hammond-Smith, but the number of instances in which tuberculous disease was found is in no way representative of the amount of disease existing amongst pigs generally. For all the animals had been sent to the slaughter-house for the express purpose of being forthwith killed and sold for food, and it is extremely unlikely in view of the strict inspection to be anticipated there that any animal would be so sent which the owner did not honestly believe to be quite sound and healthy.

No pigs that during life had shown signs of disease were at any time used by the Commission to provide material for the investigation of natural swine tuberculosis.

Equine Tuberculosis.

The material of Equine Tuberculosis used for the investigation was obtained from five cases of the disease occurring naturally in the horse. In two of the cases the animals had general tuberculosis, in two the mesenteric glands only were affected, and in one case the spleen alone showed evidence of the disease.

All the specimens were obtained from the Royal Veterinary College; in some cases the tuberculous horse had been examined post-mortem there. A description of the material received at Walpole Farm will be found in the table of origins of the Equine Viruses on page 10 of Volume IV. of the Appendix.

Avian Tuberculosis.

The material from which the avian viruses were obtained came in the majority of instances from the bodies of birds that had either died of tuberculosis or had been killed and proved on post-mortem examination to be tuberculous. The birds were of various species and the details are given in the table of Origins (Appendix, Vol. IV., page 174). In addition avian tubercle bacilli were isolated from six pigs tuberculous lesions of which had been sent to Walpole. In these animals the particular type of bacillus responsible for the tuberculous lesion or lesions had not, of course, been suspected. No naked-eye difference can be detected between merely local lesions produced in the pig by the avian tubercle bacillus and similar lesions produced by bovine or by human tubercle bacilli. The details of the six porcine viruses that yielded avian tubercle bacilli will be found in the report on Swine Tuberculosis (Appendix, Vol. III., page 145).

Casual Tuberculosis of certain Mammals.

The origins of the material used in the investigation of viruses obtained from casual tuberculosis of certain mammals are stated at the beginning of the particular report relating to that investigation (Appendix, Vol. IV., page 151). It should be noted that no special search was made for tuberculous disease in these animals, but the opportunity occurring, the viruses were used for investigation.

Human Tuberculosis including Lupus.

The actual lesions used for the continued investigation of cases of human tuberculosis other than Lupus were obtained from post-mortem examinations or after operations in the same manner and with the same precautions as were adopted previously (*see* Second Interim Report, page 47), but in the matter of the 28 viruses that consisted of sputum from individual human cases special precautions were taken. These have already been referred to in the present Report (page 12), but it may be noted in addition that the patients themselves took great interest in the investigation and willingly co-operated in carrying out the restrictions as to diet imposed upon them. Dr. A. S. McNalty, the Resident Medical Officer at Brompton Hospital, rendered assistance of great value in this particular investigation, and thanks of the Commission are due to him and to the Nursing Staff of the Hospital. Without such help it would not have been possible to ensure observance of the strict precautions that were prescribed to prevent possible contamination of the sputum. The only points taken into account in selecting the patients for sputum investigation were that so far as could be ascertained by clinical examination the disease in each one should be limited to the thorax, and that previous microscopic examination of the sputum should have revealed the presence therein of acid-fast bacilli in considerable numbers.

Material for the investigation into Lupus was obtained by Dr. Hammond-Smith. Considerable difficulty was experienced in discovering a sufficient number of patients suffering from this form of tuberculous disease in whom it was of extent large enough to provide material for research and who had not undergone any form of active treatment other than actual operation, such as scraping. That the required

number was obtained was largely due to the help of Dr. J. H. Sequeira, the majority of the cases having first come under his observation.

Experimental Animals.

Very little need be said in regard to the various experimental animals beyond what has been stated in the Second Interim Report. The same methods continued to be used for obtaining bovine animals; these in all cases came from Jersey and were personally selected and purchased there by Mr. Keddie. The reasons for using Jersey cattle almost exclusively for experimental purposes have already been explained, the chief of them being the circumstance that according to available information tuberculous disease among cattle in the island was either non-existent or extremely rare.

The fowls and pigeons used in the investigation of avian tuberculosis and for other experiments were obtained in almost every instance locally, there being no reason to suspect the prevalence at any time of epidemic or other disease amongst the poultry in the district. From every group of birds purchased some were set aside and kept as controls.

The quarantine station at Isleworth for dogs and monkeys was continued till it was no longer required for providing healthy animals of those species. At no time were experiments of any kind performed at Isleworth, the only work other than the careful observation of the stock animals kept there being the post-mortem and microscopic examination of such of them as died or were killed on account of obvious or suspected disease, or for the purpose of control observations.

Three Subordinate Investigations at Stansted.

Three separate investigations were undertaken at Stansted during the course of other work which, although done with the approval of the Commission and in one instance by their direction, are not referred to in the Final Report. In all three the experiments were of a preliminary nature and not sufficiently extended to enable definite conclusions to be drawn from them. The details of all of them are set out in the Appendix.

(1) *Immunity.*

The slight amount of disease produced in bovine animals by the tubercle bacillus of the human type and the possibility of utilising this resistance to one form of tuberculosis for the artificial production of an immunity to the disease readily set up in these animals by the bovine tubercle bacillus, frequently engaged the attention of the Commission during the first three or four years of their inquiry. But the great amount of investigatory work that had to be done in connection with the questions more strictly comprised within the terms of Reference precluded devotion of much time and labour to matters only indirectly concerned with tuberculosis in man.

Nevertheless, early in 1906 it was decided to carry out some tentative experiments with a limited number of calves to ascertain whether these animals could be immunised against bovine tuberculosis by previous inoculation either with large doses of feebly virulent human tubercle bacilli or with small doses of tubercle bacilli such as had already proved highly virulent to bovines. A definite scheme of procedure in this sense was drawn up after careful consideration, and the actual experiments were carried out during the following nine months by the Investigators at Stansted. The preliminary inoculations with the human viruses were performed by Dr. Cobbett at Blythwood Farm, the calves so inoculated being transferred to Walpole later on, while still apparently in perfect health. The vaccinations with bovine viruses as well as all subsequent resistance-test inoculations on both classes of calves were performed at Walpole by Drs. A. Stanley Griffith and F. Griffith, and these two Investigators submitted a report to the Commission on the results obtained. This report, together with full details of the investigation, is included in the third volume of the Appendix.

It is sufficient to say here that the experiments showed that by the inoculation of large doses of human tubercle bacilli, as also by vaccination with small doses of living bovine tubercle bacilli, the calf can in many instances be enabled to resist the

inoculation at a later period of a dose of bovine tubercle bacilli which otherwise would have set up in it severe and fatal tuberculosis. None of the above vaccinated animals was allowed to live for a longer period after the resistance-test inoculation than three months, and though in all of them some disease was found on post-mortem examination, in the great majority it was of a slight and non-progressive character.

In certain of the animals, however, resistance in this sense was not produced, calves that had been vaccinated once and even twice with slightly virulent tubercle bacilli developed some of them severe tuberculosis when inoculated with virulent bovine bacilli. The necessarily limited scope of these preliminary experiments did not provide sufficient data on which to found any opinion as to the probable duration of any resistance that might have been produced in the protected animals.

The results of these experiments were fully considered by the Commissioners after their Second Interim Report had been presented, and they decided that though the facts obtained were of considerable importance, the number of animals included in the investigation was not sufficient to enable any general conclusions to be safely drawn from them. They were unanimously of the opinion that further experiments on immunity should be carried out on a much larger scale if this were possible. Such experiments, they considered, should extend over a period of time considerably longer than that occupied by the preliminary inquiry, and should include at least 100 bovine animals. But it was eventually decided that such an extended investigation, though likely to be of great scientific and practical value, could not conveniently be undertaken by a temporary body such as a Royal Commission. The difficulty of obtaining a sufficient number of healthy calves of like age, the provision of the necessary accommodation without interfering with other investigations at Walpole, and above all the time that would have to be occupied and the heavy expense that would be involved compelled the Commission to give up the idea of carrying the investigation on immunity beyond the stage arrived at, and whilst desiring that the account of the experiments should be included in their Appendix, they themselves express no opinion as to the significance of the results so recorded.

(2) *Human Milk.*

From time to time during the course of other work at Blythwood careful observations were made on pregnant heifers by Dr. Cobbett to note the effect of inoculation of tubercle bacilli in bringing about tuberculous infection of the mammary gland and in influencing the production naturally of tuberculosis in the calves of which they were subsequently delivered; he also demonstrated the infectiveness of their milk when this secretion became established.

The results of these observations were recorded by him in the third volume of the Appendix to the Second Interim Report, the main facts being tabulated on pages 250–253. The tables showed that of five heifers infected with tuberculosis by means of subcutaneous inoculation, their milk, when the secretion had become established, was infective to guinea-pigs in two instances; that in two of the five the mammary glands were found to be tuberculously affected when the animals were killed; and that of the five calves produced by these heifers three yielded post-mortem evidence of tuberculosis of the hepatic glands, contracted presumably before birth.

An investigation was carried out by Dr. F. Griffith on the excretion of tubercle bacilli in the milk of naturally infected tuberculous cows showing no disease of the udder. This inquiry and the details of the experiments formed the subjects of the Third Interim Report and Appendix. About the same time Dr. A. Stanley Griffith carried out a series of experiments to determine whether after experimentally introducing tubercle bacilli into the blood-stream of healthy cows or heifers these bacilli could pass from the blood into the milk without producing changes in the mammary tissue. Of the eleven experiments performed nine showed that the normal mammary tissue will permit of the escape of tubercle bacilli into the milk after the bacilli have obtained access to the blood-stream in sufficient quantities. The details of this investigation are fully given in Volume III. of the Appendix to this Report, page 81.

As a result of the consideration of these facts it became a matter of some interest

to inquire whether the milk of a lactating woman, suffering from tuberculosis, might be a possible source of danger to her infant, a question to which conflicting answers have been given by different authorities, but regarding which very few reliable observations appear to have been experimentally made. Such an investigation was not practicable on a large scale, the matter not being one strictly included in the Reference, and pressure of other work together with the difficulty of obtaining suitable cases prevented more than a very few being examined. But the milk of four nursing women was tested by Dr. A. Stanley Griffith. Briefly it may be stated that each of these women was suffering from pulmonary tuberculosis, though not in an acute form. The diagnosis in each case had been made before the patient was selected, but in only one of the four cases did the woman's sputum produce tuberculosis when injected into guinea-pigs. The results of the inoculation of guinea-pigs with milk from these women were negative in all the four cases. The details of this investigation are recorded in Vol. I. of the Appendix to this Report (pages 12, 18 and 104–5). The investigation was of course too limited to enable any deductions to be drawn from it.

(3) *Action of Light-Rays on Lupus Bacilli.*

Dr. A. Stanley Griffith carried out some preliminary observations with the object of obtaining information as to how the undoubted benefit caused by treating lupus by light-rays is produced. The experiments were made with lupus tubercle bacilli isolated at Blythwood and grown on artificial media prepared there. The exposures of these cultures to the light-rays were made in the skin department of the London Hospital by permission of Dr. Sequeira and with his co-operation. The results are recorded in Vol. II. of the Appendix to this Report (page 9). They show that the growth of the tubercle bacillus is inhibited by both Finsen and Kromeyer rays, but the limited scope of the investigation did not supply any evidence as to whether this effect is produced by a bactericidal action of the rays on the bacilli or by some modification brought about by the rays in the artificial media or living tissue in which they were growing.

Investigations other than those at Stansted.

Two separate investigations, not carried out in the laboratories of the Commission, remain to be noted ; both of them were referred to in the Second Interim Report as having been undertaken but at that time unfinished. The results in each case were not sufficiently definite to enable the Commission to make use of them, and neither is referred to in the present final Report.

The first was an experimental investigation undertaken by Dr. James Miller, of Birmingham, at the request of the Commission.

Various means were being sought at that time to determine any differences that might exist between tubercle bacilli of the human and bovine types apart from their pathogenic effects on cattle and rabbits, and the work entrusted to Dr. Miller was to observe the changes that occurred on bringing living tubercle bacilli obtained from different sources into contact with living cells, and to note if any constant differences could be seen between the interactions of leucocytes with bacilli of these two types.

The cultures of tubercle bacilli with which the investigation was to be carried out were supplied from the Stansted laboratories, but the whole of the experimental work connected with it was done at Birmingham. Four strains in all were used, three being of bovine and one of human origin ; but unfortunately this last virus was subsequently found to be bovine not human in type, and, therefore, no deductions could be drawn from Dr. Miller's observations as to any contrasts in the cellular reaction induced by different types of tubercle bacillus. But he noted that although practically no difference was observed with regard to either the nature of the cells taking part in the primary reaction or in the amount of this reaction between any of the four viruses, certain minor variations, such as the duration of a period of quiescence, the formation of the giant-cell follicle and the degree of the secondary inflammatory reaction could be clearly noted in several cases. Thus

though the cellular reaction was not uniform with every virus, either in point of time or effect, these variations appeared to be merely an expression of the slight and unimportant differences not infrequently to be observed in virulence among different strains of bovine tubercle bacilli towards the calf and rabbit.

Apart from the question of differences between tubercle bacilli of the two types, Dr. Miller made careful observations of the general cellular reaction following injection of cultures of living tubercle bacilli into guinea-pigs which are of great interest in connection with Dr. Eastwood's histological examinations of dead tissues. They may be briefly summarised as follows:—

1. A period of inflammatory reaction, during which the bacilli are ingested by cells.
2. A period of quiescence, when the bacilli disappear almost entirely.
3. A period when the bacilli reappear and are enclosed within giant-cell follicles, a condition accompanied by a second inflammatory reaction. These giant-cell follicles may persist or may break down, in which latter case there is a marked increase in the inflammatory reaction.

Dr. Miller's investigation was carried out with great skill and minute care. Further observations were not undertaken on similar lines, Dr. Eastwood's histological researches having shown that there is an essential identity between the lesions caused by the bovine tubercle bacillus and those produced by the human type.

The second of these two separate investigations, referred to at page 48 of the Second Interim Report, was in the nature of a statistical inquiry, undertaken in 1904-5, with a view to obtain data more trustworthy than are supplied by "Causes of Death, Officially Certified," as to the extent of abdominal tuberculosis amongst the population generally. The method of inquiry adopted, which took as its basis a systematic examination of post-mortem records at hospitals, has already been described in the Report in question, and reason given for deeming the results which were being obtained as likely to prove of little value for the purposes of the Commission. Subsequent examination of the records collected has confirmed this view. Want of detail in the majority of hospital post-mortem records examined precluded exclusion of the possibility of lesions having been present in organs not specifically stated to have been healthy, while the lack of uniformity in the methods of making and recording post-mortem examinations in different places, as well as the different plans of procedure carried out from time to time in one and the same hospital, prevented any general conclusions as to the proportion of abdominal tuberculosis to other forms of that disease.

During the time that the experimental work was being carried out at Stansted a very large number of tuberculin tests of healthy and infected bovine and other animals was made by the resident investigators and the results systematically recorded. The number of tests actually made and the wide range of different species of animals tested make these records of considerable value, and it is proposed to publish an abstract of the facts obtained and the opinions of the investigators thereon in a supplemental volume of the Appendix to this Report. The procedure adopted for testing the non-infected animals was explained in the Second Interim Report (page 43).

At the end of this Report will be found a list of the contents of all the Reports and Appendices presented by the Commission. In this connection it is important to note that the method of this Commission has differed profoundly from the procedure usually adopted by Royal Commissions. The work has consisted entirely of a scientific research carried out under the direction and supervision of the Commission by experts at farms and laboratories devoted solely to the purpose. No witnesses have been examined, and therefore the only evidence on which the Commission's reports are based is the accumulated facts resulting from the experimental work done. During the progress of any investigation it was obviously improper that the facts coming to light should from time to time be made public in the precise order in which they were being revealed. But throughout these researches minute record has been kept of each step of experimental work, so that after Report by the Commission the fullest detail of all proceedings embodied in Appendix volumes might be available for independent judgment on fact irrespective of interpretation of fact that may have been indulged in by the Commissioners. To the same end a completely representative collection of pathological specimens carefully prepared and preserved in the course of the Commission's researches has been delivered to the

Royal College of Surgeons for permanent exhibition in the Museum of that institution.

As in Appendices to the Second Interim Report so in Appendices to this their Final Report, the Commissioners have regarded it as right and proper to encourage their Investigators each to set out not only the multitudinous facts arising from his work, but also his own views as to the bearing of the results of that work on the problems before the Commission.

No account of the practical administration of the work of the Commission, however brief, would be complete without reference to the help received from the Stationery Office, the Office of Works, and the officials of the Treasury, especially Mr. H. T. Holmes who throughout assisted the Secretary with the purely financial business.

LIST OF REPORTS AND APPENDICES PRESENTED BY THE ROYAL COMMISSION ON TUBERCULOSIS (HUMAN AND BOVINE).

First Interim Report.

Presented in May 1904.

No Appendix.

Second Interim Report.

Presented January 1907.

Appendix.—In four volumes.

VOLUME I.—The Pathogenic Effects of Bovine Viruses:

The Numerical Estimation of Tubercle Bacilli.
The Table of Origins of thirty Bovine Viruses.
Inoculation Experiments on Bovines, Goats, Pigs, Chimpanzees, Monkeys, and Lemurs.
Descriptive Charts of the Experiments with each Virus, and full Post-Mortem Notes of the larger experimental animals.
Inoculation Experiments on Dogs, Cats, the Mongoose and Hedgehog, Rabbits, Guinea-pigs, Rats, and Mice.
Detailed description and summaries of Feeding Experiments.
Plates: Photographs of Lesions produced in Bovine and other animals.

VOLUME II.—The Pathogenic Effects of Human Viruses:

The Table of Origins of sixty-two Human Viruses.
Descriptive Charts of the Experiments with each Virus, and full Post-Mortem Notes of the larger experimental animals; together with a history of the patient from which each Virus was obtained.
A Consideration of the Virulence of different strains of Tubercle Bacilli obtained from man for various species of animals; viz., Bovines, Rabbits, Guinea-pigs, Goats, Pigs, Monkeys, Baboons, Chimpanzees, Dogs, Cats, Rats, Mice, and Fowls; together with Tables of the Experiments made on each Species.
The Relative Susceptibility of Different Species of Animals to Tubercle Bacilli of Human and Bovine Origin.
Plates: Photographs of Lesions produced in Bovine and other animals.

VOLUME III.—Additional Investigations of Bovine and Human Viruses.

1. The Cultural Characters of the Bovine Tubercle Bacillus (with Plates).
2. The Cultural Characters of the Tubercle Bacilli obtained from Man.
3. Supplementary Report on the Cultivation of Tubercle Bacilli obtained from Man.
4. Report on the Changes in Reaction produced in Broth by Human and Bovine Tubercle Bacilli.

(*a*) The Changes in Reaction produced in Glycerin-broth.
(*b*) Additional Observations on the Changes in Reaction produced in Glycerin-broth.
(*c*) The Changes in Reaction produced in Glucose-broth.
(*d*) The Changes in Reaction produced in Glycerinated Litmus Milk.

VOLUME III.—*continued.*

5. Modification Experiments with Tubercle Bacilli of Bovine Origin.
   (*a*) Modification by Culture.
   (*b*) Modification by Animal Passage.
   (*c*) Influence of Glycerin on Virulence.
6. Report on the Stability of Virulence of the Tubercle Bacillus of Human Origin in Artificial Culture, including the Influence of Glycerin in Culture Media.
   (*a*) The Virulence of Tubercle Bacilli from Cultures and in Emulsions of Tuberculous Animal Tissues compared.
   (*b*) Does long-continued Cultivation on Artificial Media attenuate the Tubercle Bacillus?
   (*c*) The Influence of Glycerin in Culture Media.
7. Report on the minute non-progressive tubercles found in Calves injected with Tubercle Bacilli of Human Origin which are unable to provoke a progressive infection in this Species of Animal.
8. Report on the Distribution of Non-virulent Tubercle Bacilli of Human Origin in the body of the Calf after Subcutaneous Injection.
9. Report on the Dissemination of Tubercle Bacilli in Different Species of Animals after Subcutaneous Inoculation.
10. Report on the Influence of Individual Susceptibility and of Dose on the Severity of an Experimental Infection by Tubercle Bacilli of Human Origin.
    (*a*) The Variation in the Capacity for resisting Tuberculosis among Individuals of the same Species.
    (*b*) The Influence of Lactation.
    (*c*) The Influence of Dose.
11. Report on Congenital Tuberculosis at Blythwood Farm.

VOLUME IV.—Comparative Histological and Bacteriological Investigations on the Relationship of Human and Bovine Tuberculosis:

Part I.—General Report on the Histological and Bacteriological Investigations.
Part II.—Comparative Histology.
Part III.—Comparative Bacteriology.

Third Interim Report.

Presented January 1909.

Appendix.—(Included in the Report volume).

The Results of Inoculation and Feeding Experiments made with the Faeces and Milk of naturally Tuberculous Cattle.

Introduction.
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Full Post-Mortem Notes of the naturally infected Cows, and details of the investigations.

Final Report.

Presented 1911.

Appendix.—In seven volumes.

VOLUME I.—Investigation of Viruses obtained from Cases of Human Tuberculosis (other than Lupus):

General Results of the Investigation of 55 Cases of Human Tuberculosis.
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The Investigation of the Cultural Characteristics of 54 Viruses.

VOLUME I.—*continued.*

Consideration of the effects produced in Different Species of Animals by the Inoculation of Human Tubercle Bacilli and Bovine Tubercle Bacilli of Human Origin; and of the effects produced by feeding.
Modification Experiments with Human Tubercle Bacilli. (Detailed description of the Experiments and consideration of the Results obtained.)
Table of Origins of the Viruses investigated.
Detailed History of each Case, and Summaries of Experimental Results.
Details of the Experiments.
Plates: Photographs of some of the Cultures.

VOLUME II.—Investigation of Viruses obtained from Cases of Lupus:

Consideration of the cultural characters and pathogenicity of the Cultures isolated.
Classification of the Lupus Viruses according to cultural characters and virulence.
Tabular Summary of the Results of the Passage Experiments.
Table of Origins of the Lupus Viruses.
Detailed History of each Case and Summaries of Experimental Results.
Details of the Experiments.
Plates: Photographs of some of the Lupus Cultures.

VOLUME III.—Reports on Investigations dealing with:—

1. Certain Human Viruses of Irregular Type:

(*a*) Results of the Further Investigation of Cultures from the Viruses placed in Group III. (*see* 2nd Interim Report, page 30).
(*b*) Results of the Special Investigation of two of the Group III. Cultures (H 13. "A.D." (Calf 301), and H 49. "T.C.") which exhibited exceptional features.
(*c*) Results of the Special Investigation of the two Cultures H 60. "W.B." (Bronchial Gland) and H 90. "I.P." (Retroperitoneal Gland), isolated since the 2nd Interim Report, which exhibited the features of the two Group III. Cultures.
Plates: Photographs of Cultures.

2. The Excretion of Tubercle Bacilli:

(*a*) In the Milk of Cows and Goats.
(*b*) Into the Undeveloped Udder.

3. Investigation of Tubercle Bacilli from Cases of Swine Tuberculosis:

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4. Report on Immunity Experiments.

Including also Reports (submitted to the Commission in 1906) on:—
(i.) The Stability of Virulence of Tubercle Bacilli in the Living Animal, and
(ii.) Experiments with Mixed Viruses, in artificial culture, and in the body of a living animal.

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1. Investigation of Tubercle Bacilli derived from Tuberculosis occurring naturally in the Horse:

General Results of Experiments with cultures from the original material, and of passage experiments; and consideration of cultural characters.
Table of Origins of the Equine Viruses.
Summaries of Results of Inoculation Experiments with each Virus; and Details of the Experiments.
Plate: Photographs of Cultures of Bovine and Equine Tubercle Bacilli.

2. Investigation of Viruses obtained from five cases of Casual Tuberculosis of various Mammals:

Viz.: The Gnu, Antelope, Rhesus Monkey, Chimpanzee, and Cat.

3. Investigation of Avian Tubercle Bacilli obtained from Birds and Swine:

Summary of Results of Investigation:
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Cultural Characters of the Avian Tubercle Bacillus.
Summaries of the Results of the Experiments on different species of animals; and Details of the Experiments.
Plate: Photograph of Cultures of Avian, Human and Bovine Tubercle Bacilli.

VOLUME IV.—*continued.*

4. Modification Experiments with Tubercle Bacilli derived from Animals other than Man :

Summary of Results.
(*a*) Experiments with Avian Tubercle Bacilli.
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(*f*) Experiments with Tubercle Bacilli of slight Virulence for the Calf and Rabbit.
(*g*) Comparative Inoculation Experiments on Rabbits with Serum and Glycerin Serum Cultures ; and
Details of the Experiments.

5. Investigation of Artificially Mixed Cultures :

(*a*) On Calves.
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OF THE

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APPOINTED TO INQUIRE INTO THE RELATIONS OF

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PART I.

REPORT.

Presented to both Houses of Parliament by Command of His Majesty.

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DARLING AND SON, LIMITED, BACON STREET, E.
1911.

[Cd. 5761.] *Price* 6*d.*