ON THE RELATIONSHIP OF HUMAN TUBERCULOSIS TO THAT OF BOVINES.*

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IN the memorable address delivered by Professor Koch in the summer of 1901 before the British Congress on Tuberculosis, he stated that "a number of young cattle which had stood the tuberculin test, and might therefore be regarded as free from tuberculosis, were infected in various ways with pure cultures of tubercle bacilli taken from cases of human tuberculosis; some of them got the tubercular sputum of consumptive patients direct. In some cases the tubercle bacilli or the sputum were injected under the skin, in others into the peritoneal cavity, in others into the jugular vein. Six animals were fed with tubercular sputum almost daily for seven or eight months; four repeatedly inhaled great quantities of bacilli, which were distributed in water and scattered with it in the form of spray. None of these cattle (there were nineteen of them) showed any symptoms of disease, and they gained considerably in weight. From six to eight months after the beginning of the experiments they were killed. In their internal organs not a trace of tuberculosis was found. Only at the places where the injections had been made small suppurative foci had formed, in which few tubercle bacilli could be found. This is exactly what one finds when one injects dead tubercle bacilli under the skin of animals liable to contagion." From these and other data he felt "justified in maintaining that human tuberculosis differs from bovine, and cannot be transmitted to cattle."

It seemed to him very desirable, however, that these experiments should be repeated elsewhere, in order that all doubt as to the correctness of the assertion might be removed.

Such a statement, emanating from an authority whose deliverances on the subject of tuberculosis in its various aspects had hitherto remained almost unimpeachable, naturally claimed attention, not only from those interested professionally in the matter, but also from the lay public and those likely to be affected commercially by the issues which the statement involved. And, accordingly, since the announcement was made, experiments have been undertaken in this and other countries calculated to test the validity of the assertion. Tubercle is a disease which develops slowly, and hence many of these are not yet completed, while the results of others have been published in a fragmentary form.

Difficulty in determining whether or not Bovine Tuberculosis can be transmitted to Man.

The question of whether tuberculosis can be transmitted from bovines to man must of course always remain unproven experimentally;

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and although case upon case has been recorded where, apparently, the disease had been transferred to the human subject by the ingestion of food contaminated with the bacillus of tubercle derived from the cow and from other means of accidental inoculation, yet these always lack the element of certitude to be obtained where the disease can be excited experimentally, under conditions which exclude the possibility of error. The source from which the contaminated ingesta have been derived (owing to the prolonged period of incubation) may have been overlooked or forgotten by the time that the disease begins to show itself, and even if it can be shown that at a particular date the individual did consume food which was undoubtedly contaminated, there is always the uncertainty of determining whether this or some other source of contagion was the cause of the outbreak. Examples are numerous where, so far as it is possible to judge, the disease has been transmitted to children through contaminated milk; but plausible and self-evident as many of these appear to be, still they must be admitted in proof with an element of reserve, owing to the conditions being so complicated and liable to fallacy. No doubt the evidence in favour of a direct transmission of the disease from the cow to man is very strong, and up till the time of Koch's assertion to the contrary, was admitted on all hands; but, for the reasons above detailed, all such evidence, for or against, must remain in a manner conjectural. It lacks scientific verification.

One argument employed by Koch as showing that tuberculosis is seldom conveyed to man through the ingesta is the rarity with which a primary lesion of the intestine is met with in abdominal tuberculosis of children. This fact has long been familiar to pathologists. From personal observation, one of us has taught for the last twenty-five years that abdominal tuberculosis of children is seldom accompanied by a tubercular lesion of the intestinal mucosa, while in those cases where the lungs have been the primary seat of the disease, where cavities have formed, and where the discharge from these cavities containing the bacillus has been swallowed in quantity and over a lengthened period, the intestinal mucosa will frequently be found to be the seat of tubercular deposit and ulceration. In this case, however, the bacillus passes into the alimentary canal in such abundance that it would certainly be strange did the absorbents of its mucous membrane not pick it up and develop a tubercular lesion in their substance. The lower urinary viæ become auto-infected in tubercular disease of the kidney; the trachea and larynx become secondarily infected from the passage through them of the expectoration from a disintegrating tubercular lung; and it may be said that wherever the like conditions prevail, wherever a discharge containing the bacillus of tubercle comes in contact with a surface provided with absorbents, there is a liability to that surface becoming secondarily tubercular. Still it is to be borne in mind that such auto-infection of a mucous membrane over which the bacillus of tubercle has been passing by no means necessarily takes place. The discharge from a phthisical lung may have been expectorated for years without the mucosa of the trachea or larynx showing a single tubercle.

The argument against the transmissibility of bovine tuberculosis to man through the ingesta, founded upon the rarity of primary tubercular disease of the intestine, has absolutely no weight unless it can be disproved that the bacillus of tubercle is capable of passing through the intestine to the abdominal glands without occasioning an intestinal

lesion : and the fact that primary abdominal tuberculosis is met with so frequently in children without implication of the mucous membrane of the intestine seems to point the lesson that such a thing is not only possible, but that there is a strong probability in its favour. It is only by experiment, however, that such a question can be answered, and, as shown by our first series of experiments, there cannot be a shadow of doubt on the subject. Even where the abdominal glands in calves were rendered extensively tubercular by the consumption of sputum containing the tubercle bacillus, in not one instance was the mucosa of the intestine found to be the seat of a tubercular lesion.

Transmission of Human Tuberculosis to Bovines.

Whatever doubt, however, overshadows the question of the transmissibility of bovine tuberculosis to man, the settlement of the converse—whether human tuberculosis can be conferred upon bovines—ought surely to be capable of demonstration by experimental methods, and it is to this aspect of the question that we have addressed ourselves. Is the bacillus of man capable of inducing tuberculosis when introduced by various channels into the system of the cow? If so, then the presumption is highly in favour of the opposite being true, and its confirmation would tend to establish the identity of the organism in the disease of both hosts.

Chauveau (Second Congress for the Study of Tuberculosis, 1891, as well as several previous communications) announced long ago that calves could be infected not only by feeding them with material derived from phthisical lungs of cattle, but also that like material taken from the human lung had the same capability. In the experiments with human tubercle all the animals became rapidly and extensively tubercular, and it was upon the evidence afforded by these experiments that the alleged danger of consuming the flesh and milk of tubercular cattle, and the precautions taken against this danger, were chiefly founded.

Question of different Species of Bacillus.

Koch's assertion that tuberculosis of the cow cannot be transmitted to man was supported by the assumption that the bacilli belong to different species, and he came to the conclusion that the chief means of disseminating the disease in man is through the agency of human sputum, the dangers of contracting tuberculosis through infected meat and milk being unimportant. Experiments and statistics, he alleged, went to demonstrate that human and bovine tuberculosis are two different diseases.

In cultures, bovine bacilli, as a rule, are shorter, thicker, more oval, and less granular than those from a human source. But can much reliance be placed upon these differences as a means of diagnosis? Are these differences anything else than the effect of environment? When we find that human bacilli taken from different subjects vary so much among themselves in regard to their length, breadth, granularity, etc., are we to assume that morphological peculiarities can rank as a sufficient basis of distinction between bacilli of the cow and those taken from the higher animal? Hueppe, for instance (*Berl. klin. Wochenschr.*, xxxviii., 1901, p. 877), declares that it is only necessary to pass the bacillus of the ox and that of man through the system of the guinea-pig in order to render it impossible to distinguish the one from the other.

It must be evident, therefore, that mere peculiarities in the morphological characters of the bacillus constitute but a feeble basis to found a theory of difference of species upon.

Relative Virulence of the Tubercle Bacillus.

For long it has been admitted that the bacillus of bovine tuberculosis is more virulent for most animals than that taken from a human source. Villemin noticed this when the evidence on the subject of the contagiousity of tuberculosis was in its infancy; and Smith, Dinwiddie, Frothingham, Baumgarten, Gaiser, Ravenel, and De Jong have all confirmed his observation. It has, further, been demonstrated by Delépine that the human bacillus varies in its powers of contagion from time to time when taken from different subjects. Arloing, moreover, has found that certain varieties of the human tubercle bacillus, which at first infect only the guinea-pig, may be rendered capable of communicating the disease to rabbits after several passages through the system of the first animal.

It is also well known not only that the bacillus may alter in culture morphologically, but that in certain instances it may lose a great deal of its pathogenic powers after several generations—that it will, in fact, reproduce the disease after a time only when inoculated upon the peritoneum.

But even granting that the human bacillus is less virulent for cattle than that of bovines, it by no means follows that bovine tubercle is not as readily inoculable upon man as upon other animals. The fact that bovine bacilli are perhaps the most virulent of any known, and that they can be inoculated on such a variety of animals is pretty strong *prima facie* evidence of such being the case.

McFadyean put the matter very clearly in his address at the British Congress on tuberculosis. He said: "It cannot be admitted that the low virulence of human bacilli for cattle proves, or even makes it probable, that bovine bacilli have only a feeble pathogenic power for man. That might have been held to be probable if it had been shown that bovine bacilli were very virulent only for cattle, but since it is well established that these bacilli are highly dangerous for such diverse species as the rabbit, horse, dog, pig, and sheep, and, in short, for almost every quadruped on which they have been tried, it appears to be highly probable that they are also dangerous to man.

The truth seems to be that the bacillus of tubercle, like other pathogenic bacilli, whether taken from a natural source or under cultivation, may possess different degrees of infectiosity, and that the result obtainable by inoculation depends greatly upon the sample employed. For this reason it seems to us there may be an element of fallacy in many of the experiments performed by Koch and Schütz. They employed bacilli admittedly derived from a human source, but a large proportion of these were in the state of artificial culture, and hence may have lost part of their naturally weak powers of infection. The question to be settled seems to us to reside in whether the bacillus taken immediately from its natural habitat, without being subjected to any influence which might modify its powers of reproduction, is capable of transmitting the disease to the bovine host, and accordingly our experiments have been designed with a view to throw light upon this.

Criterion of Infection.

A very important matter to agree upon before drawing conclusions from experimental tuberculosis is what the criterion of infection is to be. For want of a clear definition of this, considerable misunderstanding has resulted in the interpretation of the results obtained by Koch and Schütz. A number of their experiments are put down as doubtful or negative, apparently because the lung or some other important viscus did not show evidence of disease or evidence only of a minor degree of the same.

If the inoculated virus dies out at the point of introduction, and if it fails to produce tubercle elsewhere, the case is clearly negative; and if the bacillus is found only in the local lesion, such cases surely are legitimately to be ranked as doubtful. But if the bacillus is found locally, say in a cheesy abscess, and if the next superior lymph-glands are altered, show a tubercular structure characterized by giant cells, caseation, etc., and if the diseased parts are capable of reproducing the disease on the guinea-pig, such a case, we maintain, must be held to show evidence of infection, even although it be thus limited in its range. If not, then we might as well argue that because a lesion in man is confined to a limited group of glands or the neighbourhood of a joint, it is not to be reckoned as tubercular, even although the affected parts show a tubercular structure, contain the bacillus, and are capable of producing a general tuberculosis in the guinea-pig.

If, again, the inoculation of a peripheral part causes the development of a local lesion or not, and if the animal be found to be suffering from a widely disseminated tubercular lymphadenitis, spreading upwards from the point of inoculation, but without implication of any of the larger viscera, then surely this also must be considered as evidence of the disease having been conferred upon the new host. And should, in addition, the lungs and other viscera be involved, of course there cannot remain much doubt as to what the inference should be. The evidence which, we think, will be admitted by most experimenters to be conclusive of the disease having been contracted, is that the bacillus is growing and reproducing itself upon the new host, and inducing a greater or less amount of tissue disturbance, taken along with the power such affected tissues have of exciting tuberculosis when inoculated upon the guinea-pig. It is idle to argue, as Koch and Schütz have done, that some of their cases exhibited no more evidence of tubercular infection than would be elicited by the introduction of dead bacilli. Time has evidently much to do with the extent to which the lesion has proceeded, and human tubercle evidently develops slowly in the cow.

Arloing's Criticism of Koch's Results.

In a criticism of the experiments made by Professors Koch and Schütz (*Arch. f. wissens. u. prakt. Thierheilkunde*, xxviii., 1902, p. 169), Arloing (*La Presse Médicale*, No. 13, February 12, 1902) draws attention to certain discrepancies, due apparently to this want of definition of what is to be considered infection and what not, and which go in a manner to vitiate the conclusions they arrived at.

Thirty-four animals of various kinds were inoculated by Koch and Schütz with human bacilli or with tubercular sputum, and twenty-one with bacilli of bovine origin. The twenty-one animals inoculated with bovine tuberculosis all took the disease in a grave form: some of them died from tuberculosis in a month, others in a month and a half to two

months. On the contrary, of the thirty-four animals inoculated with human tuberculosis, thirty, they say, gave a negative result, and four a result which was doubtful, and this series comprised experiments made by ingestion of tuberculous material, intravenous injection, and inhalation.

On reading over the details of these experiments, however, Arloing is struck by the fact that three more of the thirty would be considered to have been tubercular by anyone not already prejudiced, thus bringing up the number infected to seven—namely, five pigs, one calf, and one sheep. Here, for instance, he says, is an experiment made by them on the calf, and which was returned by them as doubtful, which, he maintains, was clearly positive. The animal was allowed to inhale tubercle bacilli, with the following result: The appetite of the animal during the course of the experiment was always good, but it began to cough after the first month, and continued to do so more strenuously till the time of death. The autopsy revealed "some encapsuled and clustered tubercular collections in the right lung, the size of a pea, flukes in the bile-ducts"; on microscopic examination the "presence of human tubercle bacilli in the diseased parts of the lung," while "guinea-pigs inoculated with the diseased portions of lung-tissue developed general tuberculosis."

This case, ranked as doubtful by Koch and Schütz, according to Arloing is positive, and there seems on the face of it good reason for believing that it was. The animal began to cough during the first month after inhaling the bacillus, and with augmented frequency up till the time of death. There were tubercular deposits in the right lung; these contained tubercle bacilli, and they reproduced tuberculosis on being inoculated upon the guinea-pig. It is hard to see what further proof was required of the animal having developed pulmonary tuberculosis during the time it was under observation.

Another case quoted by Koch and Schütz as negative, and which Arloing declares is clearly positive, is as follows: The animal experimented upon was a pig, and the experiment consisted in the ingestion of tubercular sputum.

Pathologico-anatomical Appearances.—Some caseous and calcified nodules, the size of a pin's head, in the posterior-pharyngeal lymph-glands. All other organs sound.

Microscopic Appearances.—Tubercle bacilli were found in the nodules of the said lymph-glands.

Inoculation on the Guinea-pig.—Guinea-pigs inoculated with the infected nodules developed general tuberculosis.

As Arloing remarks, this case is classified as negative because there was an absence of pulmonary tubercles, and adds that this manner of interpreting the results is entirely conventional. So far as he is concerned, he recognises in these two cases simply different degrees of infection.

A third experiment, called negative, consisted in the subcutaneous inoculation of human tubercle bacilli, also on the pig.

Pathologico-anatomical Appearances.—A caseous tubercular mass at the point of inoculation of the virus on the posterior left limb. Tuberculosis of left superficial inguinal glands. Catarrhal pneumonia of slight degree.

Microscopic Appearances.—At the point of injection, and in the left superficial inguinal glands, tubercle bacilli were found. Other organs sound.

Inoculation of the Guinea-pig.—Guinea-pigs inoculated with material taken from the point of infection developed general tuberculosis, while others inoculated with pieces of the affected lung remained sound.

This experiment, Arloing asserts, represents an example of infection arrested at the adjacent lymph-glands. The virus not having exhausted itself locally, the experiment, he declares, is positive, and there is nothing against the supposition that the disease might have spread in time to the lungs.

MM. Koch and Schütz, he adds as a rejoinder, have misemployed their experiments. They have departed from the principles of the experimental method, in which count must be taken of facts which are positive and of those which are negative, and in which a definition of the one and the other is an essential point. In short, they are not entitled to formulate the categorical inferences at which they have arrived. He avers it to be incontestable that they have not interpreted their results as anyone else, experienced in the matter, would have done. In their ardent desire to prove that human tuberculosis differs radically from that of bovines, they have included under their doubtful results examples of very evident infection from the human subject, and he emphasizes the fact that some of their cases, even where the lymph-glands were involved at a sufficiently great distance from the point of inoculation, were tabulated as negative because other organs were not the seat of tuberculosis.

In summarising his review of the present state of the tuberculosis question, he (*La Presse Médicale*, No. 13, February 12, 1902) comes to the following conclusions :

1. The virulence of tuberculosis is variable, and capable of adapting itself to certain organisms; consequently it is not surprising that the bacillus of human tubercle manifests less activity on certain animals than the bacillus of the bovine disease.

2. Human tubercle, and cultures from it, are capable of tuberculating the cow, the sheep, and the goat.

3. Should it prove to be incapable of doing so, and such cases occur, there is no reason for concluding that this indicates a bacillus absolutely distinct.

4. He is compelled to admit the unity of Koch's bacillus in the case of man and of animals.

5. He rejects the criterions of Koch and Schütz, in which they make a subdivision between human and animal tuberculosis.

6. Koch and Schütz were not entitled from their experiments to draw the conclusions they arrived at.

7. It is right to maintain in a large measure the precautionary edicts with regard to meat, and, above all, those relating to milk, suspected to harbour the bacillus of tuberculosis.

It may be added that similar conclusions have been arrived at by Ravenel, Delépine, De Jong, Behring, and others.

*General Account of the Experiments.**

The following experiments were undertaken at the instance of the Agricultural Committee of the University of Aberdeen and the

* In these experiments the clinical observations, the testing with tuberculin, the feeding of the animals with pure milk, and their housing in stalls free from infection, were intrusted to, and carried out by, Mr. M'Lauchlan Young.

Highland and Agricultural Society, and were designed to test the validity of the assertion that human tuberculosis differs so much from bovine that it cannot be transmitted to cattle.

All the primary experiments were made upon calves, but the guinea-pig was employed for confirmation purposes in a large number of instances.

The shed in which the calves were housed had never been used for animals previously; it was newly fitted up with stalls and windows, and was washed throughout with lime previous to the commencement of the experiments. The animals were fed at first entirely upon milk, later on with a little linseed-meal added, and a handful of hay twice daily. The milk was taken from cows which had been tested with tuberculin and failed to react. The utensils used for feeding were galvanized iron buckets. The flasks for conveying the milk were new, and were boiled to begin with. The dairyman who brought the milk was never allowed to come nearer than 200 yards from the shed. Moss-litter was used in the stalls, and every precaution taken to keep them clean. When the second series of experiments commenced the stalls were thoroughly cleaned, the whole shed limed, and the utensils used for feeding boiled.

FIRST SERIES.*

EXPERIMENT No. 1.—*A black Aberdeen-Angus female calf, ten days old, fed with tubercular sputum mixed with milk on eighteen different occasions, and over a period of sixty-nine days.*

Post-mortem Examination.—The animal was slaughtered, and the autopsy was made immediately after death. The carcass was well nourished, and there was a good deal of gas in the paunch. The mesenteric glands were all very much enlarged, especially those skirting the intestine. They constituted huge tuberos and continuous chains running along the margin of the bowel. On section they were found to contain a grayish point here and there, but otherwise they were of homogeneous consistence, and of a dull pink colour in their midst, more grayish coloured at their periphery. The intestine, stomach, and abdominal organs generally were free from disease; there was a total absence of ulceration or any other morbid affection of the intestinal mucosa, and there was not the slightest evidence of peritonitis.

The retro-pharyngeal glands were all increased in size, but not to such an extent as in other cases. The tonsils were enlarged, and, on section, presented a hæmorrhagic appearance, with numerous gray-yellow points.

Microscopic examination failed to reveal the presence of the tubercle bacillus in the enlarged mesenteric glands or tonsils, although the structure of these organs was suspiciously tubercular in appearance. They showed giant cells surrounded by circumscribed reticular lymphadenoid tissue, and the areas in which this appearance was noticed had a tendency to necrose.

Two guinea-pigs were inoculated, accordingly, in the right thigh with portions of the swollen mesenteric glands, clipped out from their centres with all due precautions. A collodion dressing, as in all other cases, was applied to the surface. The animals were kept isolated in a clean

* The animals in this series were all tested with tuberculin, with negative result, previous to the commencement of the experiments.

cage. It should be noted that all the guinea-pigs used for inoculation purposes had been under observation for from four to six weeks or more before the operation was performed, and were in perfect health at the time of inoculation.

After an interval of ninety-one days both guinea-pigs were killed. One of them proved to be perfectly sound, but the other was overrun with tubercular deposits. Immediately above the point of inoculation there was a round caseating and softening mass a little larger than a pea. Microscopic examination of the debris showed the bacillus of tubercle in abundance. The deep inguinal and retro-hepatic glands were enlarged and caseous, and throughout the substance of the liver and spleen great numbers of caseating tubercles were diffusely scattered abroad. The lungs were also beset with similar nodules, and the post-mediastinal lymph-glands were enlarged and caseous. The kidneys and suprarenal capsules seemed to be free from disease.

Summary.—A calf, ten days old, fed on tubercular sputum on eighteen occasions through a period of sixty-nine days. Post-mortem examination showed that the mesenteric glands were much enlarged; the retro-pharyngeals also enlarged, but not to such an extent as the mesenteric. Microscopic examination of the mesenteric glands failed to reveal the tubercle bacillus, but showed that giant-cells were present, with a reticular structure around them, and with a tendency to necrosis. Absence of intestinal tuberculosis. Inoculation of two guinea-pigs with the enlarged mesenteric glands produced diffuse tuberculosis in one instance after an interval of ninety-one days, while the other guinea-pig remained sound.

EXPERIMENT NO. 2.—*A black Aberdeen-Angus bull calf, fed with the same tubercular sputum as that employed in Experiment No. 1, and under exactly the same conditions. The animal was slaughtered sixty-six days after the commencement of the experiment.*

Post-mortem Examination.—The carcass was well nourished, and there was a good deal of gas in the paunch. The mesenteric glands, as in other cases, were all enlarged. Complete cords of them ran along the skirt of the mesentery adjacent to the bowel. The intestine and stomach were quite healthy. The tonsils were as large as pigeons' eggs, and were hæmorrhagic. Within them were minute yellowish points which were not suppurating. The retro-pharyngeal glands were all enlarged. The bacillus of tubercle was found in the mesenteric glands, but sparsely distributed. Numerous giant-cells with surrounding reticular structure were discovered in their substance, chiefly towards the periphery.

Two guinea-pigs were inoculated in the right thigh with pieces of tissue cut out from the interior of the tonsils; the wound was dressed with collodion. One of them was allowed to live for ninety-one days, the other died from some intercurrent disease. In the former a lymph-gland in the right groin a short way above the point of inoculation was found to be enlarged to the size of a large pea; it was caseating, and a film preparation made from it showed the tubercle bacillus in fair amount. The iliac and prevertebral glands, together with the large gland between stomach and liver, were all much enlarged, and in a state of caseation, while tubercular cheesy nodules were scattered through the substance of both liver and spleen. The other organs and tissues of the body seemed to be in a healthy condition.

Summary.—A ten-days-old calf, fed with tubercular sputum from the same case, and under similar circumstances, as in Experiment No. 1, killed after sixty-six days. Mesenteric glands all enlarged; tonsils much enlarged and hæmorrhagic; retro-pharyngeal glands also enlarged. Giant-cell structure in mesenteric glands with presence of tubercular bacillus sparsely distributed. Absence of intestinal tuberculosis.

Of two guinea-pigs inoculated from the swollen tonsils, one died prematurely from some intercurrent disease, while the other developed general tuberculosis.

EXPERIMENT NO. 3.—*A Hereford bull calf, two weeks old, fed with the same tubercular sputum as that employed in Experiment No. 1. Died thirty-seven days after the commencement of the experiment.*

Post-mortem Examination.—The carcass was somewhat emaciated, especially towards the flanks, but not to any great extent. The abdomen was distended with gas, which, as afterwards found, was contained in the rumen. The hair had a somewhat staring appearance, but in other respects the external appearances were normal.

The peritoneal cavity was free from gas or liquid, and there was complete absence of any signs of peritonitis, either recent or of old standing. The mesenteric glands in the neighbourhood of the cæcum and commencement of the large intestine were all much enlarged. Those lying closest to the bowel were of greatest size, and they were continued along the course of the meso-colon in festoons of consecutive chains. They were in some instances the size of a small walnut, in others approached that of a filbert, and the smallest of them were of the bulk of a large pea. The glandular enlargement within the abdomen appeared to be pretty much concentrated in the above-mentioned area. In all cases the affected glands were found to be fairly hard, and nearly every one of them on being cut into showed grayish-yellow points the size of a millet-seed or smaller, which looked like incipient tubercle nodules. The glands, as a rule, were somewhat anæmic, but, occasionally, round the tubercle-like points just referred to there was a congested area with sometimes a focus of hæmorrhage within it.

Both surfaces, serous and mucous, of the entire alimentary canal were examined with the greatest care from mouth down to rectum, but with the exception of about 12 inches of the mucosa of the small intestine being slightly congested, there was a complete absence of organic lesion. Both mucous and serous coats were perfectly free from tubercular deposit or ulceration.

The right tonsil showed two or three grayish-yellow nodules alike with those in the mesenteric glands. The opposite tonsil was apparently quite sound. About half a dozen of the retro-pharyngeal glands were found to be enlarged, and contained the same nodules as in the case of the mesenteric.

The outlines of the lobules of the liver were a little more accentuated than usual, and the cut surface had a somewhat gelatinous aspect. At the point of entrance of the blood-vessels there were three or four enlarged glands with the same tubercle-like points within them as described in those of the mesentery.

The carcass otherwise appeared to be healthy, not a vestige of

tubercle having been found in any other organ. The lungs and bronchial glands were quite free from any disease.

The enlarged mesenteric and retro-pharyngeal glands, the liver, and the right tonsil were hardened in methylated spirit for future microscopic examination. Sections were cut from several of the affected glands and from the tonsil, but in none of them could the bacillus of tubercle be demonstrated. The natural reticular structure of the gland was opened out and its meshes infiltrated with lymph-cells, and this infiltration was especially marked in the grayish-yellow points previously referred to. The centres of these nodule-like masses showed a tendency to necrosis and disintegration, as if they were commencing to suppurate or to undergo caseation. Giant-cells were absent, although the reticulum in many parts looked exactly like that of tubercle.

Within the blood contained in the bloodvessels of the lymphatic glands there was a streptococcus. This led to the supposition that the animal had died from a septicæmia, not from the direct effects of tuberculosis. Whether the glandular enlargements in the abdomen and retro-pharyngeal region were tubercular or not remains doubtful. Comparing the appearances presented by them, however, with those found in the other calves, placed under like experimental conditions, it is probable that they were. The absence of giant-cells may be accounted for by the tubercles having been comparatively young, and the failure to find the tubercle bacillus microscopically is what may be looked for in a certain proportion of cases, even where the structure of the part is manifestly tubercular. It is to be regretted that in this case re-inoculation was not practised on the guinea-pig; but from the fact of the calf having evidently died from some disease other than tubercle it was not considered at the time of the post-mortem examination to be worth while doing so, more especially as a comparatively small period of time had elapsed since the commencement of the experiment. There is this to be added in favour of the glandular enlargement being tubercular—namely, that, as in other experiments, the lesion took the form of a lymphadenitis, and that the glands affected lay along the digestive tract.

Summary.—A calf, two weeks old, fed with same tubercular sputum as in experiment No. 1, died thirty-seven days after commencement of the experiment, apparently from septicæmia. Mesenteric glands enlarged. Absence of tubercle bacillus, absence of giant-cell structure, absence of intestinal tuberculosis.

EXPERIMENT NO. 4.—*A Hereford female calf, three weeks old, fed with the same tubercular sputum as that employed in Experiment No. 1, and under exactly the same conditions. The animal was slaughtered sixty-five days after the commencement of the experiment.*

Post-mortem Examination.—The autopsy was made within a few hours after death. Nothing of an abnormal nature was to be noticed externally. None of the tangible lymph-glands felt enlarged, and the animal was well nourished. The paunch was distended and tympanitic from accumulation of gas within it. The peritoneal cavity, however, was perfectly free from gas accumulation.

Nearly every mesenteric gland was enlarged to such an extent as to constitute a tumour-like object. They varied in size from a large horse-bean to a walnut, and ran in chains along the intestinal border of the mesentery, mainly that attached to the small intestine. A large

gland lay over the right iliac vessels. On section the glands presented a homogeneous aspect, but were congested and even hæmorrhagic in parts, pale and anæmic in others. There were comparatively few yellow points within them, although occasionally these were met with. None of them had suppurated.

The retro-pharyngeal, cesophageal, and tracheal glands were all the subject of enlargement even to a greater degree than the mesenteric. They contained, moreover, plenty of yellowish-gray points, which in all respects resembled young tubercles.

There was a round ulcer on the dorsum of the tongue, the size of a sixpence, with raised and indurated edges. It ran only partially through the mucosa, and the neighbouring tissues were not infiltrated to any extent.

The other internal organs seemed to be quite sound; not a vestige of tubercle was found in any of them. The gastro-intestinal tract was perfectly free from morbid appearance of any kind. The mucosa of the intestine was examined carefully for tubercular infiltration or ulceration, but not the slightest indication of such was discovered. The left mammary gland was considerably enlarged and hæmorrhagic, and showed numbers of minute yellow points in the hæmorrhagic areas.

Microscopic Examination.—The cause of the enlargement of the glands and tonsils seemed to be a lymphadenitis, but whether this was tubercular or not may be a matter of question. The small-cell infiltration of the infected glands and tonsils was dense, and in some of the follicles there was commencing disintegration. This disintegration, however, did not look like ordinary caseation, unless it may have been this form of tissue necrosis just commencing. The fact of abscesses being nowhere present is against the notion of its being the result of absorption of pyogenic organisms. On the other hand, there was an absence of giant-cell structure, and the bacillus of tubercle could not be demonstrated microscopically in any of the affected parts.

Two guinea-pigs were inoculated in the right thigh with portions of two of the largest mesenteric glands. After three and a half months they were killed, and proved to be quite healthy. There was not a trace of tubercular deposit either in the lymph-glands or in other organs, and the piece of tissue inoculated seemed to have become absorbed.

The affected mammary gland was much congested, but was free from tubercular structure. The yellow points were composed of gland-tissue with cloudy epithelium in a state of desquamation.

The ulcer on the dorsum of the tongue seemed to be a mere erosion. It did not show any tubercular structure, nor were tubercle bacilli recognisable in its floor or edges.

Considered on its merits, this case presents various interesting, and in some respects anomalous, features. Thus there was pronounced enlargement of the tonsils and the lymph-glands lying along the gastro-intestinal tract. The glands appeared identical in appearance with those from other cases in which the tubercle bacillus was demonstrated microscopically, and in which tuberculosis was induced in guinea-pigs by inoculation of the affected tissues. There was an absence of supuration in all parts of the body, and the animal did not develop signs of pyæmia or septicæmia. On the other hand, the enlarged glands did not present a giant-cell structure, and the tubercle bacillus could not be demonstrated within them, while inoculation experiments on guinea-pigs proved negative. It is hard to conceive what the cause of the

glandular enlargement had been if not tubercular. A chronic lymphangitis, confined to the gastro-intestinal tract, without any tendency to suppurate, is a condition which, on the face of it, is strongly suggestive of tuberculosis from absorption, and is the kind of lesion to be looked for in an experiment such as the above. It cannot be too strongly emphasized that human tubercle grows slowly on the calf, and quite possibly, had longer time been afforded in this case, indubitable evidence of the ingrafting of the disease would have been forthcoming. Taken along with the appearances presented by other cases, it seems probable, at least, that the glandular enlargement was tubercular, but so sparsely distributed was the bacillus throughout the parts that it failed to reveal itself either on microscopic examination or after inoculation.

Summary.—A calf, three weeks old, fed with tuberculous sputum as in Experiment No. 1, killed after sixty-five days. Enlargement of mesenteric lymph-glands and of tonsils strongly suggestive of a tubercular lymphadenitis. Absence of giant-cell structure, absence of tubercle bacillus, failure to reproduce on the guinea-pig.

EXPERIMENT NO. 5.—*A Shorthorn bull calf, ten days old, fed with the same tubercular sputum as that employed in Experiment No. 1, and under exactly the same conditions. The animal was slaughtered sixty-five days after the commencement of the experiment.*

Post-mortem Examination.—The animal seemed to be somewhat out of condition, as manifested in the staring and dry condition of the hair. The mesenteric glands were all enlarged to such an extent that they immediately arrested attention. When the intestine was drawn out huge tumour-like masses, consisting of these glands, swollen and prominent, were seen running along the mesentery in chains and festoons, those nearest the intestinal attachment being again most prominent. The largest were about the size of a pigeon's or small hen's egg; a great many were of the bulk of a walnut. Their texture, as seen on section, was homogeneous, with grayish-yellow points here and there; they had a somewhat anæmic appearance, and were of a pinkish-gray colour.

Those running along the iliac vessels were also increased in size, and took the form of a continuous chain.

The cesophageal and retro-pharyngeal lymph-glands were of enormous size. On each side of the neck one of the retro-pharyngeal glands was as large as a hen's egg, and on being incised showed distinct yellow miliary points on a congested basis. The whole of the glands of the neck, indeed, seemed to have undergone enlargement, and ran in prominent chains or were clustered in masses.

The mucous membrane of the small intestine for a distance of several feet was red from congestion, and on its surface lay a quantity of grayish-yellow catarrhal discharge. The lungs showed congested patches, which on section seemed to be hæmorrhagic, and occasionally some of them had yellowish centres. They were about half an inch in breadth, and a quarter of an inch in depth. There were from six to seven of them. Numbers of petechial hæmorrhages were found on the surface of the heart.

The tonsils were both enlarged and exhibited grayish, very tubercular-looking points on section. Otherwise the organs were sound.

From four to five mesenteric glands were placed in sterile bottles and surrounded with ice, and on the following morning two guinea-pigs were

inoculated subcutaneously with portions of them in the right thigh. It should be mentioned that a scraping taken from the fresh retro-pharyngeal glands failed to show tubercle bacillus.

After the parts had been hardened in spirit, sections were cut of them and stained so as to exhibit their histological structure, and also with a view to demonstrate the tubercle bacillus. In the mesenteric and other enlarged glands there was a distinct lymphadenomatous structure, with occasional giant-cells here and there. In the tonsils, however, the structure was eminently tubercular. Scattered through their substance were rounded lymph-cellular aggregations, apparently enlargements of the natural follicles, with a reticular fibrous meshwork as a basis. Within these rounded cellular aggregations were excellently developed giant-cells of large size, and containing often as many as ten to fifteen or more nuclei. They seemed to be intimately bound up with the reticulum of the nodule by means of processes which projected from their margins.

On staining sections of the tonsil with carbol-fuchsin for the tubercle bacillus, the organism was found scattered thinly through the substance of the gland. The bacillus was of fairly large size, and lay, as a rule singly, in the meshes of the reticular tissue.

The two guinea-pigs, inoculated with pieces of the mesenteric glands, were killed after eight weeks. They both proved to be highly tubercular, the tubercles spreading from a caseous abscess at the seat of inoculation. The deep inguinal and retro-hepatic glands were all enlarged and caseous; the liver and spleen were filled with typical caseous tubercles, and similar deposits were abundant in the lungs. The mediastinal glands were also enlarged and caseous. The lesions in both animals were practically alike, and had advanced to very much the same degree.

Summary.—A calf, ten days old, fed with tubercular sputum as in case No. 1; animal killed sixty-five days afterwards. Intense tumefaction of mesenteric, oesophageal, and retro-pharyngeal lymph-glands and tonsils. Giant-cell structure within these parts, with presence of tubercle bacillus. Absence of intestinal tuberculosis. Inoculation on guinea-pig positive.

No. 6.—*A Shorthorn calf, one week old.*

The animal died, apparently from an attack of diarrhoea, before the feeding experiments began. As showing the purity of the calves utilized for the series of experiments, this animal, which was taken from the same lot as the others, failed to react with tuberculin, and was found to be free from tubercular disease.

Summary.—Animal died before inoculation; failed to react to tuberculin; carcass free from tubercle.

SECOND SERIES.*

EXPERIMENT NO. 7.—*A brown-and-white "cross" bull calf, two weeks old, inoculated subcutaneously on the inside of the right thigh with several pieces of a group of enlarged glands removed from the left side of the neck of a woman.*

Inoculation of the Glands.—The glands all presented numerous cheesy foci, but were not suppurating. A pocket of skin was raised up, and

* The animals in this series of experiments were not tested with tuberculin previous to inoculation, as it was thought that doing so might interfere with the

the pieces inserted at the upper extremity of the pocket. The operation was conducted with strict antiseptic precautions. The glands had not touched an antiseptic, and hence were not washed. The pieces introduced into the wound were removed from the centre of the gland, and collodion dressing was used for covering the wound after the introduction of a catgut stitch. The glands inoculated had been placed immediately after removal in a sterile bottle and surrounded with ice. The temperature at the time was below freezing-point.

The history of the patient from whom the glands had been obtained was as follows:

H. M., a domestic servant, aged twenty-six, noticed a swelling five years ago on the left side of her neck, which she attributed to a decayed tooth. The swelling continued to increase in size, but slowly, and at the time of operation, there was an indurated chain of glands on the left side of the neck, along the border of the sterno-mastoid. The glands were matted together, but movable as a mass. There was slight redness over the upper and most prominent part of the mass, where there was likewise a sense of softness. Some isolated enlarged glands were also felt low down, immediately above the clavicle, and some others were felt in the posterior triangle of the neck.

On the right side some circumscribed glands of fair size were felt along the border of the sterno-mastoid, and a few were also perceptible in each axilla, but none in the groins.

The teeth were very carious, and were removed a fortnight before operation. The redness increased while under observation in hospital. The patient was very anæmic but not strumous-looking. Tubercular implication of other organs of the body could not be made out. There was an absence of any family history of tuberculosis.

Seventeen days after inoculation on the calf a nodule as large as a hazel-nut was felt above the point of inoculation. It was hard, and located about one inch above the entrance to the inoculation pocket. The wound had healed perfectly by first intention, and the animal seemed in good enough health.

Fifty-five days from the date of inoculation this nodule was no larger, and there was an absence of any appreciable enlargement of the glands in the corresponding groin.

Sixty-four days after the inoculation the animal was tested with tuberculin, and reacted, the initial temperature being 101.9° F., that after tuberculin testing, 106.4° F.

Post-mortem Examination.—The animal was killed on the following day, and the post-mortem examination was made immediately afterwards. The carcass was well nourished. A soft nodule the size of a horse-bean or a little larger was found at the upper extremity of the inoculation pocket, from which, when incised, a soft, cheesy mass was ejected. In the groin of the same side there was a group of glands all more or less enlarged, the largest being about the size of a small walnut. They were five in number, and on cutting into the largest one two yellow points were revealed, distinctly tubercular in aspect. The rest of the gland was homogeneous in consistence, and grayish-pink in colour. There was no appearance of any glandular implication between the cheesy focus of inoculation and those enlarged glands found in the groin. The glands in the left groin were not enlarged.

Along the line of the iliac vessels, and running up the whole length of the dorsal spine, the glands were almost all in a state of enlargement,

success of the experiment. This idea, as shown in our subsequent experiments, is apparently erroneous.

and on section they presented, in most cases, yellow points evidently tubercular. Most of the mesenteric glands were much enlarged, some of them ranging in size from a walnut to a pigeon's egg, and showed in many instances the same yellow points. The glands over the stomach were likewise enlarged, and ran in chains, while some of them were so prominent as to resemble the "pearly" or "grape-like" variety of bovine abdominal tubercle.

On tracing the prevertebral glandular enlargement upwards, it was found that the post-mediastinal group was similarly affected, and a continuous chain was found running along the side of the trachea and oesophagus. The retro-pharyngeal glands also participated in the enlargement; two of them were deeply congested, and showed grayish-yellow points which might be tubercular. In none of the other organs was there a sign of tubercular or other disease. There was no appearance of peritonitis or pleurisy. The mucous membrane of the small intestine was a little congested, but evidence of tubercular implication was completely wanting.

Film preparations of scrapings from the cheesy nodule at the point of inoculation and from the mesenteric glands, showed the presence of the tubercle bacillus. The bacilli seemed to be larger and broader than the ordinary human tubercle bacilli, and contained several deeply-stained points in their interior.

Summary.—A two-weeks-old calf, inoculated subcutaneously in the right thigh with pieces of tubercular gland taken from the neck of a woman, reacted to tuberculin sixty-four days after inoculation; animal killed sixty-five days after inoculation. Local tubercular lesion with glandular enlargements in groin of same side, not on the opposite. Marked enlargement of pelvic, abdominal, post-mediastinal, tracheal, and oesophageal glands. Absence of tubercular implication of other organs. Tubercle bacillus found in the enlarged glands, and focal lesion.

EXPERIMENT No. 8.—*A black Aberdeen-Angus bull calf, two weeks old, inoculated in the inner aspect of the right thigh with scrapings from tubercular glands taken from the neck of a boy.*

The history of the patient from whom the glands were obtained was as follows: W. M., a boy, aged six years, had suffered for a year or two from a swelling, evidently glandular, on the left side of the neck. The swelling had slowly increased in size up till lately, when it grew more rapidly, and became red on the surface.

On examination a large, red and fluctuating swelling was noticed on the left side of the neck. A hard mass was felt below it, which was very adherent to the skin. There was no swelling on the other side of the neck nor in the axillæ. The teeth were carious, and the patient was anæmic and strumous-looking. The family history was very tuberculous.

The glands immediately after removal were placed in a sterile wide-mouthed bottle, and were not subsequently washed, as they had not touched any antiseptic. They were kept in ice overnight, the temperature at the time being below freezing-point. The calf inoculated was a fortnight old, and appeared to be in perfect health. It was not tested with tuberculin previous to the commencement of the experiment. A pocket of skin was raised up from the thigh, and pieces of the glands were introduced into its depths. The glands presented cheesy foci, and the pieces introduced were taken from these. Everything was done

with antiseptic precautions, and the inoculation wound was dressed with collodion.

Seventeen days after inoculation a hard coil was felt running up from the wound for a distance of from 2 to 3 inches. The animal's hair seemed to be a little staring, but otherwise it was well enough. The wound had healed by first intention.

Sixty-five days after inoculation the cord-like induration had vanished, but an enlarged gland was felt in the groin as large as a filbert.

Seventy-four days from the time of commencement of the experiment the animal was tested with tuberculin, and gave a reaction, the initial temperature being 101.5° F., rising to 103° F. sixteen hours afterwards.

Post-mortem Examination.—The animal was killed on the following day, and the post-mortem examination was made immediately afterwards.

The carcass was well nourished. There was a complete absence of any indication of the point of inoculation, either in the shape of a nodule or cicatrix, and the part was perfectly healed. In the right groin there was an enlarged and indurated gland about the size of a hazel-nut. All along the course of the iliac vessels and front of the spine, as far up as the pharynx, the lymph-glands were continuously enlarged, and showed in most cases yellowish-gray points on section. The mesenteric glands were much swollen, some of them being as large as pigeons' eggs. In one part of the mesentery attached to the small intestine they took the form of a continuous nodulated cord about a foot in length. The intestine was quite healthy. The case, in fact, seemed to be very much alike with No. 7, only not quite so far advanced, and with an absence of the focal cheesy deposit at the point of inoculation.

Scrapings taken from the enlarged glands did not show the tubercle bacillus, and, accordingly, two guinea-pigs were inoculated in the right thigh with small portions excised from the mesenteric glands most affected. One of these guinea-pigs died, unfortunately, before time was afforded for tubercular lesion to develop. The other was killed fifty-seven days afterwards, and showed absence of disease of any kind.

It is unfortunate that in this case one of the inoculated guinea-pigs died prematurely. The appearances post-mortem of the inoculated calf, however, were so closely alike with those observed in others as to constitute a strong argument for the lesions having been tubercular.

Summary.—A calf, two weeks old, inoculated subcutaneously on inner aspect of right thigh with scrapings of tubercular glands taken from a boy, seventy-four days after inoculation reacted to tuberculin; killed on seventy-fifth day. Absence of local lesion. Some amount of glandular enlargement. Absence of tubercle bacillus and of giant-cell structure. One inoculated guinea-pig died prematurely, the other was free from tubercle after fifty-seven days.

EXPERIMENT NO. 9.—A "cross" bull calf, three weeks to a month old, inoculated subcutaneously in the right leg with tubercular glands removed from a lad thirteen years of age.

About eight years ago a swelling developed on the right side of the patient's neck, which, his father says, disappeared several times but always returned. For the last two to three years, however, the swelling has not shown any tendency to disappear. About a year ago an enlarged gland was removed in hospital, but he

was brought back again in the beginning of October of 1901, when more glands were excised. He returned later on to be operated upon again, and the glands utilized for inoculation were removed at the time of this last operation.

The boy was of average height, well nourished, and took his food heartily.

His father and mother are both alive and healthy; he has one brother and two sisters alive and strong, and one brother and one sister dead, one of them having died, it was said, from inflammation of the lungs, the cause of death in the other case not being known.

There was slight flatness in the infra-clavicular region and percussion was somewhat impaired. Nothing abnormal was made out on auscultation.

Several long scars, the result of previous operations, were found at different parts of the neck. The present glands were removed from both sides of the neck by incision. The largest gland was taken from the right side of the neck, and some pus escaped from it on removal. A large gland was also excised from the left side of the neck, but pus was not found in it.

The glands were placed at once in a sterile bottle. They were found to vary in size from a small pea to a walnut, were cheesy in the centre, and several of them were in a state of suppurative liquefaction. Two pieces were selected for inoculation, the one cheesy, the other suppurating. They were introduced into a pocket of skin, on the inside of the right thigh of the calf.

Thirteen days afterwards a hard nodule the size of a large pea was felt about 1 inch above the point of inoculation. The wound had healed by the first intention.

Post-mortem Examination.—Twenty-two days after the animal had been inoculated it died, apparently from an attack of enteritis, the mucous membrane of the intestine being much congested. The pieces of inoculated tissue had formed a caseous nodule adherent to the surroundings, but there were no glandular enlargements or other signs of tuberculosis in any part of the body.

Summary.—A three-weeks-old calf, inoculated subcutaneously in right thigh with tubercular cervical glands from a boy, died twenty-two days afterwards from enteritis. Inoculated tissue had formed a caseous nodule adherent to surroundings, but as yet there were no glandular enlargements or other signs of tubercular infection.

EXPERIMENT No. 10.—*A "cross" bull calf, about seven weeks old, inoculated in the right leg with tubercular cervical glands removed from a boy.*

The boy from whom they were removed was fourteen years old, and one of a family of six, all being healthy. The father and mother were said to be free from tubercular disease, but the father suffers from general paralysis, and is in an asylum. The boy was healthy enough until three years ago, when an acute abscess formed in the right side of the neck. It was opened and healed early, but the swelling never passed quite away. Two months ago another swelling showed itself at the side of the old incision, but was not treated in any way until the time of operation, when the whole mass was completely removed. There was no evidence of tubercle in any other part of the body.

The glands were received in a sterile bottle, and were found to vary in size from a large pea to a large hazel-nut or small walnut. One had begun to suppurate. A smearing from one of them showed the presence of the tubercle bacillus.

Pieces were cut from several of these glands and introduced into a pocket of skin on the inner aspect of the right thigh of the calf.

Forty-eight days afterwards a nodule the size of a filbert was

detected immediately above the inoculation pocket, but the glands in the groin were not enlarged. Eighty-five days after inoculation the animal was tested with tuberculin. The initial temperature was 101.5° F., and it rose in sixteen hours to 102.8° F. The animal was killed and examined on the following day.

Post-mortem Examination.—The carcass was in good condition, and at the point of inoculation there was found to be a soft swelling the size of a filbert, which on being incised looked homogeneous and fleshy, while within it were nodular points which felt and looked like tubercles. One of these nodular foci on being incised showed a cheesy centre. Within the groin on the same side was a gland the size of a small walnut, and filled with cheesy pus. At a little distance from this large gland there was another of smaller size, but distinctly enlarged, which did not prove to be caseous. Another enlarged gland still, the size of a filbert, was found a little above the groin.

In the opposite groin there were two enlarged glands, one the size of a hazel-nut, the other that of a pea. The larger of the two on being opened was found to present a homogeneous surface and was not caseous.

The glands along the iliac vessels on both sides were much enlarged, especially those on the right side, and the enlargement was continued up in a chain in front of the spine. The mesenteric glands were universally enlarged, and some of the smallest were quite black from hæmorrhage into their substance, while the majority of them on being opened were found to contain cheesy pus in considerable quantity. The glandular enlargement was quite as great in other cases, but the caseous softening was more in evidence than in the case of any previous experimental animal. The glands at the hilum of the liver were also much enlarged, and constituted an aggregated tumour-like mass, which on being cut into showed numerous cheesy points typically tubercular in appearance. There were a few fibrous adhesions of the diaphragm to the right margin of the liver, but the liver itself, along with the kidneys and spleen, was free from tubercle.

About the middle of the right lung there was an oval-shaped and half-organized adhesion of the two pleuræ, measuring about 5 by 2½ inches, which on being separated showed much hæmorrhage into the costal layer. This adhesion corresponded in site with an indurated mass in the lung-substance, about the bulk of a middle-sized orange, with fairly well-defined margin, and perfectly devoid of air. On cutting into it the mass proved to be a tubercular infiltration of the lung-substance, the smallest nodules being about the size of a millet-seed, and grayish in colour, the largest about the size of a large pea, and far advanced in caseation and softening. Within the mass were several distinct tubercular cavities containing softened cheesy *débris* resulting from the complete dissolution of the nodules above described. The whole infiltrated mass had a tough fibrous character, as if from fibrous infiltration. On the left side there was an almost exactly similar condition, with adhesion of the pleuræ, and tubercular infiltration of a circumscribed portion of lung-tissue, only not so far advanced. There were, likewise, several phthisical cavities in the infiltrated part. The remainder of the lung-substance on both sides was free from tubercular disease, and did not in any way seem to be abnormal, and the pleuræ, otherwise than above described, did not seem to be involved. The bronchial and tracheal glands were all very much enlarged, some of them about the bulk of a large walnut, and they showed numerous

gray tubercle points in their substance. The œsophageal glands were also enlarged, but to a less degree than in some other cases.

There was no evidence of peritonitis or pericarditis. On the surface of the heart there were groups of petechial hæmorrhages, but no tubercle in connection with them.

Two guinea-pigs were inoculated in the right thigh with portions of the mesenteric glands, and were killed fifty-four days afterwards. Both gave a positive result, the primary gland above the point of inoculation and the mesenteric glands being, in each instance, enlarged and caseous, while the spleen, liver, and lungs were the seat of a tubercular eruption.

Summary.—A seven-weeks-old calf, inoculated subcutaneously on right thigh with tubercular cervical glands taken from a boy, eighty-five days after inoculation showed slight reaction to tuberculin. Cheesy tubercular formation at point of inoculation. Cheesy gland in right groin. More or less general glandular enlargement. Tubercular patch with corresponding localized pleurisy in each lung.

Inoculation of two guinea-pigs with the enlarged glands, both positive.

EXPERIMENT NO. 11.—A “cross” bull calf, seven to eight weeks old, inoculated in the right thigh with a piece of lung taken from a man who died from general miliary tuberculosis.

Nearly every organ throughout the man's body was beset with an eruption of gray nodules about the size of a millet-seed. Both lungs were literally filled with them from apex to base, the spleen, liver, kidneys, and mesenteric glands were all much involved, and the individual's death was ultimately to be accounted for by the advent of tubercular meningitis. Judging from the general appearance of the nodules and the absence of excavation, the case seemed to have been one running an acute course.

The piece of lung inoculated was kept in ice, during freezing weather, in the interval between removal from the body and the time of inoculation. A smearing taken from it showed the bacillus of tubercle.

Forty-eight days after inoculation the wound was found to have healed perfectly by first intention, and there was no indication of a nodule at the point where the pocket of skin had been made, while there was an absence of any feeling of enlargement in the glands of the groin or elsewhere. The coat was, however, a little staring, and the nose dry.

Eighty-six days after the experiment was made the animal was tested with tuberculin, and gave a reaction. The initial temperature was 101.4° F., and in twelve hours it rose to 104° F.

The animal was slaughtered on the following day.

Post-mortem Examination.—At the seat of inoculation there was a small, firm, fibrous cord. The inguinal glands on the same side were considerably enlarged and congested, but did not contain any definite yellow tubercles. The corresponding glands on the opposite side were also somewhat enlarged. There was a distinct chain of enlarged glands running up the spine in the abdominal region, which, however, did not show any yellow tubercles. All, nevertheless, contained small hæmorrhagic areas. The mesenteric glands were not markedly enlarged, and none of them was congested or hæmorrhagic. There was an absence of punctiform hæmorrhage into, or evidence of inflammation of, the peritoneum. The liver, kidneys, and spleen were all normal. The lungs also appeared to be healthy, with the exception of two or three

small solidified areas at the base of the left. The largest of these was about the size of a horse-bean, but none of them presented definite tubercular characters. The bronchial glands on both sides were very much tumefied, and running downwards from them on each side of the aorta there was a chain of glands, enlarged and elongated. All of these showed extensive caseous deposits, in many cases becoming calcareous.

With the exception of a few punctiform hæmorrhages on its visceral layer the pericardium appeared to be normal. The cervical glands were all increased in size, notably the retro-pharyngeals, which were also very congested, and on section showed numbers of small hæmorrhagic areas, but no definite tubercles. The tonsils were slightly enlarged, and there was a small caseous patch in the left.

Two guinea-pigs were inoculated in the right thigh with fragments of the caseous bronchial glands. Fifty-two days after inoculation they were killed, with the result that one was found free of tubercle, the other was eminently tubercular. In the latter, a caseous tubercular eruption was found all through the liver and spleen.

Summary.—Inoculation of a seven to eight-weeks-old calf with lung-tissue taken from a man who died from diffuse miliary tuberculosis. Inoculation made subcutaneously on right thigh. Eighty-six days after inoculation animal reacted to tuberculin; killed on eighty-seventh day. A fibrous cord-like induration at point of inoculation. Great glandular enlargement with caseation. Two or three small solidified areas at base of left lung. One of two guinea-pigs inoculated with the caseous bronchial glands became tubercular.

EXPERIMENT NO. 12.—*A "cross" bull calf, from seven to eight weeks old, inoculated in the right thigh with urine containing tubercle bacillus, taken from a man suffering from genito-urinary tuberculosis.*

The man from whom the urine was obtained had a tubercular testicle, with evidence of a tubercular kidney. The urine contained tubercle bacilli in great quantity, they were peculiarly large and long, and presented a few, but only a few, metachromatic points. The urine was allowed to stand in ice for a couple of days, and the sediment, which was very fine, was injected subcutaneously with a sterile syringe.

Forty-five days after the commencement of the experiment there was a suspicion of an enlarged gland in the groin of the inoculated leg, but nothing distinctly evident. There was an absence of any nodule at the seat of inoculation.

Ten days after this, the animal was tested with tuberculin. The initial temperature was 101° F., and it rose to 102° F. in twelve hours.

The animal was killed on the following day.

Post-mortem Examination.—There was no evidence of lesion at the seat of inoculation. The superficial inguinal glands were somewhat enlarged, but did not present any tubercular points. One of them, however, showed distinct patchy congestion. The abdominal pre-vertebral glands were not enlarged, with the exception of a few on the right side of the promontory of the sacrum. The mesenteric glands, although swollen, were not so large as in some other cases; the biggest was about the size of a walnut. None of them presented any tubercular points, but several showed small hæmorrhagic areas. There were also numbers of small pin-head hæmorrhages into the mesentery. The liver, spleen, and kidneys were quite healthy.

Towards the anterior margin of the lower aspect of the right lung there was a tubercular deposit about the size of a horse-bean, and on the area of pleura corresponding to this a small tubercular patch about a quarter of an inch in diameter. There were several small tubercular patches on the pleural surface of the middle and lower aspects of this lung. The parietal pleura also, on this side, showed numerous tubercular patches, situated mostly at its upper and posterior parts.

The bronchial glands were enlarged, and showed congested areas on section. Situated to the left of the aorta, just behind the left primary bronchus, was a large gland, almost the size of a hen's egg. On section this exhibited numbers of yellowish caseous patches, and at one part an area of yellowish colour and calcareous consistence. The cervical glands were not markedly enlarged, unless in the retro-pharyngeal region, where they were of considerable size on both sides, and deeply congested. Many of them were the size of walnuts, and on section were found to be studded with numerous pin-head hæmorrhages. The tonsils did not appear to be enlarged, and did not contain any tubercle points; but they were very dark-red in colour, probably from congestion.

Film preparations taken from the retro-hepatic lymph-glands, as well as from the caseating deposits in the lung-tissue, revealed the presence of the tubercle bacillus. The bacilli seemed to be of the usual size, and morphologically showed nothing of note.

Summary.—A calf from seven to eight weeks old, inoculated subcutaneously in the right thigh with human urine containing tubercle bacillus; fifty-five days after inoculation animal reacted slightly to tuberculin. Prevertebral, mesenteric, bronchial, and retro-pharyngeal glands, enlarged and caseous. Tubercular deposits in right lung. Bacillus of tubercle in affected parts.

THIRD SERIES.*

EXPERIMENT No. 13.—A “cross” bull calf, a few weeks old, inoculated in the right thigh with portions of cheesy tubercular glands taken from the neck of a young woman.

The patient had suffered from these for several years, and some of them were removed from the same locality five years ago. Pieces cut out from the enlarged and caseous glands were introduced into a pocket of skin on the right thigh. Fifty-two days afterwards a nodule about the size of a filbert was distinctly perceptible at the point of inoculation. A fortnight after this it had increased perceptibly in size, and continued to do so up till the time the animal was killed, one hundred and forty-six days after the experiment was commenced. A week before killing the animal it was tested with tuberculin. The initial temperature was 101·3° F. at 8.30 p.m. The following day at 6 a.m. it had risen to 104·1° F., at 9 a.m. to 105·6° F., while at 11 p.m. it stood at 105·1° F., and at 2 p.m. had sunk to 103·8° F.

Immediately before death the temperature in the rectum was 101·8° F., pulse 78, respirations 28.

Post-mortem Examination.—The carcass was well nourished. At the seat of inoculation in the right thigh a fluctuating swelling the size of a pigeon's egg could be seen, and was readily felt underneath the skin.

* The animals in this series were all tested with tuberculin before the commencement of the experiments, and with negative result.

On the same side there was an inguinal gland the size of a large walnut, which, however, did not fluctuate as in the case of the other swelling, but was hard and nodular. With these exceptions, external examination failed to reveal any lesion. On removing the hide, the tumour at the seat of inoculation was found to be closely adherent to it, and evidently was not a mere glandular enlargement. It consisted of a tough fibrous capsule, with a caseous centre almost completely liquefied. The inguinal swelling was composed of three or four glands bound together in a group, each member of which showed distinct evidence of incipient caseation, most advanced at the centre. In the thickened capsule, in which these caseous areas were enclosed, there were numerous yellow miliary tubercles. The caseous degeneration had not, however, gone so far as at the primary focus of inoculation.

On opening the abdomen a glandular enlargement, the size of a hen's egg, was found in the right iliac region, which seemed to lie in close relationship with the external iliac vessels (Fig. 1). It felt hard and nodular, and on being incised showed advanced caseation with innumerable grayish-yellow tubercle points scattered through it. The gland was, in fact, a typical example of what is commonly found in bovine tuberculosis. It was employed for inoculating calf No. 19. The glands lying in front of the vertebral column, right up to the level of the tonsils, were all more or less enlarged and indurated, but were not advanced in caseous degeneration. Some of them exhibited small grayish points in their substance, but this was not by any means general. The bronchial glands were also enlarged, but not caseous. The tonsils were of at least twice the normal dimensions, felt indurated, and on section presented a gelatinous and cedematous appearance, but were free from caseation. The mesenteric glands were enlarged and indurated pretty universally, the largest of them about the dimensions of a big walnut. They presented minute grayish points on section, but these were few in number; the majority of them had a smooth gelatinous cut surface. The spleen contained two tubercular nodules, each the size of a small pea, which were commencing to caseate, but, with this exception all the other organs were healthy.

Microscopic Appearances.—Film preparations from the enlarged and cheesy lymph-glands showed the presence of tubercle bacilli. The bacilli were in a state of active segmentation, and their chromatic points stained deeply. Numbers of stained bodies having a close resemblance to Schrön's capsules were also present.

A calf (see Experiment No. 19) and a guinea-pig were inoculated subcutaneously with pieces of the cheesy gland found in the right iliac region. The calf was two days old, and the inoculation was made in this case, and in that of the guinea-pig, into the right leg.

Sixty days afterwards the guinea-pig was found dead with its body literally filled with tubercle. In no case, perhaps, have we ever seen more intense tubercular dissemination following upon inoculation of any tubercular virus. A tubercular abscess had formed at the point of inoculation; the glands leading up from this were as large as horse-beans and in a state of cheesy degeneration. The whole of the lymph-glands throughout the body seemed to have become tubercular from the region of the masseter muscles downwards. The liver and spleen constituted almost uniform masses of yellow tubercle, and the lungs contained many nodules (see Fig. 2). The pericardium, however, as so often happens in general tuberculosis, seemed to be quite free from tubercular infection.

A smear taken from the spleen showed innumerable tubercle bacilli. They seemed to differ morphologically from those found in the calf from which the inoculation on the guinea-pig was made. They were not so long and not so beaded, but were very sharply defined, and in a state of segmentation.

The virus used in inoculating this guinea-pig seems to have been of extreme virulence. When it is considered that the lesions found were only a little over two months in production, and that practically the whole of the organs—lymphatic glands included—were infiltrated with tubercle, it must be acknowledged that the virus thus transmitted through the system of the calf was of no ordinary potency for the guinea-pig, and produced lesions in excess of those usually following the introduction of the bacillus taken directly from man.

Summary.—A "cross" calf, a few weeks old, inoculated subcutaneously in the leg with human tubercular glands taken from the neck; the animal was killed one hundred and forty-six days after inoculation, and a week before death gave a typical tubercular reaction. The post-mortem examination revealed a tubercular abscess, the size of a pigeon's egg, at the point of inoculation, tubercular inguinal glands, an intensely tubercular and cheesy iliac gland, great enlargement of the entire prevertebral and mesenteric glands, enlargement of the tonsils, tubercle deposits in the spleen. Presence of the bacillus tuberculosis in the affected parts. A guinea-pig inoculated from the iliac gland became intensely tubercular in sixty days, and died therefrom.

EXPERIMENT NO. 14.—A white-and-black "cross" bull calf, a few weeks old, inoculated in the right leg with human tubercular glands taken from the neck.

In a month the wound had healed perfectly without leaving any nodule or other local manifestation. One hundred and thirty-five days after the commencement of the experiment the animal was tested with tuberculin with the following result: The initial temperature at 8.30 p.m. was 101.8° F., while on the following day it rose to 102.6° F. at 6 a.m., at 9 a.m. it was 103.4° F., at 11 a.m. 104.8° F., and at 2 p.m. 102.2° F.

Post-mortem Examination.—One hundred and sixty days after inoculation the calf was slaughtered, the temperature immediately before death being 101.4° F., the pulse 100, and the respirations 28. It was in good condition, and there was a complete absence externally, either at the point of introduction of the virus or elsewhere, of any indication of the animal being tubercular. The inguinal glands, those along the iliac vessels, and the prevertebrals, all seemed to be normal. The mesenteric glands, however, and more especially those in connection with the small intestine, were more or less enlarged, some of them forming tumour-like objects varying in size from a pigeon's egg to that of a small hen's egg. They were free from caseation, and as a rule were moist and gelatinous, but occasionally some minute points of a grayish-yellow colour were visible on the cut surface.

Within the left lung, towards its base, there was a nodule the size of a hazel-nut which was distinctly tubercular. It was tuberoso in contour and advanced in caseation. A bronchial gland in connection with this lung was found to be enlarged and caseous, and showed distinct tubercles scattered throughout its substance. The remainder of the lung and the other organs seemed to be quite healthy.

Film preparations made from the lesion in the lung and from the

FIG. 1.—ILIAC GLAND FROM CALF No. 13, USED IN
INOCULATING CALF No. 19.

FIG. 2.—GUINEA-PIG INOCULATED FROM CALF No. 13, SHOWING
THE BODY FULL OF TUBERCULAR GLANDS AND NODULES.

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FIG. 3.—LUNG FILLED WITH TUBERCLE, FROM
CALF No. 16.

cheesy tubercular gland showed tubercle bacilli in fair abundance, some of them very short, others longer.

Summary.—A “cross” calf, a few weeks old, inoculated subcutaneously in the leg with human tubercular glands taken from the neck, one hundred and thirty-five days afterwards gave a fairly typical tubercular reaction; was slaughtered one hundred and sixty days after inoculation, and showed enlargement of the mesenteric glands, with a distinct deposit of tubercle in the left lung and a corresponding enlarged cheesy bronchial gland. The pulmonary deposit and the cheesy bronchial gland both contained tubercle bacilli.

EXPERIMENT No. 15.—*A white-and-chestnut “cross” bull calf, a few weeks old, inoculated with human tubercular sputum introduced subcutaneously into a pocket of skin in the right thigh.*

The sputum was rich in tubercle bacilli, which were beaded extensively, and about 1 c.c. was employed.

Fifty-five days afterwards the wound had healed completely, and there was no manifestation at the point of introduction or elsewhere.

One hundred and twenty-nine days after inoculation the animal was tested with tuberculin. At 8.30 p.m. the initial temperature was 102.6° F., at 6 a.m. 103.5° F., at 9 a.m. next day 104.8° F., at 11 a.m. 103.6° F., and at 2 p.m. 103° F.

Post-mortem Examination.—One hundred and fifty-five days from time of commencement of the experiment the animal was slaughtered. Immediately before death the temperature was 102.4° F., pulse 88, and respirations 24. The animal was in good condition. There was a complete absence of any local lesion at the point of introduction of the sputum, and none of the superficial lymph-glands appeared to be enlarged. The mesenteric glands, however, were all more or less the subject of enlargement, and several of them had distinct cheesy tubercular nodules within them, varying in size from a millet to a hemp-seed. The others presented a homogeneous and gelatinous appearance. Those that were cheesy belonged to the small intestine. The intestine itself was, nevertheless, quite healthy. There was a considerable excess of peritoneal liquid, serous and somewhat blood-stained, and from 6 to 8 ounces in quantity. The bronchial glands were also somewhat enlarged, and one of the longest on being incised showed distinct cheesy tubercular nodules alike with those seen in connection with the mesentery. The carcass otherwise seemed to be quite sound.

Film preparations made from the bronchial glands showed the presence of tubercle bacilli, long, and with chromatic points fairly well stained.

Summary.—A calf, a few weeks old, inoculated subcutaneously with human tubercular sputum, one hundred and twenty-nine days afterwards gave a reaction of more than 2° F. to tuberculin. An absence of local lesion; tubercular mesenteric and bronchial glands containing tubercle bacillus. Duration of the experiment one hundred and fifty-five days.

EXPERIMENT No. 16.—*A “cross” bull calf, ten weeks old, twice tested with tuberculin, the last time ten days before the commencement of the experiment, and on both occasions with negative result, made to inhale tubercular human sputum in the form of spray.*

About 50 c.c. of human tubercular sputum containing numerous bacilli were mixed up with 450 c.c. of sterile water and strained through

sterile muslin. Half of this was sprayed into the nostrils of the above calf. The spraying was repeated on three other occasions with other sputum prepared in the same way, and during a period of one hundred and forty-five days, after which the animal was killed. On these occasions, however, instead of the spray being introduced directly into the nostril of the animal, a box was adapted to fit over the head with an opening in it into which the nozzle of the spray-producer was inserted. The box was thus filled with a cloud of spray, which the calf could not fail to inhale. The box was not opened for some five to ten minutes after the spraying had ceased, and when presumably the spray had settled down on its sides. The sputum on all occasions contained numerous bacilli. The last inhalation was made seventy-two days before the death of the animal.

Eight days before the calf was killed it was tested with tuberculin, and gave the following result: The initial temperature was 101.2° F. on the evening of injection of the tuberculin, and on the following day it rose to 104.8° F., 106.3° F., and fell again to 104.6° F. and 102.7° F.

Post-mortem Examination.—Immediately before the animal was killed the temperature in the rectum was 102.4° F., pulse 68, respirations 22. The mesenteric glands were, perhaps, a little larger than normal, and showed a faint gray point occasionally on section, but did not present any signs of being tubercular. The hepatic lymph-glands were also a little enlarged, but otherwise the abdominal organs were free from disease of any kind.

On both sides of the chest the costal pleura covering the intercostal spaces showed numbers of tubercles. On the left side there were three such nodules, but on the right there were a great many more. They ran in rows corresponding with the intercostal lymphatics, and were situated mostly in the upper half of the membrane. They had the usual flat character of bovine tubercle of the pleura with shreds of fibrous tissue adhering to them.

The upper third of the right lung was infiltrated with a mass of tubercle nodules varying in size from a pea to a walnut, all tending to become cheesy and to calcify (Fig. 3). The affected area of the lung was bound to the costal wall by fibrous union. Numerous miliary and larger tubercular nodules were found attached to the visceral pleura, some of them having quite a grape-like character. Throughout other parts of the lung there were several localized deposits of tubercle, some of them advanced in caseation. One of these, the size of a walnut, was encapsuled by fibrous tissue, and on section was found to be beset with tubercle points.

The left lung was not so far advanced in tuberculosis as the right and the pleuræ were free from adhesion. Scattered through its substance there were circumscribed groupings of tubercular nodules having the same characters as those in the organ of the opposite side, and on the pleura overlying these there were usually some gray miliary points.

The bronchial and tracheal glands were all very much enlarged and indurated, and their substance was found to be beset with miliary cheesy points to such an extent that in most cases hardly a vestige of the natural gland remained. In other cases they were grayish-brown in colour, gelatinous and watery in consistence, and small groups of tubercle nodules were scattered at intervals throughout them. The trachea and large bronchi were free from tubercle, and otherwise were in a healthy condition.

The other organs were free from disease.

Examined microscopically, both the thoracic glands and the nodules in the lung were found to contain tubercle bacilli in fair abundance. They were of only medium size, and were rarely beaded. There were a good many Schrön's capsules.

Summary.—A calf about ten weeks old twice tested for tuberculosis with negative result. Was allowed to inhale tubercular human sputum mixed with water on four occasions, and was killed one hundred and forty-five days after commencement of the experiment. Lungs both found to be extensively tubercular, along with the pleuræ and the corresponding lymphatic glands. Abdominal and other organs free from disease.

EXPERIMENT NO. 17.—A "cross" bull calf, about ten weeks old, twice tested with tuberculin with negative result, last time about ten days before the commencement of the experiment, sprayed with the same human tubercular sputum, after the same manner, and at the same intervals as in Experiment No. 16.

Eight days before slaughter the animal was tested with tuberculin, with the following result: The initial temperature on the evening of administration of the tuberculin was 101.5° F., and on the following day 102.1° F., 103° F., 102.5° F., and 101.8° F. Immediately before death the temperature was 102.4° F., respirations 26, pulse 68. The animal was allowed to live one hundred and forty-five days after the commencement of the inhalations.

Post-mortem Examination.—The carcass was in good condition. The mesenteric glands were possibly a little larger than in health, but not to any notable extent. They presented a healthy appearance on section, and were perfectly free from tubercle. There was one minute gray-coloured point about the size of a pin's head in the liver, which might have been tubercular, but this was doubtful. All the abdominal organs otherwise were healthy.

The right lung showed numbers of tubercles scattered throughout its substance in groups and patches. They were yellow-coloured, caseous, and occasionally calcareous and encapsuled. In size they varied from a millet-seed to a large pea or horse-bean. The visceral pleura showed many miliary tubercles scattered over its surface, and chiefly opposite the deposits in the lung-substance.

In the left lung there was an aggregated mass of tubercles alike with those in the right, and located towards the apex. The costal pleura on both sides showed a few incipient tubercles.

The tracheal glands were much enlarged and indurated, their substance filled with miliary tubercles, cheesy and calcareous. Some of the bronchial glands were also enlarged and tubercular. The tonsils and all other organs were quite healthy.

Examined microscopically, both the deposits in the lung and the thoracic tubercular glands were found to contain tubercle bacilli in all respects resembling those in No. 16.

Summary.—A calf, about ten weeks old, twice tested for tuberculosis with negative result, was allowed to inhale tubercular human sputum mixed with water on four occasions, and was killed one hundred and forty-five days after commencement of the experiment. Lungs both extensively tubercular, along with the pleuræ and the corresponding lymph-glands. Abdominal and other organs free from disease.

EXPERIMENT No. 18.—A “cross” bull calf, about ten weeks old, twice tested with tuberculin, last time about a week before operation, and on both occasions with negative result, had tubercular sputum injected into the internal jugular vein.

About 6 c.c. of the tubercular sputum mixed with sterile water was injected into the left jugular vein. Some of it escaped into the surrounding tissues in making the injection.

Six days thereafter the wound had healed, and the animal seemed to be in perfect health. A few weeks subsequently, however, a swelling began to form in the neck opposite the point of injection, and eighty-one days after the commencement of the experiment this had gained the dimensions of a large pigeon's egg. As felt through the skin it appeared to fluctuate, but the skin covering the mass was still fairly movable. The animal was in good enough condition at the time of death. It was slaughtered after the expiry of the eighty-one days.

A week before death it was tested with tuberculin. The initial temperature at 8.30 p.m. was 101.3° F., at 6 a.m. next day 102.5° F., at 9 a.m. 104.6° F., at 11 a.m. 105.1° F., and at 2 p.m. 102.5° F.

Immediately before death the temperature was 103° F., the respirations 32, and the pulse 66.

Post-mortem Examination.—On reflecting the skin of the neck it was found to be perfectly free from any adhesion to the nodule at the point of injection. The nodule was found located exactly over the internal jugular vein, and about the middle of the neck. It was composed of a tough fibrous capsule enclosing a cyst-like cavity filled with broken-down and almost completely liquefied cheesy debris. After the liquid contents were discharged the walls presented a rough appearance from pieces of caseous tissue adhering to them.

At the root of the neck, on the same side as that on which the above was present, there was a gland about the size of a small walnut. On section it presented a homogeneous and gelatinous surface. On the right side there was another gland in a similar condition, and about half as large again. In front of the spine, a short distance above the bifurcation of the trachea, there was a group of much enlarged glands, one of them the size of a pigeon's egg and much indurated. On section they all showed cheesy necrosis, the large ones being far advanced in the degeneration.

Several of the mesenteric glands were enlarged to twice or three times their natural size, but none of them seemed to be caseous. On section, as a rule, they presented a homogeneous and gelatinous aspect. The tonsils were a little larger than usual, but were also quite homogeneous on section. The spleen showed five tubercular nodules, each about the size of a small pea, and commencing to undergo caseation.

Film preparations from the cheesy glands in the chest showed the tubercle bacillus.

A calf (see Experiment No. 20) and a guinea-pig were inoculated successfully from the largest of the cheesy glands found in the thorax in front of the spine. The calf was one day old, and the inoculation was made subcutaneously in the right thigh.

Summary.—A calf twice tested for tuberculosis with negative result; human tubercular sputum injected into the internal jugular vein and partly into the tissues around; killed after eighty-one days. A caseous tubercular focus at the point of injection, tubercular glandular swellings at the root of the neck and in the thorax, tubercle of the spleen.

FOURTH SERIES.

Two calves were employed in this series, and the purpose of the experiments was to ascertain whether the tubercle bacillus from man, inoculated upon the calf, gained in virulence by being reinoculated upon a second calf.

EXPERIMENT No. 19.—A "cross" bull calf, two days old, inoculated subcutaneously in the right thigh with fragments of the large tubercular iliac gland taken from calf No. 13.

For some weeks after inoculation the condition of the animal did not seem to be materially altered. In due course, however, a tumour began to form at the point of introduction, which went on gaining in size up to the time the animal was slaughtered, 112 days after the commencement of the experiment. For some weeks previous to death it fell off in condition, became emaciated, and suffered from loss of appetite and cough. Indeed, there was every prospect of its dying a natural death had the duration of the experiment been extended for a few days, a likelihood which was enhanced by the advent of an exhausting diarrhoea.

Post-mortem Examination.—The carcass was emaciated. At the seat of inoculation in the right thigh there was a round ulcer from about a quarter to half an inch in diameter, covered by a somewhat corrugated scab. Beneath this, and chiefly located in the subcutaneous areolar tissue, was an indurated mass the size of a small hen's egg, which on being cut into showed a fibrous basis interspersed with numerous miliary tubercle points, some gray-coloured, others yellow and caseous.

A superficial inguinal gland of the same limb was enlarged to about the size of a Brazil nut, and contained numbers of different-sized caseous and calcareous tubercle points and patches.

The deep iliac glands on the same side were much enlarged, one of them reaching the size of a walnut, and were filled with tubercular points. Over the upper part of the sacrum and the lower lumbar vertebrae there was a mass of enlarged glands, nearly all of which showed small tubercle points on section. The glands along the abdominal spine were similarly enlarged and tubercular; and several at the hilum of the liver were in the same condition. The intestinal and mesenteric glands appeared to be normal throughout. The mucous membrane of the lower third of the small intestine was congested, but did not present any signs of tubercle. The cervical and pharyngeal glands and the tonsils were quite normal.

The liver showed a tubercle point the size of a pin's head, and several nodules were distributed throughout the spleen, the largest of which was about the size of a pea. They were grayish in colour, and could be enucleated with ease.

On the left parietal pleura were numbers of flat tubercular deposits from a quarter of an inch to two inches in diameter. The pleural surface of the diaphragm was covered with a tubercular eruption, the nodules and patches varying in size from a millet-seed to a penny piece. The patches were half fibrous in character, and were not as yet in a state of caseation. Some of the largest of them were cedematous, and, consequently, had a somewhat mucoid aspect. The abdominal surface of the diaphragm was quite free from tubercle. There was a fibrous adhesion of the pleurae posteriorly on the left side. The right pleura also showed a few tubercular areas.

The whole of the upper two-thirds of the left lung was infiltrated with tubercle nodules from a millet-seed to a large walnut in size, and most of them in a state of caseation and liquefaction; others hard, fibrous, and partially encapsuled. They projected into the visceral pleura, and hence formed tumour-like masses bossing the surface. The remaining third of the organ appeared to be free from tubercle, and was apparently sound. The bronchial glands in connection with this lung were all very much enlarged, and were filled with tubercle points mostly in the gray stage. They constituted quite a tumour-like mass surrounding the root of the organ.

The right lung showed some miliary nodules located mostly in the visceral pleura at its upper aspect, some of them situated in the lung-substance. The remainder of the organ seemed to be free from tubercle, and was not otherwise altered. The corresponding bronchial and œsophageal glands were somewhat enlarged, but not to the same extent as those on the opposite side. On cutting into them numerous tubercle points were disclosed scattered throughout their substance.

Film preparations made of the caseous tubercles in the lungs showed an exceedingly short variety of tubercle bacillus which stained equally throughout. Similar preparations made from the tubercular inguinal gland also showed the bacillus, but in this case it was mostly of the large variety, and beaded to a remarkable degree, although mixed with those shorter, and which resembled in all respects the above-described from the lung.

Summary.—A two-days-old calf, inoculated subcutaneously with a tubercular lymph-gland taken from another calf rendered tubercular by inoculation of human cervical lymph-glands. The result—emaciation, cough, loss of appetite, and diarrhœa, with the presence of a focal lesion at the point of inoculation, and profuse general tuberculosis.

EXPERIMENT No. 20.—A "cross" bull calf, a few days old, inoculated subcutaneously from the large caseous thoracic glands described under Experiment No. 18.

The inoculation was made on the inner aspect of the right thigh, and the wound was dressed as usual with collodion. For some weeks after inoculation very little alteration was noticed in the condition of the animal, but for a week or two before death it began to fall off in condition, took its food badly, and for five days before death was unable to stand. It died a natural death ninety-six days after the commencement of the experiment.

The post-mortem examination showed that the carcass was in poor condition. There was a complete absence of any nodule at the point of inoculation, and all vestige of the inoculation wound had vanished, along with the inserted pieces of cheesy gland. There was not even any show of thickening of the skin at the point of insertion. In the inguinal region of the inoculated limb, however, there was a gland the size of a small hen's egg, which on being incised was found to be infiltrated with yellow miliary tubercles. The cortex of the gland showed an almost continuous mass of these. Caseation was fairly well advanced in most of them, and in parts of the gland they were calcareous.

Within the pelvis, on the same side, there was another large gland lying in contact with the iliac vessels. It was a little smaller than that above described, but was in an identical condition, being filled with gray and yellow miliary tubercles.

The inguinal glands of the opposite side were of natural size, but the iliac gland corresponding to that just referred to was a little enlarged, and contained three distinct miliary tubercle points.

The abdominal prevertebral glands were all more or less enlarged, but not cheesy.

The spleen contained about half a dozen tubercle nodules each the size of a small pea and calcifying.

There was slight fibrous adhesion of the pleuræ of the right lung towards the apex. Both lungs were infiltrated in all their parts, but mostly towards their apices, with tubercle nodules, varying in size from a pea to a hazel-nut or larger. The surroundings were congested, and on incising the nodules numbers of gray and yellow cheesy points were exposed on the cut surfaces. The costal pleuræ of both lungs showed numbers of characteristically flat tubercles running in rows along the intercostal spaces.

The left hock-joint was a good deal swollen and cedematous. On opening into it one of the cartilages was found to be in a state of disintegration, evidently tubercular in its nature. It was readily detached, and left a congested and exposed surface underneath. On cutting into the end of the bone a congested area corresponding to the detached cartilage was disclosed.

Microscopic Examination.—Film preparations made from the iliac and inguinal lymph-glands, and from one of the nodules in the lungs, all showed the presence of the tubercle bacillus. In the case of the glands the bacillus was of a very short variety, without any tendency to bead or to develop deeper-stained points of any kind. In the lung, the long variety was almost equally mixed with the short. The former was beaded, and twice as long as the latter.

Summary.—A few-days-old calf inoculated subcutaneously with a tubercular lymph-gland taken from another calf rendered tubercular by injection of human tubercular sputum into the internal jugular vein. The result—general falling off, and death from natural causes ninety-six days after commencement of experiment, profuse general tuberculosis.

General Summary of Results.

The experiments just described were arranged in four series with the view of ascertaining whether by various methods of procedure the bacillus of tubercle, removed directly from the human body, can be ingrafted upon the system of the calf. There cannot, we think, be the slightest suspicion of any of the animals having been tubercular from natural causes. They were purposely all chosen very young, and most of them were tested with tuberculin and failed to react. Contrary to what has sometimes been alleged, the tuberculin did not seem to interfere with the production of a positive result.

In the first series the object of the inquiry was to ascertain whether human tuberculosis could be communicated to the calf by feeding with tuberculous sputum. One of the animals in this series died from natural causes (diarrhœa) while under observation, but before the experiment commenced, and the examination of the carcass showed that it was free from tubercle. Another of the series died from septicæmia thirty-seven days after the experiments began, but showed, notwithstanding the short lapse of time, unmistakable enlargement

(tubercular?) of the mesenteric glands. There was, however, no evidence microscopically of the bacillus of tubercle being present in the gland tissue, nor did the glands exhibit the structural features of the disease. There remain, therefore, only four of the original six animals of this series for consideration—namely, those described under experiments 1, 2, 4, and 5; and it is notable that, in the whole of them, the only lesions discoverable were in connection with the tonsils and the lymph-glands in communication with some part of the alimentary tract. The mesenteric glands in particular were much involved; their great size was a most remarkable feature, and the fact that they showed a tubercular giant-cell structure and reproduced the disease on reinoculation into the guinea-pig proved that the enlargement was due to tubercular agency. Microscopic examination, moreover, showed the presence, in certain of them, of the tubercle bacillus.

Each of the animals had been fed on eighteen occasions with tubercular sputum from a single patient.

Calf No. 1 was allowed to live for sixty-nine days. Microscopic examination failed to demonstrate the bacillus in the enlarged mesenteric glands, but revealed a giant-cell structure in their substance, while inoculation on the guinea-pig was followed by a positive result.

In the case of calf No. 2, which was killed after sixty-six days, the whole of the lymph-absorbents along the alimentary tract from the tonsils downwards were enlarged. Microscopic examination of the enlarged mesenteric glands revealed the presence of a giant-cell reticulum together with the bacillus of tubercle lying in the reticular parts, while inoculation on the guinea-pig was, as in case No 1, followed by a positive result.

Calf No. 4 was killed after sixty-five days, and in it there was found enlargement of the tonsils and mesenteric lymph-glands suggestive of a tubercular lymphadenitis. The glands, however, showed neither a giant-cell structure nor the bacillus of tubercle, and they failed to reproduce the disease on being inoculated on the guinea-pig. In accordance, therefore, with these negative results, although the appearances were very suspicious, we must conclude that this experiment proved negative.

Calf No. 5 was killed after sixty-five days, and showed intense tumefaction of the lymph-absorbent-glands, connected with the alimentary canal, the presence of a giant-cell structure within them, and of the tubercle bacillus, with a positive result on inoculation of the affected parts upon the guinea-pig.

In the whole of this first series of experiments there was a complete absence of any intestinal tubercular lesion, and we must conclude, therefore, that the bacillus of tubercle can pass through the intestine without infecting it, and, nevertheless, be sifted out by the mesenteric lymph-glands, and render them tubercular.

In the second series, the object was to ascertain whether the human disease could be communicated to the calf by subcutaneous inoculation. In four of the experiments (Nos. 7, 8, 9, 10) the material inoculated was taken from caseous cervical glands removed from individuals who, so far as could be ascertained, were free from tubercular disease elsewhere.

Calf No. 7 was killed sixty-five days after inoculation in the thigh, and the examination of the carcass showed a local tubercular focus at the point of introduction of the diseased gland, glandular enlargements

in the groin of the same side, and marked enlargement of the pelvic, abdominal, post-mediastinal, tracheal, and œsophageal glands, but without tubercular implication of other organs. The tubercle bacillus prevailed in the affected parts.

Experiment No. 8 was alike with that detailed under No. 7. The result, although closely resembling that of No. 7, differed from it in several respects, more especially in the fact of there being an absence of focal lesion, absence of giant-cell structure, absence of tubercle bacillus, absence of positive result on inoculation upon the guinea-pig, although one of the two guinea-pigs employed died prematurely from ulterior causes. It coincided, however, with the result obtained in No. 7 in so far as the chains of lymph-glands leading up from the seat of inoculation had become much enlarged. As, however, there was no evidence to hand showing that these were tubercular, we must regard this experiment as having also proved negative.

Calf No. 9 died on the twenty-second day, apparently from enteritis: but even after this short period there was a cheesy focus at the point of introduction of the fragments of diseased gland.

In the case of calf No. 10, inoculated in the same manner as the other three with caseous cervical-glands, the animal, after eighty-five days, had developed a tuberculosis affecting the chains of lymph-glands running up from the inoculated limb, and in each lung there was a large tubercular patch with corresponding pleurisy. Inoculation of the guinea-pig with the affected glands had a positive result.

Calf No. 11 was inoculated in the thigh with a piece of human lung affected with miliary tubercle. The animal was allowed to live for eighty-seven days, by which time a fibrous cord-like structure had formed at the point of inoculation, and the glands leading up from this through the inguinal region, the abdomen, the thorax, and the cervical region were enlarged and caseous, while inoculation of these upon the guinea-pig gave rise to general tuberculosis.

For the inoculation of calf No. 12 human urine containing the bacillus of tubercle was employed. It was injected subcutaneously into the right thigh. The animal was killed after fifty-five days, when its lymph-gland system, particularly that in connection with the lungs, was found to be extensively tubercular, cheesy, and calcareous. The right lung and pleura were also involved, and the affected parts showed the presence of the tubercle bacillus. These lesions, as so often happens, occurred without there being any focal deposit at the seat of introduction.

The third series of experiments had for its object the repetition of some of the foregoing made with caseous glands, the subcutaneous inoculation of tubercular sputum, the inhalation of tubercular sputum, and the injection of the same into the internal jugular vein.

Calf No. 13 was inoculated subcutaneously with fragments of tubercular glands taken from the neck, and in the course of one hundred and forty-six days developed a widespread tuberculosis. There was a focal lesion at the point of inoculation, with enormous tubercular enlargement of the inguinal, iliac, and other glands throughout the body, enlargement of the tonsils, tubercle of the spleen. The affected parts showed the tubercle bacillus, and a guinea-pig inoculated from a tubercular iliac gland developed a general tuberculosis of an unusually intense type within sixty days, and died therefrom.

The experiment in calf No. 14 was alike with the foregoing, and the

animal was killed one hundred and sixty days afterwards. Although there was again an absence of any focal lesion at the point of introduction of the virus, yet there was the same lymph-glandular tubercular enlargements as in so many other like experiments, together with a distinctly tubercular deposit in the left lung.

Calf No. 15 was inoculated subcutaneously with human tubercular sputum, and one hundred and fifty-five days after the operation it was slaughtered. The autopsy revealed the usual tubercular enlargements of lymphatic glands with an absence of focal lesion of any kind.

Experiments Nos. 16 and 17 were conducted collaterally under exactly the same conditions. They consisted in allowing the animals to inhale from time to time, in an enclosed chamber, a spray consisting of phthical sputum mixed with water.

Two calves, twice tested with tuberculin, with negative result, were allowed to breathe this spray on four occasions, and were allowed to live one hundred and forty-five days from the commencement of the experiment. They both developed widespread tuberculosis of the lungs and pleuræ, while other organs remained free from the disease.

In the case of calf No. 18, 6 c.c. of tubercular sputum mixed with water were injected into the internal jugular vein, some of it escaping into the tissues around the vessel in performing the operation. Killed after eighty-one days, a caseous tubercular focus the size of a pigeon's egg was found at the seat of inoculation, together with tubercular-glandular swellings at the root of the neck and in the thorax, while tubercle nodules were found disseminated in the spleen.

The fourth series included two experiments (19 and 20), and the purport was alike in both—namely, to prove whether or not the human bacillus gains in virulence by being transferred from one bovine host to another. Two calves, a few days old, were inoculated subcutaneously in the hind leg with fragments of tubercular lymph-glands removed from the carcasses of two other calves (Nos. 13 and 18) which had previously been inoculated successfully from human cervical glands. Each animal developed a widespread tuberculosis far more virulent than that of the primary host, clearly demonstrating that the human bacillus, once ingrafted on the calf, becomes acclimatised to its new surroundings, and has its power of inducing lesions thereby enhanced.

Conclusions from Results.

We hold that our experiments prove—

1. That, although human tubercle is probably not so virulent for the calf as that derived from bovines, yet it can be readily inoculated upon that animal.
2. That this holds good whether the tubercle inoculated be derived from tubercular lymph-glands, tubercular lung, tubercular sputum or tubercular urine.
3. That it produces this positive result irrespective of whether it be introduced by feeding the animal with the tubercular material, by subcutaneous inoculation upon a peripheral part, by respiring a spray containing the bacillus, or by injection into the venous system.
4. That the organs most affected are those in immediate connection with the part operated upon.
5. That the lymphatic system is constantly involved in the resulting tuberculosis.

6. That when administered by the mouth, tubercular sputum induces an abdominal lymph gland tuberculosis without necessarily the intestine being in any way involved.

7. That when tuberculosis from a human source has been ingrafted upon a calf, it gains enormously in virulence by being reinoculated upon a second calf.

8. That the morphological characters of the bacillus may vary according to circumstances, and are no guide to the source of the organism under observation.

9. That the above facts go to favour the view that the human bacillus and that of bovines are identical, but modified somewhat by their environment.

10. That our results are a direct contradiction of those alleged to have been obtained by Koch and Schütz.

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THE DURATION OF THE LIFE OF PATHOGENIC BACTERIA IN MINUTE PARTICLES OF WATER AND ON DUST PARTICLES (F. Kirstein, *Ztschr. Hyg. u. Infektionskrank.*, 39, 1902, No. 1; *Exp. Rec.*, 39, 4).—The purpose of the experiments which are reported in this article was primarily to determine the length of time during which pathogenic bacteria which are associated with particles of dust or minute drops of moisture may remain alive in rooms subjected to ordinary illumination with diffuse sunlight. Experiments with the tubercle bacillus showed that this organism preserved its vitality when thrown out in moisture in the form of the finest possible particles for at least four days. Tubercle bacilli which had been thrown out in a spray in that manner, and collected eight days after the spraying, were found to have lost their virulence. The period at which the tubercle bacilli die under conditions mentioned is, therefore, between four and eight days. The experiments of other authors along this line with the tubercle bacillus are discussed in this connection. It was argued that the great variation in results obtained by different authors is due largely to the fact that the tubercle bacilli were encased in drops of moisture or sputum of very different size in different experiments. The author found that where tubercle bacilli were protected from the action of diffuse sunlight and desiccation in particles of sputum of considerable size, the organisms preserved their vitality for a period of three months or more.

In similar experiments with the organism of fowl cholera it was found that these bacilli lost their vitality after a period of seventeen hours. Similar experiments were also made with a number of staphylococci and streptococci, and similar results were obtained. In all cases it was found that when the organisms were not protected by a thick film or other substance from the action of the light and air, their vitality disappeared within a few days at most, and usually within a few hours.