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STUDIES ON TUBERCULOSIS IN DOGS, AND ON A CASE OF HUMAN TUBERCULOSIS CONTRACTED FROM A DOG

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INTRODUCTION.

From a study of the available literature it would appear that so far no case has been recorded of a human having contracted tuberculosis from a dog [Lovell and White (1940), Feldman (1947), Glover (1949)].

Of interest, however, was the case reported by Lewis-Jonnson (1946), where a healthy three-year-old boy was bitten in the forearm by a tuberculous cat, and subsequently died of bovine tuberculosis. Buss (1954) refers to a case, where the owner of a horse, which he regularly tended, contracted the bovine type of tuberculosis from the skin of this animal.

The recorded incidence of tuberculosis in the dog seems to vary a good deal. Calmette (1923) referred to the frequency of this disease in dogs, which apparently frequented cafés and restaurants in company with their owners (and where they probably contracted the disease from infected sputum). Scott (1930) was of opinion that tuberculosis in dogs had probably been overlooked in the past, due to the atypical naked-eye appearance of the lesions. Cooper and Lurie (1926) believed the dog to be less susceptible than the guinea-pig and the monkey. The dose that caused a fatal disease in the guinea-pig and rabbit, if given to the dog in amounts proportional to the body weight, produced only slight pulmonary involvement, while all the other organs remained free. They noted no difference in the susceptibility of the dog to the bovine or human strain. According to Mills *et al* (1940), the route by which the dog is apparently most easily infected, and by which it probably receives its natural infection, is through the respiratory tract. They consistently produced tuberculosis in the lungs of dogs by means of intrabronchial insufflation of virulent bacilli of the bovine or human type in suitable doses. Lovell and White (1940) recorded 25 cases of tuberculosis in 543 dogs autopsied. Of these 18 were due to the human bacillus, three resembled the human type, whereas in four cases the bovine type was identified. Gunn (1943) was of opinion that the dog possessed a high degree of natural resistance to tuberculosis. The most successful method of infection was by means of intrabronchial insufflation of the virulent bacilli of the human type. Feldman (1946) expressed the opinion that dogs were probably equally susceptible to the human and bovine types, but there were few characteristic symptoms in dogs, and in consequence the disease was seldom recognised. Wilson and Miles (1947) deal with the pathogenicity of tuberculosis in different species, and interesting data are reflected in Table No. 27 of their textbook. They state that the human and bovine types occur occasionally in dogs. According

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to Jennings (1949) the natural incidence of tuberculosis in dogs is approximately 40 per cent. Glover (1949) is of the opinion that the dog has a high degree of resistance to both the human and bovine types. The human type was more prevalent—70 per cent as compared with 30 per cent due to the bovine type. Robinson recorded a case of tuberculosis in a Great Dane post-mortemed at Onderstepoort (S.A.) in 1940 (private communication). The virulence and cultural characteristics justified him in regarding the strain as a human type. From hearsay reports, it would seem that there have been several cases of tuberculosis diagnosed in dogs in South Africa.

Materials and Methods.

Dog No. I.—Aged Alsatian, from the Animal Welfare Society Clinic, Cape Town (O/C Dr. Brownlie) was *in extremis* on the 25th July, 1953. Before it was killed, it showed nervous symptoms resembling distemper. In view of this and the neoplasm-like lesions observed in the caeco-colic lymph nodes, tuberculosis was not suspected. Tuberculosis was only subsequently diagnosed in the sections prepared from this case for histological examination.

Dog No. II.—Alsatian, aged about 8 months, also from the Animal Welfare Society Clinic was extremely emaciated and listless on the 28th August, 1953. At post-mortem there were marked changes of cachexia and general atrophy of the skeletal muscles. The lesions were somewhat similar to those observed in dog No. I, except that they were more pronounced and widespread. In view of the information gained in dog No. I, a diagnosis of tuberculosis, complicated with a heavy ascaris infection, was made, and specimens and smears were collected for histological examination, as well as material in 50 per cent glycerine for biological investigations.

Human case of Tuberculosis.

De Kock who carried out the above autopsies, and all those on the experimental animals, developed a small granuloma-like nodule about the size of a half-a-pea on the lateral aspect of the right middle finger near the nail. The nodule did not increase in size, but remained circumscribed, with no evidence of spread. When a diagnosis of tuberculosis was made in the sections of dog No. I, it was decided to remove the nodule for histological and biological studies. It was excised on the 16th October, 1953, approximately $2\frac{3}{4}$ months after the dog No. I was autopsied. Because the wound did not heal, a further operation was carried out on 23rd October, 1953, and the wound treated with streptomycin dry dressings. With the addition of parenteral dihydro-streptomycin sulphate and oral isonicotinyl hydrazine, rapid and complete healing of the wound occurred. It should be stressed that prior to the post-mortem on dog No. I, De Kock had at no time handled or come into contact with any material suspicious of tuberculosis.

The specimens in 10 per cent formalin were sectioned and stained with haematoxylin-eosin, and Ziehl Neelsen (Z.N.). In some sections the Giemsa stain was also applied. The blood and organ imprint smears were stained with Giemsa, and the majority of organ smears with Z.N.

Guinea-pig No. I was injected intramuscularly on the 16th October, 1953, with an emulsion of portion of the nodule on the finger excised on the 16th October, 1953. The rest of this nodule was cultured in Kirschner's medium (see Table 1). The guinea-pig revealed no symptoms of disease until it was

killed for post-mortem on 10th March, 1954, approximately 5 months after inoculation, when it showed well-marked lesions of tuberculosis in the lymph nodes, spleen, liver and lungs. Specimens were collected for histological and biological investigations.

Guinea-pig No. II was injected intramuscularly on the 10th March 1954, with an emulsion of the lung of guinea-pig No. I. It was killed for post-mortem on the 28th April, 1954 (see Table 1), and showed lesions of tuberculosis in the lymph nodes, spleen, liver and lungs.

The strain of bacilli from the nodule on the finger, and a strain isolated from specimens of dog No. II at Onderstepoort Research Institute* were grown in Kirschner's medium, and were inoculated into guinea-pigs, rabbits, and dogs (see Tables 1 and 2).

Except for guinea-pigs III and IV, which were listless and off their feed prior to being killed, none of the other animals revealed any clinical evidence of tuberculosis, whereas all showed lesions of this disease.

Culture Methods.

All cultures of tubercle bacilli were carried out in Kirschner's liquid medium. The nodule strain, the dog strain (ex Onderstepoort Institute), as well as the numerous cultures from experimental animals, behaved like the human type of *M. tuberculosis*, in that there was better growth in the presence of glycerine, than in the medium without glycerine.

Terminology.

The following terms are adopted in this paper: monocyte, macrophage, epithelioid, and Langhans giant cell. The monocyte of the blood and the macrophage of the tissues, according to Lurie (1932), probably represent physiological states of the same cell. Approximately 40 per cent of the leucocytes of the rabbit with multi-lobulated nuclei, and pseudo-eosinophilic cytoplasmic granules, were named amphophiles by Kracke (1947). According to Downey (1938) the rabbit blood, besides eosinophiles, basophiles, monocytes, and lymphocytes has approximately 40 per cent of so-called heterophiles, pseudo-eosinophiles or amphophiles. In this paper the term "heterophile" is applied to this type of cell.

RESULTS.

These can conveniently be considered under the following headings:-

1. Tuberculosis in dog I and II—Natural cases.
2. Tuberculosis of the skin nodule—Human case.
3. Experimental investigations in guinea-pigs, rabbits and dogs.

In Table 3 the distribution of the lesions of tuberculosis in the lungs, liver and spleen has been tabulated.

1. In the natural cases of tuberculosis in dogs I and II, pathogenesis was of the nature of an incomplete primary complex in the alimentary tract, with dissemination of the disease into the liver and the lungs. No tuberculosis was

* We are indebted to Dr. E. M. Robinson, who submitted the culture. It was prepared from material of dog No. II post-mortemed in Cape Town.

observed in the spleen. In dog No. I primary lesions were present in the caeco-colic lymph nodes, whereas in dog II, the mesenteric lymph nodes were also affected. The mucous membranes of the alimentary tract in both dogs showed no evidence of erosions. The naked eye appearance of the changes in the caeco-colic lymph nodes (dog I), and in the mesenteric lymph nodes, and much thickened mesentery (dog II), resembled a neoplasm. In both cases there was a peritonitis with effusion, and the presence of plaques on the visceral serosa. The changes in the peritoneal cavity were more prominent and wide-spread in dog No. II and it also showed pleuritis and adhesions to the costal pleura, as well as a heavy ascaris infestation.

The lymph nodes of both dogs showed a marked disintegration of the lymphoid tissue by clusters of macrophages and epithelioids, some with evidence of necrobiosis. Neutrophiles were not infrequent, and in dog No. 2 there was well-marked caseation. Long slender acid-fast bacilli, sometimes bent and beaded, and in clusters or bundles, were frequent in the imprint smears and sections of the lymph nodes stained with Z.N. The cytoplasm of some of the macrophages in the sections stained with Giemsa revealed a number of parallel channels. When stained with Z.N. long slender acid-fast bacilli were observed in some of these channels. In the Giemsa stained smear of the caeco-colic lymph node of dog No. I, a few leptospira were identified. The sections of plaques on the visceral serosa revealed numbers of acid-fast bacilli.

The early tubercles observed in the alveolar walls of the lungs, and in the periportal zones of the liver, were mainly composed of clusters of macrophages and epithelioids. In the liver they occurred as round foci of cells in dilated sinusoids. These organs revealed no caseation, and in none of the sections of dogs I and II were Langhans giant cells, calcification or healed lesions observed.

The brain sections of dog No. I showed chromatolysis of some of the ganglion cells, especially in the cerebellum, and intranuclear inclusions could be demonstrated in the glia cells.

2. The small granuloma on the finger showed a necrotic centre, and here and there the presence of epithelioids, and a few Langhans giant cells. Around the periphery was an irregular zone of lymphocytic cells. Neutrophiles were infrequent. There was an abnormal proliferation of the epithelial cells of the germinative layer, and this extended as an irregular network of papillae into the cutis. There was no definite encapsulation of the nodule, and no acid-fast bacilli could be identified after prolonged search, although the subsequent cultures of the nodule proved to be positive for tuberculosis.

3. The various injections in animals are reflected in Tables 1 and 2. All animals injected, and cultures made, proved to be positive for tuberculosis. The distribution of the lesions in the lungs, liver and spleen are tabulated in Table 3. Except in guinea-pigs Nos. III and IV, none of the animals revealed any symptoms before they were killed. In fact dogs III and IV actually improved in condition during the course of the experiment, probably as a result of better hygiene and feeding. Guinea-pig No. I inoculated with an emulsion of the skin nodule was killed approximately five months after it was injected, whereas guinea-pigs II and VI were killed approximately six weeks after inoculation, and rabbits I to IV approximately three months after injection. Rabbits and guinea-pigs including guinea-pig No. I showed well-defined lesions of tuberculosis, as indicated in Table 3. Only in rabbit III was there evidence of calcification in the lesions of the lungs. Rabbits I to III revealed parasitic cysts in the liver,

and in rabbit No. III these cysts (*Cysticercus pisiformis*) were of enormous dimensions, and caused marked distension of the abdominal cavity. It, however, manifested no clinical symptoms, before it was killed.

All the subcultures in Kirschner's medium from specimens of guinea-pigs and rabbits proved to be positive for tuberculosis.

The lesions of tuberculosis in dogs III and IV inoculated with fairly large doses of tubercle bacilli, were extremely mild, when they were killed approximately three months after injection. No acid-fast bacilli could be demonstrated in the organ imprint smears, or in the sections stained with Z.N., although the subcultures from specimens of both dogs proved to be positive for tuberculosis. The lesions observed in the lungs resembled irregularly shaped nodules in the thickened alveolar walls. They were chiefly composed of macrophages and epithelioids, surrounded by lymphocytic cells. Langhans giant cells, caseation, or calcification were not observed in any of these nodules. In both dogs, especially in the lungs of dog No. IV, there was in places hypertrophy of the muscles of the bronchi, and here and there hyperplasia of the overlying epithelial cells. In the spleens of both dogs III and IV, there were a few early lesions of tuberculosis, without caseation. In the livers no tubercles were identified, but the periportal zones showed irregular foci of macrophages and lymphocytes, whereas neutrophiles were infrequent. Dog No. III showed the presence of an ill-defined tubercle, without caseation, in the cortex of the kidney.

The disease in dogs III and IV infected experimentally with tuberculosis was decidedly milder, and the lesions less extensive when compared with the natural cases (dogs I and II).

The examination of the *blood smears* of the guinea-pigs and rabbits made at post-mortem revealed no specific changes. In dogs I and II (natural cases) neutrophiles and monocytes appeared to be increased in number, with an apparent reduction of lymphocytes. In dog No. II there was an increase in the number of eosinophiles in the blood, and it was not clear whether this was in any way related to the heavy ascaris infection in a comparatively young dog. eosinophiles were, however, also more frequent in the blood of dogs III and IV.

Discussion.

From the literature quoted, it would appear that this was the first case where man contracted the *human type* of tuberculosis from a dog. A small wound on the finger became infected at post-mortem of a natural case of tuberculosis in a dog, in which acid-fast bacilli were very frequent in the lymph nodes and peritoneum. The small granuloma that developed on the finger, remained completely localised, until it was successfully excised approximately three months after the post-mortem on the infected dog.

In the case of the three-year-old boy, bitten by a tuberculous cat referred to above, sores developed at the site of the bite on the fore-arm, while adenitis appeared in the right coronoid fossa and the right axilla, and the lungs became the site of miliary changes. The patient died $3\frac{1}{2}$ months after the bite, and from the lesions produced in the rabbit injected with parts of the organs of the child, it was believed that the bovine type was responsible.

Skin lesions of tuberculosis developed on the little finger of the owner of a horse, affected with skin tuberculosis, and believed to be due to the bovine type. The lesion on the finger revealed poor healing and later showed a wart-like

thickening, with congestion and pus formation. Approximately three years after the infection, a diagnosis of tuberculosis of the hand was made histologically, and the treatment then applied had the desired effect. A year after, the skin lesions of the horse gave a suspicion of tuberculosis and filtrates prepared from the lesions provoked miliary tuberculosis in various organs, when injected into guinea-pigs and rabbits. Acid-fast bacilli were identified, and although no cultures were made, the bovine type was suspected.

According to Wilson and Miles tubercle bacilli when growing in the skin are apparently liable to undergo a modification in virulence, so that both the human and bovine types become less pathogenic for experimental animals. Although guinea-pig No. I injected with material from the skin nodule on the finger showed no symptoms for approximately five months, at post-mortem it revealed well-marked lesions of tuberculosis in the lungs, liver and spleen, and lymph nodes.

From the literature it would appear that it is difficult to diagnose tuberculosis in dogs clinically. It would also seem possible that cases of tuberculosis of dogs are not diagnosed at post-mortem, in view of the fact that the lesions often resemble neoplasms, especially sarcomata [Scott (1930), and Jennings, (1949)]. Feldman (1947) also referred to the circumscribed neoplastic-like lesions in tuberculosis of dogs. In Dodd's case (1952), an aged dog revealed widespread lesions of miliary tuberculosis or disseminated "neoplastic" nodules in the thoracic and abdominal cavities. In view of the naked eye neoplastic-like appearance of the lesions in the caeco-colic lymph nodes of dog No. I, the first natural case referred to above, a diagnosis of tuberculosis was not made at autopsy. This case was further complicated by nervous distemper, and a leptospira infection.

Some believe that the dog is more resistant to natural infection than guinea-pigs, rabbits and monkeys, and that infection with the human type occurred more often. According to Cooper and Lurie (1926), a dose of tubercle bacilli that would cause a fatal disease in the guinea-pig and marked pulmonary involvement in the rabbit, would, if given to the dog in amounts proportional to body weight, produce a slight pulmonary involvement, while all the other organs would remain free. As mentioned before, Mills *et al.* (1940) and Gunn (1943) maintain that tuberculosis can be produced in dogs by intrabronchial insufflation of virulent bacilli and the majority of natural cases probably occur as a result of infection via the respiratory tract.

Lovell and White (1940) state that incomplete primary tuberculosis of the stomach and intestine usually occurs in canines, involving only the lymph nodes in those sites, and that tuberculosis of the serous membranes is also common in these animals.

In dogs I and II (natural cases) incomplete primary tuberculosis was associated with the alimentary tract, with involvement of the caeco-colic and mesenteric lymph nodes. The adjacent visceral peritoneum was also affected. Were the spread and susceptibility in these natural cases (dogs I and II) compared with the experimental cases (dogs III and IV) in any way influenced by distemper in dog No. I, and a heavy ascaris infection in dog No. II? From the literature it would, however, appear that there is a difference of opinion as regards the possible factors that might or might not influence the resistance of dogs to tuberculosis. The large doses of tubercle bacilli injected intravenously into dogs III and IV, might have been responsible for the infection. In view of the small number of dogs involved in these observations, it was not possible to draw final conclusions.

The human type of *M. tuberculosis* was diagnosed in all the cultures of Kirschner's medium prepared from specimens of the human skin nodule, and of the guinea-pig, rabbits and dogs. The nature of the disease in rabbits also pointed to the human type of organism. The long, slender, bent, and beaded forms of bacilli, usually in bundles, identified in the organ imprint smears and sections stained with Z.N., resembled the human type. According to Wilson and Miles (1948), the human bacilli tend to be long, thin, and curved, and show granular staining, whereas the bovine type tend to be short, straight and thick, and show uniform staining.

The nature of the lesions in dogs has been referred to by several authors. With the intravenous injection in the dog, the liver according to Cooper and Lurie (1926) appeared to be the conspicuous organ involved, although the lung developed considerable tuberculous lesions, where the spleen remained free, except in large doses. Feldman states that Langhans giant cells do not occur in dogs, and that acid-fast bacillary forms were often numerous in caseous portions of the lesions. In the cases of dogs described by Lovell and White, apparently none of the lesions showed necrosis. They were composed of epithelioids (macrophages), lymphocytes, plasma cells, and large numbers of neutrophiles, whereas giant cells and calcification were extremely rare. Innes (1940) was of opinion that in dogs the classical tubercle was conspicuous by its absence from the lungs and the lymph nodes. The predominating cell appeared to be the large macrophage, and polymorphs were either scanty or absent. Multinucleated giant cells were said to be absent, whilst calcification was almost invariably absent. The disease in most dogs passed almost invariably into the disseminated stage. According to Gunn, who infected dogs by intrabronchial insufflation, polymorphs predominated in the lung lesions in the early stages, whereas large mononuclears rapidly increased, and dominated the field after two days. Dodd (1952) referred to the absence of the lesions in the spleen in the case of tuberculosis described by him. Lurie (1932) was of opinion that by gradual transition the large mononuclears were transformed into the early epithelioid cell.

It would appear therefore that the variation in the nature of the lesions of tuberculosis in the dog probably depends on the stage of infection. In dogs I and II (natural cases), lesions of tuberculosis were advanced in the abdominal cavity, whereas in the liver and lungs several tubercles were observed. Langhans giant cells, caseation, and calcification were not observed in any of the lesions. The spleen in both cases showed no evidence of tubercles. The macrophage, and to a certain extent the epithelioid were the predominant cells in the tubercles, and polymorphs were rare or scanty.

In dogs III and IV infected intravenously with large doses of tubercle bacilli, there was a very mild spread of the disease. Small tubercles occurred in the lungs and in the spleen, and in none of these were Langhans giant cells, or caseation seen.

The lesions in the liver on the other hand did not resemble those of tuberculosis. It would therefore appear that classical tubercles, as maintained by Innes, did not manifest themselves in these dogs.

SUMMARY.

1. Apparently this is the first case on record in which tuberculosis of the skin in man was contracted from an infected dog through a wound. The infection probably occurred when handling the heavily infected lymph nodes and serous membranes of dog No. I at post-mortem.

2. In view of the rather obscure nature of the lesions, and the fact that this case was complicated with nervous distemper, tuberculosis was not suspected in this dog, until diagnosed histologically.

3. The nodule on the finger, which remained completely circumscribed, was successfully excised approximately three months after infection.

4. In the two dogs with natural tuberculosis the infection was of the nature of an incomplete primary complex in the abdominal cavity.

5. Although large doses of tubercle bacilli were injected into two dogs intravenously, the disease was much milder, and less widespread than in the two natural cases.

6. In all the dogs clusters of macrophages and epithelioids dominated the picture in the lesions, whereas neutrophiles appeared to play an insignificant part. There was no evidence of Langhans giant cells and calcification, and in the liver, spleen and lungs no caseation was observed.

7. In view of the morphology of the tubercle bacilli, the nature of their growth in culture media, and of their behaviour in rabbits, it was concluded that the human type of organism was involved in all these cases.

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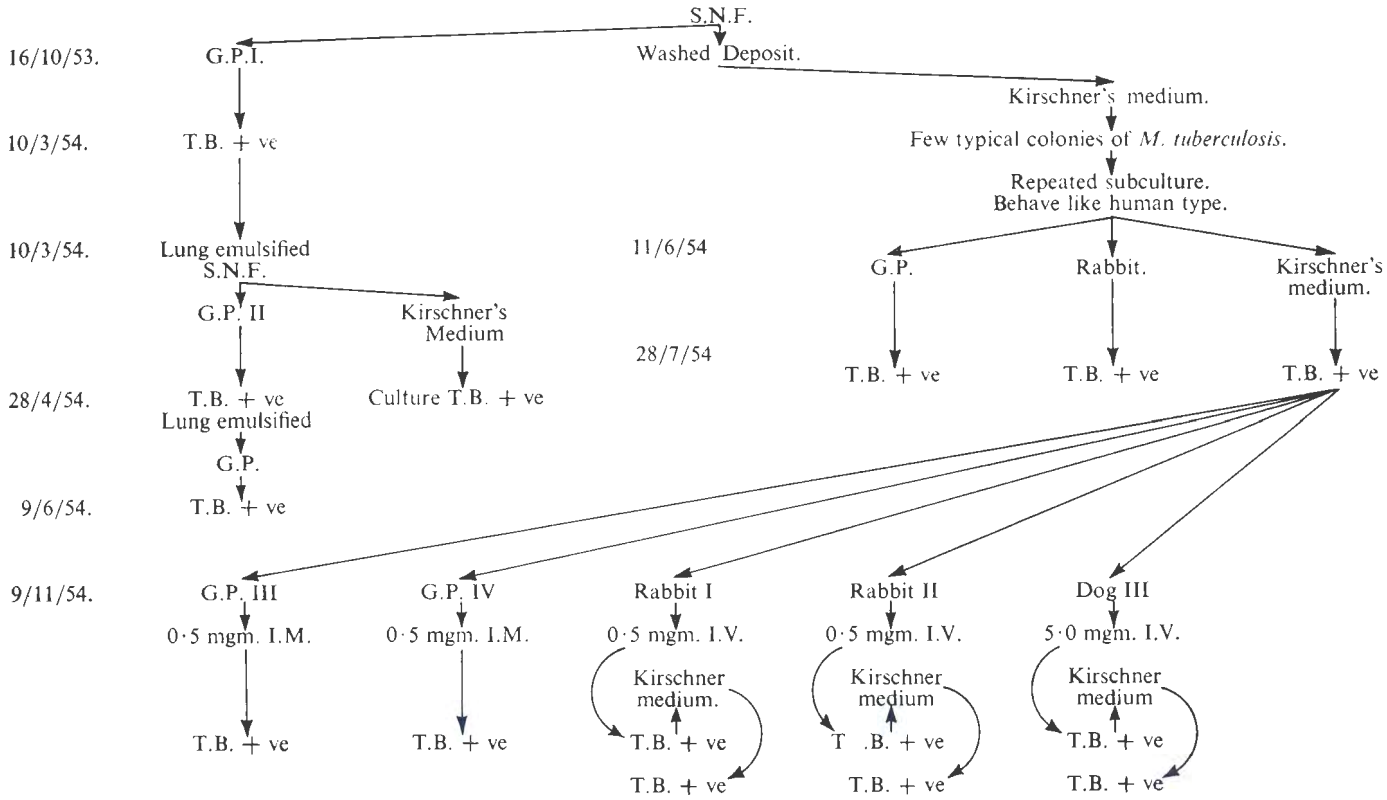
TABLE I.

Nodule of skin of finger emulsified in saline with powdered glass.
After standing to allow glass to settle out.

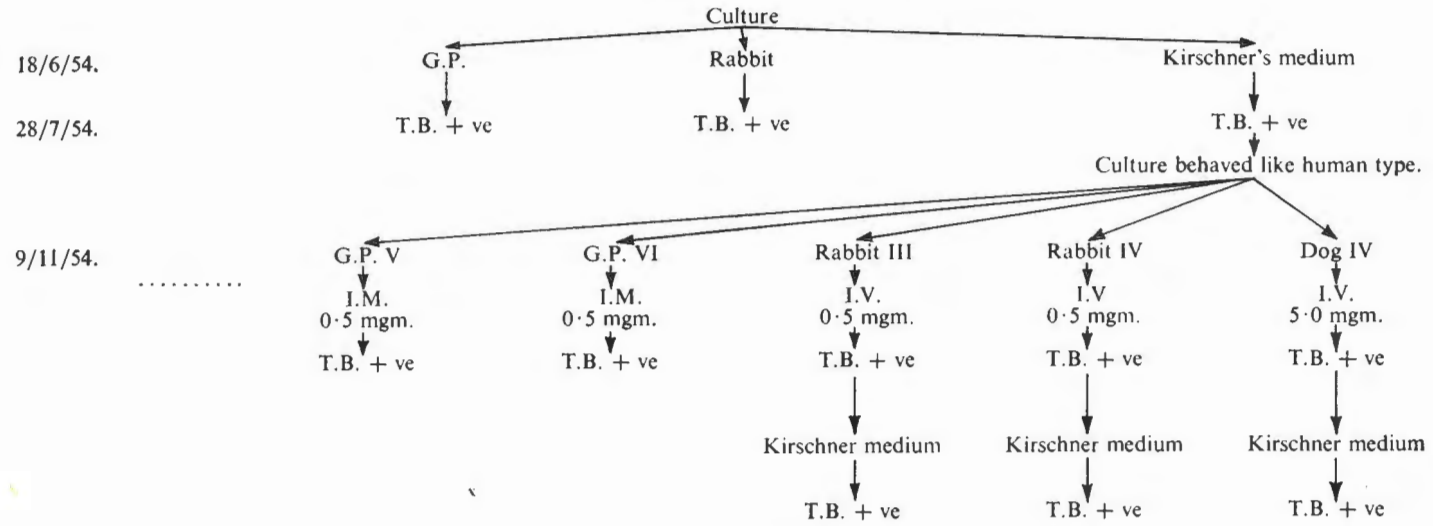


ABBREVIATIONS:—

S.N.F. = Supernatant Fluid.
+ ve = Positive—Tuberculosis.
I.M. = Intramuscular.
I.V. = Intravenous.

TABLE 2.

Culture of *M. tuberculosis* from Dog II ex Onderstepoort.



NOTE:—The following amounts (representing wet weights of organisms) were inoculated into the animals referred to in Tables 1 and 2:—

0·5 mgm. Intramuscularly in guinea-pigs,
0·5 mgm. Intravenously in rabbits,
5·0 mgm. Intravenously in dogs.

TABLE 3.

Distribution of Lesions in Lung, Liver and Spleen.

Animal.	Lungs.				Liver.				Spleen.				Cultures of Tubercle Bacilli from Organs.
	Tubercles.	Langhans giant cells.	Caseation.	Acid-fast bacilli.	Tubercles.	Langhans giant cells.	Caseation.	Acid-fast bacilli.	Tubercles.	Langhans giant cells.	Caseation.	Acid-fast bacilli.	
Dog I[d]	++	—	—	—	++	—	—	+	—	—	—	—	(O)
Dog II[d]	++	—	—	++	++	—	—	++	—	—	—	—	++
Dog III[d]	++	—	—	—	X	—	—	—	++	—	—	—	++
Dog IV[d]	+	—	—	—	X	—	—	—	+	—	—	—	+
G.P. I	++	—	++	++	++	+	—	+	+++	—	+	+	+
G.P. II	++	—	++	++	++	+	—	+	+++	++	++		(O)
G.P. III	+++	—	—	—	+++	+	++	++	+++	+	++	++	(O)
G.P. IV	++	—	—	+	++	+	—	++	++	+	—	++	(O)
G.P. V	++	—	—	—	++	+	+	+	++	+	+	+	+
G.P. VI	+	+	—	—	+++	+	+		++	—	+	+	+
Rabbit I	++	+	—		+	—	—		—	—	—		+
Rabbit II	++	+	+		++	—	—		+	—	—		++
Rabbit III	++	C +	++	++	—	—	—		+	—	—		++
Rabbit IV	++	—	—										+

ABREVIATIONS:—

(i) +, ++, +++ : degree of lesions present.
(ii) X : proliferation of macrophages, etc. in the periportal zone.
(iii) C : calcification.
(iv) O : cultures were not prepared.
(v) d : dogs I and II were natural cases, whereas III and IV were experimentally infected.

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