TUBERCULOSIS IN MAN, DOG AND CAT.

An investigation into the inter-relation of tuberculosis between humans and their domestic pets.

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PREFACE.

This study is the account of an investigation, extending from 1953 to 1961, into the relationship of tuberculosis between man and his domestic pets, the dog and cat; and was undertaken to establish the significance of these animals as agents in the transmission of infection between humans in tuberculous households.

The need for accurate observation of both human and animal subjects necessitated a combined medical and veterinary approach, which resulted in the findings that tuberculous animals not only constituted a definite hazard to their human contacts, but also that apparently healthy animals, in contact with active tuberculosis in humans, could carry infection, an unexpected, and hitherto unreported occurrence.

Quite fortuitously, an opportunity arose to establish diagnoses of tuberculosis in chimpanzees at a local zoo by the use of B.C.G. as a skin test; and it was decided to adapt this method as a diagnostic test in dogs and cats, with particular regard to the unexpected findings in the apparently healthy animals.

The subsequent trial of B.C.G., in parallel with that of the reputedly unreliable P.P.D. tuberculin confirmed the efficiency of B.C.G. as an alternative to P.P.D. which proved unacceptable.

To provide background for the investigation and, at the same time, a basis for a code of hygiene for domestic pets in the home, an ecological questionnaire was circulated to seven hundred and fifty pet owners at home and abroad.

Both preliminary and definitive reports of the findings, together with certain recommendations, have been published in scientific and technical lay journals in U.K. and U.S.A.; and the author was awarded the McCunn Travelling Scholarship to enable him to accept the invitation of the American Thoracic Society, to present the findings detailed in this study, at their Joint Meeting with the American Tuberculosis Association at Cincinnati, Ohio, on 23rd May, 1961.

It is hoped that the investigation will not only reduce the transmission of bacterial and viral infection within the home, and stimulate further research on these problems, but may culminate in legislation making tuberculosis in dogs and cats a notifiable disease.

The author is indebted to Mr. I.M. Lauder, Lecturer in Medicine at the University of Glasgow Veterinary Hospital, to his veterinary colleagues, Dr. W.F.H. Jarrett, Mr. D.D. Lawson, Dr. W.B. Martin and Mr. J.M. Taylor, and to Dr. C.B.S. Roberts and Dr. W. McNaught, lately of the Pathology Department of Ruchill Hospital, for their co-operation in the investigation.

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of Glasgow, Dr. A.W. Lees, Consultant Chest Physician, Glasgow Northern Division, Dr. T.J.R. Miller, Medical Director, Glasgow Mass Radiography Service, Dr. J.H. Lawson, Medical Superintendent, Ruchill Hospital, Mr. S.H. Benson, Director-Secretary of the Glasgow and West of Scotland Zoological Society, the Central Infusion Fluids Laboratory of the Western Regional Hospital Board, and the Feline Advisory Bureau.

"The whole-making, holistic tendency, or Holism (from ὅλος : whole), operating in or through particular wholes, is seen at all stages of existence, and is by no means confined to the biological domain to which science has hitherto restricted it."

" Wholes of various grades are the real units of nature."

--- General The Right Hon. J.C. Smuts.
Holism and Evolution, 1926.

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INTRODUCTION.

Villemin was the first to demonstrate the susceptibility of domestic animals to tuberculosis when, in 1868, he reported the successful infection of horses, cats and dogs. While the possibility of a mammalian contribution to the epidemiology of tuberculosis among humans had attracted the passing attention of many of the early workers, the concept received a major reverse when Koch, speaking of bovine tuberculosis in 1901, said, "I do not deem it advisable to take any measures against infection by the milk and flesh of tubercular cattle". Despite the terrible legacy of this early setback, bovine tuberculosis was eventually tackled so vigorously that, although it was still recognised as one of the eight most important zoonoses in Europe, by the World Health Organisation in 1952, today it has been virtually eradicated from the British Isles.

While tuberculosis in dogs and cats shared the ill effects of Koch's remarkable, ex cathedra statement, it was excluded from the restitution which followed his rebuttal. Not only did the problem lack full recognition, but what little it regained failed to secure the type of positive action which so successfully dealt with its bovine counterpart. This may be partly explained by the early emphasis on the value of dogs and cats as experimental animals, an emphasis tending to restrict study more to the place of these animals in the laboratory than in the field of epidemiology.

These aspects, however, were not completely neglected; and, indeed, were stimulated, from time to time, by reports of natural incidences in various countries.

Among dogs, naturally occurring tuberculosis was reported by Faulenborg and Plum, in incidences ranging from those of Fröhner in Berlin, of 0.04%, and Eber in Dresden, of 2.75%, in the 1890's to those of Smythe (1929), in the British Isles, who recorded a rate of 0.3 to 0.4% among dogs attending the out-patient clinic at the Royal Veterinary Hospital, and Lovell and White (1940) who found tuberculosis at 4.6% of 543 autopsies. In 1955, two years after the inception of this investigation, an analysis of 175 dogs, submitted consecutively for pathological examination, at the University of Glasgow Veterinary Hospital, over a period of four months, showed that eight had tuberculosis in all organs, a rate of 4.5% (Hawthorne et al., 1957).

The position among cats was not greatly different. Dobson (1930), in a study at the Veterinary College in Edinburgh, found evidence of tuberculosis in 11 out of 505 cats examined at autopsy between October, 1925 and June, 1927. Dobson's rate of 2.1% was to be compared with rates between 2% and 11%, reported from Europe by Petit, Yost and Nieberle. In 1941 Lovell and White reported tuberculosis in 3.6% of all their autopsies of cats.

Feldman (1955) collated information regarding the type of mycobacterium responsible for 182 cases of tuberculosis occurring naturally in dogs in the British Isles, Europe, the Dutch East Indies and U.S.A.. 137 were of human type, 44 were bovine and one was avian. In cats, of the 56 cases in the literature up to 1941, 52 were bovine; and the remaining four were reported as human, although the data did not permit complete confirmation of this point. Jarrett (1955), however, recorded a case of tuberculosis due to bacilli of the human type, occurring in a cat, a finding confirmed by the standard virulence tests in guinea pig and rabbit.

Viewed quantitatively, the problem seemed fairly extensive, perhaps affecting dogs a little more than cats. Qualitatively, it appeared that humans more often caused the infection of dogs, while cattle more frequently infected cats.

Despite the prevalence of disease indicated in the literature, investigations of the sources of animal infection appeared superficial; and were generally confined to enquiry as to the existence of a history of tuberculosis in the owner's family. Thus the collective reports of Lovell and White (1940), Smythe (1929), Stableforth (1929) and Hjärre and Herlitz (1935) showed family histories of tuberculosis in 17 out of 83 cases investigated. On the other hand, Lesbouyries (1926) stated that 8 out of every 10 tuberculous dogs in Paris lived an extra-domiciliary existence in cafes or restaurants, a finding confirmed by Scott (1930), who recorded 51 out of 100 dogs, with tuberculosis of human type, as having been exposed in restaurants, while a further 23 had been in contact with sick persons.

His opinion was that dogs, with infection of bovine origin, obtained their infection by frequenting abattoirs; and that tuberculosis in cats was due to drinking milk, and not to contact with humans.

Much of the existing, epidemiological information had a circumstantial, rather than a factual basis.

By 1953 tuberculosis had become an infection almost universally associated with a falling death rate, a reduced morbidity, and a decrease in the number of new cases being notified. Already the outlook had so changed that the possibility of eradication was being given a place in social thinking. With the amelioration of the situation, it became possible to study aspects of the disease which would have been regarded as trivial a decade before. An outstanding problem was the continuing succession of new cases among family contacts; and it was considered that fresh light might be shed on this subject by an ecological investigation, which could be defined as a study of the inter-relation between organisms and the environment.

This approach involved treatment of the problem under investigation as a zoonosis which is a disease capable of natural transmission between vertebrate animals and man. Study of the zoonoses entails examination of the inter-relation between man, animals, a causal organism and the environment, thus, for example, man, cows, M. tuberculosis of bovine origin, and the community environment, constitute the ecological factors related to the zoonosis of bovine tuberculosis; and are linked together, in a dynamic concept, by the transfer of the zoonotic infection by a "food chain".

The question, which this study set out to answer, was: could man, dogs and cats, and M. tuberculosis of human or bovine origin, be linked together, in the environment of the home, as a zoonosis; and if they could, what was the dynamic state of that zoonosis, and what was its present place in the epidemiology of the disease?

THE PLAN OF INVESTIGATION.

The investigation of the inter-relation of tuberculosis between humans, and dogs and cats, required a combined medical and veterinary approach; and had five objectives:

A. To ascertain the prevalence of tuberculosis among apparently healthy dogs and cats owned by humans with active pulmonary tuberculosis.

B. To ascertain the prevalence of tuberculosis among humans in contact with tuberculous animals.

C. To evaluate the use of B.C.G. as a test to detect the presence of past or present infection in dogs or cats.

D. To compare B.C.G. with P.P.D. tuberculin as an aid to diagnosis.

E. To acquire sufficient information about domestic pets, their owners, and their homes, to allow accurate assessment of the ecological factors.

To implement A and B, it was arranged that a Veterinary Surgeon would examine the apparently healthy dogs and cats owned by sputum positive patients in the Sanatorium Wards of Ruchill Hospital for Infectious Diseases, while a Chest Physician of the Glasgow Chest Service would examine the owners of morbid dogs and cats routinely admitted to the University of Glasgow Veterinary Hospital for investigation, and found to be suffering from

FIGURE I.

M.M.R. Centre,
10, Elmbank Street,
GLASGOW. C.2.

University of Glasgow Veterinary Hospital,
Bearsden Road, Bearsden, Glasgow.

Telephone No. Bearsden 2278.

Tuberculosis is on the decrease but there is still much to be done before it can be eradicated. Among other things, more knowledge is needed about many aspects of the disease in order that full benefit can be obtained from new drugs and techniques.

It is not generally known that dogs and cats can carry the same tuberculosis germ that affects humans but because these animals are highly resistant to tuberculosis, very few become ill enough for the disease to be detected. On the other hand, it is not known accurately how many can carry the germ without any signs of illness at all and it is here that recent research has shown that the number of apparently healthy animals carrying tuberculosis is higher than expected.

Up to the present, the method of detecting these potentially dangerous animals has been very difficult. Now, by means of a simple skin test, it may be possible to detect an infected, but apparently healthy dog or cat, within a fortnight.

Before the method can be used on a wide scale, a large number of dogs and cats have to be tested to confirm the success of the work already completed. It is hoped you may be able to contribute to this important research by arranging for your visitors to bring a dog or cat from your home to the Veterinary Clinic here in the Hospital, during a pre-arranged Wednesday evening visiting hour. While the visitors are in the wards a veterinary surgeon will carry out a simple skin test, the result of which, when observed within a fortnight, will supply the required information; and, at the same time, ensure the health of your pet, and home.

If there is a dog or cat in your home, and you are prepared to help, you will be visited shortly by a doctor who will answer any questions and arrange a suitable appointment.

A specimen of the explanatory letter to in-patients with active tuberculosis, and their relatives, at Ruchill Hospital.

tuberculosis. Where no apparent source of infection was found among owners or their families, an attempt would be made to trace the source of the animals' infection among previous owners and close neighbours.

To implement C and D, four groups of animals were required. The main group (GroupI) consisted of apparently healthy dogs and cats in contact with human tuberculous patients with positive sputa. To examine this group a Veterinary Out-Patients' Clinic was opened at Ruchill Hospital, where visitors to appropriate patients in the Sanatorium Wards brought with them their household pets, (See Figure I).

During the visiting hour, and after a full, physical examination, including the taking of specimens of urine, and rectal and pharyngeal exudates for culture, each animal had an area of 3 square cms. shaved in both scapular regions. Then 0.1 ml. of B.C.G. (75 mgm. per ml.) and 0.1 ml. of P.P.D. tuberculin (100,000 I.U. per ml.) were injected intradermally into the right and left scapular areas respectively. Subsequently these animals were kept under surveillance in their own homes, and the nature of the skin reactions carefully recorded. Special attention was paid to the number of days elapsing between B.C.G. inoculation and the point of ulceration of the resultant papule.

The basis for this part of the investigation was that B.C.G. would produce an early, immune, 'positive' reaction at the site of injection in an animal already infected, and possessing antibodies to M. tuberculosis, whereas a late, non-immune, 'negative'

FIGURE IIB.

ANIMAL

X-Ray REPORT ....

....

CLINICAL SIGNS ....

....

....

TUBERCULIN TEST ....

LARYNGEAL SWAB ....

FAECES ....

OTHER BACTERIOLOGY ....

....

TYPE ....

oooOooo

HUMAN

X-RAY REPORT ....

....

....

CLINICAL SIGNS ....

....

CLINICAL SYMPTOMS ....

....

....

SPUTUM TEST ....

LARYNGEAL SWAB ....

GASTRIC LAVAGE ....

BRONCHIAL LAVAGE ....

TYPE ....

A specimen of the combined questionnaire and case record sheet - back.

FIGURE IIA.

THE ANIMAL HEALTH SCHEME

SERIAL No ....
DATE ....

Completion of this form will help the Veterinary Surgeons and Doctors to assess the disease risk in your home.

1. Name of Owner: ....

   Address: ....

2. Name of Animal: ....

   Age: ....

   Breed: ....

   Sex: ....

   Colour: ....

3. Have there been any previous illnesses or injuries of YOUR Animal? ....

4. Does your animal live in the house or outside? ....

   Does it sleep in the same room as a member of the household? ....

   Does it get on, or in, any bed in the house? ....

5. Where does your animal eat? ....

   Does it receive scraps from the table? ....

   Does it have its own feeding bowl ....or................

   Does it use one of the household plates? ....

   If so, is the utensil washed in the communal sink or wash basin? ....

6. Where do you wash your animal? ....

7. Is your animal wholly or partly house trained? ....

   If house trained, Does it use the Streets ....
   Public Parks ....
   Waste Ground ....
   Garden ....
   Sawdust Box ....
   Coal Bunker ....

8. Has your animal any reprehensible eating habits? ....

9. Has your animal had any contact with tuberculosis? ....

A specimen of the combined questionnaire and case record sheet - front.

reaction would occur in an animal not previously infected. By combining the experience of B.C.G. in chimpanzees and in humans, it was decided empirically that the early, immune, 'positive' reaction could be expected to occur at any time up to 14 days, the earlier, the more reliable; and the late, non-immune, 'negative' reaction would occur later than 14 days, and up to 4 weeks, after the initial injection.

In addition to Group I, the group of apparently healthy dogs and cats in contact with active tuberculosis in humans being examined at Ruchill Hospital, it was decided to test three additional groups as controls at the University of Glasgow Veterinary Hospital. These were: Group II, a group of animals known to have acquired a natural tuberculous infection; Group III, a group of non-tuberculous morbid dogs and cats with no known history of exposure; and Group IV, a group of healthy dogs and cats artificially immunised against tuberculosis by B.C.G. one year previously. This last group was included to produce an experimental check on the working of the test with particular regard to the interval between inoculation and ulceration of the papule.

To implement E, a combined case record sheet and questionnaire (Figure IIA) was prepared containing simple questions about the animal under investigation, and its home, for completion by the owner, either by himself, or under the guidance of the investigator. The reverse side of the questionnaire (Figure IIB) contained the

FIGURE IIIB.

IF HOUSE-TRAINED, DOES IT USE THE STREET/Public Parks/Waste Ground/ Garden/ Sanitary Tray/Coal Bunker.

IF SANITARY TRAY, PLEASE DESCRIBE MATERIAL USED - (e.g. sand, peat, proprietary ....product)

HAS YOUR CAT ANY REPREHENSIBLE HABITS? (e.g. eating sputum) give details ....

....

HAS YOUR CAT HAD ANY CONTACT WITH TUBERCULOSIS? ...YES/NO.(If.!YES!.please.give.details)

....

WHAT OTHER PETS DO YOU KEEP? ....

WHAT HAPPENS TO YOUR CAT AT HOLIDAY TIMES? ....

WHERE DID YOU OBTAIN YOUR CAT? ....

HAVE YOU ANY SPECIAL REASON FOR OWNING A CAT? ....

First Fold

CONFIDENTIAL

Mass Radiography Centre,
10 Elmbank Street,
GLASGOW. C.2.

Second fold

Third fold

TUCK IN

A specimen of final questionnaire - back.

FIGURE IIIA.

Mass Radiography Centre,
10, Elmbank Street,
Glasgow, C.2.

Tel: CITy 5667/8.

University of Glasgow Veterinary Hospital,
Bearsden Road,
Glasgow.

Tel: Bearsden 2278.

____
Code No.

FELINE ADVISORY BUREAU

30 Canynge Square, Bristol, 8.

QUESTIONNAIRE

____

Your co-operation is invited in answering the following questions. The information is needed to enable a panel of doctors and veterinary surgeons to study the ways in which infections may pass from your cat to you, or from you to your cat. A questionnaire should be completed in respect of each cat in your home; and the completed forms stamped and posted at your earliest convenience. The findings of this special study will be advised to you at a later date.

OWNERS NAME .... Married/Single/Widowed.

ADDRESS ....

NUMBER OF CHILDREN IN HOME ....

TYPE OF HOME - Flat/Detached/Semi-detached/Terrace/Institution.

INCOME GROUP OF OWNER - less than £500/less than £1,000/less than £2,000.

NAME OF CAT .... AGE .... SEX 1. Male
2. Male/Neuter.
3. Female.
4. Female/Neuter.

HAS YOUR CAT EVER BEEN ILL OR INJURED? (Please give particulars)

WAS A VETERINARY SURGEON CONSULTED? ....YES/NO..................................

DOES YOUR CAT LIVE MAINLY INSIDE OF OUTSIDE THE HOUSE? ......INSIDE/OUTSIDE...........

DOES YOUR CAT SLEEP IN THE SAME ROOM AS ANY MEMBER OF THE HOUSEHOLD? ....YES/NO.......

IS IT ALLOWED ON, OR IN, THE BED? ....YES/NO...................................

IS YOUR CAT FED WITH THE FAMILY? ....YES/NO...................................

DOES IT RECEIVE SCRAPS FROM THE TABLE? ......YES/NO...................................

DOES IT HAVE ITS OWN FEEDING BOWL? ....YES/NO...................................

DOES IT USE ANY OF THE HOUSEHOLD PLATES? ....YES/NO...................................

ARE UTENSILS USED BY THE CAT WASHED IN THE HOUSEHOLD SINK OR WASHBASIN? ...YES/NO.....

IS YOUR ANIMAL WHOLLY OR PARTLY HOUSE-TRAINED? ......WHOLLY/PARTLY/NOT................

A specimen of final questionnaire - front.

case records of animal and owner. In this way not only was any inter-relation, such as positive sputa, immediately apparent, but at each stage of the individual examination each case was, of necessity, considered as a whole, as a dynamic unit consisting of human, pet, organism and environment.

The experience gained from the use of this questionnaire during the preliminary survey, formed the basis of the expanded version (Figures IIIA and IIIB) which was circulated at a later stage, through the agency of the Feline Advisory Bureau, to 750 individuals in the British Isles, Western Europe and the United States of America.

TABLE I.

FINDINGS AMONG APPARENTLY HEALTHY ANIMALS IN CONTACT WITH ACTIVE TUBERCULOSIS IN HUMANS - BACTERIOLOGICAL TESTING ONLY.

	ANIMALS INVESTIGATED	ANIMALS WITH POSITIVE BACTERIOLOGY	PERCENTAGE
DOGS	25	4	16.0
CATS	23	3	13.0
COMBINED	48	7	14.5

Observations.

A. The Animals in Contact with Tuberculous Humans.

Table I shows that growths of M. tuberculosis were recovered from four dogs and three cats (14.5 per cent) of 48 apparently healthy animals exposed to active tuberculosis in humans for a material time. M. tuberculosis was cultured from normal saline swabs of pharynx and rectum inoculated on to Lowenstein's medium. To provide for the inhibition experienced with certain bovine strains on that medium, parallel inoculations were made on to Dorset egg medium. To exclude quick-growing saprophytes cultures were examined weekly, and early growths discarded. Slow-growing saprophytes were excluded by limiting the acceptance of positive findings to secondary cultures, and using direct examination for confirmation at this stage.

All growths accepted as positive were examined to determine whether the strain isolated was of human or bovine origin. All of the isolated growths were eugonic, warty, and with varying degrees of yellow pigmentation. The standard virulence tests on guinea pigs produced lesions typical of the human strain. 10 mgms. of moist culture of the bacilli obtained from two of the dogs and three of the cats were inoculated subcutaneously into rabbits. The inoculations resulted in a localised lesion of the type associated with the human strain, in each of five rabbits when these were killed at twelve weeks. In the three dogs and three cats obtained for

TABLE III.

INCIDENCE OF TUBERCULOSIS AMONG HUMANS EXPOSED TO INFECTION FROM TUBERCULOUS DOGS.

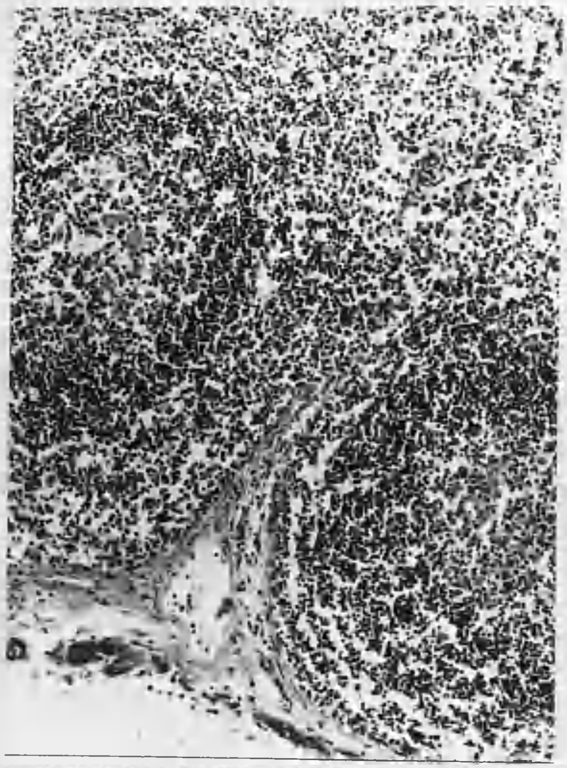
Number of Dogs dying of tuberculosis	Number of Humans in close contact	Humans with evidence of active tuberculosis at a material time
31	354	41 (11.86%)

TABLE II.

FINDINGS AMONG HUMANS IN CONTACT WITH ACTIVE TUBERCULOSIS IN DOGS.

CONTACT INVESTIGATION	NUMBER	PERCENTAGE
Owner, or family had tuberculosis.	16	51.6
Neighbour had tuberculosis.	5	16.1
Previous owner had tuberculosis.	2	6.4
Probable contacts traced	23	74.1
No contacts traced	8	25.9
GRAND TOTAL	31	100.0

FIGURE IV.



A cat lymph gland showing 'sinus catarrh'. There is marked congestion and an excess of lymphocytes with obliteration of the germinal centres. The cells of the sinuses show proliferation.

autopsy, no lesion typical of tuberculosis was found; and each was normal apart from a small apparently non-specific, inflammatory lesion, generally solitary, and usually associated with a lymph gland, best described as showing sinus catarrh, and forming one of a normal chain closely associated with either the alimentary or respiratory tracts. M. tuberculosis was not visible in Ziel Nielsen stained sections of these glands, nor was it grown from cultures of the material.

Figure IV illustrates a lymph node from one of the cats from which a positive culture of M. tuberculosis had previously been recovered from a pharyngeal swab. It shows marked congestion and an excess of lymphocytes with obliteration of the germinal centres. The cells of the sinuses show proliferation.

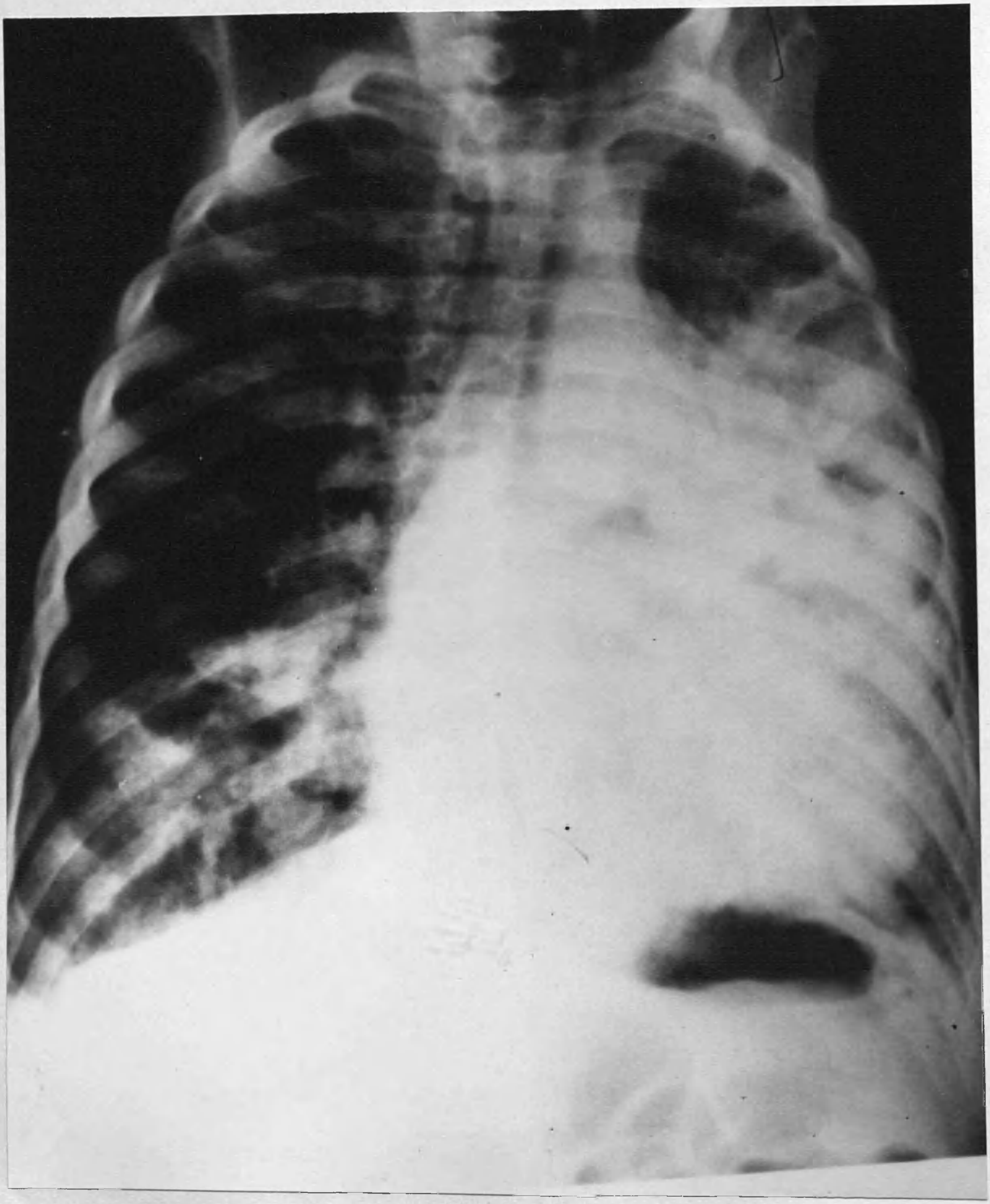
B. The Humans in Contact with Tuberculous Animals.

Table II shows the findings among the human contacts of 31 dogs dying with tuberculosis. Thirty households and an hotel were examined; and in sixteen cases the owner, or member of his family, had evidence of tuberculosis. In seven cases the probable contact was traced either to a neighbour, or a previous owner. In eight cases no contacts were traced.

Table III shows the incidence of tuberculosis among the humans exposed to infection from the thirty-one tuberculous dogs.

354 humans of all ages lived in fairly close contact with the morbid animals during their lifetime; and among them 41 humans

FIGURE V.



The postero-anterior chest x-ray of the more ill of the two chimpanzees, showing tuberculous infiltration at the base and in the mid zone of the right lung, and in the lower two thirds of the left lung.

were found who had evidence of active tuberculosis at a material time, (i.e. a period when transfer of infection could have taken place between human and animal).

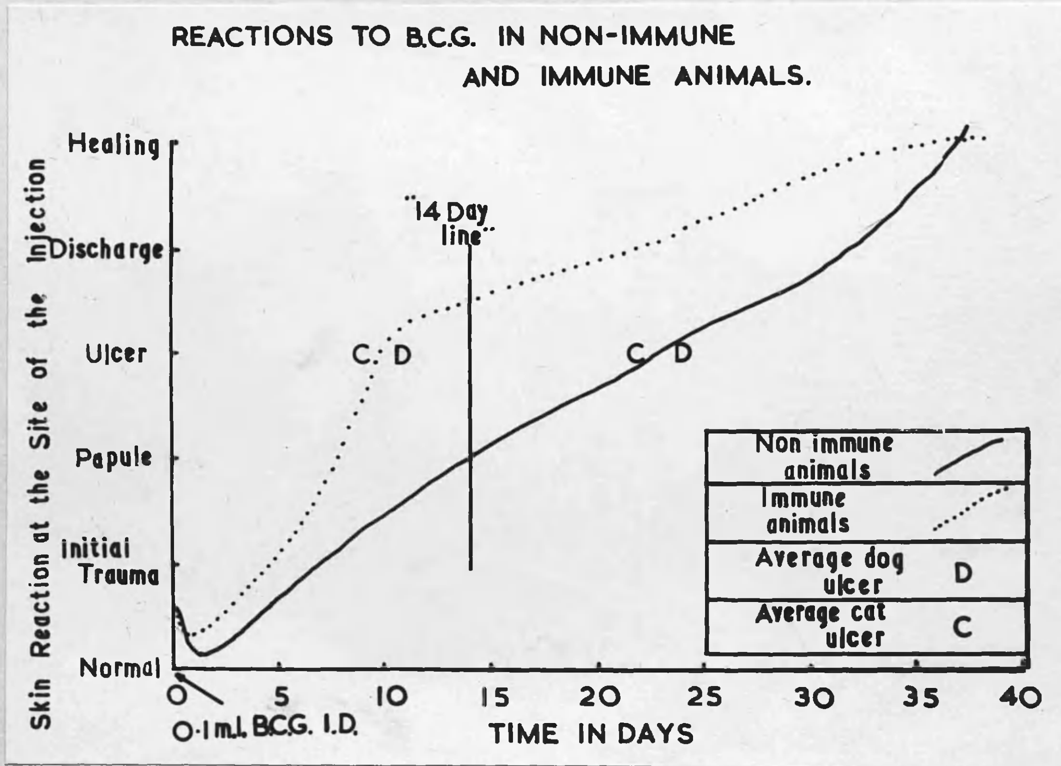
C. <u>The Use of B.C.G. as a Test.</u>

<u>Figure V</u> - During 1958 an opportunity arose to examine two chimpanzees at a local zoo. These animals had been ill for a few months with respiratory infections which had failed to respond to the usual anti-biotics. The possibility of a tuberculous infection was considered; and in view of the unreliability of tuberculin as a test of allergy in this species, it was decided to use B.C.G. as a diagnostic measure.

0.1 ml. of B.C.G. (75 mg. per ml.) was injected intra-dermally into the flexor aspect of the forearm of both animals. The result was an allergic systemic reaction within three days in the more ill of the two animals, and the appearance, within 5 days, of a papule in each animal, larger in the case of the more ill animal, at the site of injection. These papules proceeded to central necrosis within 7 days of the date of injection. Presumptive diagnoses of tuberculosis were made in respect of both animals; and these were subsequently confirmed both radiologically and later at autopsy, by which time culture of the stools had produced growths of M. tuberculosis of human origin.

<u>Figure VI</u> is a diagrammatic representation of the basis for using B.C.G. as a test to distinguish between non-immune and immune

FIGURE VI.



The diagram illustrates the effects of intradermal inoculations of 0.1 ml. of B.C.G. at the sites of injection, the changes in the skin being recorded along the co-ordinate and the time elapsing from the injections along the abscissis. The continuous line indicates the average, late, non-immune, 'negative' reaction of the healthy dogs and cats, reaching the point of ulceration about 23 days; and the dotted line shows the average, early, immune, 'positive' response in the group of dogs and cats, either naturally infected or artificially immunised to tuberculosis, ulcerating at 10 days. Symbols show the average ulceration times of all the dogs and all the cats separately; and the clear separation of the 'positive' and the 'negative' reactors from each other, and from the arbitrary "14 day line".

animals. The co-ordinate illustrates the pathological progress of the skin reactions at the sites of inoculation, from the transient reactions due to the trauma of the injection through the successive stages of papule, ulcer and discharge to healing. The abscissis shows the time in days from the day of inoculation. The "14 day line" is an arbitrary point in time, calculated empirically, and later confirmed by experiment, occurring 14 days after inoculation. Papules ulcerating before this time were interpreted as early, immune 'positive' reactions signifying infected animals: while the papules ulcerating after this time were taken to indicate the late, non-immune, 'negative' reactions of non-infected, healthy animals.

The solid line shows the average group response of the non-infected animals i.e., the late, non-immune 'negative' reactions. Ulceration of the papules, the critical point of the test, did not occur until after the "14 day line". The average time of ulceration in the group of apparently healthy dogs tested, was 22 days, and, in the group of apparently healthy cats, 24 days.

The dotted line illustrates the average, early, immune, 'positive' response of the infected animals. The point of ulceration was reached within 14 days. The group reaction times for these animals, either naturally infected or artificially immunised, were 9 and 11 days, for cats and dogs respectively.

The skin reaction to the injection, referred to in the diagram as initial trauma, was probably a simple tissue reaction to

TABLE IV.

THE USE OF B.C.G. AS A TEST IN 69 DOGS AND CATS.

GROUP	DESCRIPTION	DOGS		CATS		DOGS AND CATS COMBINED	
		Numbers Tested	Positive Reactors	Numbers Tested	Positive Reactors	Numbers Tested	Positive Reactors
I	Animals in contact with tuberculosis.	13	8	9	3	22	11
Control II	Known tuberculous animals.	13	12	-	-	13	12
Control III	Non-specific morbidity.	11	3	8	-	19	3
Control IV	B.C.G. Immunised.	8	6	7	7	15	13
I,II,III, IV.	COMBINED.	45	29	24	10	69	39

FIGURE XIV.

The Technique of B.C.G. Testing: A similar ulcer to that in XIII above, in a cat previously immunised with B.C.G.,

FIGURE XIII.

The Technique of B.C.G. Testing: The ulcer illustrated developed 11 days after inoculation in a dog previously immunised by B.C.G.; and represents, in effect, an experimentally-produced early, immune, 'positive' reaction.

FIGURE XII.

The Technique of B.C.G. Testing: The small indurated papule illustrated was photographed 22 days after the inoculation; and is typical of the late, non-immune, 'negative' reactor.

FIGURE XI.

The Technique of B.C.G. Testing: The three reactions illustrated had developed 11 days from the initial inoculation and indicate an early, immune 'positive' reactor. Arrow 1 points to the ulcer produced by 0.1 ml. of B.C.G., arrow 2 to the smaller reaction produced by using 0.05 ml. of B.C.G. and arrow 3 to the faint rosette produced by the needles of the 'Heaf gun' using the 2 m.m. setting.

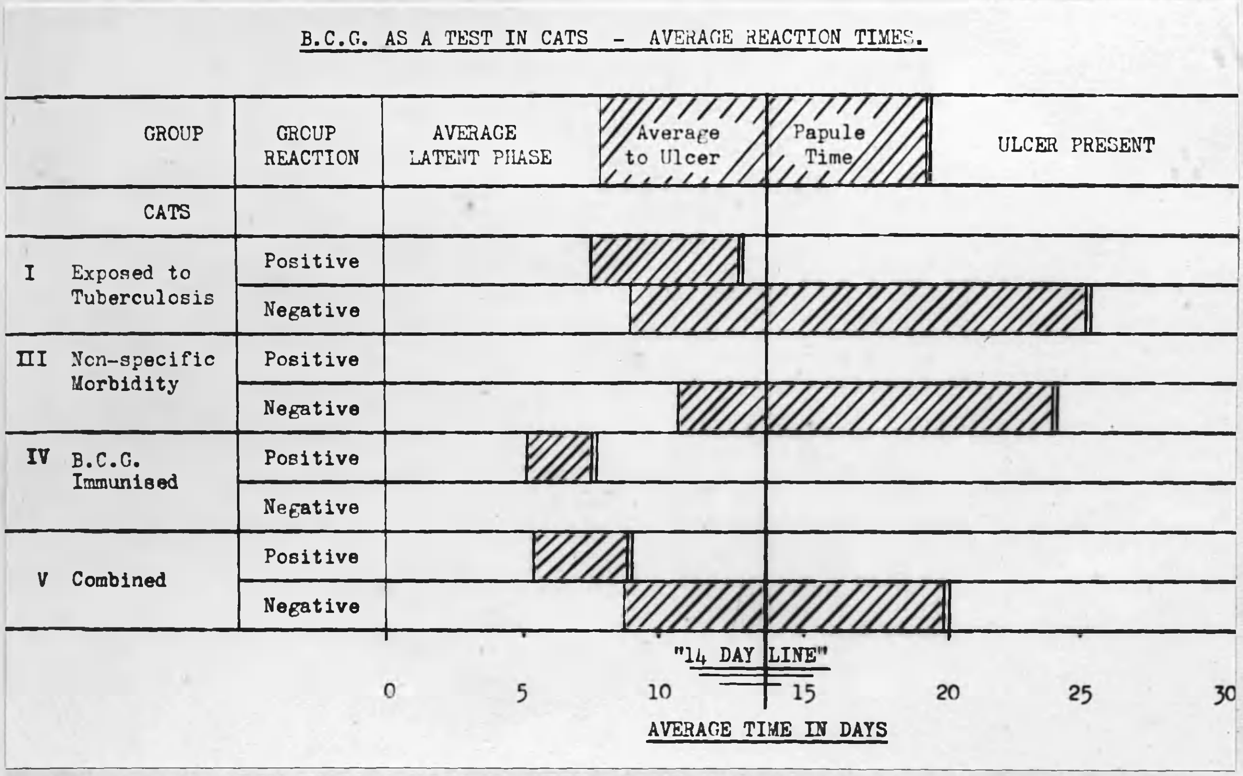
FIGURE X.

The Technique of using B.C.G. as a Test: the erythematous reaction developing at the site of inoculation at 48 hours, in a dog which subsequently ulcerated at 10 days, i.e., an ultimate, early, immune 'positive' reactor.

FIGURE IX.

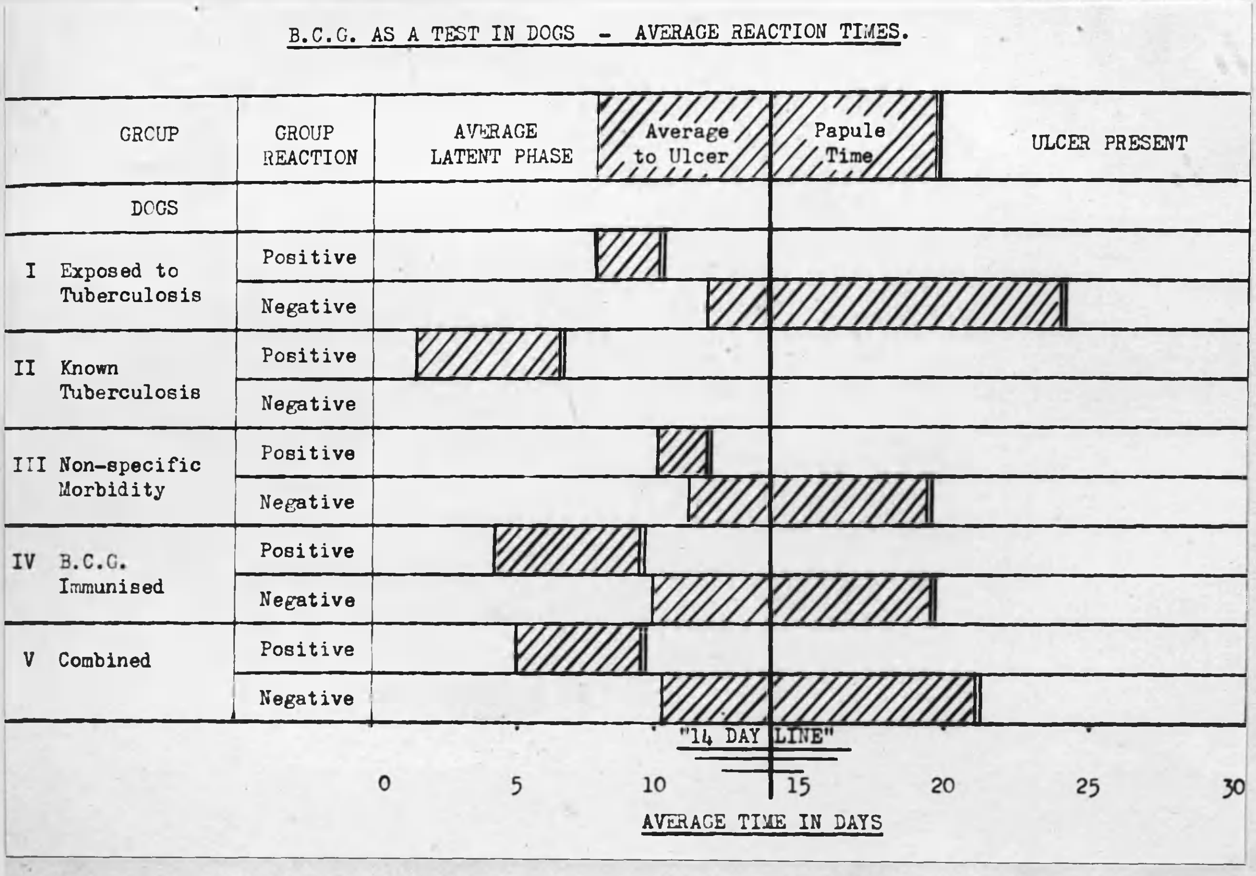
The Technique of B.C.G. Testing: 0.1 ml. B.C.G. has been injected intradermally into a shaved area in the right scapula of the dog. The Tuberculin syringe, fitted with a Luer needle, has been withdrawn and is being used to indicate the successful production of the weal.

FIGURE VIII.



The shaded areas represent the average papule to ulcer time in respect of three groups of cats tested with B.C.G.. The earliest point of ulceration occurs in those cats previously immunised by B.C.G. (Group IV).

FIGURE VII.



The shaded areas represent the average time elapsing from the formation of the papule to the point of ulceration (indicated by the double line) in respect of the four groups of dogs tested by B.C.G.. The earliest point of ulceration occurs in the group of dogs with known tuberculosis (Group II).

protein; and generally lasted less than 12 hours.

Figures VII and VIII are diagrams amplifying the information in Figure VI above, by showing the average time in days for the papule to appear, and to proceed to ulceration, in the different groups of dogs and cats which were tested. The wide separation of the point of ulceration between infected animals, giving early, immune, 'positive' reactions, and non-infected animals, exhibiting late, non-immune, 'negative' reactions, is apparent.

Figures IX to XIV illustrate the technique of using B.C.G. as a test. Figure XI contrasts the positive reactions obtained by intra-dermal inoculation with those from using the "Heaf gun", at the 2 m.m. setting. The use of the "Heaf gun" was discontinued early in the investigation, as unsatisfactory.

Table IV illustrates the application of B.C.G. as a test in the four groups of animals.

In Group I (apparently healthy dogs and cats in contact with active tuberculosis in humans) 11 out of the 22 animals tested gave an early, immune, 'positive' reaction. M. tuberculosis of human origin, established by the same methods as detailed under Table I above, was recovered from one cat among the positive reactors.

In Group II, consisting of dogs known to have tuberculosis, 12 out of 13 animals gave early, immune, 'positive' reactions.

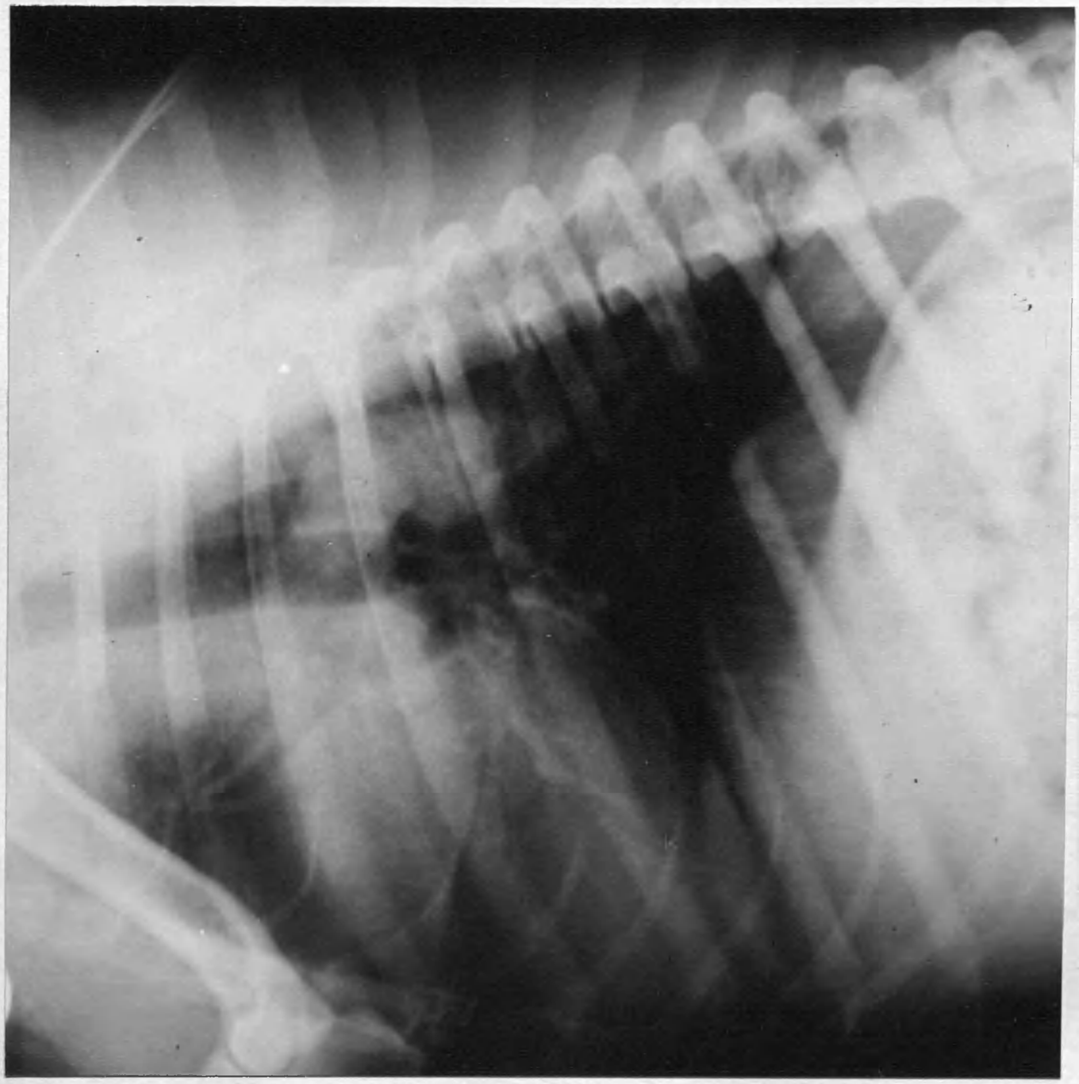
In Group III, 19 dogs and cats ill with non-tuberculous conditions, 3 dogs gave 'positive' reactions; and in Group IV,

TABLE VI.

THE COMPARISON OF B.C.G. AND P.P.D. IN THE PRODUCTION OF POSITIVE REACTIONS.

	NUMBER TESTED		'POSITIVE' REACTIONS	
	B.C.G.	P.P.D.	B.C.G.	P.P.D.
DOGS	45	32	30 (66.6%)	11 (37.5%)
CATS	24	22	10 (41.6%)	3 (13.6%)

FIGURE XV.



The lateral chest x-ray of an apparently healthy dog with an early, immune, 'positive' reaction to B.C.G.. The enlarged gland is clearly seen above the heart shadow and below the vertebral column. Autopsy confirmed that the gland, and several adjacent glands, were tuberculous.

TABLE V.

AUTOPSY RESULTS IN ANIMALS GIVING A "POSITIVE" REACTION TO B.C.G..

GROUP	DESCRIPTION	Number Tested	Positive Reactors	Autopsies obtained	Tuberculosis confirmed
I	Animals in contact with tuberculosis.	22	11	3	1
Control II	Known tuberculous animals.	13	12	13	13
Control III	Non-specific morbidity.	19	3	19	-
Control IV	B.C.G. Immunised.	15	13	2	-
I,II,III,IV.	COMBINED.	69	39	37	14

consisting of 15 dogs and cats artificially immunised against tuberculosis one year previously, 13 gave 'positive' reactions.

Table V shows the autopsy results. In Group I only one animal, a dog, out of the three obtained for autopsy, had macroscopic and microscopic evidence of tuberculosis confirming the B.C.G. reaction. The cat, which had produced the growth of M. tuberculosis in life, was one of the two negative animals; and, apart from lymphoid hyperplasia of the appendix, only exhibited an enlarged mesenteric gland, showing sinus catarrh.

Among the controls, all the animals in Group II, and none of the animals in Groups III and IV, revealed pathology typical of tuberculosis.

Figure XV is the lateral chest x-ray of the dog from Group I, the group of apparently healthy animals in contact with active tuberculosis in humans, in which an early, immune, 'positive' reaction to B.C.G. had suggested the presence of infection. The lymph gland shown on the x-ray, together with several, smaller adjacent glands, were later confirmed to be tuberculous at autopsy.

D. The Comparison of B.C.G. with P.P.D..

Table VI shows the results of testing 45 dogs and 24 cats with B.C.G., compared with the results of testing 32 dogs and 22 cats with P.P.D. tuberculin. Among dogs, 66.6% gave 'positive' reactions using B.C.G., compared with only 37.5% using P.P.D.; and in cats, 41.6% gave 'positive' reactions with B.C.G., compared

TABLE VIII.

MORBIDITY DUE TO INFECTION IN 227 CATS.

VETERINARY DIAGNOSES IN ORDER OF PREVALENCE	GROUP A. 18 MORBID CATS IN CONTACT WITH TUBERCULOSIS		GROUP B. 92 MORBID CATS WITH NO KNOWN CONTACT WITH TUBERCULOSIS		WHOLE GROUP (227 cats)	
	No.	Rate%	No.	Rate%	No.	Rate%
SPECIFIC INFECTION.						
Tuberculosis.	1	5.5	-	-	1	0.4
UNSPECIFIED INFECTIONS.						
"INFLUENZA".	9	50.0	27	28.2	36	16.0
Abscesses.	4	22.0	18	19.6	22	9.7
Gastroenteritis.	-	-	19	20.6	19	8.4
Respiratory.	3	16.5	12	13.2	15	6.6
Eye.	-	-	6	6.4	6	2.6
Ear.	-	-	5	5.4	5	2.2
Bladder.	2	11.0	2	2.1	4	1.7
Discharging sinuses, (chest and face).	2	11.0	-	-	2	0.8
Skin.	1	5.5	2	2.1	3	1.3
Larynx.	1	5.5	2	2.1	3	1.3
Lymph glands.	1	5.5	2	2.1	3	1.3
Kidney.	1	5.5	2	2.1	3	1.3
Mouth.	-	-	1	1.0	1	0.4
Peritoneum.	-	-	1	1.0	1	0.4
Tonsil.	-	-	1	1.0	1	0.4

TABLE VII.

THE COMPARISON OF THE USE OF BACTERIOLOGY WITH B.C.G. IN THE EXAMINATION OF 70 ANIMALS IN CONTACT WITH ACTIVE TUBERCULOSIS IN HUMANS.

	BACTERIOLOGICAL EXAMINATION (25 dogs and 23 cats)		B.C.G. EXAMINATION (13 dogs and 9 cats)	
	M. Tuberculosis recovered.	% of Total	'Positive' Reactors	% of Total
DOGS	4	16.0	8	61.5
CATS	3	13.0	3*	33.3
TOTAL	7	14.5	11	50.0

* M. tuberculosis recovered from 1 cat.

with 13.6% using P.P.D..

Table VII compares the results of the bacteriological investigation of 48 apparently healthy dogs and cats, in contact with active tuberculosis in humans, with the testing of 22 animals, in a similar category, by B.C.G.. Growths of M. tuberculosis were recovered from 14.5% of the animals tested by bacteriology; whereas 'positive' reactions were observed in 50% of the animals tested by B.C.G..

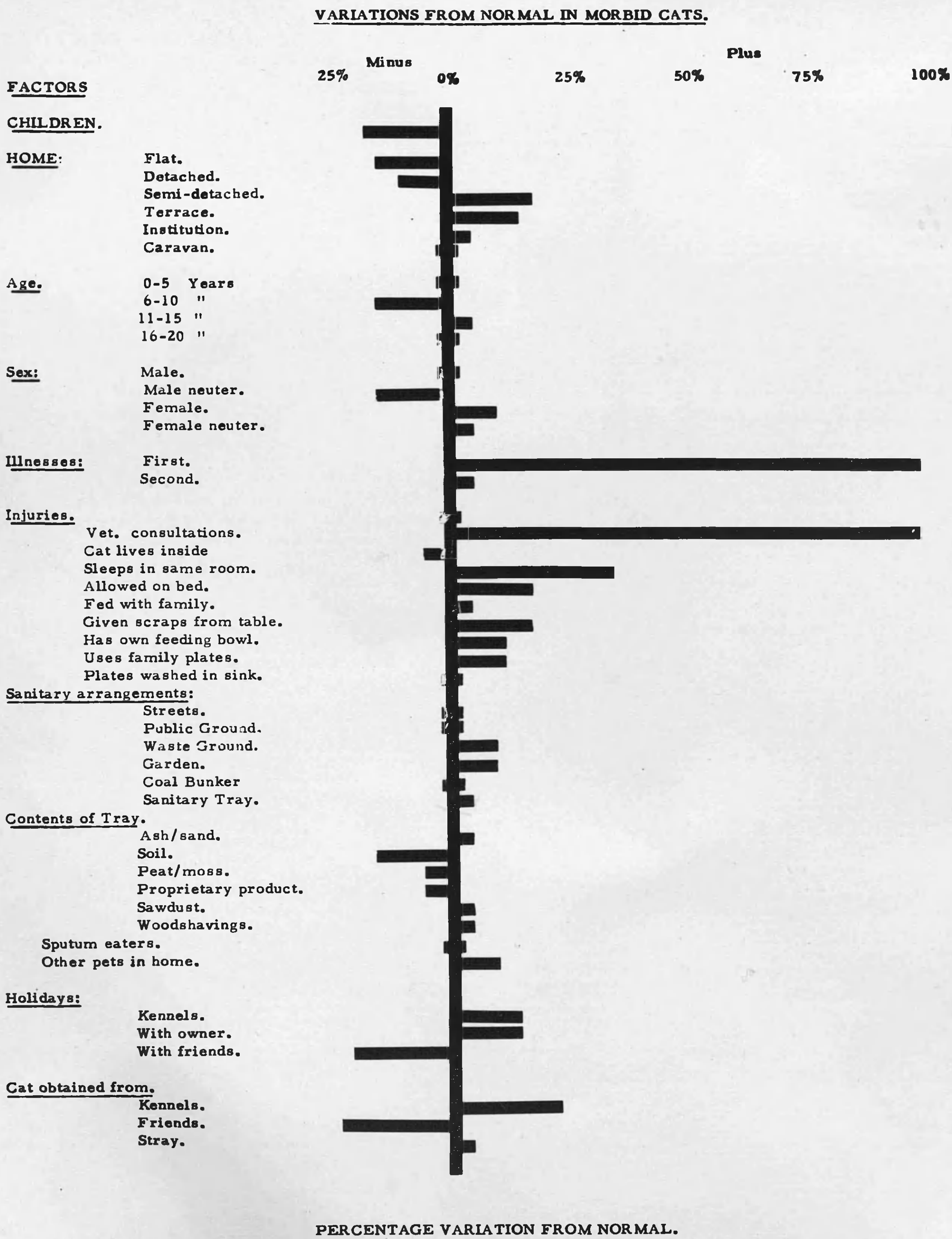
E. The Ecology of the Domestic Pet.

Table VIII shows the morbidity due to infection in 227 cats, whose owners had correctly completed the questionnaire (Figures IIIA and IIIB) distributed by the Feline Advisory Bureau to a cross section of cat owners, selected by income group, in each community. Although only one third of the questionnaires were returned, they came from homes evenly distributed throughout the five social classes.

The animals fell into three groups. Group A consisted of 20 cats, 18 of them morbid, with a history of exposure to tuberculosis. Group B consisted of 92 morbid cats, with no known history of exposure to tuberculosis, and Group C of 115 normal cats.

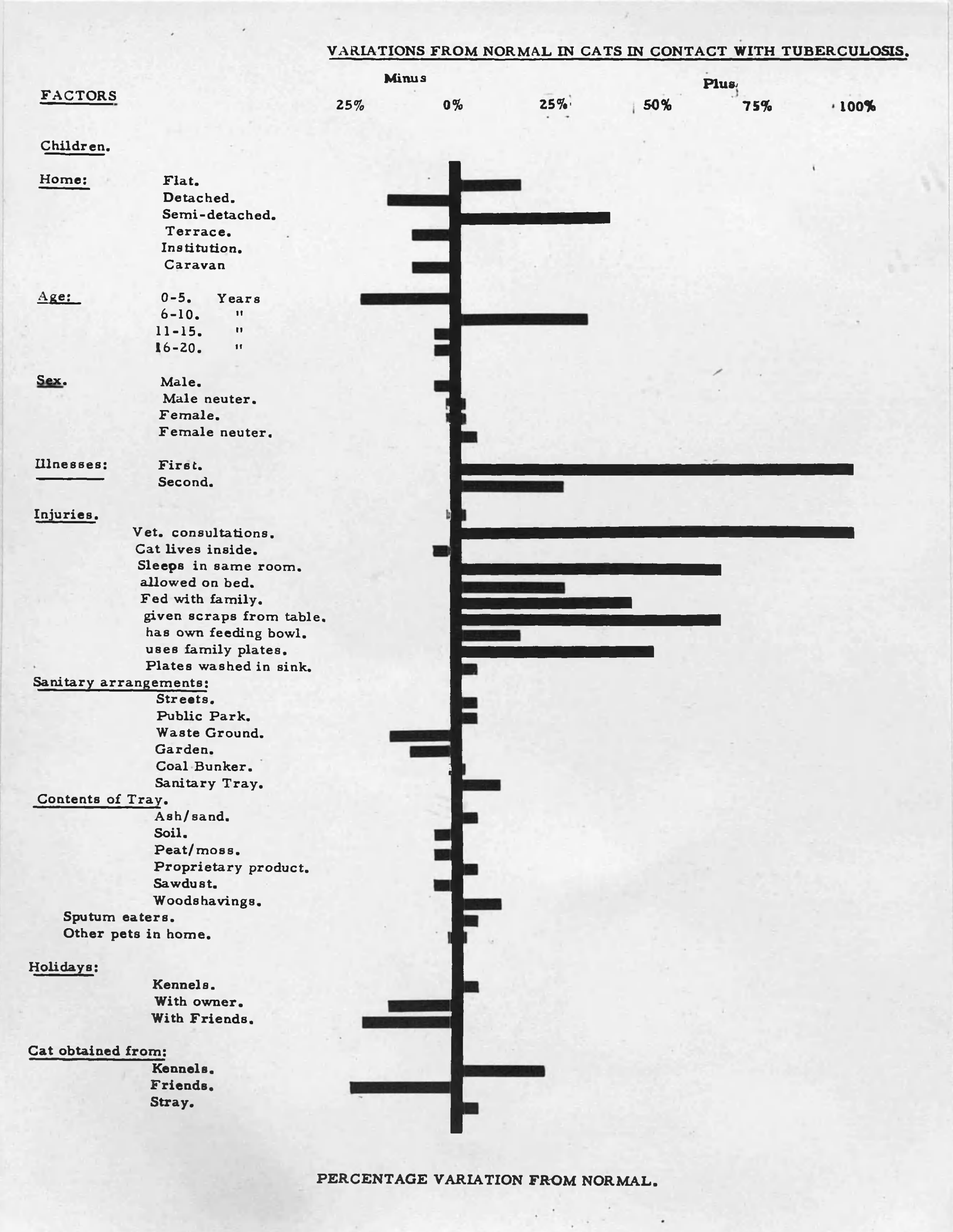
One Group A cat had a confirmed diagnosis of tuberculosis, giving a rate of 0.4% for the combined groups; and the infective morbidity rate was higher among Group A, compared with Group B animals.

FIGURE XVII.



The Variations from normal in morbid cats.

FIGURE XVI.



The Variations from normal in cats in contact with tuberculosis.

TABLE IX.

MORBIDITY DUE TO NON-INFECTIVE CONDITIONS IN 227 CATS.

CONDITION	NO.	RATE%
Allergic		
Asthma	2	0.8
Excema	10	4.4
Traumatic		
Fractures	5	2.2
Dislocations	4	1.7
Burns	1	0.4
Infestations		
Tapeworms	7	3.5
Fleas	1	0.4
Metabollic		
Hormone Deficiency	5	2.2
Diabetes	1	0.4
Mechanical		
Obstruction (Hair balls)	5	2.2
C.N.S.		
Paralysis	2	0.8
Epilepsy	1	0.4
Mental Defect	1	0.4
Gynaecological	3	1.3
Neoplastic	2	0.8
Urogenital (Stone)	1	0.4
Hepatic (Hepatitis)	1	0.4
Blood (Anaemic)	1	0.4
Haemorrhagic (Intestine)	1	0.4
Mastitis	1	0.4
Eye (Cataract)	1	0.4
Vitamin Deficiency	1	0.4

Table IX shows the morbidity due to causes other than infection with the highest incidence in the group of allergic conditions.

In the 227 animals the total morbidity rate was 48.5%, of which total, the infective morbidity rate was 56.4%.

The total morbidity rate among Group A cats was 90% compared with 44.4% among Group B.

Figure XVI is a diagram in which the ecology of the Group A cats (morbid cats exposed to tuberculosis) is compared with that of Group C (normal cats). The ecology of the normal cats is represented by the thick, vertical line, while that of the morbid cats by lateral branches, indicating the percentage deviation, either plus or minus in frequency, from normal. Thus, for example, 65% more Group A cats slept in the same room as their owner than did Group C; and 20% less cats, in Group A, were obtained from friends than the normal, Group C cats.

Figure XVII is a similar diagram to Figure XVI, this time illustrating the ecology of the 92 Group B cats in comparison with the Group C animals.

A combination of the findings in Figures XVI and XVII reveals a number of ecological differences in Group A and B, the morbid animals, compared with Group C, the normals.

Group A cats had a higher proportion of second illnesses than Group B.

More of both Group A and B animals were allowed to sleep in their owners' bedrooms, were allowed on their beds, were fed

TABLE X.

COMPARISON OF THE DEGREE OF PROPINQUITY EXISTING BETWEEN 37 DOGS AND 21 CATS, AND THEIR OWNERS, IN THE AVERAGE HOME.

Detail	PERCENTAGES CONFORMING. Dogs	Cats	Combined
Animal lives in house.	100	100	100
Animal sleeps in same room.	51	47	50
Animal gets on, or in, bed.	40	19	34
Animal eats with family.	61	61	62
Animal has scraps from the table.	75	71	74
Animal has own feeding utensil.	94	95	94
Animal uses household plates.	18	9	15
Animal's utensil washed in communal sink.	91	90	91
Animal washed in family sink or bath.	67	-	67
Animal "house-trained".	91	95	93
Animal uses streets.	40	33	36
Animal uses public parks.	2	-	1
Animal uses waste ground.	24	-	15
Animal uses garden.	35	23	30
Animal uses sawdust box or coal bunker.	16	9	13

with the family, received scraps from the table, and were permitted to eat from the family plates, than in normal, Group C animals.

Comparison of the hygienic arrangements were less significant, although Groups A and B more frequently used the so-called "sanitary" tray, than Group C animals.

Sputum eaters, the time-honoured mode of infection of the tuberculous dog or cat, were confined exclusively to Group A cats; but other pets in the home were more frequent in Group B cats.

Groups A and B together were more gregarious than Group C, in that they were more often boarded-out at Kennels, or accompanied their owners on holiday, compared with the normal cats, who tended to be left at home with friends.

Finally, the morbid groups A and B, were acquired more frequently by their owners from Kennels or as strays, than the normals, Group C, which were acquired more often from friends (a known source).

Table X, based on the questionnaire incorporated in the case record sheet (Figure IIA), gives details of the hygienic arrangements in the homes of a representative sample of dogs and cats. It shows that dogs and cats enjoy almost the same degree of propinquity to their owners.

DISCUSSION.

The Prevalence of Tuberculosis during the Investigation.

Among humans, tuberculosis continued to decline during the period of the investigation. According to the report of the Medical Officer of Health of Glasgow, both death and notification rates decreased to 286 (27 per 100,000) and 1,159 (108 per 100,000), respectively in 1959, a trend shared by the positive reactors to Mantoux testing, further reduced from 20.9% in 1959 to 19.3% in 1960 among schoolchildren between 13 and 14 years of age. In March 1957, however, the Mass Miniature Radiography Campaign detected 8,000 (11.5 per thousand) new, active cases of pulmonary tuberculosis among residents of the City, over 14 years of age.

Among animals the position was more difficult to assess, with the exception of bovine tuberculosis, which was well documented. The West of Scotland had been an attested area since the early fifties, but it was only recently that this had been the position throughout the country. Thus in the West, during the period from 1955 to 1959, the Staff of the Animal Health Division of the Ministry of Agriculture, Fishery and Food, reported that only 0.06% of the dairy herds produced positive tuberculin reactors, compared with 0.15% for the whole country (including England and Wales). At these levels, and with the pasteurisation of all milk, the dairy herds appeared to be in greater need of protection from humans than vice versa.

The incidence of tuberculosis in morbid dogs in the 1955 to 1959 period in Glasgow and the West of Scotland was estimated at 2 per thousand. At the University of Glasgow Veterinary Hospital, tuberculosis was detected at 2.2% of all autopsies made in 1955. This figure fell to 1.7% in 1957 and 1958 but rose again to 2.2% in 1959. All bacilli recovered were of human origin.

Among cats, tuberculosis was estimated as 1% of all autopsies during the same period; and again examination of the bacilli revealed only bacteria of human origin.

Irregularly over this period tuberculosis was found in other species. The cases included two chimpanzees in a local zoo, a pig from the Glasgow Abbattoir with M. tuberculosis of human origin (Jarrett, 1960), a horse and a pony, detected at autopsy following death in a road accident, (Lauder, 1961).

The dominant impression was one of a considerable pool of free infection almost exclusively of human origin, maintaining a fairly steady, if diminishing, incidence in all ages of the human population, and their domestic animals.

A. The Prevalence of Tuberculosis among Apparently Healthy Animals in Contact with Active Tuberculosis in Humans.

A total of 70 animals in this category were investigated (Table VII), 48 by bacteriological methods and 22 by B.C.G..

M. tuberculosis of human origin was recovered from 7 animals, 4 dogs and 3 cats, among the 48 animals examined by culture of rectal and pharyngeal swabs; and 11 animals, 8 dogs and 3 cats, gave an early reaction among the group of animals examined by B.C.G..

The seven animals having 'positive' bacteriology in the group of 48 animals, were re-examined within three months of the recovery of the positive specimens, and were found to be negative. At autopsy, apart from isolated enlarged glands, showing non-specific inflammatory changes, no lesions typical of tuberculosis were found.

Of the 11 animals giving an early reaction to B.C.G. only 3, one cat and two dogs, were obtained for autopsy. In the cat, a growth of M. tuberculosis of human origin had been recovered from a swab taken at the same time as the B.C.G. inoculation, but at autopsy no lesion typical of tuberculosis was found, although there were non-specific inflammatory changes at the ileo-caecal junction. The two dogs were negative bacteriologically. At autopsy one had no detectable tuberculous lesions but the other (Figure XV) had enlarged mediastinal glands showing typical tuberculous pathology.

The recovery of organisms from the gastro-intestinal tracts of animals without loss of virulence had also been reported by Floyd and Page (1943), who demonstrated the physical ability of M. tuberculosis to survive in the gastric juices of dogs for periods of one to twelve hours without impairment of virulence.

In the present series, growths recovered from both pharynx and rectum were of similar virulence in guinea pigs. Explanation of the recovery of M. tuberculosis, at intervals varying up to three months after separation of these animals from their apparent human source of infection, without demonstrable tuberculous lesions at autopsy, may lie in the work of Kuwabara (1938), who showed that cats, naturally highly-resistant to M. tuberculosis of human origin, could survive the presence of bacilli for as long as two months, without histological evidence of lesions at autopsy. In this connection, it was perhaps significant that the one animal with definite pathological evidence of tuberculosis, out of the ten examined at autopsy, was a dog. Heppleston (1949), infected rabbits by droplets of human tubercle, and recovered bacilli from macroscopically normal lung tissue, several weeks after primary infection; and Griffith (1942), recovered living vole bacilli from the apparently unaltered spleen of fowls after 141 days. It would thus appear that the findings made in this study are not an uncommon occurrence in circumstances where the genetic, or acquired, resistance of the host is high, or where the virulence of the organism is low for the host in which it is being tested.

An alternative explanation for the recovery of M. tuberculosis from these apparently healthy animals, might lie in relating the recovery of the bacilli to an atypical pathological reaction, noted in each of the animals obtained for autopsy. In these animals at least one moderately enlarged lymph gland was found adjacent to either the gastro-intestinal, or the respiratory tract, and showing a lymphocytic infiltration of varying degree, described as sinus catarrh (Figure IV). Human and veterinary medicine has little to offer in the way of detailed information regarding the early evolution of tuberculosis, in the latent period between infection and tubercle formation (6 to 8 weeks in humans); and it could be that these predominantly lymphocytic, focal reactions, represented the pathology of the latent stage of the infection. Innes (1949), describing the histological changes of early infections of M. tuberculosis of human origin, in the horse, reported that the most striking feature apparent in the lymph glands was sinus catarrh, which might easily be mistaken for a non-specific effect, and certainly could not be assumed, on histological examination alone, to be due to mycobacterial infection.

Innes compared the lesions in the horse to those of Boeck's sarcoid in man. Sarcoidosis in man, according to Scadding (1950), may be the response of the reticulo-endothelial system to various agents, two known, the tubercle bacillus and beryllium, and one or more as yet unknown. It is tempting to speculate that the reactions noted in the lymph glands of the animals in this study, might be sarcoid-like reactions to M. tuberculosis.

While further studies of the significance of the pathology of these lymph glands might provide new information on either the early, latent phase of a tuberculous infection, or the aetiology of sarcoidosis, it must be concluded, on the evidence of this study, that the recovery of M. tuberculosis from these animals, probably indicated the presence of the bacilli as commensals, a finding which need not preclude their proliferation in the gastro-intestinal tract. Evidence that this process may be attended by the production of natural immunity, is supported by the fact that one cat, which produced a growth of M. tuberculosis, was also an early, immune, 'positive' reactor to B.C.G., a finding which might also suggest that the sinus catarrh of the lymph gland was evidence of its immunological reaction.

The dangers of the apparently healthy domestic pet, with its reservoir of viable and virulent bacilli, and its undoubted contribution to the succession of the tubercle bacillus among the other members of the household, would indicate the advisability of proscribing the animal for a period of several months, following the detection of an active case among the humans.

B. The Prevalence of Tuberculosis among Humans in contact with Tuberculosis in Dogs.

This part of the investigation was to some extent hampered by a marked reluctance on the part of most owners to submit either themselves, or their families, to examination even after being informed that the household pet had died of tuberculosis, and that they themselves had inevitably been exposed to an increased risk of infection. Many remained quite resolute in their attitude, and sometimes this restricted the scope of examination to a minimum, although this generally included a single x-ray. Occasionally, a study of the Tuberculosis Register showed definite concealment. In these circumstances, it was hardly surprising that Mantoux testing of the children was allowed in only two families; and that attempted "follow-up" by repeat x-rays was rarely successful.

Despite these shortcomings, it was generally possible to trace at least one human with an active, or recently active lesion, who had been in contact with the dead animal, for a material length of time.

In five cases, however, the apparent tuberculous human contact was a neighbour, and in two cases, a previous owner. It was in one of these homes that the two children were Mantoux positive reactors, although their parents had negative x-rays; and it was a reasonable inference that the dog, infected in its daily contact with a tuberculous neighbour, had in turn been responsible for the Mantoux conversion of the children, earlier than might be expected in children of comparable ages.

Where no known contact was traced the fault probably lay with the inadequacy of the single x-ray without "follow-up", and the failure to examine every contact. At the same time the existence of a completely extraneous source could not be excluded, as instanced by the circumstances surrounding the infection of one dog, A, which had almost certainly been acquired from another dog, B, owned by an immediate neighbour; and with which A had played, until the other dog, B, had sickened and died of tuberculosis four years previously.

The investigation of the source of an animal's infection has been undertaken by a number of workers: Lovell and White (1940) reported a history of tuberculosis in the owners' families in 3 out of 22 cases; Smythe (1929) found evidence in 4 out of 20 cases; Stableforth (1929) 4 out of 16 cases; and Hjärre and Herlitz (1935) 6 probable sources for 25 tuberculous animals. In these studies 17 (20.4%) probable human sources were identified among the 83 cases investigated, compared with 23 (74.1%) from 31 cases investigated in the current study.

The question of whether the pet more often infected the human, or the human the pet, remained open, and must remain so with tuberculosis at its present ubiquitous stage; but the probability was that the human more often infected the pet; and the reverse was less common, except in the case of small children, now normally protected by B.C.G.. While the definition of the hazard of the tuberculous animal to its owner must await a more comprehensive, and inflexibly applied study of the human contacts, including tuberculin testing, the present investigation made it clear that the risk from the tuberculous pet differed little from that of the tuberculous human.

In one instance, growths of M. tuberculosis of human origin, were recovered from both the owner and her cat. Beyond being able to note that both growths looked the same, and had similar virulence for guinea pig and rabbit, there was no specific, bacteriological technique available, which was capable of relating one growth positively with the other. The solution of this problem would go a long way towards establishing the frequency of both human to animal, and animal to human infections; and must await the refinement of such techniques as infra-red spectroscopy, and the identification of the mycollic acid fraction of the bacillary capsule.

Despite the incomplete nature of this section of the current investigation, summation of the active cases among the 354 known, close, human contacts gave a total of 41 (11.86%) humans with evidence of active disease at a material time. Considered as a whole, contacts of tuberculous household pets constituted a group with an exceptionally high yield of tuberculosis. Accordingly, it was quite certain that the diagnosis of tuberculosis in a domestic animal should be notified immediately to the Public Health Authority in the confidence that even a partial examination of the accessible human contacts, will produce at least one active case in every nine human contacts examined.

C. The Use of B.C.G. as a Test to Detect the Presence of Past or Present Infection in Dogs and Cats.

Technique.

Originally it had been hoped that the use of B.C.G. might be simplified by using the "Heaf gun", a multi-puncture instrument producing a rosette of punctures in the skin (Figure XI, arrow 3), 2 mm. in depth, through a surface layer of test material, but the method failed to produce a standard skin reaction, as did sub-cutaneous inoculation, probably because of variations in the skin thickness between one animal and another. The most satisfactory technique was the injection of 0.1 ml. of the test material intra-dermally to produce a 'bleb'. The most suitable region for testing was the scapular area because it was the most accessible to the operator and the least accessible to the animal (Figures IX to XIV). The performance of the test should not exceed the competence of the average veterinary technician after a little practice. The interpretation of the test, on the other hand, must be made by a veterinary surgeon.

Basis for Using B.C.G. as a Test.

The practical basis for the use of B.C.G. as a test was based on experience with two chimpanzees at a local zoo. 0.1 ml. of B.C.G. was injected intra-dermally into the flexor aspect of the forearm of both animals. The result was an allergic systemic reaction within three days in the more ill of the two animals, and the appearance, within four days, of a papule, larger in the case of the more ill animal, at the site of injection. These papules proceeded to central necrosis within 7 days of the date of inoculation. Both animals were later confirmed to be suffering from active tuberculosis (Figure V).

The theoretical basis for the use of B.C.G. as a test was based partly on practical experience with the two chimpanzees, and partly on the reports of the use of B.C.G. as a test in humans by Ustvedt and Aanonsen (1948), and by Friedman and Silverman (1952), who interpreted papules of 2 mm. in diameter or more, and still present on the 8th day, as positive, specific, early reactions; and papules appearing after the 12th day and up to 20 days, as primary, late reactions denoting humans not previously infected with tuberculosis.

In dogs and cats a more definite end point was required than the appearance of the papule; and it was decided to base the study on the point of ulceration of the papule. Experience showed that ulceration was a fairly definite event taking place within 24 hours; and one which produced, in the group of dogs and cats under investigation, and the controls, a clear, though not absolute, division between the early and late reactors on either side of fourteen days from the date of inoculation. This led to the selection of the fourteenth day after inoculation as the critical day separating 'positive' from 'negative' reactors.

The Results of using B.C.G. as a Test.

A 'positive' reactor rate of 50% was detected in the Group I animals (Table IV), and of 15% in the Group III animals. While these numbers were too small to permit accurate assessment, there was a superficial similarity between the percentages produced in these animals and the type of percentages which might be expected in similar groups of humans. Thus humans exposed to active tuberculosis in the same home might be 100% Mantoux positive, while the rate in the general population might be about 30%, (it was 19.3% among school leavers in Glasgow in 1960).

Again in Groups I and III animals, the traditional, greater susceptibility of the dog, compared with the cat, was apparent, using B.C.G. as a test: 8 dogs out of 13 in Group I and 3 dogs out of 11 in Group III, compared with 3 out of 9 cats in Group I and no cats at all in Group III, giving positive reactions.

In Groups II and IV, the natural and experimental controls respectively, the 'positive' reactor rates were, for all practical purposes, 100%. The one failure in the dogs dying of tuberculosis (Group II), was an animal, moribund with disseminated disease when inoculated, a condition, analogous to acute miliary tuberculosis in the human, where a tuberculin-neutralising factor in the serum can produce Mantoux negative results, even with the 1/100 dilution of Old Tuberculin (Lees, 1951). Friedberg and Fröhner had similar experiences using tuberculin subcutaneously in animals with advanced tuberculosis.

The two failures in Group IV, were early cases immunised by the Heaf gun, which was later found to be mechanically incapable of producing any immunity at all in some animals.

Interpretation of the B.C.G. Reaction.

While the majority of reactions were associated with ulcers occurring clearly before or after the '14 Day Line' occasionally ulceration occurred on, or around, this time. It was found helpful in these cases to take into account the length of time elapsing from inoculation to the appearance of the papule, The earlier its appearance, the more probable the 'positive' nature of the response.

A further helpful point in the interpretation of the 'positive' reactors was noted among the naturally infected, and artificially immunised animals, of Group II and Group IV (Figures VII and VIII), namely, that the more extensive and active the infection, the earlier the point of ulceration. A quick reaction reaching the stage of a papule within 48 hours, and ulceration within a week, was strongly indicative of active tuberculosis. An animal in this category might be expected to exhibit clinical evidence of tuberculosis, supported either by an abnormal x-ray of thorax or abdomen (Figure XV), or, less often, positive bacteriological findings.

The gradations of response noted among the 'positive' reactors might be regarded as analogous to the variations in response to Mantoux testing in humans: the brisker the response, the more probable the presence of demonstrable disease.

Lurie et al. (1952), showed that when B.C.G. was injected intra-cutaneously into races of rabbits, genetically resistant and genetically susceptible, to human type tubercle bacilli, the nodule at the site of injection in the resistant race grew and ulcerated more rapidly than in the susceptible race. When these races were artificially immunised by B.C.G. the naturally resistant strain developed allergic sensitivity to tuberculin more quickly than the naturally susceptible strain. They concluded that on this basis, B.C.G. could serve as an index of native resistance.

In the current investigation, essentially a field, as opposed to a laboratory study, it was not possible to differentiate between genetic and acquired resistance; and while it would be tempting to classify all the animals giving the early, immune, 'positive' reactions without apparent tuberculous pathology, as previously infected, the possibility that their early reactions were an index of genetic resistance could not be dismissed. At the same time, genetic resistance was not often considered as an invalidating factor in the interpretation of the Mantoux test in humans; and it may be that B.C.G. 'positive' reactor rates of 50% in apparently healthy animals, exposed to tuberculosis in humans (Group I), and 15% in morbid animals, with no history of exposure (Group III), were true indices of acquired immunity.

The ground has now been prepared for a large scale study of dogs and cats, including strays. In the meantime, a dog or cat producing an early, 'positive' reaction to B.C.G. should be regarded as a tuberculosis suspect, and the reaction to B.C.G. as an aid to diagnosis, in conjunction with the usual clinical and laboratory procedures for the investigation of tuberculosis.

D. The Comparison of B.C.G. with P.P.D. as an Aid to Diagnosis.

A study of the literature relating to the efficacy of tuberculin as a diagnostic test of tuberculosis in dogs and cats indicated a wide variation in results. Friedberger and Fröhner (1908) found that in some instances non-tuberculous dogs gave positive reactions. Cobbett and Griffith (1913) found that only 6 out of 11 tuberculous cats reacted to tuberculin sub-cutaneously. Grobon (1925) observed that only 27.5% of infected cats, and 62% of infected dogs, gave positive reactions to sub-cutaneous injections of tuberculin, Colwell and Mills (1940) were most successful, observing 89.1% positive reactors among experimentally infected dogs. Ten of this group, including 3 negative reactors, were re-infected by virulent bacilli; and 100% reacted positively with 0.01 tuberculin. Among 18 dogs immunised with B.C.G., 83.3% were positive, and 16.6% were negative or doubtful. Francis (1956), using P.P.D. in experimentally infected dogs, obtained only slight and irregular results. Summarising the position, Francis (1958) reported that allergy to tuberculin was irregular in dogs, and developed little in cats.

In the current series the same animals were tested with B.C.G. and P.P.D. simultaneously. Nearly twice as many dogs, and more than three times as many cats, gave positive reactions to B.C.G. compared with P.P.D., but even this comparison tended to give a false impression of the efficacy of P.P.D.. A study of the individual P.P.D. reactions showed that these were very variable; and frequently did not occur at all, even in known tuberculous (Group II), and previously immunised (Group IV) animals. In addition, despite the use of a standardised technique, the tissue response to P.P.D. was minimal compared with B.C.G.; and in many cases it would have been difficult to interpret the reaction to P.P.D. had it been unaccommmpanied by B.C.G..

With B.C.G., on the other hand, only 3 animals in the known infected group (Groups II and IV, Table IV) failed to produce positive reactions; and of these, one was moribund, and the other two were tested by an unsatisfactory technique (the Heaf gun).

The apparent superiority of B.C.G. over P.P.D., as a test in humans was well-documented. Boiron (1952), examining 2,000 humans not previously tested, concluded that B.C.G. was more sensitive than tuberculin; and produced a positive in all cases where a tuberculin skin test was positive, and in 15% of cases where the tuberculin skin test was negative. Ustvedt and

Aanonsen (1948) also concluded that B.C.G. was more sensitive, and definitely more specific, than Pirquet and Mantoux tests. Novak (1950) found that a positive Pirquet test was always associated with a positive B.C.G. test, but a positive B.C.G. test, in persons with a negative tuberculin test, always differentiated the infected from the non-infected.

It was concluded in the series under investigation that B.C.G. appeared to be markedly more sensitive and constant than P.P.D. in the production of skin reactions of diagnostic value.

A current problem of great interest has been the rising incidence of active tuberculosis in elderly males. The rate in men over 60 years, examined by the Glasgow Mass Radiography Service in 1960 was 9.1 per thousand compared with 3.6 per thousand in the community as a whole. There was no corresponding rise in females. Reports by Bellomo (1952), Amazon (1943) and Giannini and Sloan (1957), showed an increasing proportion of negative tuberculin reactors with successive age groups. In addition, Amazon (1943), and Groth-Petersen and Wilbek (1955), found radiological evidence of previous tuberculosis in many elderly persons with negative tuberculin tests. Unlike the morbidity rates, the proportion of negative tuberculin reactors in elderly women was even larger than in elderly men. A further study of B.C.G. in artificially immunised dogs and cats, analysed according to age and sex might prepare the ground for a B.C.G. survey of elderly, human, Mantoux negative reactors. Not only could the accuracy of the Mantoux reaction be independently assessed in the same patient, but the artificial stimulation of immunity by B.C.G., might alter the apparent, existing susceptibility of the examinee, to new, or the exacerbation of old, disease with advancing years.

E. The Ecology of the Domestic Pet.

The preliminary studies, based upon the questionnaire incorporated in the case record sheet (Figure IIA), showed that, in the average home, a dog's life was not greatly different from a cat's (Table X); and so it was decided that a survey of cats would suffice for both.

Certain of the results had interest outside the scope of the investigation, such as the finding that two thirds of all cat owners were childless; and an even higher proportion had no children living in the home, as objects of care and affection.

The main impressions from the study in morbidity (Tables VIII and IX), were the wide, and human, range of ailments to which the cat was subject; and, at the same time, the preponderance of the conditions arising from infection.

It was in the field of infection and infestation that the interests of the medical and veterinary professions coincided, a fact more clearly realised by the veterinary surgeons than the doctors. Whereas the medical practitioner had remained pre-occupied by the patient and his disease, in recent years the veterinary practitioner had looked increasingly beyond the immediate problem towards the wider one of the inter-relation of animal and human morbidity.

Once again, point had been given to the need for a better understanding by doctors, of the inter-dependence of certain human diseases on the whole environment, by the reports of Ashton (1960) and Duguid (1961), on human infestations by Toxocara canis, the common round worm of the dog. This hitherto reputedly rare condition for which there was no treatment, had caused blindness in man, who can be infested from eggs, excreted by puppies up to six months old, when excretion stops. The part played by the cat round worm, T. cati, was still unknown. The fundamental importance of this, and related problems, however, was that the possibility of their existence should have a place in medical thinking.

The Zoonoses Committee of the World Health Organisation listed 60 diseases capable of affecting man, a list which has grown and will grow, with further research. Even at present the zoonotic agents were many and varied. Among the bacterial infections were salmonellosis and leptospirosis. There were the Rickettsial diseases comprising three types of human typhus, and Q Fever. Important virus diseases included B. virus encephalitis, lymphocytic choriomeningitis and Newcastle disease;

and there were the arbor viruses, about which knowledge was still growing, forming a group of over 100 human infections in the U.S.A. and the tropics.

When these infections were considered in the light of the infective morbidity rate of 56.4% in the group of cats investigated, the possibilities of the current study became apparent as the basis for further research into other bacterial and viral zoonoses. The association of respiratory disease, between cat owners and their pets, was well known. Was there a relationship between cat influenza (16% of the morbidity in 227 cats), and cat scratch fever or virus pneumonia in the human? And what of the better known viruses? Somerville (1959) recovered poliovirus, type I, from a budgerigar; and the human patient died of poliovirus of the same type.

In the present series, it would be hard to escape the conclusion that at least some of the infections of the Group A and B cats, had originated in their owners. The tuberculous Group A cat had almost certainly been infected by its tuberculous owner. Again the cats in Group A had a higher infective rate than the Group B animals; and a proportion of the difference might be presumed tuberculous. Discharging sinuses were commonly, and lymphadenitis occasionally, due to tuberculosis in cats. Had the current investigation been able to undertake parallel bacterial and viral assays of the owners, much of value would have been learned.

The total rate of tuberculosis of 5.5% in Group A, the cats exposed to tuberculosis, was not greatly at variance with the rate expected among human members of a tuberculous household, and the rate of 0.4%, or 4 per thousand, not so different from the community average incidence of 3.6 per thousand in Glasgow and the West of Scotland in 1960. While these similarities might be statistically unsound, viewed together they tended to unite human and animal disease in a feasible way, as parts of the same epidemiological problem.

With regard to the ecological diagrams (Figures XVI and XVII) they demonstratedthe ample opportunities which existed for the interchange of infection in the average household. The high rates of infective illness among the animals in households with poor hygienic arrangements, suggested that the health, of both humans and animals, would benefit from certain elementary precautions. The household pet should not be allowed in the bedroom, or on the bed; and should not be fed with scraps from the table, nor share the household plates, which should be washed separately from the animal's feeding bowl. Ideally, the animal should have access to a garden or waste ground, in preference to parks or streets, indeed, the less it was in contact with other animals, and the less it travelled outwith the home, and its environs, the healthier the animal, and, probably the household. Kennels would not appear to be the healthiest source of a pet, nor the ideal place to board one.

There remained the question of whether or not tuberculosis of human origin could act as a zoonosis of dogs and cats.

As far as the human was concerned, the present study revealed an active rate of 118.6 per thousand in contacts of dogs dying with tuberculosis, compared with 3.6 per thousand among the general population in the same community. It would be difficult to refute the fact that the dying animals (one had been ill for over two years) had made a considerable contribution towards the reservoir of free infection in their respective households.

The animal contribution to the problem was more difficult to assess, but here again, the recovery of M. tuberculosis from 8 out of 70 animals in contact with active tuberculosis in their owners, pointed to the freedom with which viable organisms could be transmitted within a household. That these bacilli were recovered from apparently healthy animals indicated that each was acting as a "silent host", a condition well recognised among the zoonoses, where highly resistant animals often functioned effectively as reservoirs for their parasitic organisms, without the formation of anti-bodies.

A further factor in favour of zoonosis was that all of the growths isolated were of human origin (although a single bovine strain was encountered in a dog in 1961). As far as cats were concerned this was exceptional, as only one fully authenticated case of human tuberculosis in a cat has been recorded in this country (Jarrett, 1955). All organisms were of standard virulence, irrespective of their origin from a morbid or an apparently healthy animal, showing that the latter was a true "silent host", and not just an animal dependent for its apparent good health on attenuation of the commensal bacillus.

There remained the ecological bond. In this instance, the simple food cycle, such as a mosquito feeding on a human in malaria, was replaced by the sophisticated relationship of a man with his domestic pet.

It thus seemed probable that M. tuberculosis of human origin could act as a zoonosis, involving man, and dog and cat, in the environment of the home.

The current dynamic state of the zoonosis appeared to be one in which the human was more susceptible than the dog, and the human and dog more susceptible than the cat, in a situation where morbidity was declining in all three. As long as the environment remained stable, the epidemiological significance of the zoonosis was probably small in relation to the position occupied by infection passed from human to human.

SUMMARY.

1. An account is given of an investigation, extending over eight years, into the inter-relation of tuberculosis between man, and his domestic pets, the dog and cat; with particular reference to the ecological aspects of the infection, whether or not it was a zoonosis, and if so, its epidemiological significance.

2. The method of investigation was by a combined medical and veterinary approach, aimed at ascertaining the incidence of tuberculosis among apparently healthy animals in contact with active tuberculosis in humans, and among humans in contact with animals dying of tuberculosis.

3. The investigation included an attempt to refine existing methods of diagnosis of tuberculosis in dogs and cats, by the development of B.C.G. as a test of immunity, in place of P.P.D. tuberculin, which was found to be both ineffective and unreliable.

4. A questionnaire was devised to elicit the required ecological details; and then distributed by the Feline Advisory Bureau to 750 individuals in the British Isles, Western Europe and the United States of America.

5. M. tuberculosis of human origin, was recovered from 4 dogs and 3 cats in a group of 48 animals, exposed to active tuberculosis in their owners, and from one cat in a further,

similar group of 22 animals. The presence of these bacilli, which were of normal virulence, was not accompanied by pathological changes typical of tuberculosis; and it was concluded that the bacilli were probably present as commensals in highly resistant animals.

6. The atypical pathological changes, described as sinus catarrh, in isolated glands of the animals producing growths of M. tuberculosis, suggested further studies to determine if these changes might be related to sarcoidosis or an early, latent, phase of a tuberculous infection in a highly resistant animal.

7. The dangers of the apparently healthy domestic pet, excreting viable and virulent tubercle bacilli, indicated the advisability of proscribing the animal for a period of several months, following the detection of an active case among the human members of the household.

8. Three quarters of the human contacts of 31 dogs dying of tuberculosis were traced, half of them to the owner, or a member of his family, but in seven cases to a neighbour or a previous owner. Of the total of 354 human contacts, 41 (11.86%) were found to have had active tuberculosis at a material time in their association with the sick animal.

9. While the definition of the exact hazard of the tuberculous animal to its owner needed a more comprehensive, and inflexibly applied study of the human contacts, including

Mantoux testing, and a new method of identifying identical growths obtained from owner and pet, the present investigation made it clear that the diagnosis of tuberculosis in a domestic animal, should be subject to the same statutory notification to the Public Health Authority, as was required in the case of a tuberculous human.

10. The intradermal injection of 0.1 ml. of B.C.G., producing a papule which ulcerated before 14 days (average interval from injection to ulceration, 9 days for cats and 11 days for dogs), was interpreted as the early, immune, 'positive' reaction of the infected animal; whereas a papule ulcerating after 14 days (average interval from injection to ulceration, 22 days for cats and 24 days for dogs), was taken as the late, non-immune, 'negative' reaction of the un-infected animal. The earlier the appearance of the ulcer, i.e., an accelerated, early, immune, 'positive' reaction, the more likely the animal to be suffering from an active tuberculosis infection.

11. In the group of animals exposed to active tuberculosis in their owners, 8 out of 13 dogs, and 3 out of 9 cats gave early, immune, 'positive' reactions to B.C.G.. M. tuberculosis of human origin was recovered from one cat; but at the autopsies of the cat, together with two of the dogs, the only changes pathognomonic of tuberculosis were detected in one of the dogs. Among the control animals, immunised either naturally, or artificially by intra-

dermal inoculation of 0.1 ml. of B.C.G., all gave early, immune, 'positive' reactions to B.C.G., except one moribund animal.

12. While the investigation had prepared the way for a large scale study of dogs and cats, in the meantime an animal producing an early, immune, 'positive' reaction to B.C.G. should be suspected of tuberculosis; and the reaction itself regarded as an aid to the customary clinical and laboratory procedures of investigation.

13. The trial of P.P.D. tuberculin in parallel with B.C.G. in the same animals, showed that B.C.G. was markedly more sensitive and constant, than P.P.D., in the production of skin reactions of diagnostic value.

14. A future study was outlined in which the elderly, negative reactor to Mantoux testing could be independently assessed; and the rising incidence of fresh disease in the elderly human male perhaps reduced, by the use of B.C.G. as a test.

15. The information collated from the return of 227 correctly completed questionnaires showed that cats were subject to a wide range of illness among which the morbidity rate due to unspecified infection was 56.4%, a rate to which a confirmed diagnosis of tuberculosis contributed 0.4%.

16. There was need for a better understanding of the interdependence of medical and veterinary science in the field of

infection; and this might best be given expression by an investigation of the bacterial and viral aetiology of the high morbidity rate due to infection in cats, and its relation to their human contacts.

17. Ecological diagrams, detailing the habits and practices of cats and their owners in the home, demonstrated the salient differences between groups of healthy and morbid cats; and described the ideal circumstances in which a pet should be obtained and maintained.

18. Factors in favour of human tuberculosis being an incidental zoonosis of household dogs and cats were: the incidence of 118.6 per thousand among humans in contact with dogs dying of tuberculosis; the recovery of virulent and viable bacilli from 8 out of a group of 70 apparently healthy dogs and cats in contact with active tuberculosis in humans; that the causal organism was exclusively of human origin throughout the investigation; that the home was demonstrated to be ideally suited for free interchange of infection; and that the relationship between owner and pet was infinitely stronger, and more effective, than the usual ecological bond based on the "food chain".

19. The dynamic state of the zoonosis at present was one in which the human was more susceptible than the dog, and the human and dog more susceptible than the cat, in a situation where morbidity was declining in all three. As long as the

environment remained stable, the epidemiological significance of the zoonosis was probably small in relation to the position of infection passed from human to human.

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