by inserting on the inside of the mould a very thin layer of cotton-wool. The mould is then immersed in a 10 per cent. formalin solution for about fifteen days. The whole block, which keeps its form extremely well, is easily dislodged afterwards and cut into frontal slices 1/2 to 1 cm. thick with a brain knife. The slices are washed in running water for two days, then immersed in methy-

FIG. 2.—Sketch of x-ray photograph showing left perihilar shadow.

lated spirit for twenty-four to forty-eight hours, which causes the return of the normal post-mortem tissue colour. To obtain permanent specimens the sections are placed in large Petri dishes filled with the following solution: gelatin, grains 105; thymol, m5; glycerin, 31.75; distilled water, 31.5. Sagittal, oblique, or lateral sections may be obtained in a similar manner.

Examination of the sections enables their situation, form, and relation to other parts to be studied accurately, and permits easy comparison with x-ray photographs taken with the same orientation.¹ Two examples may be

FIG. 3.

FIG. 3.—Sketch of sagittal section of thorax at *a b* (in Fig. 2), showing area of infiltration in left lung (anteriorly) giving rise to the left perihilar shadow. *H* = heart; *V* = vertebra; *R.L.* = right lung; *L.L.* = left lung.

FIG. 4.

FIG. 4.—Similar sagittal section showing area of infiltration in posterior part of left lung, also giving rise to a left perihilar shadow in an antero-posterior x-ray.

given to illustrate the great importance of such a comparison. A good deal has been written about "perihilar tuberculosis." Figs. 2, 3, and 4 explain how an antero-

FIG. 5.

FIG. 5.—Sketch of x-ray photograph showing shadow of varying density in right lung.

FIG. 6.—Sketch of lateral section of right lung at axis *c d* (in Fig. 5), showing that varying density of shadow is due to superimposition of two areas of similar density.

FIG. 6.

posterior photograph may easily suggest a perihilar lesion if one only thinks in terms of two dimensions. An antero-posterior x-ray photograph will often show a shadow of varying density, suggesting different types of lesion. Comparison with the post-mortem sections may, however,

demonstrate that the difference in appearance is due to the superimposition of lesions situated at different depths in the antero-posterior diameter, and actually at the same stage of the pathological process (Figs. 5 and 6). It may therefore be pertinent to conclude by stressing the importance of lateral or oblique x-ray photographs in every case of pulmonary tuberculosis.

It is a pleasure to express my thanks to Dr. Armand-Delille and to Dr. Lestocquoy for their kindness in giving me the opportunity of becoming familiar with their methods, and for the loan of the photograph.

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ON THE LACK OF EVIDENCE OF TRANSMISSION BY HUMAN BEINGS OF TUBERCULOSIS DUE TO THE BOVINE TYPE OF BACILLUS

BY

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The stimulus for research into the incidence of disease due to the bovine type of tubercle bacillus, and the virulence of that organism for the human subject, was supplied by Koch when, at the Washington Congress in 1908, he asserted that it was less virulent than the human type, and that it had never been demonstrated as a cause of chronic pulmonary tuberculosis in human beings. Investigation has gone on in several countries since that time, and has led to a fuller appreciation of the role of the bovine bacillus in the pathogenesis of human tuberculosis.

The results were summarized in a paper by Griffith and Munro,¹ which also gave an account of ten new Scottish cases of chronic pulmonary tuberculosis due to bovine organisms. Munro, in 1925, began to isolate and type the organisms from every case admitted to the sanatorium with tubercle bacilli in the sputum, and this work is still going on. For the past two years I have been privileged to assist in this, and am indebted to Dr. Munro for permission to use his figures and clinical notes. Up to September, 1933, 595 Glenlondmond strains have been isolated and typed, and of these twenty-three proved to be bovine, while in one case a mixture of bovine and human type bacilli was found, giving a percentage incidence of bovine type of 4. In addition two bovine strains were isolated from a total of forty specimens examined from Ayrshire. Isolation was effected chiefly by cultural methods, rarely by animal inoculation, and in no case did failure to isolate occur, so that no anomalous virus was missed.

Consideration of the group of cases of chronic pulmonary tuberculosis due to the bovine organism reveals several interesting points, and we are concerned here with only one of these. While they are clinically and radiologically indistinguishable from cases due to human bacilli, there is an apparent epidemiological difference at present unexplained—namely, the complete lack of proof of transmission from one human subject to another. How otherwise it is with tuberculosis due to human type bacilli is well known. It is recognized that the disease is produced as the result of contact, more or less prolonged and repeated, with some source of infection, usually an open case of pulmonary disease, and therefore becomes manifest as a "familial" or, more accurately, a "household" disease. So much is this the case that careful inquiry is always made into the family history with a view to

discovering the source of infection, and when two or more members of a family are found suffering from tuberculosis it is assumed that transmission occurred from one to the other.

It is a matter of some practical importance to ascertain whether, in the case of the bovine bacillus, similar transmission from human to human does occur. There is no apparent reason why it should not, but only examination of a large number of cases and full bacteriological investigation of those which show a family history of tuberculosis can settle the issue. Out of the twenty-four cases in the Glenomond series only four instances occurred in which more than one member of the family suffered from tuberculosis, and in only one of these was an opportunity of full bacteriological examination available. In his series of English cases Dr. W. M. Cumming also had one opportunity to type the bacillus where two brothers were found suffering from open pulmonary disease, and he has kindly allowed me to include notes of that case here. These two cases will be reported in some detail, since they show how presumptive evidence of familial disease due to the bovine bacillus was disproved by bacteriological examination.

CASE I

A female, aged 20, was admitted to Glenomond on January 28th, 1933. Her mother had had treatment (not in Glenomond) in 1931, and her sputum at that time was positive for tubercle bacilli. She died at home in September, 1933. The daughter was said always to have been fit as a schoolgirl, and, apart from scarlet fever at 14, had had no previous illness. From the time she was 7 until she was 16 she went for a holiday every summer to a farm. She began to train as a nurse in 1929, and developed a cough in the winter of 1932. This lasted a fortnight and returned a month later, but she remained at work until the time of her admission to Glenomond. On admission she was found to have a root-spread into the left lung and infiltration in the right upper lobe. The tonsillar glands were palpable, but no other glands were felt. Sputum was positive for tubercle bacilli, and a bovine type organism of full virulence was isolated. When it was realized that this organism was a bovine type, a specimen of the mother's sputum was obtained and a human type organism was isolated.

Bacteriological Examination

Sputum from the daughter was inoculated on Corper's potato and modified Loewenstein's egg medium on January 30th, 1933. The virus was dysgonic. On February 28th, 0.01 mg. of pure culture was injected intravenously into a rabbit of 2,500 grams. Thirty-five days later it was killed when very ill and weighing 2,200 grams. Generalized tuberculosis typical of bovine infection of full virulence was found at necropsy. A dysgonic virus was isolated and grown from the spleen. Sputum was sown on egg medium on three subsequent occasions, and each time a dysgonic virus was isolated. On two tubes sown on April 22nd several heaped-up colonies appeared when the culture was about two months old. One of these was subcultured on glycerinated egg medium, and a moist dysgonic growth resulted. Another colony was lifted off and 0.01 mg. inoculated intravenously into a rabbit of 2,000 grams. Necropsy forty-three days later showed the same picture as previously, except that no prominent superficial tubercles were seen on the kidneys. These examinations were done in order to exclude the presence of human type bacilli. This sputum contained only bovine bacilli.

Sputum from the mother sown on potato and egg medium gave rise to a luxuriant growth typical of human type tubercle bacilli. In order to detect the presence of bovine bacilli, 2 mg. of pure culture were inoculated subcutaneously into a rabbit of 2,510 grams. After fourteen weeks it was killed when apparently healthy, and minimal lesions were found in the lungs. No tubercles were present in the kidneys and spleen. This sputum contained only human type bacilli.

CASE II

This case was investigated by Dr. W. M. Cumming at Bradford City Sanatorium, Grassington, Yorkshire. A miner,

aged 48, was found to be coughing up sputum containing bovine type tubercle bacilli, and the strain was isolated on two occasions in 1932. In February, 1933, sputum from his brother, aged 60, was examined, and yielded a typical eugonic strain. This was inoculated into a rabbit, which was killed when in good health two months later. Necropsy showed the typical picture of human type infection, and the strain isolated from the kidney of the rabbit was also typically eugonic.

CASES WITH PRESUMPTIVE EVIDENCE OF FAMILIAL INFECTION

In the cases reported above there was presumptive evidence of familial infection with bovine bacilli, but this was disproved by complete bacteriological examination, which showed that one member of the family was coughing up bovine bacilli alone and the other human bacilli alone. In addition to these cases there were three instances in the Glenomond series in which two members of the family suffered from tuberculosis, but where bacteriological confirmation was not available.

Case 1.—A female, aged 11, was admitted to Glenomond on May 12th, 1933, suffering from advanced bilateral pulmonary tuberculosis with cavitation. She had a gland abscess in the neck at the age of 2. A bovine organism of full virulence was isolated from the sputum on three occasions. Her mother died of pulmonary tuberculosis at home in December, 1931.

Case 2.—A male, aged 33, was admitted to Glenomond in 1933 suffering from generalized tuberculosis, and died at home in August, 1933. A bovine organism of full virulence was isolated from the sputum. A brother died at home of pulmonary tuberculosis in 1926.

Case 3.—A male, aged 31, was admitted to Glenomond in 1921 suffering from tuberculosis of spine and lupus, and died there in August, 1923. Ten days before he died he coughed up material from which a bovine organism of attenuated virulence for the rabbit was isolated. A daughter, aged 6, had excision of glands of the neck in 1926.

One of the ten cases reported by Griffith and Munro is that of a female, aged 32, who had two sisters and one brother, who died of "acute tuberculosis" several years previously.

DISCUSSION

The measures taken for the control of tuberculosis depend upon a knowledge of the epidemiology of the disease, and in the case of human type infection the mechanism of spread is sufficiently well understood to permit the promulgation of preventive measures, which are—at least theoretically—adequate. The purpose of this paper is to draw attention to a serious gap in our knowledge of the epidemiology of bovine type infections—namely, whether transmission can occur from one human being to another, or whether the condition is self-limiting and the extent of bovine type infection in man is dependent solely on the amount of tuberculosis in cattle.

At present, administrative measures designed to eradicate human tuberculosis of bovine origin are directed towards improvement of milk supply and the quality of dairy herds. The value of such is less apparent if proof of propagation of the disease from human to human is forthcoming. Of possibly greater economic importance is the danger of the introduction of tuberculosis into a clean herd by a person working among cattle while suffering from open pulmonary tuberculosis and coughing up bovine type bacilli. It is a common experience that a person who is delicate and has a "weak chest" is sent to the country and often to a farm for a "change of air." In five out of twenty-six cases of pulmonary tuberculosis due to the bovine bacillus investigated at Glenomond there was close association of the patient with cattle. If such people move about from one farm to another, as, for example, in changing their employment, the possibilities are obvious.

It is realized that the mere occurrence of familial disease due to the bovine bacillus will not prove transmission by humans unless infection from a common source is definitely excluded, and, indeed, it is remarkable that heretofore no instance of this kind has been recorded.

In the absence of proof of transmission to contacts, it is of interest to inquire whether there is any peculiarity of the bovine bacillus or of the disease produced by it which would point to a limitation of spread of the disease by infected human subjects. An outstanding feature of tuberculosis of bovine origin is the high incidence of glandular disease in children in the 0-5 years group, and the disproportionately low incidence of visceral disease in the later age periods. This disparity is not related to the virulence of the bovine bacillus, but suggests that it has a lower invasive power than the human type, so that extension beyond the lymphatic system occurs less readily and so the majority of bovine infections in childhood do not lead to late visceral disease. But when spread does occur beyond the lymphatics the organism shows a high virulence and a tendency to produce multiple lesions and in some cases a marked degree of generalization, similar to that resulting from experimental inoculation in rabbits. This combination of low invasive power and high virulence recalls the cultural characteristics of the organism, and may be in some way related to the latter. Bovine bacilli are dysgonic on all artificial media, and are difficult (as compared with human bacilli) to establish in primary culture, but by subculture they can be induced to grow luxuriantly. Their persistence and tenacity of life when once established in culture is well illustrated in the case of a mixed growth of human and bovine bacilli which, when kept in the incubator for some months, yielded only dysgonic cultures, the eugonic element having apparently died out.²

If it is not accepted that the bovine bacillus has a lower invasive capacity, and has greater difficulty in causing progressive disease in man, is there an alternative explanation of the low incidence of visceral tuberculosis in adults? It has been suggested that mutation of type occurs in the human body, so that an infecting bovine organism after many years in human tissues acquires the characteristics associated with human type bacilli, and becomes manifest as such in chronic pulmonary tuberculosis in adults. Against this it may be pointed out that the type characteristics of tubercle bacilli are remarkably stable, less than 3 per cent. showing divergence in cultural character or virulence from standard types, and no range of transitional strains is found. Further, attenuation does not appear to be related to the age of the patient. For example, a bovine strain isolated at Glenlomond from a case of hyperplasia of the large bowel in a patient aged 58 was found to be of standard virulence, and strains isolated from pulmonary cases where the personal history of tuberculosis extended over periods of three, five, and seven years were also of standard virulence. One strain was isolated from sputum on two occasions with an interval of four years between, and no alteration in virulence was found.

Another point worthy of consideration is the number of bacilli observed in the sputum of cases due to the bovine bacillus. In the earlier cases investigated at Glenlomond it was noticed that the bacilli were present in very small numbers, but this does not hold good for the more recent cases, where sputum rich in tubercle bacilli has been obtained. In one case they were present in enormous numbers, and this virus was grown from the sputum only after many attempts, although easily isolated by animal inoculation. So far as contact infection depends upon the number of bacilli thrown off in sputum, there seems to be no reason why it should not occur as easily with bovine as with human type cases.

CONCLUSION

There is no proof that spread of bovine type tuberculosis by humans occurs.

There are opportunities for contact infection under conditions similar to those which cause spread of tuberculosis due to human type bacilli.

It is suggested that the bovine bacillus has a lower invasive capacity than the human, and produces progressive disease less readily.

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ARTIFICIAL PNEUMOTHORAX

AN AFTER-HISTORY OF 113 CASES

BY

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In a recent paper on the effect of fluid complicating artificial pneumothorax the after-history of forty cases was considered in detail. These forty were exactly half the number of sputum-positive cases in which I was able to induce a pneumothorax between 1924 and 1930, and in which for various reasons refills have ceased. All cases have been followed up to November, 1933, so it is now possible to compare results (1) in forty cases that did not develop fluid and forty that did, and (2) in the total eighty cases with "successful" inductions, and thirty-three "control cases" where induction was not successful. At the time when induction was decided on, each case was allocated to a "choice" I, II, or III in accordance with the type and extent of disease, but these subdivisions have not been included in the present summary.

TABLE I.—Cases Successfully Induced: No Fluid. Still Alive

	T.B. +	T.B. - and No Sputum	Totals
Completed treatment ...	4	21	25
Re-expanded	1	2	3
Refills stopped for fresh disease in other lung	2	3	5
Totals	7	26	33

Thirty-three of the forty cases that did not develop fluid during the treatment are alive, and twenty-six of these are sputum-free or have negative sputum. Four of these had laryngeal tubercle: all four are soundly healed. Under the heading "completed treatment" are given those in whom refills were carried on for at least three years and until such time thereafter as it was considered safe to re-expand the lung. Four of twenty-five in this category are now sputum-positive; two became positive again soon after re-expansion, and in both phrenic evulsion was performed, while one of them also had sanocrysin, but both have developed signs of disease in the better lung. The other two became positive at intervals of a year and two years after the re-expansion.

"Re-expanded" cases are those where for no apparent reason the lung re-expanded during the treatment by refills. Of three such patients two again became sputum-positive; one refused any surgical intervention, and has now extensive bilateral disease; the other had severe haemoptysis, and Mr. Tudor Edwards performed thoracoplasty with such success that the patient has been symptomless and fit for work for two years.

In five cases refills were stopped because fresh disease appeared in the better lung; two remain sputum-positive;