

# HUMAN CONTAGION AND TUBERCULOUS INFECTION IN CHILDHOOD

BY

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The relative importance of heredity and contagion in the production of non-bovine tuberculosis, both in children and adults, has long been a subject of discussion. While many have sought the solution of this problem by statistical examination of the records of cases of clinical tuberculosis, the influence of exposure on tuberculous infection\*, as opposed to manifest disease, has been less frequently studied.

There are, however, indications in the earlier literature that the very high incidence of tuberculous infection, which mass investigations with tuberculin tests revealed in the apparently healthy children of the densely populated continental cities of twenty years ago, was largely attributable to contact with open tuberculosis in the home and its vicinity.

## Earlier investigations.

As early as 1909, Mantoux and Lemaire reporting 16 per cent. of reactors to tuberculin in a series of apparently healthy Paris children aged 1—2, 51 per cent. among those 2—4 years old, and 66 per cent. in the age-group 4—7, described their clinical material as 'sortant d'un milieu essentiellement misérable et fortement tuberculisé.' These authors contrast their figures with the lower percentages obtained in a better quarter of Paris. Similar findings were recorded in Lille by Calmette, Grysez and Letulle (1911), who pointed out the extreme frequency of reactors among children in towns where familial contagion was most intense. Lille was an example of such a town, and the figures given by these workers for its general population were only slightly lower than those reported by Cohn (1910) about the same time in another European city (Posen), for children who were drawn exclusively from tuberculous homes. Pollak (1911) found positive von Pirquet reactions in 96 per cent. of a series of infants under two years of age, living in tuberculous surroundings in Vienna, but his material largely consisted of sick infants brought up for treatment.

If contagion in the home is potent in producing tuberculous infection in children, a higher incidence of infection, as shewn by the tuberculin reaction, would be anticipated in children who are home-contacts† of open tuberculosis than among those who hail from non-tuberculous

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\*The term 'infection' which appears repeatedly in this paper signifies that the individual has at some time been infected with the tubercle bacillus. This does not necessarily imply that any active focus of disease is present.

†The term 'home-contacts' is used throughout this paper to denote children who have cases of tuberculosis living in their homes. It does not include children who have been exposed, in their homes or elsewhere, to tuberculous relatives, etc., if the latter do not reside with them. The term 'tuberculous households' is used in the same sense, and 'non-contacts' and 'non-tuberculous households' in exactly the opposite sense.

households. Tuberculosis, however, was rife, and the working-class population congested in many large continental cities at the time of the earlier investigations, to such an extent that a child, even though a member of a non-tuberculous household, was brought into frequent contact with tuberculous adults,—relatives, friends and neighbours,—in its home or the vicinity. The result was that, excluding infants, the risk of exposure run by a working-class child, who came from a non-tuberculous home, was not much less than the risk incurred by a child who was living in contact with open tuberculosis. Under these conditions it might be expected that, so far as the poorer classes were concerned, the direct comparison of the frequency of tuberculin reactions among these two groups of children would have led to confusion rather than to advancement of knowledge. Although we have been unable to find any continental urban statistics of this nature published at this period, the first enquiry in a large American city provides a case in point. This was a careful investigation carried out by Fishberg (1914, 1915) on a series of destitute Jewish children under 15 years of age, living in a congested tenement area of New York. These children were divided into two groups: (1) those whose parents were tuberculous, and (2) those whose homes were free of tuberculosis. The results were as given in Table 1.

TABLE 1.

NEW YORK INVESTIGATION (FISHBERG, 1914, 1915): COMPARISON OF TUBERCULIN REACTIONS IN CHILDREN WHOSE PARENTS WERE TUBERCULOUS (GRP. 1) AND IN THOSE WHOSE HOMES WERE FREE OF TUBERCULOSIS (GRP. 2).

Age	Group 1	Group 2
1—3	Positive reactions in 55 per cent.	Positive reactions in 33 per cent.
3—5	“ “ “ 69 “ “	“ “ “ 41 “ “
5—7	“ “ “ 65 “ “	“ “ “ 50 “ “
9—11	“ “ “ 71 “ “	“ “ “ 69 “ “
13—15	“ “ “ 76 “ “	“ “ “ 76 “ “
All ages	“ “ “ 67 “ “	“ “ “ 53 “ “

Fishberg, apparently believing that the slight disparity was due to a small difference in technique, was led to conclude that ‘the difference between those who lived in a tuberculous milieu and those who had no contact with consumptives in their homes, is apparently insignificant.’

Here, at first sight, might appear to be evidence against the potency of home contagion in determining infection. But investigations in rural communities, together with subsequent work in cities give a different complexion to Fishberg’s results. Jakob (1911), working in a rural district of Germany, found that practically all the children living in houses where there were cases of open tuberculosis, reacted to tuberculin, while in the other homes a much smaller percentage of reactors was discovered. Overland (1913) found that the majority of the reactors in the Norwegian villages which he investigated came from tuberculous homes. Slater (1924–25) studied the tuberculin reactions of a wealthy farming community in Minnesota. The proportion of children infected was extremely low, being only 10 per cent. for all cases under 16. When, however, his cases were divided into those who had lived in a house with an open case of tuberculosis (61 children) and those who did not give a history of exposure (529), a very marked difference in the percentage infected was revealed, 80 per cent. of the former reacting to tuberculin, as against 5 per cent. of the latter.

Slater’s figures for home-contact children in a country district are comparable with those obtained by Fishberg in some of the poorest and most congested parts of New York. On the other hand, the frequency of tuberculin reactions in non-contact children is entirely different in the two areas. The probable explanation lies in the different opportunities for making contacts. The environmental conditions of Fishberg’s clinical material were such that, except for infants,

the risk of exposure for children of the same age, whether of tuberculous or non-tuberculous households, was much about the same, and it is therefore not surprising that only a slight difference was obtained between the tuberculin reactions of the two groups. In rural districts, on the other hand, the chances of contact are relatively slight for those who have no cases of open tuberculosis in their homes, and consequently the effect of home contagion is manifested sharply by the marked disparity between the tuberculin reactions of home-contacts and of children from non-tuberculous households.

This disparity has been noted, though to a somewhat less degree, in the majority of recent urban figures. Recent investigations of the tuberculin reactions of children of the urban hospital class in Europe and America shew that the incidence of infection is much lower than that reported a quarter of a century ago in many continental cities. It is also less than that recorded more recently for children of the lowest social status, such as destitute orphans drawn from highly congested and unhygienic surroundings. This difference in incidence of infection which has accompanied the improvement of environmental conditions and the decline in the tuberculosis death rate, indicates a decreased risk of exposure. Affecting, as might be expected, the non-contact population to a greater extent than children of tuberculous households, it has allowed the influence of contagion in the home to manifest itself, even in cities, by a significant disparity in the tuberculin reactions of the two groups.

#### Recent investigations.

More recently, Manning and Knott (1915) tested 228 children under 16 in Seattle, a comparatively modern town where housing conditions were much better than in the poorer quarters of most large continental or American cities. 166 of these children were living in intimate contact with active adult cases of tuberculosis; the remaining 62 children had no history of exposure. The percentage of reactors in the first group was more than twice that found among the latter (51 per cent. as against 23 per cent.).

Bernard and Debré (1920) made some interesting observations in Paris with the von Pirquet reaction on infants aged 0—2, who had been separated from their tuberculous mothers and placed in a creche. Of 58 infants whose mothers had bacilli in their sputum, 40 (69 per cent.) were found to be infected, as shewn by a positive tuberculin reaction, while of 65 infants where bacilli had not been discovered in the mothers' sputum or where the parents were not tuberculous, only 8 reacted (12 per cent.). All the infants who had been in contact with open tuberculosis for more than six months before separation were infected, all but one of the non-reactors having been removed 1 week to 3 months after birth. On the other hand, many of the infected infants had been in contact for only a few months. The infected group was followed up in order to discover if there was any association between the duration of contact and the ultimate prognosis. 40 per cent. of the infected infants died of tuberculosis, usually in the month following separation, and even though apparently healthy at that time. The other 60 per cent. of the infected infants were well when examined 2 to 24 months after separation. The duration of contact in both the survivors and the fatal cases of the infected group was from 2 to 3 months. The authors draw the conclusion that a certain time is required for contact to produce infection, but that this almost invariably results if the duration is prolonged to about 6 months. But their further conclusion, that separation of an infant from its tuberculous mother, may, even if already infected, save its life, is not warranted by the evidence which they give in this paper, for 40 per cent. of them died, and there was nothing to show that their fate would have been better or worse had they been left with their parents. This work does, however, suggest that separation of a contact infant which is not yet infected, is, if carried out early enough, the best way of preventing infection and of avoiding the possible fatal issue of this infection.

In a later paper Bernard, Debré and Lelong (1925) report the results achieved by 'L'Œuvre du Placement Familial des Touts-Petits,' founded in Paris in 1920.† They compare the fate during the first four years of life of (a) 265 infants with negative tuberculin reactions, separated from their tuberculous parents either at birth or later; (b) 171 infants separated when already infected,\* but 'rigorously selected' according to the circumstances of their exposure; and

†A more recent account of the working of this system is given by Bernard (1927).

\*See Footnote, p. 191.

(c) 66 infected infants who remained with their tuberculous parents. The tuberculosis death rate of the first group was nil; none of them developed clinical tuberculosis or even a positive von Pirquet reaction while under observation. 17 of the 171 infants in the second group developed clinical tuberculosis which was fatal in 13 (7.5 per cent.), meningitis and pulmonary disease accounting for most of the deaths. 82 per cent. of the third group, the infected infants who were left with their tuberculous parents, are stated to have died of pulmonary or meningeal tuberculosis, the majority in the first year of life. The rationale of separation of infants of the poorer classes before tuberculous infection has occurred thus appears to have been established. The advantage of separating infants already infected seems less certain, as the 'rigorous selection' of the 171 infected children for segregation makes them hardly comparable with the 66 infected infants who remained with their tuberculous parents. Nevertheless, the contention of these writers that this is the proper course to take is supported by their statement that of 13 infected infants who had passed the 'rigorous test,' but whose segregation was refused by their parents, 8 perished. It is interesting to compare the figures of Bernard and his co-workers with those of Walquist and Myers (1925) who followed up 71 tuberculin-positive infants under 2 (21 under 1) who were attending the out-patient clinic of the Lymanhurst school for tuberculous children, Minneapolis, the majority having been brought up not because of symptoms but mainly because of exposure. 96 per cent. of these infants gave a history of exposure: 73 per cent. to tuberculous parents, 11 per cent. to tuberculous siblings, and 11 per cent. to several sources of contagion. A tuberculosis fatality rate of only 8 per cent. was recorded, which was no higher than that found by Bernard and his associates among infants who were segregated after infection. This suggests that under favourable conditions the outlook for infected infants remaining in contact with tuberculosis is far from hopeless.

Schram (1921-22) investigated the von Pirquet reactions of 300 children from tuberculous homes in a poor quarter of Oslo. He obtained positive reactions in as many as 53 % of 113 infants under 1 year of age, and found that by 8 years four-fifths were infected. The incidence of infection was higher for those whose parents had positive sputum than for those whose family contacts had negative or no sputum, or whose source of contagion was a lodger. The value of Schram's work is unfortunately seriously affected by the lack of normal controls, and by the omission of clear details as to the age of those contacts whom he found to be clinically tuberculous, for the inclusion of such cases would naturally tend to raise the proportion of tuberculin reactors. A similar want of controls occurs in a paper by Barchetti (1921), who reported 73 per cent. of tuberculin-positive reactors in a series of 51 infants of tuberculous mothers in Vienna. Roepke (1923) working in Mannheim, found that the percentage of children in tuberculous households who reacted to tuberculin was greater if the source of contagion was an advanced case than if in an early stage of the disease.

The observations of Lampton (1923) on the spread of tuberculous infection in families indicate that the incidence of infection varies with the type of the tuberculous infective agent, being higher if this is an open case than if latent or healed.

Falk (1923-24) examined 68 children under 13, whose parents had open tuberculosis: 91 per cent. gave reactions with tuberculin (6 out of 10 infants less than a year old), the percentage being 100 in the case of 20 children of fatal cases. Girls seemed more likely than boys to receive infection from tuberculous mothers.

Austrian (1924) reported the results of an investigation carried out from 1915 to 1920 at a tuberculosis dispensary in Baltimore. He found that actually fewer children aged 0-9 years who had been exposed to a known case of clinical tuberculosis reacted than those with no known exposure. The figures were 67 per cent. (241 cases) and 74 per cent. (65 cases) respectively. Drolet (1924-25) published the tuberculin reactions of 1234 children with a positive parental history of tuberculosis, and of 461 with a negative parental history. His cases were drawn from a tuberculosis dispensary in the East-side district of New York over the period 1912-1916. In the first group 48 per cent. of those under 5 years reacted, 69 per cent. of the children aged 5-9, and 78 per cent. of the age-group 10-14. The corresponding percentages for the children of non-tuberculous parents were very similar, being 47, 64 and 74. The findings of Austrian and Drolet might be construed as evidence against the importance of family contagion in determining infection. But their controls are open to the serious objection that they were apparently

all children attending a tuberculosis dispensary, to which they must have been sent because of symptoms suggesting tuberculosis to their parents, since none of them were home-contacts; whereas many, if not most, of the home-contact series had been brought up because of exposure alone. For this reason the non-contact controls would be expected to be infected to a greater extent than the general non-contact population. The statistics of Sill (1918) appear to support the validity of this objection, for they were obtained, only a few years after Drolet's investigation, among children from non-tuberculous families of the hospital class living in the same district of New York. A much lower percentage of infected children was recorded, his figures being 10 per cent. for the age-group 4—5, 16 per cent. for children aged 8—9, and 48 per cent. for those who were 10—13 years old.

Myers and Magiera (1925), working in Minneapolis, examined with the von Pirquet test 761 contacts aged 0—19 years, the majority of whom were brought up because of exposure, or for symptoms which had suggested tuberculosis to their parents. All but 12 were under 16 years of age. These were compared with 784 cases (all but 25 less than 16 years old) with no known exposure to tuberculosis. Reactions were obtained in 57 per cent. of the contact group and in 29 per cent. of the control group.

Opie and McPhedran (1926), in Philadelphia, made a careful study of the spread of infection among children exposed to a tuberculous parent or sibling, using the intracutaneous (Mantoux) test as an index of infection. As controls they used children of families in which there was no case of tuberculosis. The percentage of reactors among 272 children who were home-contacts of open tuberculosis (bacilli in sputum) rose from 80 per cent. in the age-group 0—5, to 100 per cent. at 20, while in 179 non-contact controls the percentage rose from 23 per cent. among those aged 0—5 to 100 per cent. at 20. The results are shewn graphically on Chart 1. Of 124 children, one or both of whose parents suffered from open tuberculosis, 11 were found to have manifest disease themselves. These workers noted that reactions were more frequent among children in contact with a tuberculous parent (86 per cent.) than when in contact with a brother or sister (65 per cent.). Children whose parents, brothers, or sisters, had tuberculosis without bacilli detected in the sputum shewed a frequency of positive tuberculin reactions no greater than that found among the non-contact controls (44 per cent.). They ascribed these differences to varying duration and intimacy of contact. In a similar manner Opie and McPhedran observed the frequency of latent pulmonary foci in both groups of children by radiological examination, and found that, as with tuberculin reactions, the proportion rose with age, but was higher in the home-contacts than in the controls. The same differences were noted with regard to contact with open and closed tuberculosis, except that the incidence of latent lesions among the latter was greater than among the non-contacts.

From this résumé of the literature it will be apparent that considerable caution must be exercised in interpreting the results of investigations on the influence of contagion in the home on tuberculous infection. In many instances the clinical material has largely consisted of children from tuberculous households, brought up for symptoms suggestive of, or in some cases actually proved to be, manifest tuberculosis, with the natural result that a very high percentage of reactors has been obtained. Suitable controls are essential. Not infrequently they have been omitted altogether. In some of the published series the non-contact controls were composed of children brought up on suspicion to a tuberculosis dispensary, while a large proportion of the contact cases had attended only because of exposure. This is an unfair comparison.

It is best, in order to avoid two variables, to exclude all cases of suspect or definite clinical tuberculosis both from the series of home-contact children and from the control series of non-contacts. In this manner the most accurate estimate of the potency of contagion in the home in producing infection, as opposed to manifest or clinical tuberculosis, will be obtained.

**Present London investigation.**

The present investigation comprises a study of 118 London children of the hospital class, who came from tuberculous households. They were aged 0—15 years, 94 being less than 11 years old. The majority were brought up to hospital on account of exposure, or for some non-tuberculous complaint. All suspect or definite cases of clinical tuberculosis were excluded. This series was compared with 513 clinically non-tuberculous children of the same class and district, but whose homes were free of tuberculosis. These non-contact controls were also aged 0—15 years (438 being under 11 years of age), and were tested over the same period (twelve months) in 1929, by the same observer.

Many of the home-contact cases were drawn from the contact clinic of the North Islington Tuberculosis Dispensary, under the charge of Dr. W. E. Snell. The remainder were patients under the care of one of us (B.S.) in the Children's Department of the Royal Northern Hospital and in the out-patient department of the Hospital for Sick Children, Great Ormond Street.\* The controls were drawn from the latter two sources.

TABLE 2.

COMPARISON OF TUBERCULIN REACTIONS IN HOME-CONTACTS OF  
PULMONARY TUBERCULOSIS AND NON-CONTACT CONTROLS.

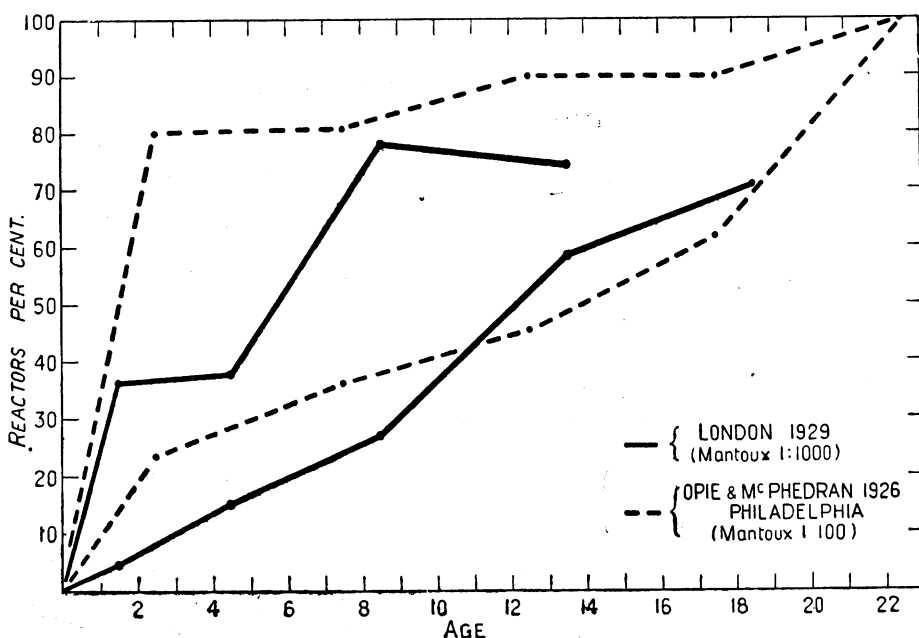
Age last birthday	Home-contacts of pulmonary tuberculosis			Non-contact controls		
	Number tested	Number positive	Percentage positive	Number tested	Number positive	Percentage positive
0—2 ... ..	11	4	36	109	5	4.5
3—5 ... ..	21	8	38	112	17	15
6—10 ... ..	36	28	78	217	58	27
11—15 ... ..	19	14	74	75	44	59
16—20 ... ..	2	2	—	28	20	71
21— ... ..	14	13	93	118	106	90
0—10 ... ..	68	40	59	438	80	18
0—15 ... ..	87	54	62	513	124	24

The intracutaneous (Mantoux) test was used, and the reaction of each case to 0.1 c.cm. of 1/1000 dilution (0.1 mgrm.) of Old Tuberculin (Burroughs Wellcome & Co.) was ascertained. The tuberculin, of which the same batch was used throughout, was put at our disposal through the kindness of Dr. R. A. O'Brien, Director of the Wellcome Physiological Research Laboratories. It conformed to the Frankfurt standard, and in addition was standardized by the intracutaneous method on guinea-pigs.

\*Part of this work was carried out while one of us (P. D'A.H.) held a Research Studentship at the Hospital for Sick Children, Great Ormond Street.

Of the 118 children under 16 years, 87 (68 under 11) were home-contacts of a relative who had pulmonary tuberculosis : in 50 of these cases (42 under 11) tubercle bacilli were present in the sputum ; in the remaining 37 cases (26 under 11) the sputum result was negative or not known. 31 children under 16 (26 under 11) were home-contacts of a relative who had non-pulmonary tuberculosis. The relatives with pulmonary tuberculosis were parents or siblings in all but four cases, where a grandparent (one case), uncle (one case), or aunt (two cases), was responsible. The relatives with non-pulmonary tuberculosis were parents or siblings, the latter predominating.

CHART I.



Tuberculin reaction of non-contacts and of home-contacts of pulmonary tuberculosis. The upper two curves are home-contacts ; the lower two curves are non-contacts.

The results of the pulmonary contacts in the different age-groups are compared with those of the non-contact controls of the same age in Table 2 and Chart I. It will be seen that, as with the curves of Opie and McPhedran, the incidence of infection increases from infancy to adolescence in both the home-contact and the non-contact series, but that the curve of the home-contacts runs above that of the non-contacts up to the age of 16. By 6 years of age half, and by 10 years three-quarters, of our home-contact series were infected, whereas only one-fifth and one-third of our non-contact controls were positive reactors at these respective ages. Similarly, by 5 years three-quarters of the home-contacts of Opie and McPhedran shewed positive reactions as compared with one-quarter of their non-contacts. In other words, most of the tuberculization of home-contacts takes place in infancy and early childhood,

i.e., in the home environment ; whereas at the present day most of the infection of non-contacts is received in middle and later childhood and in adolescence, i.e., during a period when the principal activities of the individual are away from the home. Both groups, however, are tuberculized to the same extent when adult life is reached. But the most striking difference is to be found in the shape of the two sets of curves. The home-contact curves obtained by Opie and McPhedran and ourselves rise rapidly at first, and then assume a more gradual slope ; the control curves, on the other hand, approximate to straight lines. This difference in shape is of some epidemiological interest. It indicates that the tuberculization of home-contacts has its maximum rate in infancy and early childhood, whereas the tuberculization of non-contacts occurs at approximately the same rate from birth to manhood. Such a dissimilarity is in keeping with a difference in the mode of contagion. Children in tuberculous households are subjected to contagion which is intense from birth, but children whose homes are free of open tuberculosis make their contact with the disease mainly outside the home, and with a frequency which increases as they grow up.

TABLE 3.

TUBERCULIN REACTIONS IN HOME-CONTACTS OF VARIOUS  
TYPES COMPARED WITH NON-CONTACT CONTROLS.

Group	No. tested aged 0—10	Number positive	Percentage positive
Home-contacts of pulmonary tuberculosis ... ..	68	40	59
Home-contacts of open pulmonary tuberculosis (bacilli in sputum) ... ..	42	29	69
Home-contacts of pulmonary tuberculosis where sputum result is negative or unknown ... ..	26	11	42
Home-contacts of non-pulmonary tuberculosis ...	26	4	15
Non-contact controls ... ..	438	80	18
Bedroom contacts of open pulmonary tuberculosis (bacilli in sputum) ... ..	34	24	71

Of the 68 children aged 0—10 years in our series, who were home-contacts of pulmonary tuberculosis, 59 per cent. reacted, as compared with 18 per cent. of 438 non-contacts of the same age (see also Table 3). These differences are more marked if the pulmonary home-contacts are divided into home-contacts of open pulmonary tuberculosis (bacilli in sputum), and home-contacts of pulmonary tuberculosis with negative or unknown sputum result. The percentages of children aged 0—10 in each of these groups, who were positive reactors, are compared with the non-contact controls of the same age in Table 3. It will be seen that positive reactions were obtained in 18 per cent. of the non-contact controls aged 0—10, in 42 per cent. of home-contacts of pulmonary tuberculosis with negative or unknown sputum result, and in as many as 69 per cent. of home-contacts of pulmonary tuberculosis with sputum known to contain



bacilli. This greater infectivity of open as compared with closed pulmonary tuberculosis is in agreement with the results of other workers already quoted.

The home-contacts of open pulmonary tuberculosis were next divided into those who had slept with the infective relative, and those who slept by themselves or with a non-tuberculous member of the family (Table 3). The percentage of tuberculin reactions among 34 bedroom contacts of open pulmonary tuberculosis, whose ages were 0—10, was found to be 71 per cent., a figure which is no higher than that of all the open pulmonary home-contacts together (69 per cent.). Since, however, four-fifths of the pulmonary home-contacts were bedroom contacts the statistical error of this comparison is considerable.

Comparison of the percentage of children infected when living with a parent, with that obtained when the tuberculous member of the household was a sibling, is not given, as the great preponderance of the parental contacts makes the figures of too little value.

In 26 children, aged 0—10, living with a relative (parent or sibling, the latter predominating) who had non-pulmonary tuberculosis, the percentage infected (15 per cent.), in marked contrast to the open pulmonary contacts, was no higher than in the non-contact group (438 cases, 18 per cent., see Table 3). While the numbers are small, they suggest that a positive family history of tuberculosis is only of importance in determining infection in so far as it yields a potential intimate source of contagion. If a familial inherited predisposition to infection existed, as many believe, we should expect this to be evident to some extent in children living in tuberculous families, no matter what the type of tuberculosis be. This point is of fundamental importance, and further work on a larger scale is required to decide it. If it can be shewn that children whose parents suffer, or have suffered, from non-pulmonary tuberculosis, have no higher incidence of infection, as shewn by their tuberculin reactions, than children with a negative parental history of tuberculosis, then the conception of inherited familial tendency to tubercular infection (in the sense already defined in this paper) will be rendered untenable.

In an attempt to throw further light on this problem, the non-contact controls were divided into those who had no tuberculous relatives, one tuberculous relative, and two or more tuberculous relatives. Each parent was carefully questioned on these points. The relatives include any of the following:—sibling, grandparent, uncle, aunt, great-uncle, great-aunt, great-grandparent, or first cousin—whether living or dead. It was not found practicable to classify according to the proximity of relationship. The comparisons are in any case crude, on account of the difficulty of eliciting family histories from hospital patients. The results for the children, aged 0—10, are given in Table 4. It will be seen that 22 per cent. of those with one tuberculous relative reacted, as compared with 15 per cent. who had no tuberculous relatives, while 46 per cent. of the children who had two or more tuberculous relatives gave reactions. While none of these relatives was living in the same house as the children tested (i.e., they were all non-contacts in the sense used through-

out this paper), many of them had pulmonary tuberculosis, and occasionally or frequently met the children concerned. These children, therefore, had a greater chance of becoming infected than children who had no tuberculous relatives, and who in consequence seldom met tuberculous adults. It will be noted that a smaller proportion of children with two or more tuberculous relatives, not living in the same house, were infected, than of children who had a relative with open pulmonary tuberculosis actually living with them (46 per cent. as against 69 per cent.). On the other hand, reactions were found no more frequently among home-contacts of non-pulmonary tuberculosis than among children who had no tuberculous relatives at all, the percentage being 15 in both cases.

The results which we have obtained for the infection incidence among pulmonary home-contacts are lower than those of many workers quoted (e.g., Pollak, Schram, Falk). This may be partly accounted for by the fact that we have excluded all suspect cases of clinical tuberculosis. By so doing we believe that we can obtain the best estimate of the influence of home contagion on the acquisition of tuberculous infection. It is also possible that the hygienic conditions in the homes of the children tested were better than in some investigations; this would tend to lower the infection incidence.

TABLE 4.

TUBERCULIN REACTIONS IN VARIOUS TYPES OF NON-CONTACT CONTROLS.

Children who are not home-contacts but have—	No. tested aged 0—10	Number positive	Percentage positive
2 or more tuberculous relatives* ... ..	35	16	46
1 tuberculous relative ... ..	50	11	22
No tuberculous relative ... ..	353	53	15
Total = non-contact controls ... ..	438	80	18

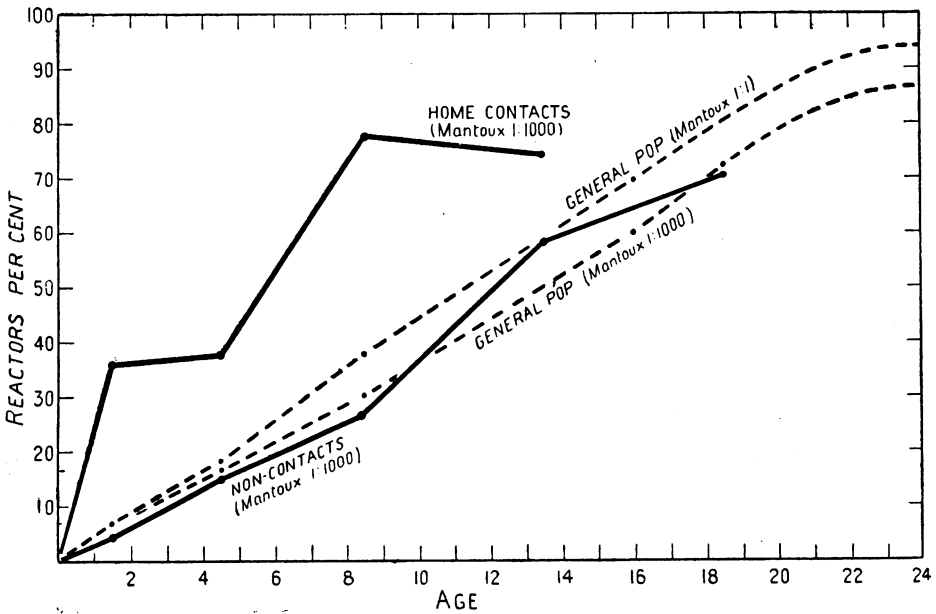
Our figures are open to at least two criticisms. In the first place the number of home-contact cases in each age-group is small, partly owing to the exclusion of clinically tubercular and suspect cases. This is admittedly true, but the statistical error is reduced by the adequate number of non-contact controls. The second possible objection is that while we have used the most delicate available test, the intracutaneous, we only give the figures for a dilution of 1/1000 tuberculin. Opie and McPhedran proceeded as far as a dilution of 1/100 before classing a patient as a non-reactor. The reactions in our control series are also given for a 1/1000 dilution. While this is the dose commonly accepted as standard by workers in this field, a significant percentage

\*Sibling, grand-parent, uncle, aunt, great-uncle, great-aunt, great-grand-parent, first cousin—living or dead.

of additional reactors may be obtained, as Schroeder (1924) and one of us (Hart, 1930) have found, if stronger concentrations are used on cases negative to the standard dilution. If this occurred with the present control series more than with our home-contacts the differences which have been shewn between them would be less marked.

As a check, therefore, on our results the following procedure was adopted. The non-contact series which we have used as controls in this investigation does not form a true sample of the clinically non-tuberculous population, because the latter naturally contains some home-contacts. The non-contact controls were, in fact, obtained by extracting all the home-contacts from a series of 751 clinically non-tuberculous subjects of all ages, who formed a fair sample of the hospital class of north and central London in 1929. We have used this original series as a check on our results. The reactions to 0.1 c.cm

CHART II.



Tuberculin reactions of non-contacts and of home-contacts of pulmonary tuberculosis, compared with tuberculin reactions of general population (hospital class) of London, 1929. All clinically non-tubercular.

of a 1/1000 dilution of tuberculin was ascertained for all the 751 cases. A random sample of those who failed to react were tested with 0.1 c.cm. of a 1/100 dilution, and so on, with 1/10 dilution, and finally with 0.1 c.cm. of a 1/1 dilution (100 mgrm.). By this means the full sensitiveness of the intracutaneous method was brought into play, and by adjustment the reaction of all the 751 cases to a 0.1 c.cm. of a 1/1 (i.e., undiluted) tuberculin, which is the maximum intracutaneous dose, (100 mgrm.), was ascertained. The figures are not tabulated here, but those for 1/1000 dilution and for undiluted

tuberculin are plotted as curves and shewn on Chart II. The latter curve represents the maximum frequency of tuberculin reactions in the clinically non-tuberculous hospital class of London in 1929. Both curves, as expected, run above that of the non-contact series tested to 1/1000 dilution, but nevertheless both are much lower than the home-contact curve for 1/1000 dilution, shewing that the difference found between the latter group and non-contact cases is not a chance disparity nor due to insufficient dosage.

### Discussion.

We are now in a position to discuss the relative significance of heredity and contagion in determining tuberculous infection, as opposed to tuberculous disease, i.e., clinical or manifest tuberculosis. This distinction is vital to the present issue. That the factors are not the same in the two cases is strikingly shewn by comparing the statistics of the mortality rate of tuberculosis with those of the incidence of tubercular infection. The incidence of infection in urban populations rises from birth to adult life, as shewn on Chart 2 for London. On the other hand, the mortality rate of tuberculosis is high in infancy, falls rapidly after 2 or 3 years of age, remaining low in middle childhood; it rises again in adolescence to a high plateau in adult life (Registrar-General, 1927, 1928, 1929; Census of England and Wales, 1921). Thus in middle childhood, although infection is occurring as fast as at other ages, the mortality from tuberculosis is at its lowest.

It is believed by some that children with a strong family history of tuberculosis are more likely than other children to acquire tuberculous infection, because of an inherited predisposition, although contagion must finally determine this infection. According to those who hold this view, if two sets of children, one with a strong tuberculous ancestry, the other free of this taint, are exposed to the same infective agent, the former is more liable to become infected than the latter. There are several reasons for rejecting this view.

(1) The conception of familial diathesis is unnecessary. Children from tuberculous households have, as shewn in this paper, a much higher incidence of infection than those whose homes are free of tuberculosis, this being greater when the tuberculosis is active or open than when it is closed or healed. The severer the condition, the more likely is infection to take place. Children with a tuberculous parent or sibling living in their home are more frequently infected than those whose tuberculous relatives visit them occasionally; the latter more frequently than those who have no tuberculous relatives at all. All these findings are satisfactorily explained by variations in frequency, intimacy and duration of contact, without having recourse to a belief in hereditary predisposition.

(2) The percentage of tuberculin reactions among children exposed in tuberculous households to parents, brothers or sisters with non-pulmonary tuberculosis appears to be no higher than among children of non-tuberculous

households ; nor does it even exceed the frequency of tuberculin reactions found in those who have no tuberculous relatives at all. An inherited familial tendency to tuberculous infection should be evident, to some degree, in children living in tuberculous families, whatever the type of tuberculosis. But our figures (though the number of cases is small) suggest that a positive family history of tuberculosis is of importance in producing infection only in so far as it yields a potential intimate source of contagion in the shape of an open pulmonary case. Further work on a larger scale should decide this matter.

(3) Infants intimately exposed to a tuberculous individual who is not a member of the family rapidly acquire infection. Schloss, Holt and others have described this in the case of nurses. Schloss (1917) found that all but two of the infants in a ward where there was a nurse who had advanced tuberculosis, were infected, and gave positive tuberculin reactions. The two non-reactors were breast-fed by their mothers. In another ward where this nurse had only been temporarily, one-third of the infants were infected. Opie (1927) quotes Holt, who cites the case of ten infants infected within 14 months by a tuberculous midwife who used the mouth-to-mouth method of artificial respiration in the new-born.

(4) Infants separated from their tuberculous parents before infection has occurred, and placed in other families, appear to be no more liable to acquire infection in early life than infants of non-tuberculous parents.

We believe that the simplest view of the spread of infection in children of tuberculous families is as follows. Children with a strong family history of tuberculosis are more likely to become infected than other children, only because of the increased chance of contagion from an open case of pulmonary disease. This risk is naturally greatest if the patient lives in the children's home, and least when he only visits them occasionally. If the tuberculous relative has never seen the children, or is suffering from healed or non-pulmonary tuberculosis, they are, we suggest, no more likely than other children to become infected. We believe, further, that if two sets of children, one with a strong tuberculous ancestry, the other free of this taint, are exposed to the same infective agent, both are equally liable to acquire infection. Such a view is not inconsistent with a conception of heredity as a determinant of the subsequent course of this infection once it has taken place. The consideration of this matter, however, is beyond the scope of this communication.

#### **Practical conclusions.**

We believe that the facts presented in this paper, and the subsequent discussion, have a practical bearing on the prevention of tuberculosis, for they justify or suggest definite lines of action, some of which are already in force in this and other countries. It is clear that the system of allowing infants to remain with tuberculous parents, as practised in England, is the unnecessary cause of the loss of many lives. The recent careful study of the Lancashire Group of Tuberculosis Officers (1929) emphasizes this point. These

workers found that the tuberculosis death rate of 1,500 young children in tuberculous households in that county greatly exceeded that of the general population of Lancashire, which formed a control. The death rate from non-pulmonary tuberculosis (meningitis in two-thirds of the cases) among children living with an adult with positive sputum, was nine times greater in the age-group 0—1, fourteen times greater in the age-group 1—2, and nineteen times greater in the age-group 2—5. The actual tuberculosis death rate for children under 2 years of age in tuberculous households in which an adult relative had pulmonary tuberculosis (open or closed) was 1·7 per cent. ; and 2·5 per cent. where the adult was the mother, and had a positive sputum. The substantial majority of these infants remained in contact with the tuberculous adult in their homes, except during the several months' institutional treatment undergone by some of the latter. Assuming, for the purpose of argument, that the figures which we have given for the frequency of tuberculin reactions among infants in tuberculous households, in which a relative has pulmonary tuberculosis (Table 2), to hold good for Lancashire, about a third of these infants, under two years of age, are infected. This would give a tuberculosis death rate of 5 per cent. to 8 per cent. for infected infants under two in tuberculous households of Lancashire, figures which are of the same order as that (8 per cent.) found by Walquist and Myers for contact infants under 2 years of age who were known to be infected. It is interesting to compare the fate of children in tuberculous families noted by the Lancashire Tuberculosis Officers with that reported for the Papworth Colony by Varrier-Jones (1927). He states that there has been 'a complete absence during 11 years of clinical tuberculosis in the 133 children of men and women who are definite cases of the disease and in most instances show tubercle bacilli in the sputum from time to time.' Whether the superior environmental and hygienic conditions of Papworth produce this result by diminishing the risk of massive and repeated infection, by influencing the course of the infection, or by preventing it altogether, it is impossible to decide without knowledge of the tuberculin reactions of the children in the colony. The researches of Bernard and his co-workers, already mentioned, suggest that each of these factors may play a part.

From Varrier-Jones' statement the Papworth system would appear to prevent the spread of tuberculosis in families. As an alternative, while prophylactic immunization (Calmette, 1928) is still on trial, the most effective preventive measure would be to separate infant from parent before infection has taken place. The Grancher system, when applied to uninfected infants for a period of several years, appears to be successful in France (Bernard, Debré and Lelong, 1925 ; Bernard, 1927). If infection has already occurred, as shewn by a positive tuberculin reaction, the value of separation is less certain, and it is possible that as much can be done by supervision at home. The present short period of separation during the institutional treatment of an adult is shewn from the Lancashire study to be totally inadequate.

**Summary and conclusions.**

1. Tuberculin reactions are more frequent among children of tuberculous households than among children whose homes are free of tuberculosis.

2. Children living with a tuberculous parent or sibling shew tuberculin reactions more frequently than children with tuberculous relatives who do not live with them ; and the latter more frequently than children with no tuberculous relatives.

3. A larger percentage of reactors is found among children who are living with a relative suffering from open tuberculosis than when the tuberculosis is closed.

4. These findings are adequately explained by variation in frequency, intimacy and duration of contact, without assuming the existence of inherited predisposition.

5. In a small series of children, living with a parent or sibling who had non-pulmonary tuberculosis, tuberculin reactions were no more frequent than among children of non-tuberculous households, and children with no tuberculous relatives at all. If further work, embracing a larger number of cases, confirms this finding, the view that children of tuberculous ancestry inherit a predisposition to tubercular infection will be rendered untenable.

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