Chapter III

Comparison of the Groups (continued)

Section D.

It appears likely that part of the differences observed in Table 4 (see Chapter II) could be explained by differences between the mean ages of the four Groups with a consequent loading of contact histories among the older Group of patients, and it is necessary to make a correction for this. Observation has shown that the greater bulk of patients in each Group occurs between 18 and 23 years. If this portion of each Group is compared with the same portion of the other Groups, the results obtained would be free from any bias due to this factor.

Table 5 shows the data for patients in the four Groups who were 18 to 23 years old in 1950 when this material was gathered. By taking moving averages in groups of three, it is possible to determine (a) the proportion of 18 to 23 years old patients in each group with a positive contact history, and (b) the average number of contacts per patient in each group. These points have been studied already in columns 4 and 5 of Table 4 (see Chapter II), but now being studied with a correction for the differences between the ages of the groups. The results are shown in Figs. 1 and 2.

From Fig. 1 it may be concluded firstly that 1 out of 4 patients of Group D reveals a positive contact history, while 1 out of 3 in Group A, 1 out of 2 in Group C, and 2 out of 3 in Group B do so. It would appear therefore that after passing through primary tuberculosis (Group A), further contact with tuberculous persons may be necessary in order to acquire post-primary tuberculosis (Group B); it will be shown later that this may well be a false deduction. Secondly, it is noted that the trends of the graphs of Groups D and A are similar, and the trends of Groups C and B are similar.

Now, on general grounds, we may accept that everyone makes more and more contacts with tuberculous persons as one ages, but at what rate is uncertain. The gradients of the graphs of Groups D and A are both 0.026 rise per year. Two hypotheses are possible from this: (a) if this value is applicable to the population at large, then everyone will have made contact with one tuberculous person by 38½ years. Since the annual tuberculin conversion rate was about 3 per cent in 1950 (Springett 1952), the population should show in theory 100 per cent conversion by 34 to 36 years. This conclusion is supported by Heaf (1946). My calculated value of 38½ years for 1950 from different data is quite close to Springett's value. Thus the gradients of the graphs of Groups D and A could be representative of the population at large; and (b) assuming that the rise of 0.026 per year starts at birth, the expected level at 18½ years should be 0.488, and at 21½ years, 0.559 (Fig. 1). This does not agree with the graph.
of Group D. It must be noted, however, that 1950 is an instant in a lifetime, and, while the population starts life in a healthy state, some people enter Groups A, C and B earlier than others, while the others remain in Group D. It may be valid therefore to deduce further that, while a contact history rate of 0.026 per year is consistent for the population at large, if an individual is to remain permanently in Group D (healthy soldiers), then either his contact history rate must be roughly half of the above figure (i.e. 0.013 per year), because the observed level of the graph of Group D is almost half that of the expected level, or, what is more likely since the greater bulk of the population is healthy at 20 years, a history of contact with tuberculous persons does not start until several years after birth (about 12 years). It will be shown later that this is the case, and this result is also in agreement with Springett (1952).

Thirdly, the graphs of Groups C and B show a fall in the older age groups when a continued rise would be expected. However, the more severe grades of patient expected in Groups C and B were probably excluded from military service in the first place, but this implies that these patients with severe grades of chronic non-tuberculous chest diseases as well as those with severe post-primary tuberculosis would yield a high proportion with positive contact histories. The average levels of the graphs of Groups C and B in Fig. 1 in relation to the other graphs support this suggestion.

Fig. 2 shows that the average number of contacts per patient of Group D (healthy soldiers) is nearly 0.33 and remains level, while for Group B (post-primary tuberculosis) it is nearly 1.0 and also remains level. Groups A (primary tuberculosis) and C (non-tuberculous chest conditions) occupy an intermediate position, run very close to one another, and take a declining course. Several points can be made from these results: first, the primary tuberculosis group (A) shows a mean of 0.7 contacts per patient. It is almost axiomatic that in order to acquire primary tuberculosis it may be necessary to contact one tuberculous person, but it is equally true that primary tuberculosis need not necessarily appear having contacted that tuberculous person; the fact that Group A falls short by 0.3 of 1.0 contact per person does not invalidate the series. Second, the trend of the graph of Group A is contrary to expectation in
that more contacts per person are made between 19 and 20 years than between 20 and 22 years. This may be explained by the fact that primary tuberculosis tended to occur at this period among the 19 to 20 year olds after an episode of relatively heavy contact with tuberculous persons, and remembering that the greater bulk of this group suffered from pleurisy with serous effusion. Third, the graph of the non-tuberculous chest disease group (C) shows an unusual trend. It tends to confirm that this is a heterogeneous group not only in respect of their non-tuberculous chest conditions but also in respect of their natural history of tuberculosis. The graph suggests that some of the patients are similar to those of Group D (those with doubtful M.M.R. abnormalities which were not substantiated later, those with a negative tuberculin reaction, and those with miscellaneous conditions with no tuberculous connection), and that others are on the verge of entering Group B (mainly the 18 years old patients), and that others have had their primary complexes (as is known from their X-rays and tuberculin reactions). Fourth, the average number of contacts among the post-primary tuberculosis group (B) is highest of all and remains level at nearly 1.0 contact per person. It is distinctly higher than the graph of the primary tuberculosis group (A), and this suggests that a number of contacts are made after having had primary tuberculosis and before the post-primary disease ensues. These fresh contacts could be important in establishing this fresh disease. On the other hand, the opposite may be argued, because the average number of contacts per patient in Group B does not exceed unity which is the minimum necessary in order to acquire primary tuberculosis. Is the appearance of post-primary disease determined partly therefore at the time of the primary infection? Fifth, it is interesting that the two groups of patients which in nature form the extremes of the natural history of tuberculosis (Group D composed of healthy soldiers, and Group B patients with post-primary tuberculosis) should exhibit graphs which are virtually horizontal. This finding suggests that the maximum average number of tuberculous persons which one may contact and remain healthy is 0.35 (rather a theoretical figure), while the minimum average number of tuberculous persons which may be contacted in order that post-primary tuberculosis may result is 1.0 (a more practical figure).

Summary of these findings suggests that the difference in contact histories noted in col. 4 of Table 4 (see previous article), and the difference in the number of tuberculous contacts encountered (col. 5) remain significant after making allowance for the differences in the mean ages of the four groups. It would also suggest that after having had primary tuberculosis, further contact with tuberculous persons is made before post-primary tuberculosis results. Are these further contacts responsible, however, for producing further disease?

Section E.

Since one of the main purposes of collecting this material has been to make a further study of contact histories in tuberculous and non-tuberculous persons alike, the histories of these patients were taken in fairly complete detail. This allows me to date the start of each individual known contact by each soldier with reasonable certainty. It can be assumed therefore that the graphs presented in Fig. 1 are the results to date (i.e. 1950) of the various contacts made from birth onwards by the
soldiers who were 18 to 23 years old then. But by what route, and at what pace have these graphs been formed? Study of each soldier's contact history allows me to decide how many contacts had been made from birth until 6, 11, 14, 17, 18, 19 and 20 years later. Fresh graphs can be produced at these periods for each of the four disease groups, but for ease of interpretation each graph is represented in Fig. 3 by a point, and the points referring to each disease group have been linked together. Several points arise from this figure.

While it appears likely that all four Groups were part of a homogeneous group up to the 10 to 12 years period, it may be important to note that even here the primary tuberculosis Group (A) and the post-primary tuberculosis Group (B) show a higher proportion of patients with a positive contact history than do the other two Groups. Beyond this period, the primary tuberculosis Group (A) remains close to the healthy control Group (D) until 17 years and thereafter it deviates sharply. Fairly intense contact with known tuberculous persons is therefore being made from 17 years until 20 years when the primary complex or some complication of it, e.g. pleural effusion, becomes apparent. It is clear that increasing contact with tuberculosis can be made for almost three years before the disease is acquired, at 20 years of age. It will be recalled that four patients (see Group 5 in Chapter I) showed healed primary complexes. This number in a total of 70 patients with primary tuberculosis of varying activity will not seriously affect the trend of the graph of Group A. Indeed, Group A is the logical group for these four patients, and activity or inactivity matters little in these discussions. A point of more importance, however, which ought to be mentioned here is the reliability of the clinical assessment of the patients with primary lesions. The relationship of the results of Group A to those of the other groups as shown in Table 4 and in Figs. 1, 2 and 3 suggests (a) that the criterion of accepting into Group A only those cases which were manifestly apparent as primary lesions has been reasonably accurate, and (b) that, while a few dubious primary lesions may have been placed in Group B, no case of post-primary tuberculosis appears to have been placed in Group A erroneously.

The post-primary tuberculosis Group (B) shows a graph in Fig. 3 with the same gradient as the graph of Group A, but starting to rise about the age of 13 years. I assume that when the Group B graph reaches at 17 years the height which Group A attained at 20 years (i.e. 0.384) the majority of patients in Group B will be passing through the phase of primary tuberculosis. The period between 17 and 20 years is the time in which they develop post-primary tuberculosis, and it is noteworthy that the gradient of the graph does not show any tendency to alter during this period, until the twentieth year when there is a slight falling off. Thus further contacts are being made, as has been shown already, but at the same rate as before the period of primary infection. If the graph had flattened in this period, support would have been given to the theory of endogenous exacerbation of the primary focus and its sequelae; that is to say that further contacts were unnecessary for the appearance of post-primary tuberculosis. If the graph had climbed more steeply, support would have been given to the theory of superinfection. The present finding is capable of three interpretations:

(1) that both endogenous exacerbation and superinfection occur;
(2) that neither method is responsible for post-primary tuberculosis; or

(3) that both methods are responsible for post-primary tuberculosis.
(3) that, regardless of (1) or (2) above, the gradient is an indication of smouldering relatively localized community epidemics. That is to imply that the contacts met during the 13- to 17-year period were responsible both for the primary disease which progresses in the Group B patients without halt to post-primary tuberculosis, and also for the disease appearing in the new contacts met between 17 and 20 years. Should this be the case, it is incorrect to call these latter persons "contacts."

Explanation (2) above is unlikely, and (1) and/or (3) appears to be correct. The slight tendency for the Group B point at 20 years (Fig. 3) to flatten out could be due partly to the patient being admitted to hospital so that he now begins to lose possible contacts, and partly to the fact that each patient is unlikely to be aware at this time of all likely contacts which he has encountered recently because they only become fully apparent some months later once they are diagnosed.

The gradient of the graph of Group C occupies a position intermediate to that of Group D on the one hand, and to those of Groups A and B on the other. This lends further support to the view that Group C is heterogeneous as far as tuberculosis is concerned, as well as with regard to their non-tuberculous disease. Further still, nearly all graphs which are represented by single points in Fig. 3 assume a more or less horizontal course, but the graphs of the points relating to Group C at 17 years to 20 years take a downward course from left to right across the other graphs which help to compose the lines for Groups A, B and D. It may be deduced from these later graphs of the course of Group C, as was concluded from earlier information, that while a few patients in Group C are healthy, some are free from tuberculosis,

![Graph](http://jramc.bmj.com/)

Fig. 3
some are on the verge of developing primary tuberculosis (i.e. resemble Group A), and some are on the verge of post-primary tuberculosis (Group B).

Similar graphs have been constructed for the retrospective incidence of the number of contacts per patient, based on the results given in Fig. 2, and the same trends have been noted. These graphs have not been reproduced here. In particular, the individual graphs of Group C at 17, 18, 19 and 20 years are very oblique, running downwards from left to right, and cutting across the graphs of the other groups which tend to remain horizontal throughout.

Discussion—Part I

Table 4 (see Chapter II) shows that the contact history of those with primary tuberculosis (Group A) is not overburdened by contact with known tuberculous persons. This is contrary to many publications (Blacklock 1947; Kayne 1935). It is not unreasonable, however, since the ages of these patients range from 16 to 32 years. Tuberculosis is a universal disease and the majority in Great Britain has experienced its primary infection by 35 years. It is impossible to expect everyone to yield a history of heavy contact with tuberculosis within the family or elsewhere. Many publications infer that the earlier in life a person acquires primary tuberculosis, the more ought suspicion to be placed on the person’s close associates. Primary tuberculosis is merely an incident in other people’s lives and often passes unnoticed. This series differs from previous reports because the latter show a significant contact history among those with primary tuberculosis (Israel et al. 1941; Lloyd et al. 1936). The present series, however, was derived from youths who were healthy recently and who had passed rigorous medical examinations before call-up. Further, it is recognized that the average age over which tuberculin conversion occurs naturally is rising gradually (Dawson of Penn 1941; Daniels et al. 1948; Hart 1932; Heaf 1946; Springett 1952), and, as pointed out above, the later in life at which this episode occurs, the less chance will there be of finding the probable source of infection, and therefore of Group A revealing a mean contact history rate which differs significantly from that of the healthy soldiers (Group D).

Next, the results of the post-primary tuberculosis Group (B) in Table 4 suggest strongly that contact with tuberculous persons is important in acquiring post-primary disease. The significance of the results is not abolished by making an allowance for the difference in average ages (Figs. 1 and 2). The possibility must be considered that the results could be due to patients of Group B knowing that they had tuberculosis, and therefore to them having searched their memories more thoroughly than the patients of the other groups. If this were the case it would be reasonable to expect the patients of the primary tuberculosis Group (A) to do likewise, for they too were tuberculous, and being laymen, it is unlikely that they could make any satisfactory differentiation in their own minds between primary and post-primary disease. That Group A failed to show this tendency suggests that the above surmise is invalid.

A further feature, shown in Table 3 (see Chapter II), is that only 3 years separates the average ages of the primary and post-primary tuberculosis Groups (A and B), and the difference between the mean periods of military service is 2½ years. Three years is a very short period in the history of tuberculosis, and it has to be considered
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how post-primary tuberculosis is related to primary disease. The proximity of the mean ages of these two groups is as important a finding as the finding that Group B gave a greater number of patients with a contact history. These two results tend to be self-contradictory, but Fig. 3 helps to explain them. Previous workers, observing similar results, have been content to state that further contact with tuberculous persons following primary infection favours the development of post-primary tuberculosis. However, Fig. 3 shows that Group B reveals a greater proportion of patients with a positive contact history at 20 years because these patients entered a tuberculous environment at an earlier age than did those of any other Group. The graph suggests that this occurred about 12 years of age (i.e. the year 1942). This is important for, in conjunction with the other graphs, it suggests that Group B experienced its primary infection about 17 years (this age being the point where the graph of Group B attains the present level of Group A), while for Group C it was 18½ years, and for some soldiers of Group D it will be 22 to 23 years.

Beyond this age of 17 years the graph of Group B continues to rise on the same gradient. Two possible explanations for this were detailed earlier; firstly, that superinfection and endogenous exacerbation both occur, and secondly, that the gradient of the graph is an indication of minor smouldering epidemics in various communities. The latter possibility is an attractive one, for there is not only a 3 to 4 year build-up of background contacts between 12 to 13 years and 16 to 17 years when the primary infection is thought to have occurred, but there is a 3 to 4 year interval between the primary infection at 16 to 17 years and manifest post-primary tuberculosis at 20 years (5/12 of which was discovered by M.M.R., and was relatively asymptomatic). There is also a 3 to 4 year interval between the onset of significant contact histories in the primary tuberculosis Group (A) compared with the post-primary tuberculosis Group (B), (i.e. 17 years compared with 12 to 13 years respectively). Under these circumstances it would seem more likely that post-primary tuberculosis is a sequel to the primary infection, although my results do no more than suggest that this is so. This does not exclude the possibility of superinfection being the method of acquiring post-primary disease in individual instances. The two explanations suggested above are compatible with one another, and each may be partly responsible for producing the graph.

(To be concluded, with references)
Table 5. Number of Patients, Positive Contact Histories and Number of Contacts.
18 to 23-year-old Patients of the Four Experimental Groups.

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<th>GROUP B</th>
<th></th>
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<td>No. with Contact History</td>
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<td>225</td>
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</table>

Notes: (a) Figures in **bold print** refer to number of contacts.
(b) Figures in ordinary print refer to patients.
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