RESULTS OF RE-EXAMINATION BY MASS RADIOGRAPHY

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It is generally known that in England and Wales at the present time the maximum rate of mortality from tuberculosis occurs late in life for males, whilst in females the greatest mortality occurs in young adult life. There is little evidence of the source of these fatalities in later life in males : are they associated with a high attack rate of new disease in this period of life or are they due to breakdown of lesions acquired perhaps two or three decades previously ? This analysis of mass radiography results was undertaken in the hope that some evidence of relative attack rates at different periods of life might be obtained.

Methods

During 1946 it was noticed that a considerable proportion (one-third) of persons attending a particular mass radiography unit in London had previously been examined by the same unit. It was a routine practice to note the fact of previous examination at the unit, so that it was possible, by having the record cards specially re-scrutinized, to obtain in age groups for each sex the numbers who had previously attended the unit. *X*-ray examination by other mass radiography units or elsewhere was not noted as a routine, so that individuals previously *x*-rayed elsewhere are included in the " not previously examined " group.

It was possible similarly to classify the patients with tuberculosis recalled for medical interview into those who had and those who had not been previously examined at the unit, and, by relating these figures to the numbers *x*-rayed, to obtain the incidence of tuberculosis in the two groups " previously examined " and " not previously examined." When a tuberculous lesion requiring investigation was found in a person who had been previously examined the recorded result of that previous examination was obtained and, if normal, the miniature film was re-scrutinized. Thus, these cases were further classified, either as radiologically new or as previously present. The mean interval between examinations was also estimated from the records : from this and the number of cases developing in a group of known size it is possible to calculate an " annual attack rate "—that is, the number of new cases occurring per annum per 1,000 at risk—in various age and sex groups. This annual attack rate is then compared with the annual mortality rate and with the incidence of disease found at first examination by mass radiography.

For my convenience the period of study was originally made to coincide with the period for which minimal lesions found by this unit were being recruited to the Prophit Survey (January, 1946, to April, 1948, for women ; January, 1946, to October, 1948, for men). Subsequently, further analysis was carried out so that the results of re-examinations of males in 1949 are included. The present paper deals not only with minimal lesions but with all tuberculous lesions found and considered to require clinical investigation after large-film reporting. All such cases have been reviewed and categorized either as " active " or " stable." For the purpose of this analysis " active " includes all cases showing, within an observation period of six months : (1) cavitation, (2) radiological progression, (3) isolation of tubercle bacilli, or (4) symptom-complex and/or signs of active disease : the presence of one or two commonly found symptoms such as cough did not lead to classification as " active."

Cases classified as " stable " either showed none of these features in a six-months observation period or, in a few cases, were classified as inactive on the result of the initial clinical examination. Although cases showing regression within six months are strictly active, for the present analysis they have been included in the stable group.

The mass radiography unit concerned is a static one examining Civil Servants in the London region. Most are clerical workers, though some are Post Office workers, and a few industrial Civil Servants are also examined. The exact percentage attending from any one office or group of offices is not known from unit records, but it is understood to be low, probably less than 50%. It follows that there has been no real clearing of possible sources of infection at places of work, as might occur at repeat examinations of a factory to which a unit went regularly and obtained a high percentage of attendances.

The procedures so far outlined can give no information concerning individuals who, after a normal examination, develop clinical tuberculosis and so are prevented from reattending. Very full records of all cases of tuberculosis in Civil Servants, leading to absence from work, have been kept since 1946 by the Treasury medical adviser's department. By the courtesy of that department it has been possible to have these records compared with the files of the mass radiography unit for the years 1943–9, and so to obtain information about cases developing symptomatically after a normal mass radiography examination.

Results of Repeat Mass Radiography of Previously Normal Individuals

Males

The results are shown in Table I. It is unfortunate that such comparatively small numbers were re-examined in the 15–24 year age group. The majority

TABLE I.—*Results of Re-examination by Mass Radiography of Males Previously Normal. January, 1946, to October, 1948, and January to December, 1949*

Age (Years)	No. *X*-rayed	New Tub. Lesions		Active Initially or Within 6 Months	Stable 6 Months
		No.	No. per 1,000		
15–	2,531	12	4·7	7	5
25–	9,325	26	2·8	16	10
35–	8,119	17	2·1	4	13
45–	10,575	18	1·7	10	8
60+	925	0	0	0	0
Total	31,475	73	2·3	37	36

in this group were, in fact, over the age of 20. The reason for the small numbers is, of course, the absence of these young men on military service until well into 1946–7. On the small total available the incidence of new lesions of 4.7 per thousand in this age group is significantly greater than the incidence of 1.7 in the age group 45–59 years ; the difference between age groups 15–24 and 35–44 years is just not significant. The

incidence of 2.8 per thousand in the 25–34 year age group does not differ significantly from that in the younger age group nor from those in the older age groups : the steady decline in incidence with increasing age would seem a valid observation. The number of these cases giving evidence of activity or remaining stable for six months is also shown in Table I. There does not appear to be any constant relationship with age, and the cases are more or less equally divided between active and stable.

Females

Table II gives corresponding results for females, though covering a shorter period of time. Adequate numbers have been examined in the younger age groups, but the totals are small in the older age groups. The

TABLE II.—*Results of Re-examination by Mass Radiography of Females Previously Normal. January, 1946, to April, 1948*

Age (Years)	No. X-rayed	New Tub. Lesions		Active Initially or Within 6 Months	Stable 6 Months
		No.	No. per 1,000		
15–	4,966	34	6·8	18	16
25–	6,062	26	4·3	10	16
35–	2,575	3	1·2	0	3
45–	1,374	1	0·7	0	1
60+	36	0	0	0	0
Total	15,013	64	4·3	28	36

age group 15–24 years includes a considerable proportion under the age of 20, so that this group is not comparable with the corresponding male group. There is, again, a sharp decline in incidence of newly appearing disease with increase of age, from 6.8 per 1,000 at age 15–24 years to about 1 per 1,000 at ages 35 and over.

Only in the 15–24 year age group do the active cases outnumber the stable ones. Over the age of 34 years no new cases showing signs of activity in the six-months observation period developed in nearly 4,000 individuals examined.

Annual Attack Rates

The interval between the mass radiography examinations varied greatly. In a few cases it was less than one year ; in a few it was as great as five years. For a sample of 850 women and 550 men attending for a repeat examination in 1946 or the first half of 1947 the interval from their previous examination was determined by re-scrutiny of both the relevant record cards. The age distribution of the sample agreed closely with the age distribution of the total, indicating that in this respect at least the sample was representative. The percentages of the sample reattending at various intervals

TABLE III.—*Percentage Distribution of Intervals Between Examinations*

Interval (Months)	Female (%)	Male (%)
–15	41·0	35·5
–21	25·5	35·5
–27	10·5	12·5
–33	11·0	8·0
34+	12·0	8·5

are shown in Table III for men and women separately. The mean interval was 22.1 months for women and 19.1 months for men.

The difference in the means for men and women is not unexpected, as during 1943 to 1945 many of the younger men were in the Forces and were able to come to this unit for the first time only after completion of service. The inclusion of late 1947 and 1948 and 1949 cases in the sample would tend to increase this difference between the sexes, and for the whole material it is probable that the mean observation period is of the order of two years for women and one and a half years for men. If these figures are accepted as the best available approximation, and applied to those in Tables I and II, then annual attack rates of the order of 3.5 per 1,000 for women at age 15–24, 2 per 1,000 at age 25–34, and 0.5 per 1,000 over that age are obtained. Corresponding figures for men would be 3 per 1,000 at 15–24, 2 per 1,000 at 25–34, falling to 1 per 1,000 at 45–59. These rates must be regarded as low estimates, since cases developing symptomatically are not included.

Cases Developing Clinical Pulmonary Tuberculosis after Normal Mass Radiography

When the records of the Treasury medical adviser's department were compared with those of the mass radiography unit, a further 29 cases were found which had developed clinically manifest tuberculosis after a normal mass radiography examination. It is, unfortunately, impossible to obtain attack rates from these cases, as there are too many unknown variables—individuals might not have reattended for mass radiography ; the population covered by the Treasury medical adviser's records is not exactly coextensive with the population examined by the x-ray unit. Some cases may have developed in individuals who left the Civil Service after a normal examination at the unit ; if so, there is no method of obtaining information about them, and to this extent there is a possibility of error in the following paragraphs.

However, the age and sex distribution of the 29 cases is of interest. In females 12 cases occurred at age 15–24, six at age 25–34, and none over that age. In males four cases occurred in the age group 25–34 years, three in each of the next two older age groups, and none over the age of 60. Only one case developed in the 15–24 year age group, but, as already noted, few young men of this age had been examined by the unit.

Although it is not possible to calculate attack rates from these cases the age distribution is essentially similar to that given by the mass radiography cases (Tables I and II). The annual attack rates derived from these tables are too low, but even from this small number of cases developing symptomatically it is most improbable that such cases would alter the age and sex relationship shown by the attack rates calculated from the mass radiography results.

The interval between the normal mass radiography examinations and the onset of clinically manifest disease in these cases is of interest, as it has been suggested by some that the onset of tuberculosis is usually sudden and hence that mass radiography is of little value. In females three cases developed within one year, nine in the course of the second year, three in the third year, and three after longer intervals. For males the figures were : one case in each of the first two years, five cases in the third year, and four after a longer interval. Again there are too many unknown factors to calculate attack rates for the various years, but, from the method of working, the numbers at risk in later years cannot be greater than in the first year and are likely to become less in each successive year. These results suggest that, while some cases do undoubtedly occur shortly after a

normal chest *x*-ray film, there is a period of lowered incidence of clinically manifest disease after mass radiography, extending over a period of one year for females and over the first two years for males. The difference between the sexes may be largely due to the fact that the males examined by the unit are on the average older than the females.

Cases Showing Abnormality at Both Examinations

When re-scrutinizing the earlier miniature films of cases known subsequently to have developed tuberculosis a very strict standard was observed, as the main object was to obtain a valid attack rate of new lesions. Twenty miniature films were regarded as possibly showing lesions on which the original interpreter had made no comment—13 in women and 7 in men. All 13 women were under 35 years old, and fully half of them were reasonably passed as normal. The addition of a further six or seven cases as "new lesions" would still further increase the differences in attack rates between young adult and older females. The seven male cases with previous miniature films regarded as normal for the present analysis were more evenly distributed over the various age groups. Even if there were some newly developed cases included among these they could not seriously disturb the relationships between the calculated attack rates.

Of considerable clinical interest were the cases found to have active disease at the second examination which had definite lesions at the time of the earlier examination. In men, most of these cases were in the older age groups and had disease of a type which has usually been recognized as stable. Their importance is emphasized by the fact that there were 21 active cases in males aged 35 or over who had a lesion present at the previous examination, compared with 14 cases in this age group found to have active disease after a previously normal film.

Only two cases in women were assessed as "active" after having been previously regarded as stable. These patients were aged 30 and 34 years.

Results of Initial Mass Radiography Examinations

Males.—Many mass radiography surveys have now been reported in the literature. The results given in Table IV are shown for comparison with those of Table I, as exactly the same standards of assessment have been employed. It should be noted, however, that the results in Table IV were collected during a shorter

TABLE IV.—*Incidence of Tuberculosis in Males First Examined by Mass Radiography. January, 1946, to October, 1948*

Age (Years)	No. *X*-rayed	Active		Stable	
		No.	No. per 1,000	No.	No. per 1,000
15–	4,123	28	6·8	56	13·5
25–	13,619	108	7·9	187	13·5
35–	8,093	46	5·7	94	11·6
45–	8,657	54	6·2	105	12·1
60+	1,091	8	7·3	17	15·6

period than those of Table I. There are no significant differences between age groups in the incidence of active or stable cases found on first attendance. The incidence of active cases in each age group is about 6 to 7 per 1,000. This is higher than the figure of 3 or 4 per 1,000 usually quoted, partly because the assessment is based on a six-months observation period and not a single clinical examination. The true incidence of stable cases is greater than that shown, especially in the older age groups: cases assessed as inactive on radiological appearances alone are not included, and these cases were probably more numerous in the earlier years of the study.

Females.—The results of initial examinations of females are shown in Table V for comparison with Table II. The incidence of active lesions is high—

TABLE V.—*Incidence of Tuberculosis in Females First Examined by Mass Radiography. January, 1946 to April, 1948*

Age (Years)	No. *X*-rayed	Active		Stable	
		No.	No. per 1,000	No.	No. per 1,000
15–	9,339	72	7·7	91	9·7
25–	6,992	51	7·3	117	16·9
35–	3,537	16	4·5	57	16·1
45–	2,391	4	1·7	27	11·3
60+	112	0	0	0	0

more than 7 per 1,000—up to age 35, but falls rapidly thereafter. The incidence of stable lesions remains fairly constant—just over 10 per 1,000.

Annual Mortality Rates

For comparison with the annual attack rates the mean annual death rates per 1,000 for respiratory tuberculosis in England and Wales have been calculated for the years 1946–8 in the same age and sex groups that have been used throughout this paper. The rates are given in Table VI and show the familiar phenomenon of a rate

TABLE VI.—*Mean Annual Mortality from Respiratory Tuberculosis, England and Wales, 1946–8*

Age (Years)	Males (per 1,000)	Females (per 1,000)
15–	0·36	0·67
25–	0·62	0·70
35–	0·67	0·39
45–	1·06	0·25
60–64	1·18	0·25

high in young adult females falling to a low level in older life. The male rates start at a lower level than those for females, but rise to a high level in older life.

Discussion

This statistical analysis indicates that the attack rate of radiologically detectable tuberculous lesions is similar in the two sexes—comparatively high in young adult life, falling with increasing age to appreciably lower levels in older males and to an almost negligible level in older females. A group of cases with symptomatic onset not included in the statistical analysis gives a similar age and sex frequency distribution, suggesting that the rates calculated may be too low in absolute value but supporting their general trend.

If these results are compared with the tuberculosis death rates in England and Wales during the period under review it is seen that there is a general similarity in the attack rates and death rates for females; both are high in young adult life and fall to low levels in older life. For males, however, the results are paradoxical: the highest attack rate occurs in young adults, but the maximum death rate occurs late in life, with the rate at 60 years nearly double that in young adults. It is suggested that a considerable proportion of these fatalities are the result of breakdown of lesions that

have been present for many years and probably acquired without major symptoms in young adult life 30 to 40 years ago. The results of the first mass radiography examinations reported here have shown, as in many other mass radiography surveys, that there is a considerable pool of inactive or doubtfully active cases amongst older males. The present study has further shown that breakdown of such lesions can and does occur, and is numerically as important in older males as newly acquired active disease.

While there is now an extensive literature covering mass radiography examinations, studies giving attack rates in age and sex groups of persons previously found normal are few in number. Dick and Thompson (1946) found very few cases developing even in household contacts over the age of 30; few cases would have been missed if contacts in this age group had not been repeatedly examined after one normal film. Dick (1948) has reported the results of repeat annual mass radiography examination of a factory group and showed a very low incidence of disease arising in those previously examined, the total of significant cases being of the order of 0.3% or 0.4%. The numbers involved were not large enough to permit of analysis by age and sex groups.

In the United States, Reid (1940, 1941) has reported the results of routine annual fluoroscopy of an office group: she gives the results for the years 1930–9 in broad age groups and shows an attack rate of 3 per 1,000 in young adults aged 17–29 of either sex, falling with increasing age to 1.4 per 1,000 at 40 plus for the first five years of her study and as low as 0.4 per 1,000 in the second five years. She shows little difference between corresponding age groups of the two sexes. She herself points out that some small lesions are likely to be missed on fluoroscopy, and of course re-scrutiny is not possible with this method.

Brooks (personal communication), in analysing the results of re-examination by mass radiography of men in the Royal Navy, found an increasing incidence of newly occurring disease with increase of age up to about 45 years. The older men in this study were mostly long-service men and constitute a rather special group with regard to environmental conditions. Cases occurring symptomatically are not included. Among women over 30–35 years in the W.R.N.S., Brooks found an extremely low incidence of newly appearing disease. In view of his results for older men, and the predominance of clerical workers in the present series, further studies along similar lines in other population groups would be valuable.

Following Frost (1939), I have shown elsewhere (Springett, 1950) on statistical grounds that the present peak of mortality in late adult life in males can be satisfactorily explained as the residue of even higher rates experienced by the group when young. The analysis in the present paper brings more direct evidence in favour of the view that the tuberculosis mortality of older males is to a considerable degree determined by the extent to which they as a group acquired disease as young adults, though the attack rate of new disease in older males cannot be regarded as negligible. For women also the mortality in later life is dependent mainly on the breakdown of lesions acquired in much younger life, and is only rarely due to disease acquired for the first time in middle life or later. The risk of breakdown is smaller than in males, however, so that there is in females at the present time no postponement of the age of maximum mortality, though there was such postponement at about the turn of the century.

Conclusions

Certain practical conclusions follow from the results presented and the above discussion.

1. Mass radiography of a group not previously examined yields a greater incidence of active tuberculosis than similar examination of a group previously examined. This result is perhaps obvious, but it confirms that, until a community has been completely covered, the main effort should be concentrated on examining the greatest possible number of individuals for the first time.

2. At repeat mass radiography examinations the highest incidence of new lesions is found in young adults of both sexes. Few cases are found in older males and practically none in older females. When repeated examinations are possible the main effort should be to obtain the maximum attendance of young adults, as the chance of persons over the age of 35 years with a normal radiograph developing tuberculosis is so much smaller.

3. An essential corollary of conclusion 2 is that some arrangements must be made for further supervision of apparently healed or healing disease in older persons, particularly males, whether discovered by mass radiography or otherwise. Even annual radiological supervision in all such cases would seriously strain existing facilities in many districts. Special arrangements for their repeated examination by mass radiography is not satisfactory, as comparison of two 35-mm. films is difficult. Serial examinations require a method whereby films of one individual shall be filed together. If radiological supervision of apparently healed and healing lesions in older persons cannot be arranged, at least they and their private doctors should be informed of the finding, so that full investigation could follow immediately on the occurrence of symptoms. It must be admitted that such cases are commonly difficult ones to treat, but their detection and supervision are important from a public health aspect, and they should be advised on hygienic disposal of sputum.

Summary

Repeat mass radiography of a group of males yielded 4.7 cases of tuberculosis per 1,000 examined at age 15–24 years, declining with increasing age to 1.7 per 1,000 at 45–59 years.

Similar examination of a group of females yielded 6.8 cases per 1,000 at 15–24 years, falling to below 1 per 1,000 at 45–59 years.

Expressed as annual attack rates the results were: Women, 3.5 per 1,000 at 15–24 years; 2 per 1,000 at 25–34; 0.5 per 1,000 over 34. Men, 3 per 1,000 at 15–24 years; 2 per 1,000 at 25–34; 1 per 1,000 at 45–59. These rates are low estimates, as no allowance is made in them for cases occurring symptomatically.

These results are compared with the incidence of tuberculosis found at a first examination by mass radiography and with the annual death rate from respiratory tuberculosis in England and Wales.

It is a pleasure to acknowledge the help received from many sources in compiling this paper. The medical staff of the Ministry of Health mass radiography unit has permitted ready access to all records, while the clerical staff has given help in the special analyses of record cards. Dr. Parks, of the Treasury

medical adviser's department, gave invaluable assistance on the section dealing with cases developing symptomatically. My contribution was part of the work as Prophit Scholar of the Royal College of Physicians, and the Prophit Committee of the College made additional clerical help available for the analysis of record cards.

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TECHNIQUE OF JELLY (TUBERCULIN) SKIN-TESTING

COMPARISON BETWEEN VARIOUS TECHNIQUES AND THE MANTOUX TEST

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It is apparent that many physicians reject the jelly test and that others are dissatisfied with results from this method. To a recent questionary sent to 246 chest clinics and children's and orthopaedic hospitals in England, 190 replies were received from different individuals (77%).

Of the 190, 80 (42%) do not use jelly tests, some having abandoned them. Of the 110 using the test, the number who abrade the skin with fine sandpaper was 64 (58%); in each group about one-third (35%, 36%) were dissatisfied with results. It is of interest to note that, of those who were dissatisfied, only 2.9% read their results at 72 hours or more.

The series of tests described was undertaken in order to find the most efficient method of jelly skin-testing, to produce a simple, standard, and reliable technique, and, if possible, to determine its equivalent in terms of the Mantoux test. The investigation was carried out independently of the work published by Pointon Dick (1950), and the draft article was written before his publication; some amendments in the text were made after the publication of his findings.

Non-specific Reactions to the Mantoux Test

W.H.O. (1948) has lowered the final test dose of O.T. from 100 (1 mg.) to 10 tuberculin units (T.U.) on the grounds that there are non-specific reactions from the higher dose. It has been shown in America by Furcolow *et al.* (1941), Furcolow (personal communication), and Long and Seibert (1937) that such reactions occur with P.P.D. The former used increasing doses of P.P.D. and found that even infants under 6 months of age who had had no known contact would give a high proportion of positive reactions if the dosage was sufficient. They also stress the instability of the reaction, used by its opponents as a condemnation. Long and Seibert, using a timothy-grass (T.G.) product, found that 86% of those negative to first-strength P.P.D. and to the T.G. product in corresponding dosage, and who were positive to second-strength P.P.D., were also positive to the T.G. product in corresponding dosage.

The great advantage of the intradermal Mantoux test is claimed to be that an accurate known dosage is given. Furcolow and Robinson (1941) reported an interesting series in this connexion, injecting the same individual with the same material (P.P.D.) from the same syringe at the same time. With a dose of 1/10,000 mg. of P.P.D. they found that 3.3% were positive in one arm and negative in the other, and state that with higher dosage "much greater variation takes place"—a finding previously reported by Paretzky (1938). Heimbeck (1950) regards the Mantoux as not so good a test as the von Pirquet, mainly on the grounds of non-specificity.

Standard for Comparison.—The Mantoux test was regarded, for the purpose of this investigation, as the standard by which the various transdermal tests were measured, because it is still accepted in this country as the standard test, even at 100 T.U. dosage. It was felt that, if a test which was consistently equal to or better than 10 T.U. could be found, this would meet the objections to the use of the highest dose—objections considered by some to be exaggerated. The standard used for checking against false positive jelly reactions is therefore the 100 T.U. Mantoux test in those cases in which the 10 T.U. test gave a negative result and in which, therefore, a positive jelly test might be regarded as a false result; but from the work quoted above it appears to be more important to have a high correlation with the 10 T.U. test.

The Techniques

Deane (1946) showed that abrasion of the skin by fine (grade O) cabinet-maker's sandpaper gave 100% positive results, using O.T. jelly, in a series of children known to be positive to the 1/1000 O.T. Mantoux test, whereas without the use of sandpaper only 87.5% were positive. The series was small and no details of age grouping were given.

P.P.D. Jelly.—Technique A (P.P.D.): The skin is given a firm rub with a plug of cotton-wool soaked in acetone; the interscapular area to be tested is then stroked lightly with flourpaper six times, so as not to produce an erythema; the jelly (60% w/v) is applied and covered with leucoplast. The plaster is removed at 48 hours, and the result is read 48 to 96 hours after application. The technique is that described by Pointon Dick (1950). *Technique B (P.P.D.):* Precisely as A (P.P.D.), except that, instead of a "firm rub" with acetone-wool, a deliberate attempt is made to produce an erythema with the wool, before flourpapering. *Technique C (P.P.D.):* This is a commonly used method in clinic practice. It is precisely as B (P.P.D.), except that the flourpapering is omitted.

O.T. Jelly.—Technique D (O.T.): Identical to A (P.P.D.), except that O.T. jelly replaces the P.P.D. jelly.

Standards.—In all tests in both parts of the investigation results were accepted as positive when the jelly gave six papules or more in the shape of the original application; and for intradermal tests an area of induration not less than 5 mm. in diameter. All O.T. was kept in a refrigerator when not in use and was discarded after 21 days from the date of dilution. All tests were performed and read by me.

Results

First Series. Technique A Compared with Technique C.—Volunteers were 1,452 boys and 1,795 girls from schools in Portsmouth. The jelly tests were applied