RECENT TRENDS IN SURVIVAL OF PATIENTS WITH RESPIRATORY TUBERCULOSIS

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Mortality from most of the common infections has been falling steadily in Great Britain since the end of the 19th century. For a number of these diseases the rate of fall has increased very considerably during recent years, and the improvement has been particularly dramatic in the case of respiratory tuberculosis. The remarkable post-war change in mortality from this disease is illustrated graphically in Fig. 1, which presents the crude mortality from respiratory tuberculosis in Birmingham since 1875.

The death rate fell by half in the 35 years between 1875 and 1910, and again by half between 1910 and 1945. Since about 1947, however, there has obviously been a profound change in the epidemiology of the disease. The rate of fall of mortality has accelerated so rapidly that the crude death rate has been halved yet again in the 6 years between 1945 and 1951 (from 68 to 34 per 100,000) and more than halved in the 3 years between 1949 and 1952 (from 54 to 25).

There seems no reason to question the conclusion of Springett (1952) that medical science can claim little credit for the long slow decline in mortality between 1875 and 1925. As he points out, effective treatment hardly existed before 1920, and even up to 1940 its influence upon mortality was probably trivial. It is true of course that by making it possible to isolate an increasing number of infectious cases, the gradual expansion of hospital accommodation for tuberculous patients which resulted from inclusion of Sanatorium Benefit in the provisions of the National Health Insurance Act of 1911 made some contribution towards the decline. Nevertheless the falling death rate was for the most part an unplanned, uncontrolled, and to some extent unexpected by-product of a steady improvement in general standard of living, with all that this implies in terms of better working conditions, a more varied diet, and more and better houses.

But although it is probably true that until recently the gradual fall in mortality has been due to a rising standard of living, it is not certain whether the improvement is attributable in the main to a decline in incidence of the disease, or to a change in prognosis among those infected. It is significant, however, that in the 25 years between 1913 (when notification of all forms of tuberculosis was made compulsory) and 1938, notifications decreased more rapidly than

FIG. 1.—Crude mortality rate from respiratory tuberculosis Birmingham, 1875-1952 (semi-log scale).

deaths. In Birmingham, for example, the notification rate of respiratory tuberculosis decreased during this period by 80 per cent. (from 483 to 96 per 100,000), while the mortality rate decreased by only 41 per cent. (from 119 to 70). Although notifications are incomplete and notoriously unreliable as an index of morbidity, this striking reduction suggests that the improvement in mortality can be attributed wholly or mainly to a decline in incidence. And if this is true for the period 1913–38, it is probably also true for the preceding half century. Certainly there is no evidence which suggests that there was any substantial improvement in the prognosis of the established case between the end of the 19th century and the beginning of the second world war, and until quite recent times about two-thirds of patients with respiratory tuberculosis died within 5 years of notification (Table I).

TABLE I

REPORTED FIVE-YEAR SURVIVAL RATES OF PATIENTS WITH RESPIRATORY TUBERCULOSIS

Source	Type of Patient	Date of Notification	Proportion of Patients Surviving at Least 5 Years (per cent.)
Thompson (1943)	Sputum positive notifications from County Durham	1928–38	27
Tattersall (1947)	Sputum positive cases attending Reading Dispensary	1914–40	32
Fraser (1947)	Sputum positive notifications from City of Aberdeen and Aberdeenshire	1934–43	45
Acker (1951)	All notifications in Edinburgh	1936–44	54
Present study	All notifications in Birmingham	1930 1935 1945	30 34 45

Since 1947 there has been a sharp increase in the rate at which mortality has been falling, and it seems likely that a new factor has been introduced into the epidemiology of the disease, for although the standard of living has continued to rise since the war, there is little to suggest that this in itself has been sufficient to account for the change. There is also no reason to believe that the improvement is due to a sudden decline in incidence. Indeed, since the beginning of the war in 1939 notification rates have increased, but this increase is apparently attributable to a more intense and successful search for cases, and it seems likely that incidence has continued to fall (Lowe and Geddes, 1953). But even if morbidity is still declining, the rate of decline is certainly not

sufficient to account for the abrupt change in mortality.

It seems probable that the recent remarkable improvement in mortality must be attributed mainly to an improvement in prognosis following the introduction of effective chemotherapy. A number of carefully controlled clinical trials (notably those conducted by the Tuberculosis Chemotherapy Trials Committee of the Medical Research Council) have established beyond doubt the value of streptomycin, *p*-aminosalicylic acid, and isoniazid in treatment. But the effect of these agents upon the survival rate has not been measured. In the report which follows an attempt has been made to record how survival rates have changed in the past two decades, by examination of the subsequent histories of patients notified from Birmingham.

SOURCE OF DATA AND METHOD

The greater part of this inquiry is concerned with the year to year survival after notification of all cases of respiratory tuberculosis notified from Birmingham during each of the years 1930, 1935, 1940, 1945, 1947, 1949, 1950, and 1951. Names of patients (approximately one thousand for each of these years) and dates of notification were taken from the official register of notified cases. Persons normally domiciled within the City boundary but found to have respiratory tuberculosis while serving in the armed forces appear in the survival tables from the date on which they were entered in the Birmingham register. All other transfers to the register from outside areas, cases entered after death (*i.e.* not notified during their lifetime), and patients for whom there was no specific mention of respiratory involvement at the time of notification, have been excluded.

For each patient the following data were extracted from the records held in the Birmingham Chest Clinic: sex; age at notification; date last seen alive (or date of leaving the City); (when applicable) date and cause of death. In addition, the state of disease at the time of notification was classified in the three groups suggested by the Ministry of Health (1947):

Group I.—Cases with slight or no constitutional disturbance, no complications (tuberculous or other), and radiological findings limited to mottling involving a total area of not more than one zone.

Group III.—Cases with profound systemic disturbance or constitutional deterioration, including all with grave complications (whether tuberculous or not).

Group II.—All cases which cannot be placed in Groups I and III.

These data were used to prepare Life Tables. The method is illustrated in Table II, which is based on patients (males and females combined) notified during 1935. Mortality rates (*qx*) for this cohort were calculated for each of the 10 years succeeding notification by dividing the number of patients known to have died from respiratory tuberculosis during each year by the number

TABLE II
ESTIMATED SURVIVAL RATES OF 1,000 PATIENTS NOTIFIED FROM BIRMINGHAM IN 1935

Years since Notification (x)	Number known to be Alive on Each Anniversary of Notification	Number Lost Sight of during Each Year			Number at Risk at Beginning of Each Year	Number Dying from Tuberculosis during Each Year	Probability of Dying from Tuberculosis during Each Year (qx)	Number Alive on Each Anniversary out of 1,000 Notifications (lx)
		Untraced	Left City	Died from Other Causes				
0	995	48	30	5	953.5	349	.3660	1,000
1	563	21	13	2	545	95	.1743	634
2	432	15	6	2	420.5	58	.1379	523
3	351	17	5	3	338.5	50	.1477	451
4	276	16	10	—	263	30	.1141	384
5	220	11	4	1	212	19	.0896	340
6	185	9	6	1	177	11	.0621	310
7	158	17	3	—	148	9	.0608	291
8	129	10	—	—	124	12	.0968	273
9	107	7	2	1	102	3	.0294	247
10	94	6	1	—	92.5	4	.0432	240

presumed to have been at risk at the beginning of the corresponding year. Patients were considered to be at risk until halfway through the year in which they were last examined, had left the City, or had died from some cause other than tuberculosis. The results are summarized as the number alive (*lx*) on each anniversary out of a thousand notifications.

Much of the value of a Life Table depends upon the proportion of the population at risk which can be followed through succeeding years. In this inquiry no attempt was made to trace patients except through Chest Clinic records; a considerable wastage was therefore inevitable. For example, 8 per cent. of the 1935 notifications were not seen again or had left the city by the end of the first year, and this proportion had risen to 16 per cent. by the end of the fifth year and 25 per cent. by the end of the tenth year (Table II). However, with the exception of 1930 (for which year, owing to the inadequacy of early records, there was a greater wastage), the pattern of loss was very much the same for each of the chosen notification years. Since we are concerned mainly with secular trends in survival there is no reason to believe that the wastage seriously invalidates the conclusions.

CHANGING PATTERN OF SURVIVAL

In the preliminary analysis, sex, age, and extent of disease at notification were disregarded. Table III (see also Fig. 2, overleaf) gives survival tables for the eight notification years examined. Of all new cases of respiratory tuberculosis discovered in 1930 and 1935, only three-fifths were alive 12 months after notification, about one-third were alive after 5 years, and one-fifth after 10 years. These results are compared with previous estimates in Table I. As might be expected, the published findings vary

TABLE III
ESTIMATED SURVIVAL RATES OF 1,000 PATIENTS NOTIFIED FROM BIRMINGHAM IN VARIOUS YEARS

Years since Notification (x)	No. Alive on Each Anniversary out of 1,000 Notifications (lx)							
	1930	1935	1940	1945	1947	1949	1950	1951
0	1,000	1,000	1,000	1,000	1,000	1,000	1,000	1,000
1	608	634	546	721	714	785	842	902
2	469	523	419	621	620	709	792	—
3	390	451	351	556	564	648	—	—
4	329	384	312	501	536	—	—	—
5	299	340	274	452	501	—	—	—
6	274	310	237	426	—	—	—	—
7	250	291	210	413	—	—	—	—
8	245	273	188	—	—	—	—	—
9	229	247	164	—	—	—	—	—
10	208	240	154	—	—	—	—	—

according to locality and period, but they are in reasonably close agreement with the Birmingham evidence.

The Life Table for 1940 is even more discouraging. But it must be remembered that at this time there was delay in registration with the appropriate local authority of cases discovered in the armed forces, and that this will inevitably have an adverse effect upon survival after notification. Nevertheless delayed registration is unlikely to have contributed much to the deterioration, since the results in women (of whom a much smaller proportion served in the armed forces) were almost identical with those in men. If this view is correct, the abrupt rise in mortality at the beginning of the war must be attributed to an adverse effect of war-time conditions upon prognosis as well as to an undoubted increase in incidence of the disease.

FIG. 2.—Survival rates of patients notified from Birmingham in various years (all notifications).

FIG. 3.—Survival rates of patients with Group I disease.

FIG. 4.—Survival rates of patients with Group II disease.

FIG. 5.—Survival rates of patients with Group III disease.

Post-war Life Tables show a remarkable and consistent improvement. For example, for the years 1935 and 1947, the proportions of patients alive 5 years after notification were 34 per cent. and 50 per cent. respectively. For later years the improvement is even more striking, the proportions of patients surviving for one year being 63, 71, 84, and 90 per cent. for 1935, 1947, 1950, and 1951 respectively. Indeed, it seems likely that the 5-year survival rate for patients notified in 1951 will be as high as the one-year survival rate for 1935.

SURVIVAL RELATED TO STAGE OF DISEASE AT NOTIFICATION

It has already been mentioned that the high level of notification in England and Wales since the war has been due to more complete ascertainment, and it seems probable that this has resulted in an increase in the proportion of early lesions among the cases notified. Between 1935 and 1952 the annual number of early (Group I) cases found at the Birmingham Chest Clinic among patients examined for the first time doubled; during the same period the number of

late (Group III) cases was halved (Lowe and Geddes, 1953). Notifications are evidently being progressively diluted with cases which at one time would not have been discovered until they had reached a more advanced stage and carried a much graver prognosis. In addition, tuberculosis registers now include numbers of patients with lesions that would previously have resolved without coming to medical attention. It is likely, therefore, that quite apart from the influence of treatment, some of the recent improvement in survival after notification may be due to earlier and more complete ascertainment. Accordingly the data have been examined in relation to the stage of the disease at notification.

Figs 3, 4, and 5 indicate that there has been a remarkable improvement in survival rate among patients classified in each of the three groups. It is conceivable that the apparent improvement in prognosis of early (Group I) cases may merely reflect the inclusion of increasing numbers of patients with minimal lesions, which a decade ago would have escaped detection. But improvement in case-finding can hardly explain the dramatic change in the survival rate of patients with advanced (Group III) disease: the proportions still alive 12 months after notification were 36, 44, 59, and 73 per cent. for 1935, 1947, 1950, and 1951 respectively. And, what is perhaps even more striking, patients whose disease was advanced when notified in 1951 had a better chance (72 per cent.) of surviving for 12 months than any patient, irrespective of stage of disease, notified in 1935 (63 per cent.).

There can be little doubt, therefore, that the spectacular decline in mortality from respiratory tuberculosis in Great Britain since about 1947, although possibly associated with some decline in incidence, is largely attributable to improvement in prognosis at every stage of disease.

SURVIVAL RELATED TO SEX AND AGE AT NOTIFICATION

In the Life Tables and diagrams so far presented males and females were grouped together and age at notification was disregarded. It is well known, however, that age specific mortality patterns are quite different for the two sexes. Age and sex specific mortality rates for England and Wales in 1951 are shown in Fig. 6; female mortality rates are at their highest in early adult life (in the age group 25–29 yrs), when they are appreciably higher than corresponding male rates; the maximum male mortality rate occurs very much later (65–69 years), when it is many times greater than the female rate. (Indeed in 1951 male mortality in middle and late

Fig. 6.—Age specific mortality rates from respiratory tuberculosis (England and Wales, 1951).

life was considerably greater than female mortality at any age.) It is clearly necessary to consider the influence of age and sex on survival, and for this purpose notification data for 1935, which permitted a 10-year follow-up, were chosen.

Fig. 7 (overleaf) shows that, among patients with early lesions, males fared better than females (10 years after notification 77 per cent. of males were still alive, compared with 61 per cent. of females); but among patients with moderate or advanced disease the position was reversed. Fig. 8 (overleaf) relates survival to age at notification: under 35 years males did better than females; for the age group 35 years and over, on the other hand, the male survival rates were a little lower than the female rates. These sex differences in respect of age and stage of disease at notification are of course not unrelated, since it is predominantly among young people that early respiratory lesions are found, whereas it is among the middle-aged and elderly that advanced lesions are common.

NOTIFICATION RATES ACCORDING TO AGE AND SEX

We have so far been considering the mortality experience of Birmingham patients after notification. With the same data it was possible to examine the notification rates, and this examination revealed an interesting association between notification and age and sex which has been obscured in national figures by the way in which the data are presented.

Fig. 9 (overleaf) gives age and sex specific notification rates for England and Wales, calculated from the report of the Ministry of Health for 1951 and in the One per cent. sample Tables of the 1951 census. Sex differences in notification rates are much less conspicuous than the sex differences in mortality rates shown in Fig. 6. Above 45 years of age

FIG. 7.—Survival rates according to sex and stage of disease (Birmingham, 1935).

FIG. 8.—Survival rates according to sex and age (Birmingham, 1935).

FIG. 9.—Age specific notification rates (England and Wales, 1951).

notification rates are much higher for males than for females, but for both sexes the highest rates are in the age group 15–24 years.

The Birmingham data are presented in Fig. 10(a). By giving notification rates in 5-year age groups, they show for males a striking bimodal distribution which is not apparent from the four broad age groups given in national statistics. Male and female distributions are indeed quite different. Female notification rates follow much the same pattern as the mortality rates for England and Wales in the same year: they are comparatively high in infancy, fall during school years, increase very rapidly in the late teens, reach a peak in early adult life, and fall again with advancing

years. As might be expected, the peak is earlier for notifications (age group 20–24) than for deaths (age group 25–29). Male notification rates also rise abruptly in early adult life, reach a peak in the same age group (20–24), and thereafter decline rapidly, but after 40–44 years the rate again rises steeply, and reaches a second peak at 50–54 years, 15 years earlier than the age of maximum mortality.

In Fig. 10 (b, c, and d), the Birmingham data for 1951 are also examined according to stage of disease at notification. Female age distributions are much the same for all groups. In males Group II disease shows the characteristic bimodal distribution observed for all notifications, but Group I disease is almost entirely limited to young adults and Group III disease to the elderly. Here it must be mentioned that notification rates for young adult males are somewhat overstated, because census data underestimate the population at risk. (They relate to home population, whereas notifications include a small number of patients identified while serving in the armed forces abroad). The error introduced is appreciable only in the age groups 15–19 and 20–24; but even here it is not large and in no way invalidates the observations.

CONCLUSIONS

The history of the decline of mortality from respiratory tuberculosis in England and Wales is divided into three fairly distinct periods by the two National Health acts of 1911 and 1946. Until 1911 not only was there no effective treatment, but public services designed to control the spread of infection

FIG. 10.—Age specific notification rates (Birmingham, 1951).

were badly co-ordinated, unevenly distributed, and altogether ineffectual. Nevertheless, national mortality rates had been falling for at least half a century, and it is reasonably certain that this was due, not to an improvement in prognosis, but to a gradual reduction in morbidity mainly brought about by a rising standard of living.

Between 1911 and 1946 there was a progressive improvement in local authority services directed specifically towards the control of tuberculosis. As in the previous period, a rising standard of living was reflected in a falling mortality rate, but the introduction of more efficient anti-tuberculosis services undoubtedly helped to accelerate the

decline. Focused as they were upon identification and isolation as well as treatment, these services influenced mortality rates principally by reducing the incidence of infection in the community. Nevertheless, it seems likely that in the 10 or 15 years preceding the National Health Service Act, curative medicine was beginning to make some impression on national mortality figures. The improvement in survival rates between 1935 and 1947 supports this conclusion (Fig. 2).

The period since 1946 has been characterized by the introduction of effective therapy. Therapeutic trials have left little doubt about the value of modern treatment, and the present investigation suggests that by effecting a striking improvement in immediate prognosis it has profoundly altered the pattern of mortality. The same methods are also producing very much higher sputum conversion rates (Snell, 1953), and the consequent reduction in the amount of infectious disease is likely to accelerate further the decline of mortality.

There is thus every reason to be encouraged by the contribution which the curative services are now making to the control of tuberculosis. At the same time it should not be forgotten that for nearly 100 years mortality had been falling in the absence of specific curative or preventive therapy, and it would be unfortunate if the new methods which have recently become available should lead us to forget that tuberculosis is an infectious disease, whose course is still largely influenced by social and economic conditions. On the other hand if we apply the new methods with due regard for the continuing importance of the standard of living, it is perhaps not too much to hope that the day is in sight when this formidable disease may be removed from its long-standing position as one of the most common causes of death.

SUMMARY

Data on survival were collected for all cases of respiratory tuberculosis notified from the City of Birmingham during each of the years 1930, 1935,

1940, 1945, 1947, 1949, 1950, and 1951. The material was used to prepare Life Tables.

Of cases notified in 1930 and 1935, three-fifths survived for at least 12 months, about one-third for 5 years, and one-fifth for 10 years. Survival rates for 1940 were even poorer, but post-war rates showed a remarkable improvement. For example, the proportion of patients who survived for 12 months were 63, 71, 84, and 90 per cent. for 1935, 1947, 1950, and 1951 respectively. A similar improvement was evident whatever the stage of the disease. The proportions of Group III (advanced) cases still alive 12 months after notification were 36, 44, 59, and 73 per cent. for 1935, 1947, 1950, and 1951 respectively.

Male survival rates were higher than female rates for Group I disease and for the younger age groups, and lower for Group II and III disease and for the older age groups.

Age specific notification rates for Birmingham in 1951 showed a striking sex difference. Female rates were highest at age 20-24; male rates were also at a peak in this age group, but were again raised at age 50-54. The bimodal character of the distribution of male notification rates is obscured in national data by the wide age groups in which the data are presented.

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