THE TREND OF MORTALITY FROM TUBERCULOSIS

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TUBERCULOSIS at the present time still causes over 20,000 deaths a year in England and Wales and is one of the major medical problems of the day. The mortality of the disease has been considered several times recently in papers or discussions of the Institute (Pedoe, 1947; Elderton, 1947; Conybeare, 1948), and always it is the mortality by calendar years that has been mentioned or implied. It is the purpose of this note to draw attention to the somewhat different picture obtained when generation mortality rates for tuberculosis are examined.

The data used are set out in Table 1 and consist of the mortality rates in England and Wales for all forms of tuberculosis. For the years 1851–1920, the rates were taken or derived from Table 12 of the *Registrar-General's Decennial Supplement*, 1921, Part III. For 1921–40, the rates have been calculated from the numbers of deaths and mean populations given in the annual volumes of the *Registrar-General's Statistical Review*.

CALENDAR YEAR METHOD

Figs. 1 and 2 show the rates of Table 1 plotted in respect of decennial calendar year periods. The most striking feature is, of course, the tremendous fall which has taken place in less than 100 years. The male curves show a progressive

Table 1. Tuberculosis (all forms) death-rates per 1,000,000 in England and Wales

Period	Age group								
	0–	5–	15–	25–	35–	45–	55–	65–	75–
	Males								
1851–60	6323	1166	3400	4163	4119	3957	3479	2573	1061
1861–70	6018	967	3157	4206	4244	3969	3433	2174	740
1871–80	5798	828	2493	3785	4198	3928	3285	2025	650
1881–90	5004	727	1976	3164	3685	3611	3027	1913	732
1891–1900	4347	615	1641	2541	3251	3296	2768	1706	629
1901–10	3129	552	1353	2158	2622	2934	2574	1686	668
1911–20	1942	545	1299	1840	2204	2335	2135	1390	585
1921–30	1067	321	1083	1413	1645	1729	1437	972	398
1931–40	612	184	817	1009	1134	1390	1287	808	353
	Females								
1851–60	5232	1388	4079	4690	4293	3236	2523	1783	834
1861–70	4917	1109	3689	4482	3988	2954	2178	1354	528
1871–80	4663	956	2907	3631	3475	2535	1866	1193	452
1881–90	3987	949	2267	2932	2846	2146	1597	1058	452
1891–1900	3516	780	1670	2086	2264	1753	1344	906	427
1901–10	2636	704	1338	1651	1710	1449	1186	894	494
1911–20	1619	682	1470	1484	1401	1156	943	750	437
1921–30	881	408	1353	1230	936	729	617	511	326
1931–40	522	214	1061	929	639	481	423	358	236

Mortality of males from tuberculosis

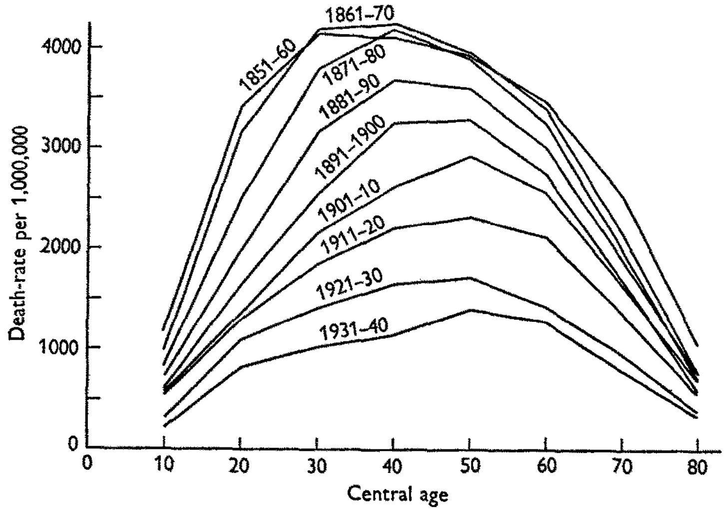

Fig. 1. According to calendar years

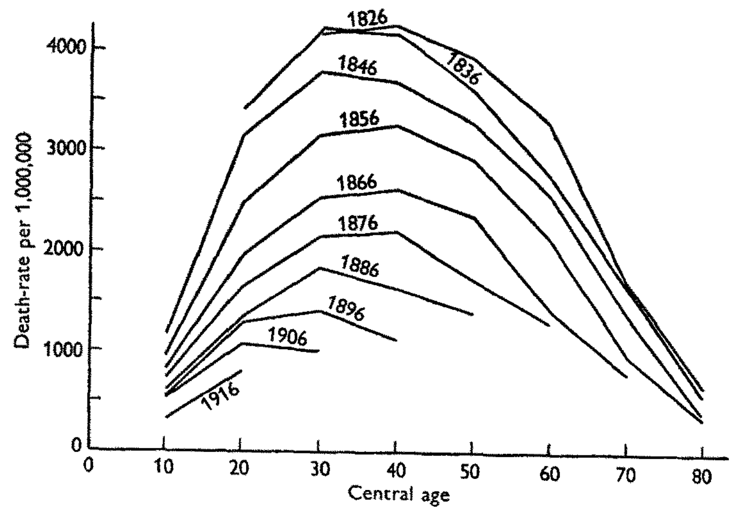

Fig. 3. According to mean years of birth

Mortality of females from tuberculosis

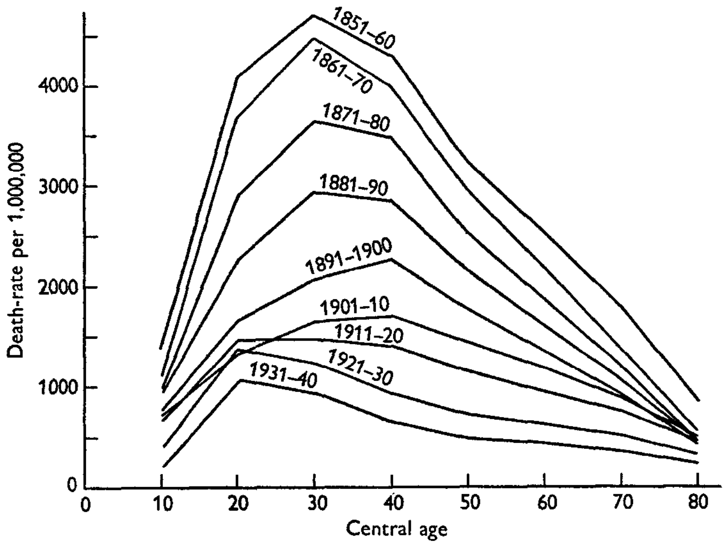

Fig. 2. According to calendar years

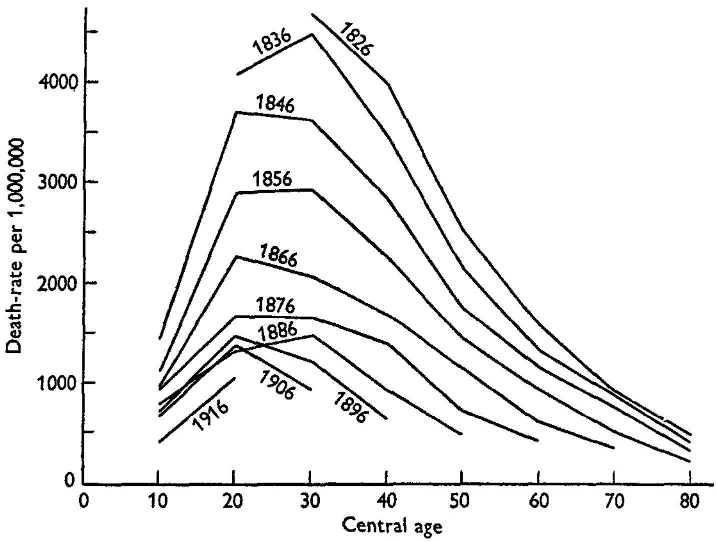

Fig. 4. According to mean years of birth

increase in the age of maximum mortality (excluding infancy). In 1851–60, the (central) age of maximum mortality was 30, but since then it has increased more or less steadily and in 1931–40 was 50. Females show a similar but less pronounced increase in the age of maximum mortality until 1901–10 when the age was 40, but the next decade had a maximum at age 30 and the two subsequent decades show maxima at age 20.

It is the calendar year aspect of tuberculosis mortality which has led to statements such as 'death from pulmonary tuberculosis has tended to be postponed to middle life' (Conybeare, 1948, p. 61), 'He was under the impression *that there had been a shift in the incidence of tuberculosis towards older ages*' (Elderton, 1947, p. 282). Figs. 1 and 2 show that by the calendar year method the statements are justified in the case of males but are rather doubtful for females. The generation approach will show these statements to be somewhat misleading.

GENERATION METHOD

The different outlook provided by the generation method in the case of the United States has been pointed out by Frost (1939), and the statistics for England and Wales show very similar features. Figs. 3 and 4 show the mortality rates experienced in England and Wales by generations of persons born during given periods. The year shown against each curve is the average year of birth. Thus, while each curve of Figs. 1 and 2 represents the rates shown on a horizontal line of Table 1, the curves of Figs. 3 and 4 each represent a diagonal.

The principal difference between Figs. 1 and 3 (i.e. male lives) is that in the latter the shapes of the curves are very similar for all generations, and the age of maximum mortality occurs nearly always at the (central) ages 30 or 40. There is no trace of the postponement of age of maximum mortality shown by the calendar year curves; in fact, the more recent generations seem to show a tendency for the age of maximum to become younger. Females (Fig. 4) show very similar features, with a somewhat lower age of maximum which is always at the (central) age 20 or 30. Although the shape of the curves is similar for all generations, it is different from that for males, being more skew and tending to the low rates at high ages in a rather different manner.

It would therefore appear that every generation experiences its own mortality and that the *relative* variations with age are rather similar for all generations (i.e. the shape of all the generation mortality curves is similar). Thus the year of birth seems to be a more fundamental function than the calendar year so far as tuberculosis mortality is concerned, and a generation which has experienced high tuberculosis mortality at the young ages continues to suffer from high mortality throughout life. In this light the progressive increase in the age of maximum (calendar year) mortality does not represent the postponement of maximum risk to later life but is rather associated with the higher rates experienced by the older lives in their young days. In any calendar year there are young lives subject to relatively low death-rates from tuberculosis and older lives who are survivors of earlier generations subject to much higher tuberculosis death-rates. It would be fallacious to infer that the young adults of to-day will show higher rates in middle age; tuberculosis is still primarily a disease of youth.

Although life tables are usually constructed on a calendar year basis, life assurance is strictly concerned with generation tables, but the difference is usually ignored except for annuities. Sometimes, however, the generation aspect is the only one applicable and Figs. 3 and 4 show that there is at present no justification for statements like 'tuberculosis from the point of view of life assurance will become a stationary rather than a decreasing risk' (Conybeare, 1948, p. 61) which is based on the calendar year aspect.

MATHEMATICAL REPRESENTATION OF TREND

The dependence of tuberculosis mortality on year of birth suggests that interesting results might be obtained if an investigation similar to that made by Rhodes (1941) for 'all causes' mortality rates were carried out for tuberculosis rates.

Table 2. Values of $G(\theta) = q_x^\theta / q_x^{1846}$

Mean year of birth	Age group								Median value (both sexes combined)
θ	5–	15–	25–	35–	45–	55–	65–	75–	$g(\theta)$
	Males								
1776	—	—	—	—	—	—	—	2·666	2·612
1786	—	—	—	—	—	—	1·851	1·859	1·855
1796	—	—	—	—	—	1·352	1·564	1·633	1·598
1806	—	—	—	—	1·201	1·334	1·457	1·839	1·524
1816	—	—	—	1·118	1·204	1·276	1·376	1·580	1·394
1826	—	—	1·100	1·152	1·192	1·176	1·227	1·678	1·260
1836	—	1·077	1·111	1·139	1·096	1·075	1·213	1·470	1·165
1846	1·000	1·000	1·000	1·000	1·000	1·000	1·000	1·000	1·000
1856	·829	·790	·836	·882	·890	·829	·699	·887	·803
1866	·710	·626	·671	·712	·708	·558	·581	—	·620
1876	·623	·520	·570	·598	·525	·500	—	—	·510
1886	·527	·429	·486	·446	·422	—	—	—	·425
1896	·473	·411	·373	·308	—	—	—	—	·385
1906	·467	·343	·267	—	—	—	—	—	·355
1916	·275	·259	—	—	—	—	—	—	·281
1926	·158	—	—	—	—	—	—	—	·156
	Females								
1776	—	—	—	—	—	—	—	2·558	2·612
1786	—	—	—	—	—	—	2·377	1·620	1·855
1796	—	—	—	—	—	2·127	1·805	1·387	1·598
1806	—	—	—	—	1·846	1·836	1·591	1·387	1·524
1816	—	—	—	1·508	1·685	1·573	1·411	1·310	1·394
1826	—	—	1·292	1·401	1·446	1·347	1·208	1·515	1·260
1836	—	1·106	1·234	1·221	1·224	1·133	1·192	1·340	1·165
1846	1·000	1·000	1·000	1·000	1·000	1·000	1·000	1·000	1·000
1856	·799	·788	·807	·796	·827	·795	·681	·724	·803
1866	·689	·615	·574	·601	·659	·520	·477	—	·620
1876	·684	·453	·455	·492	·416	·357	—	—	·510
1886	·562	·363	·409	·329	·274	—	—	—	·425
1896	·507	·398	·339	·225	—	—	—	—	·385
1906	·491	·367	·256	—	—	—	—	—	·355
1916	·294	·288	—	—	—	—	—	—	·281
1926	·154	—	—	—	—	—	—	—	·156

Kermack, McKendrick and McKinlay (1934) showed that it is sometimes reasonable to assume that 'all causes' rates could be expressed as the product of two functions, one depending only on age (x) and the other only on year of birth (θ), i.e.

$$q_x^\theta = \mathrm{Q}(x) \,.\, \mathrm{R}(\theta). \tag{1}$$

This formula can be tested by calculating, for different values of x, the function

$$\mathrm{G}(\theta) = \frac{q_x^\theta}{q_x^\mathrm{A}} = \frac{\mathrm{R}(\theta)}{\mathrm{R}(\mathrm{A})}, \tag{2}$$

where A is some chosen base year. If $\mathrm{G}(\theta)$ is reasonably constant for all values of x, then (1) should give a satisfactory representation of the trend of mortality by age and year of birth.

Table 2 shows the values of $\mathrm{G}(\theta)$ calculated from the rates of Table 1, taking A as 1846, i.e. q_x^A are on a diagonal line of Table 1; thus for males the successive values are 1166 (ages 5–15), 3157 (ages 15–25), ..., 398 (ages 75 and over). This table gives the impression that the values of $\mathrm{G}(\theta)$ for given θ are not constant but are subject to systematic trends. Further examination, however, shows that the trends are different for generations born before and after the base year 1846, and are also different for the two sexes, facts which suggest that the trends are not significant of any real effect. Also it must be remembered that statistics by cause of death are always somewhat unreliable. In this case the figures are being compared over nearly a century, during which time there has been considerable improvement in the accuracy of certifying the cause of death. Thus there does not seem to be any strong argument against assuming $\mathrm{G}(\theta)$ to be constant at all ages for given θ. For similar reasons there seems to be little ground for thinking that the values of $\mathrm{G}(\theta)$ differ for the two sexes. Ages under 5 do not fit into the scheme and have been omitted from Table 2. Rhodes found the same effect in his investigation of all causes of deaths.

Fig. 5 shows the median values of $\mathrm{G}(\theta)$, say $g(\theta)$, for both sexes combined,

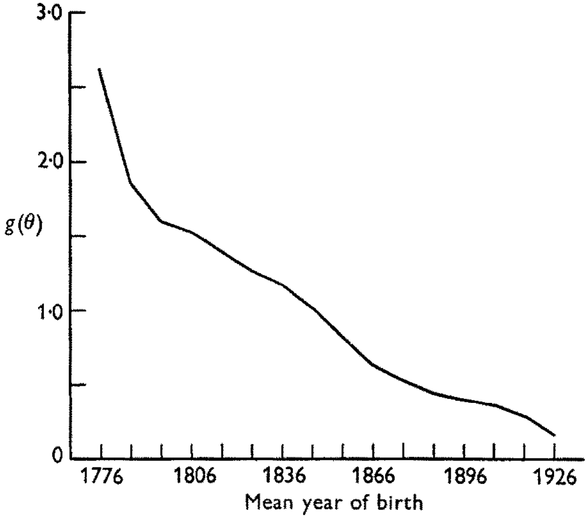

Fig. 5

plotted against θ. Median values were used, following Rhodes, instead of means, to avoid any extreme values having undue influence on the average value adopted.

Rhodes proceeded by fitting a logistic curve

$$g(\theta) = \frac{A + Be^{k(\theta-\theta_0)}}{1 + e^{k(\theta-\theta_0)}} \tag{3}$$

to the values of $g(\theta)$. This curve, which has asymptotes at A and B and a point of inflexion midway between (where $\theta = \theta_0$), gave a satisfactory representation of the 'all causes' values of $g(\theta)$. The graph of Fig. 5, however, is quite unsuitable for representation by this type of formula, and no attempt was made to fit a logistic curve. The generation effect (represented by $g(\theta)$) is therefore of quite a different type for tuberculosis from that found by Rhodes for all causes of death. It would, however, appear that, while the basic age curve $Q(x)$ has a different shape for each sex, the year of birth function $R(\theta)$ is substantially the same for both sexes. In other words, each generation experiences mortality which is the same proportion at all ages of that experienced by any other generation.

RELATION OF YEAR OF BIRTH FUNCTION TO CHILDHOOD INFECTION

Tuberculosis is an infectious disease caused by a bacillus, and it is believed that most people have been infected before they reach adult life. Sometimes the primary infection is fatal, but usually it is slight and the child recovers after an illness too trivial for its real cause to be recognized. Thus most people reaching early adult life have successfully overcome their primary infection, but there is always a possibility that the disease will break out again, either as a result of fresh infection or because bacilli lying dormant in the body again become active, probably at times when the resistance of the body is temporarily lowered by illness, strain or malnutrition. It is perhaps the extra burden of childbirth which is responsible for the earlier age of maximum mortality for females as compared with males (Figs. 3, 4).

The infectious nature of tuberculosis suggests that the year of birth function $R(\theta)$ might be better correlated with the amount of infection present in the population around the time of birth, than with the year of birth as was done in Fig. 5. A measure of the amount of infection present in childhood in the community, which has been used by Bradford Hill (1936), is the death-rate from all forms of tuberculosis at ages 0–5 ($I(\theta)$ say). This, of course, is not an ideal measure of infection and some objections were made to it in the discussion of Bradford Hill's paper but nothing better was suggested. The values of $I(\theta)$ are shown in Table 3, and in Fig. 6 $g(\theta)$ is plotted against the corresponding $I(\theta)$ for the nearest available mean year of birth.

The points appear surprisingly regular and suggest that a logistic curve

$$I(\theta) = \frac{A + Be^{ky}}{1 + e^{ky}} \tag{4}$$

(where y is the value of $g(\theta)$ measured from the point of inflexion) should fit fairly well. Both $g(\theta)$ and $I(\theta)$ are subject to error and any attempt to find a functional relation between them should take account of this fact. Since, however, it was not thought that (4) could have anything but empirical justification, the constants were determined by the method of least squares assuming $I(\theta)$ not subject to errors of observation. The formula resulting from this procedure is the regression of $g(\theta)$ on $I(\theta)$ and would be appropriate for the rather dangerous process of forecasting $g(\theta)$ from an observed $I(\theta)$. To be realistic the fitted curve must provide for a considerable reduction in $I(\theta)$ below that of the lowest point available, as shown by the last column of Table 3.

Table 3. Tuberculosis death-rates, ages 0–5, England and Wales, and corresponding $g(\theta)$

Period	1851–60	1861–70	1871–80	1881–90	1891–1900	1901–10	1911–20	1921–30	1931–40
Mean year of birth	1853	1863	1873	1883	1893	1903	1913	1923	1933
Death rate per 1,000,000 aged 0–5, both sexes ($I(\theta)$)	5780	5469	5230	4494	3930	2883	1781	975	568
$g(\theta)$ for nearest mean year of birth	·803	·620	·510	·425	·385	·355	·281	·156	—
Values of $g(\theta)$ calculated by formula (5)	·665	·580	·540	·459	·413	·340	·260	·180	—

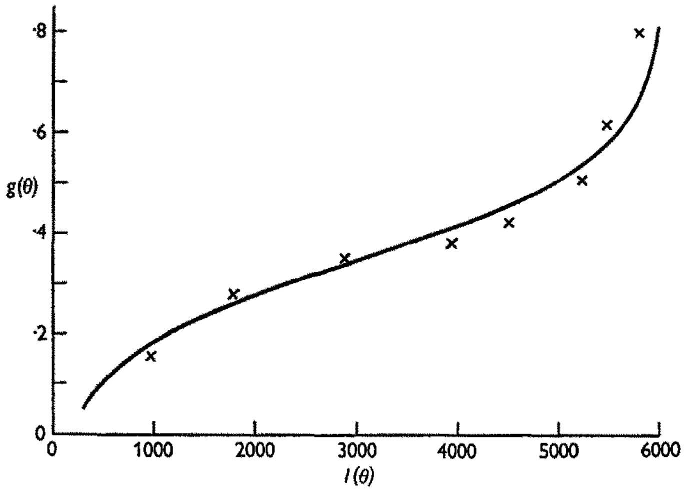

Fig. 6

Attempts to fit (4) resulted in values of A which did not fulfil this requirement. As in theory tuberculosis is a disease which can be completely eradicated, it was decided to put $A = 0$. The curve finally arrived at was

$$g(\theta) = \cdot 350 + (\cdot 2366) \log_{10}\left\{\frac{I(\theta)}{6050 - I(\theta)}\right\}. \qquad (5)$$

The calculated values of $g(\theta)$ are given in Table 3 and the curve (5) is shown in Fig. 6. The fit of the curve is not very good, but the limitations of the data and the empirical nature of the curve fitted must be remembered.

It is, of course, obvious that (5) can at the best give only a broad representation of the trend of tuberculosis death-rates, and at any time may be completely changed by some new circumstance such as the discovery of a drug which will kill the tubercle bacillus without harming its human host or the widespread use of B.C.G. vaccine. Nevertheless, it is believed that a broad mathematical relation like (5) is not without interest and use.

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