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THE LENGTHENING OF LIFE BY MODERN THERAPY IN PERNICIOUS ANAEMIA AND DIABETES

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The uses to which vital statistics are applied become every year more manifold, but this is not a cause for unmixed satisfaction. Some of these uses are embarrassing to the medical profession, not because unpleasant truths are thereby revealed, but because statistics culled from public health records and then subjected to incomplete analysis or ingenious misinterpretation are employed by interested persons to "disprove" the adequacy of this or that form of therapy or prevention.

An example of this is to be seen in the use in certain quarters of the national statistics of death from pernicious anaemia and diabetes to "prove" that the claims of medical research workers to have discovered remedies for these diseases were unfounded. As this is an instance where the misuse of figures may have unfortunate results, it seems advisable to point out wherein the fallacy lies, and to measure in as simple a manner as possible from the statistics of death what effect modern therapy has so far had upon the chances of life for those afflicted by these diseases.

Observed Changes in Death Rates

In the first place, let us inquire what has happened to the death rates since the discoveries of the new remedies. The introduction of liver therapy in 1926 was followed by an immediate fall in the standardized death rates from pernicious anaemia in England and Wales. This is shown in Table I, where the rates are expressed as percentages of the corresponding rates in the triennium 1924-6 preceding the use of the new remedy. By 1928 male mortality had fallen by 35 per cent., and female mortality by

TABLE I.—*Pernicious Anaemia. Death Rates per cent. of the Corresponding Rate in 1924-6*

	Males						Females					
	*All Ages	0-	25-	45-	65-	75 and over	*All Ages	0-	25-	45-	65-	75 and over
1924-6 ...	100	100	100	100	100	100	100	100	100	100	100	100
1927 ...	98	84	91	96	106	114	97	86	90	93	98	109
1928 ...	65	102	59	55	77	92	67	77	56	64	78	91
1929 ...	70	78	59	58	86	133	67	66	53	64	84	109
1930 ...	76	74	69	71	85	121	72	45	63	63	84	118
1931 ...	74	70	54	64	89	149	74	58	58	74	91	112
1932 ...	85	106	53	72	106	167	84	56	61	83	106	162
1933 ...	76	69	55	68	91	159	79	47	64	72	102	158

* Standardized.

33 per cent., but the rates then gradually rose again to about 85 per cent. of the 1924-6 level by 1932. In 1933, the latest year for which the deaths can yet be ascertained, there was again a fall to 76 and 79 per cent. of the 1924-6 rates for males and females respectively. The death rates at separate ages have been recorded year by year in the Text Volumes of the Registrar-General's Statistical Review, and were examined very carefully and in greater detail in a recent excellent study by Dr. A. Bradford Hill.¹ They show that although the early fall in death rates has been fairly well maintained at ages under 45, since 1928 some of the improvement has been lost at ages 45 to 65, all of it has been lost at 65 to 75, and at 75 and over there has been a considerable increase in death rate to the extent of nearly 60 per cent. (See Table I.)

If we next turn to the behaviour of diabetes mortality since the introduction of insulin in 1923, the story told by the death rates as they stand appears even less satisfying. The standardized rate (Table II) for males fell to 87 per cent. of the 1920-2 level by 1925, and then increased again to its original level by 1929, and has remained about that level since, whilst for females the rate has risen since 1922 by as much as 27 per cent. Separating into two groups of ages, under and over 55, and standardizing each rate, Table II indicates that at ages under 55 mortality has fallen by 41 per cent. for

TABLE II.—*Diabetes. Death Rates per cent. of the Corresponding Rate in 1920-2*

	Males			Females		
	*All Ages	*Under 55	*55 and over	*All Ages	*Under 55	*55 and over
1920-2 ...	100	100	100	100	100	100
1923 ...	96	79	110	104	95	112
1924 ...	92	72	108	98	75	116
1925 ...	87	67	104	104	80	122
1926 ...	92	68	112	101	74	121
1927 ...	94	67	116	112	76	139
1928 ...	97	63	126	112	79	138
1929 ...	101	73	125	123	81	155
1930 ...	99	65	128	119	72	155
1931 ...	94	62	122	123	77	157
1932 ...	99	60	131	125	75	162
1933 ...	99	59	132	127	78	164

* Standardized.

males and 22 per cent. for females since the introduction of insulin, this being offset by increases at ages over 55 amounting to 32 per cent. for males and 64 per cent. for females. A more complete analysis at separate ages is to be found in the Registrar-General's Reviews for recent years.

Expected Changes in Death Rates

What changes in the deaths and death rates would be anticipated if the remedies were fulfilling expectations? The remedies were only claimed to be "curative" so long as the treatment was continued, and from this several important consequences follow. Every patient under treatment for one of these diseases (which for clearness I shall designate by D) must eventually die of one of three groups of causes: (1) a relapse of the disease D due to failure to use a remedy of reliable potency and to continue its use with the necessary regularity; (2) some infective process or acute intercurrent disease such as influenza, or general disease such as cancer; or (3) some "local" disease, such as a heart, lung, kidney, or nervous affection.

The first of these events must be quite common owing, on the one hand, to the variety of forms in which liver therapy, for example, is being administered,² and on the other to weariness or lack of perseverance on the part of the patient. In this case the death will have been postponed by the treatment to a later age than would have been the case without it. In the event of (2) the death will usually be certified as due to the other disease, coupled with or contributed to by D, and owing to the precedence over D which is usually given to diseases of this group in the classification of deaths due to joint causes, the death will be credited for statistical purposes as a rule to the other disease, and will therefore affect the statistics precisely as though the patient had been permanently cured of D. It may be noted that a superimposed acute infective condition may not of itself kill the patient, but may lead to death from the disease D by rendering the ordinary dosage of the specific remedy inadequate. In the event of (3) the death will usually be certified with mention of D as a partial or contributory cause, and owing to the precedence in classification usually given to D over such causes as heart and lung conditions by reason of its prior incidence or supposed importance as a primary factor, the death will be credited as a rule to D, the statistical effect of the new therapy being, therefore, as in (1), to postpone the death to a later age.

Of these three events the deaths classed under (2) must be relatively few compared with the others, for, if the children's diseases are excluded, deaths from all those causes which usually take precedence in classification over diabetes or pernicious anaemia, when jointly stated with them, form only about one-quarter of the total deaths. A longer exposure to the risk of dying from this group of causes after diagnosis of the disease D must have tended to depress slightly the recorded death rates at all ages. During a severe influenza epidemic this may be of some importance; thus, during the last quarter of 1918, 122 deaths were attributed to diabetes plus influenza, and thirty-seven to pernicious anaemia plus influenza, in England and Wales, compared with about 950 and 500 classed to the diseases themselves. In normal periods the increase of such transfer of deaths to other causes owing to longer survival is not of great statistical importance.

The main effect to be anticipated on the statistics of deaths from cause D, whether the patient continues treatment until he dies of some other cause or whether he discontinues treatment and suffers a relapse, is therefore a postponement of deaths to a later age. Owing to the

increasing risk of death from causes of class (3) above as age advances, the average duration of this postponement must decrease in passing up the age scale. For simplicity of calculation let us suppose that the average duration of life after diagnosis of D was originally two years, and that the result of the new treatment was to increase this to ten years for cases arising at ages 15 to 25, to nine at ages 25 to 35, to eight at 35 to 45, and so on to four years at 75 and over, as shown in the third line of Table III. Suppose also that the numbers of new cases arising in each year are as shown along the first line of the table (the distribution corresponding very roughly to the probable distribution of ages amongst new cases of pernicious anaemia), that this incidence of new cases continues unchanged, and that permanent cures allowing complete cessation of treatment are rare. For simplicity it has been assumed that there is no variation around the average durations of life. Before the treatment was introduced the annual deaths resulting from an average duration of two years at each age would be as shown along the A line of deaths, and after the treatment had been in general use long enough for rates to become stable the deaths would be as shown along the line B.

TABLE III

	Age							Total
	15-	25-	35-	45-	55-	65-	75 and over	
New cases arising each year ...	2	8	15	20	25	20	10	100
Average life in years after diagnosis	(A 10	2 9	2 8	2 7	2 6	2 5	2 4	
No. of deaths each year ...	(A 10	2 3	6 10	14 18	19 24	21 25	14 20	100 100

According to this hypothetical scheme there would be no ultimate change in the total deaths, but in the period just following introduction of the treatment there would be at first a rapid fall in total annual deaths, and during that period the number of persons suffering from the disease who were alive at a given moment in the community would increase year by year until stability between incidence and deaths was reached. The deaths, after an initial fall, would begin to rise again until this condition of stability was attained.

The death statistics of pernicious anaemia show that the mean annual deaths in the triennium 1924-6 numbered 2,629, in 1927 there were 2,655, and then in successive years after introduction of the new therapy the numbers were 1,854, 1,955, 2,150, 2,226, 2,591, and 2,428. The total deaths, therefore, showed the expected initial fall and gradual return almost to the original level five years after the liver treatment was introduced.

Comparing the B deaths with the A deaths in Table III, there is a decline in the number at each age group under 55, no change at 55 to 65, and an increase at ages over 65. The pernicious anaemia deaths show a change of this kind when the year 1932 is compared with 1925, years having almost the same numbers of total deaths:

	0-	15-	25-	35-	45-	55-	65-	75 and up.	Total
1925	39	77	134	261	539	759	629	147	2,585
1932	31	48	89	166	398	752	820	287	2,591

There had evidently been a transfer of deaths up the age scale during the interval, resulting in a decrease of 318 deaths at ages under 55 and an increase of 331 at ages over 65.

For diabetes the position is more complicated, since there has been in progress during the whole period for which death statistics are available (except from 1915 to 1919) a steady increase in mortality rates at ages over 55. This is shown in Table IV, where the rates per million living in England and Wales are given at six age groups at various periods since 1861. The years of food restriction were marked by a fall in diabetic mortality at all ages over 35 during 1916-19, a minimal level being reached in 1918, quickly followed by a rise at ages over 45 as food became more plentiful. Ignoring this interruption in the trend, and having regard to the note below Table IV, there was no very pronounced change in the rates at ages under 55 between 1891-1900 and 1922. The standardized death rates at ages under 55 were as follows:

	1891-1900	1901-10	1912	1922
Males	49.8	50.2	50.6	51.5
Females	35.9	41.7	44.8	44.4

TABLE IV.—Diabetes. Death Rates per Million

	1861-70	1871-80	1881-90	1891-1900	1901-10	1915	1918	1920-22	1933
Males									
15-	—	—	—	—	41	74*	76*	42	26
25-	44	48	59	57	59	98*	165*	60	30
35-	55	69	79	87	78	104*	96*	69	36
45-	83	96	135	161	160	181	123	133	80
55-	136	182	282	347	415	476	299	309	325
65-	181	248	399	559	731	785	618	661	888
75 and up.	121	172	315	474	720	969	745	772	1,326
Females									
15-	—	—	—	—	31	35	36	35	25
25-	22	27	36	42	51	47	50	48	30
35-	30	35	51	56	63	68	62	62	48
45-	37	50	82	112	129	130	103	124	118
55-	58	88	161	258	357	442	286	355	470
65-	62	107	208	380	574	820	511	656	1,178
75 and up.	38	68	181	312	473	750	508	632	1,275

* Rates amongst civilians only, and therefore influenced by selection. The rates for 1913 were 41 at 15-25, 61 at 25-35, and 80 at 35-45.

The deaths to be anticipated at ages under 55 in recent years if insulin had not been introduced would therefore be given, as nearly as may be judged, by applying the 1920-2 death rates to the population at the corresponding ages in the year in question. These expected deaths in each year, 1930 to 1933, are shown in Table V, and for comparison the actual deaths registered. It is seen that there were aggregate deficiencies of deaths at ages under 55 from the expected numbers amounting to 508, 500, 532, and 530 in the four successive years. It is reasonable to suppose that these represent approximately the deaths which would have occurred at ages under 55, but were postponed by insulin to some age over 55.

At ages over 55 mortality rates are seen from Table IV to have risen continuously and very greatly from 1861 up to 1915. There was then an abrupt fall to the 1918 minimum, and by 1920-2 the 1915 level had not yet been regained. The progressive rise must represent an increasing incidence or recognition of diabetes at the higher ages, the effect of this being also enhanced in the statistics of death by more complete certification of diabetes as a cause of death at these ages. The recorded increases in death rates per million (a) between 1891-1900 and 1901-10 and (b) between 1891-1900 and 1915 were as follows:

	Males			Females		
	55-	65-	75-	55-	65-	75-
(a)	68	272	246	99	194	161
(b)	61	54	249	85	246	277

Supposing the same average annual increment in rates to have occurred between 1920-2 and 1933 as in the (b) period of 9½ years preceding the interruption produced by the war (that is, from the central point of the decade to the middle of 1915), the expected rates in 1930, 1931, 1932, and 1933 may be calculated, and by applying these to the populations the numbers of deaths expected would be as shown in Table V. The registered deaths in the four years at these ages exceeded the numbers thus expected by 567, 460, 593, 567 in the four years—that is, by 547 in the average year—and these numbers are seen to be approximately equal to the annual deficiencies of deaths at ages under 55, which averaged 517. In other words, the recent trend of the death statistics can be adequately explained by a transfer of deaths up the age scale, sufficient to postpone about 500 deaths in each year (or about one in every three) from before 55 to after that age, superimposed upon a continuation since 1921 of the pre-war trend of mortality rates at the various ages. In assessing the value of this “postponement of death” it is well to remember that the persons affected are not just “alive in bed,” but are for the most part of an age and in a condition to carry on their occupations.

TABLE V.—Diabetes. Actual and Expected Deaths, 1930-3

		Ages under 45	Ages 45-55	All Ages under 55	Deficiency under 55	All Ages over 55	Excess over 55
1930	Actual ...	682	549	1,231	508	4,428	567
	Expected	1,107	632	1,739		3,861	
1931	Actual ...	702	540	1,242	500	4,568	460
	Expected	1,112	630	1,742		4,108	
1932	Actual ...	691	527	1,218	532	4,890	593
	Expected	1,116	634	1,750		4,297	
1933	Actual ...	723	501	1,224	530	5,054	567
	Expected	1,117	637	1,754		4,487	

Lengthening of Life in Pernicious Anaemia

For a disease whose incidence of new cases may be regarded as constant over the period under review, Table III suggests a simple method of depicting and measuring the net improvement in the length of life which may be attributed to a new “maintenance treatment.” The total years of life lived after diagnosis by the 100 cases in Table III would be, under A conditions (that is, before the treatment was introduced), 200 years, and under B conditions it would be given by the sum of the products 2×10 , 8×9 , 15×8 , 20×7 , 25×6 , 20×5 , 10×4 , or 642 years, the average increase in life due to the new therapy being, therefore, 4.4 years. If the mean age at death is calculated simply from the A and B distributions of 100 deaths by ages (taking the mean ages of the groups to be 20, 30, 40, 50, 60, 70, 80), the A distribution gives 57.6 years and the B distribution 61.8 years, the difference being 4.2 years, or practically the same result as was found from direct knowledge of the incidence of cases and mean durations of life. From this and other considerations the simple method depicted in Figs. 1 and 2 emerges of assessing the average increase in duration of life of pernicious anaemia cases which has resulted since the new forms of treatment were introduced.

The mean age at death has first been calculated for each sex in each year since 1921 for pernicious anaemia, by means of the Registrar-General's records for England and Wales, and the results are given in Table VI, and represented by the continuous lines in Figs. 1 and 2. Part of the rise which is evident is merely due to the gradual increase in the average age of the living population, and, in order to allow for this, the mean age at death which would have obtained had the death rates at each age remained unaffected by the changes in treatment has been calculated for each year. The 1921-6 death rates for each sex at eight age groups have been multiplied by the populations for that sex and age, giving the expected deaths at each age, and by summation the

FIG. 1.—Pernicious anaemia. Mean age at death. Males. (— = actual; = expected at 1921-6 rates.)

FIG. 2.—Pernicious anaemia. Mean age at death. Females. (— = actual; = expected at 1921-6 rates.)

total deaths, from which the expected mean age at death for each sex has been found in each successive year. The expected mean ages at death are given in Table VI, and are represented by broken lines in Figs. 1 and 2.

TABLE VI.—Pernicious Anaemia. Mean Ages at Death

	Males			Females		
	Actual	Expected	Difference	Actual	Expected	Difference
1921 ...	55.9	56.2	-0.3	53.5	54.3	-0.8
1922 ...	55.6	56.2	-0.6	54.7	54.4	0.3
1923 ...	55.9	56.3	-0.4	54.2	54.5	-0.3
1924 ...	57.4	56.4	1.0	54.8	54.6	0.2
1925 ...	57.0	56.5	0.5	55.2	54.6	0.6
1926 ...	56.9	56.7	0.2	55.5	54.9	0.6
1927 ...	58.5	56.8	1.7	55.9	54.9	1.0
1928 ...	58.0	57.0	1.0	57.1	55.1	2.0
1929 ...	59.8	57.1	2.7	58.1	55.2	2.9
1930 ...	59.4	57.2	2.2	58.6	55.9	2.7
1931 ...	60.9	57.4	3.5	58.7	55.7	3.0
1932 ...	60.8	57.5	3.3	59.8	55.8	4.0
1933 ...	61.1	57.6	3.5	60.0	55.9	4.1

The expected mean ages at death rose from 1921 to 1926, owing to the increasing proportion of older people alive in the population, by half a year. During the same period the actual mean age at death increased slightly more rapidly, which may indicate some small improvement in the survival of pernicious anaemia cases during those years. From 1926 to 1933 the rise in actual mean age was greater than the expected rise by 3.3 years for males and by 3.5 years for females. The lengthening of life which can reasonably be attributed to the improved therapy dating from 1927 is, therefore, three to three and a half years as an average for the whole population of cases, however treated and of all ages.

The treatment has scarcely been long enough in use for a balance between incidence and mortality to be reached, and moreover, as Mills and Herring³ have recently pointed out, a further improvement is to be looked for as the importance of persistent and regular treatment to prevent relapse is gradually brought home to those who suffer from the disease. The mean age at death of 100 cases distributed as in Table III would be raised above 70 years if their expectation of life was that of the general population, so there would appear to be plenty of room for such improvement.

Lengthening of Life in Diabetes

For diabetes the actual mean age at death is shown in Table VII and Fig. 3 for each year from 1915 to 1933. The expected mean ages at death are calculated by

FIG. 3.—Diabetes. Mean age at death. (— = males; = females.)

applying the 1920-2 mortality rates at each age group under 55 to the corresponding populations in each year 1921 to 1933, whilst at the age groups over 55 the rates used are the 1920-2 rates increased successively, for reasons previously explained, by the average annual increments observed during the decade preceding 1915. The deaths thus calculated at the various ages are summed, and the mean ages thus obtained for each year are given in Table VII.

The rise in the expected mean age at death is more rapid than for pernicious anaemia, for it is produced not only by the increasing proportions of old people alive, but also by the rapid increase in the "senile" form of diabetes (or in the certification of it), whilst the incidence of the diabetes of younger ages is presumably not increasing. The simple difference between the actual and expected figures gives an approximate estimate of the average lengthening of life attributable to insulin in the whole population of diabetics, but this must be considerably less than the average lengthening of life of those who receive insulin, since a large proportion of the diabetics of advanced age, who provide such a considerable fraction of the total deaths, presumably do not require or receive insulin treatment, and therefore their expectation of life has not been affected by it. The increase since 1922 in the average age to which the whole population of diabetics lives is eight years for males and

seven for females, and after deducting the expected increases due to the population and incidence changes, the average improvement for *all* diabetics, attributable to insulin treatment of some fraction of them, is three and a half years (see note below Table VII). If insulin is being applied to only one-half of the total diabetics of all ages, these figures would have to be doubled to give the average lengthening of life of those treated by insulin.

TABLE VII.—*Diabetes. Mean Ages at Death*

	Males			Females		
	Actual	Expected	Difference	Actual	Expected	Difference
1915	52.9	—	—	56.3	—	—
1916	53.8	—	—	55.8	—	—
1917	54.3	—	—	55.8	—	—
1918	52.7	—	—	54.0	—	—
1919	53.7	—	—	55.1	—	—
1920	54.3	—	—	55.7	—	—
1921	53.7	54.1	-0.4	55.5	56.0	-0.5
1922	54.2	54.3	-0.1	56.7	56.3	0.4
1923	56.9	54.7	2.2	57.9	56.8	1.1
1924	57.9	54.8	3.1	59.7	57.1	2.6
1925	58.2	55.1	3.1	59.8	57.4	2.4
1926	58.4	55.5	2.9	60.4	57.9	2.5
1927	58.9	55.7	3.2	61.4	58.3	3.1
1928	60.4	56.1	4.3	61.5	58.7	2.8
1929	59.8	55.3	3.5	62.1	58.9	3.2
1930	60.7	56.6	4.1	63.0	59.3	3.7
1931	61.1	57.0	4.1	62.9	60.0	2.9
1932	62.1	57.1	5.0	63.2	60.2	3.0
1933	62.0	57.6	4.4	63.4	60.6	2.8

Note.—There is reason to believe that the use of 1915 rates (see Table IV) at ages 65 to 75 has led to some overestimation of the expected mean age at death for females, with perhaps an underestimation for males.

Fortunately, Table V provides a clue to the average lengthening of life of all those diabetics who in pre-insulin days would have died before 55, the great bulk of these younger diabetics being now presumably insulin-treated. In 1933, 530 deaths which would otherwise have occurred before 55 are estimated to have been postponed till after 55, and this number can be regarded as the excess of deaths transferred from the age group 45 to 55 to the group ten years older over those transferred from the group ten years younger to the group 45 to 55. The expected deaths at 45 to 55 were 637, of which 530, or 83 per cent., were transferred to an age group ten years older, which means that since 1921 the average lengthening of life at ages up to 55 is about 8.3 years. The 1932 figures give 8.4, 1931 gives 7.9, and 1930 gives 8.0 by the same methods; so we may estimate that the *average lengthening of life for diabetics who in pre-insulin days died before 55 has been about eight years*. This addition of about eight years on the average during the working period of life is no small achievement, since the majority of the patients are able to carry on their normal activities.

For diabetics over 55 years of age the average lengthening of life of the insulin-treated must, owing to the much greater risks of death from heart and other affections at the higher ages, be less than this, but it cannot be ascertained unless we know what proportion are insulin-treated.

It may be recalled that Joslin, Dublin, and Marks⁴ estimated the average duration of diabetic life from

clinical experience in America of patients of all ages during 1926–30 as 8.4 years, but concluded that by 1934 “in view of all the circumstances we believe that an average of ten years’ duration between onset and death is a conservative estimate.” In pre-insulin days the average duration was perhaps two to three years, so this would imply an average lengthening by seven or eight years for the insulin-treated of all ages.

Summary

1. It is estimated that since the introduction of the new methods of treatment in recent years there has been an average lengthening of life of all persons afflicted by pernicious anaemia in England and Wales amounting to three to three and a half years, and of all diabetics amounting to three and a half years. The changes in the distribution of deaths by ages can be explained by a greater lengthening of the duration of life for the young than for the old patients, the above being average figures for all ages.

2. These averages, based upon the Registrar-General’s statistics of deaths, naturally embrace those who for various reasons do not receive or do not continue the specific treatment, and the average advantage to the treated alone would be considerably higher for diabetes. Assuming that the rate of incidence of the diabetes which used to be productive of deaths before age 55 has not appreciably changed since 1921, it is estimated that there has been an average lengthening of life for this class of diabetics amounting to about eight years.

3. Mortality attributed to diabetes has continued to increase since 1922 at ages over 55 at a greater rate than can be accounted for by the postponement of death from the younger ages by insulin, and it is found that the increase in this form of diabetes mortality, over and above what can be thus accounted for, has been proceeding at about the same rate as during the decade preceding the war. To what extent this steady increase in deaths ascribed to diabetes at advanced ages represents a real increasing incidence, and to what extent it is due to an increasing recognition of it and mention of it on death certificates is difficult to decide.

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- ⁴ Joslin, Dublin, and Marks: *Amer. Journ. Med. Sci.*, 1924, clxxxvii, No. 4, 434.

The epidemiological report of the Health Section of the League of Nations, which now appears quarterly instead of monthly, contains in the January–March issue a survey of the incidence and mortality of cerebro-spinal fever throughout the world. In Africa the countries most affected have been Egypt and the Anglo-Egyptian Sudan. In the former, however, the number of cases has declined to less than half that for 1933, while in the latter 1934 was marked by an increased severity of the epidemic. In Asia the disease continued in endemic form at the Chinese ports. There was a severe epidemic in the island of Formosa, with 273 cases during the first six months. In Japan the number of cases rose from 359 in 1933 to 1,225 (with 663 deaths) in 1934. The incidence in Manchuria was by no means negligible, but did not reach epidemic proportions. In British India the disease showed a change from its usual sporadic character to the endemo-epidemic form, particularly in the Bombay Presidency, where there were 1,221 cases with 645 deaths, and the urban area of Calcutta (775 cases and 584 deaths). In the Near East it occurred in endemic form. In Turkey the number of cases rose from 627 in 1933 to 641 in 1934, with 206 deaths. In Europe the morbidity was highest in England and Wales (1,115 cases), Germany (1,015), Italy (557), and Poland (526). In North America the morbidity was slightly lower than in the previous year, and in Australasia and Oceania the disease remained sporadic.