STATISTICAL STUDY OF SCARLET FEVER AND DIPHTHERIA

WITH SPECIAL REFERENCE TO (1) CHANGES IN THE AGE DISTRIBUTION OF MORTALITY; (2) EFFECT OF ISOLATION ON THE PREVALENCE AND MORTALITY FROM SCARLET FEVER.

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INTRODUCTION.

In the early records of mortality there was much confusion between scarlet fever and diphtheria. According to Hirsch, after scarlet fever had been clearly differentiated from measles about the middle of the eighteenth century a new error was introduced into the doctrine of scarlet fever. Emphasis was placed on the inflammatory process in the throat which frequently occurs in scarlet fever, and this led to its being confused with diphtheria.

Although Bretonneau's classical description of diphtheria is more than a century old, the nomenclature and definition of this disease were still very confused down to about 1856–9. In 1859 diphtheria was tabulated separately from scarlet fever in the Annual Reports of the Registrar-General, and in that year 9587 deaths were returned as due to diphtheria and 19077 to scarlatina. But these early statistics of diphtheria mortality are very unreliable. There was some ambiguity of diagnosis between diphtheria and croup, and there appears little doubt that many deaths which are now recognised as diphtheria were formerly ascribed to croup. In 1879 a special committee was appointed to try and clear up the difficulty. The result was that fewer deaths were assigned to croup and mortality from diphtheria increased. The deaths from croup were often more numerous than those from diphtheria in the earlier records. In 1882, 3992 deaths were returned as due to diphtheria and as many as 4609 as due to croup, whereas in 1912, thirty years later, there were 4289 deaths from diphtheria and only 40 from croup. The standardised death rates from 1861–1910 given in the decennial periods in the Registrar-General's decennial abstracts show clearly the changes in mortality from these two diseases.

England and Wales.

Death rates per million standardised	1861–70	1871–80	1881–90	1891–1900	1901–10
Diphtheria	166	108	148	254	183
Croup	211	144	128	50	13

Many deaths which would now be ascribed to diphtheria were perhaps ascribed to croup sixty years ago. The Registrar-General was of this opinion

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and for many years, in examining the records of diphtheria mortality, he studied the two diseases conjointly. But, in the Decennial supplement for 1901–10 Stevenson made a special study of the relation of croup to diphtheria and came to the conclusion that the croup of former days was not entirely diphtheritic. In 1910 the deaths from croup numbered 261 and the practitioners certifying these deaths were asked for further information. As a result of this enquiry 123 of the deaths were transferred to laryngitis, 42 to diphtheria and 18 to laryngismus stridulus, reducing to 78 the number finally classified under croup. By 1921 the term croup had practically died out from death certification and when employed enquiries showed as a rule that it did not imply diphtheria.

Since the quinquennium 1861–5 mortality from scarlet fever has been steadily falling. This decline in mortality from scarlet fever is one of the outstanding features of the mortality in England and Wales. In 1861–5 the death rate per million persons living was 982, twenty years later it was less than half and in 1921–5 the rate of mortality was as low as 29 per million living. On the other hand, mortality from diphtheria has not declined to anything like the same extent as scarlet fever. In 1861–5 mortality from scarlet fever was more than three times that from diphtheria, but in 1921–5 the positions were reversed. The death rates per million were: in 1861–5, diphtheria 248, scarlet fever 982; and in 1921–5, diphtheria 88, scarlet fever 29.

The fatality rates for diphtheria are roughly about five times those for scarlet fever, and if one examines the statistics for London from 1892–1927—the longest series available in England and Wales—the decline in fatality has been relatively the same in both diseases. But a little caution must be exercised here. Since the early days of notification, nearly forty years ago, the diagnostic criteria have certainly improved and the standard of reporting has changed, more especially in the case of diphtheria. The introduction and popularisation of bacteriological methods may have had some influence, and probably some of the recent increase of diphtheria can be accounted for by a greater tendency to notify cases on slenderer clinical evidence.

1. CHANGES IN THE AGE DISTRIBUTION.

In the annual reports of the London County Council, Shirley Murphy frequently drew attention to the variations in the age incidence of infectious diseases. From an extensive analysis of diphtheria mortality in London he reached the conclusion that some part of the change in age incidence could be attributed to changes in nomenclature, but that the aggregation of children in elementary schools was probably the chief factor. He found an increasing tendency for children of 3–10 to die from diphtheria, an increase which dated from 1871 (the Elementary Education Act was passed in 1870). Collis inferred from a study of the mortality between 1861 and 1910 that a definite change in the age incidence of mortality from scarlet fever had occurred, leading to a tendency to a maximum in later childhood life. In a paper written in 1907

Shirley Murphy expressed the opinion that variations in the age incidence of infectious diseases occur as a natural phenomenon, probably due to variations in virulence and differences in opportunity of acquiring infection.

It is well known that changes in the character of a disease may affect the age distribution. It seemed therefore of interest to consider what effect the great decline in mortality from scarlet fever during the last sixty years has had on the age distribution of the disease. The data examined were the death rates at ages in decennial periods from 1861 to 1910 (from the Decennial supplements of the Registrar-General) and 1921–4. No change has occurred in the age of maximum mortality. It has been consistently highest in the age group 0–5 for both sexes throughout the periods examined.

In Table I the death rates in 1921–4 are compared with those for the earliest period 1861–70 by expressing the rates at each age as a percentage of those in 1861–70. Mortality at ages 0–5 in males is 3·4 per cent. of what it was in 1861–70 and 4·0 per cent. at ages 5–10, whereas at ages 15–20 mortality is 10·7 of the earlier period and over 10 per cent. for other ages up to 55. The

Table I. *Scarlet Fever. Rates per million.*

Males	0–	5–	10–	15–	20–	25–	35–	45–	55–	65–	75 and up
1861–70	4765	2229	471	149	80	48	23	16	8	5	8
1921–4	161	90	26	16	10	5	4	2	0·4	0·2	—
1921–4 as percentage of 1861–70	3·4	4·0	5·5	10·7	12·5	10·4	17·4	12·5	5·0	4·0	—
Females											
1861–70	4523	2156	537	157	106	73	33	12	10	6	5
1921–4	150	101	36	16	12	9	5	2	2	0·3	0·6
1921–4 as percentage of 1861–70	3·3	4·7	6·7	10·2	11·3	12·3	15·2	16·7	20·0	5·0	12·0

percentages are of the same order for females. The number of deaths from scarlet fever at ages over 25 years is negligible. In 1926 out of a total of 677 deaths only 51 occurred over age 25, therefore the comparison will be confined to the age groups under 25. The fall in the death rates between 1861–1924 has been greatest at ages under 10 years, the period of life chiefly affected by scarlet fever.

The next step was to compare the mortality at ages in each decennium to see if the decline at ages under 10 had been consistent throughout. The standardised death rate for each period was taken as a 100 and the death rates in each age group expressed as a percentage of the standard. This process gives the relative mortality at each age in each decennium and stabilises as far as possible differences in the age constitution over such a long period. The results are shown in Table II. The relative mortality at ages 0–5 was practically stationary for males in each decennium from 1871 to 1900, but for the two later periods the proportion has declined in both sexes. In the next age group the relative mortality has been rising since 1891–1900. In all the other age groups the relative figures have been steadily rising since

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Table II. *Scarlet fever.*

Years	Standardised death rate per million	0–	5–	10–	15–	20–25
Males						
1861–70	(867)	550 ± 3·3	257 ± 2·9	54 ± 1·5	17 ± 0·9	9 ± 0·7
1871–80	(638)	565 ± 3·6	245 ± 3·1	50 ± 1·6	17 ± 1·0	9 ± 0·8
1881–90	(303)	564 ± 4·9	250 ± 4·2	49 ± 2·2	14 ± 1·2	8 ± 1·0
1891–1900	(152)	562 ± 6·6	229 ± 5·6	51 ± 3·0	25 ± 2·2	14 ± 1·8
1901–10	(110)	533 ± 7·3	250 ± 6·5	55 ± 3·6	31 ± 2·8	15 ± 2·0
1921–4	(35)	459 ± 12·5	256 ± 11·8	73 ± 6·9	44 ± 5·5	27 ± 4·7
Differences						
1861–70, 1901–10		− 17 ± 8·0	− 7 ± 7·1	+ 1 ± 3·9	+ *14* ± 2·9	+ 6 ± 2·1
1861–70, 1921–4		− *91* ± 12·9	− 1 ± 12·1	+ 19 ± 7·1	+ *27* ± 5·6	+ *18* ± 4·8
1871–80, 1901–10		− *32* ± 8·1	+ 5 ± 7·2	+ 5 ± 3·9	+ *14* ± 3·0	+ 6 ± 2·2
1871–80, 1921–4		− *106* ± 13·0	+ 11 ± 12·2	+ *23* ± 7·1	+ *27* ± 5·6	+ *18* ± 4·8
Females						
1861–70	(847)	534 ± 3·4	255 ± 2·9	63 ± 1·7	19 ± 1·0	13 ± 0·8
1871–80	(612)	556 ± 3·8	242 ± 3·1	54 ± 1·7	17 ± 1·0	11 ± 0·8
1881–90	(298)	545 ± 5·1	257 ± 4·3	53 ± 2·3	13 ± 1·2	9 ± 1·0
1891–1900	(152)	548 ± 6·7	235 ± 5·6	56 ± 3·1	18 ± 1·8	15 ± 1·7
1901–10	(107)	517 ± 7·6	255 ± 6·7	64 ± 3·9	23 ± 2·4	17 ± 2·0
1921–4	(37)	406 ± 12·3	273 ± 11·9	97 ± 7·7	44 ± 5·4	34 ± 4·9
Differences						
1861–70, 1901–10		− 17 ± 8·3	0	+ 1 ± 4·3	+ 4 ± 2·6	+ 4 ± 2·2
1861–70, 1921–4		− *128* ± 12·8	+ 18 ± 12·2	+ *34* ± 7·9	+ *25* ± 5·5	+ *21* ± 5·0
1871–80, 1901–10		− *39* ± 8·5	+ 13 ± 7·4	+ 10 ± 4·3	+ 6 ± 2·6	+ 6 ± 2·2
1871–80, 1921–4		− *150* ± 12·9	+ 31 ± 12·3	+ *43* ± 7·9	+ *27* ± 5·5	+ *23* ± 5·0

1881–90. To test the significance of these variations, *i.e.* to see if they may have arisen as a result of a chance alone, the probable errors of the proportions were calculated from a formula[1] for which I am indebted to Mr Soper, and from these the probable errors of the differences between the earlier and later periods were calculated.

The mortalities for 1861–70 and 1871–80 are each compared separately with those for 1901–10 and 1921–4. A difference of more than three times its probable error is usually regarded as a significant one and where the differences fulfil this criterion they are italicised. It appears from this analysis, that the mortality from scarlet fever has declined relatively most at the earliest age group 0–5 and there is tendency for a greater proportion of the mortality to occur among older children and young adults. In other words, while the absolute mortality from scarlet fever has fallen at every age, the relative importance of mortality in later life has increased. It is interesting to note that the same result was found by Pope in a recent study on the epidemiology of scarlet fever in Providence. He found definite evidence of a shifting of mortality from the lower to the higher age groups.

[1] The Standard Deviation of the percentage that the death rate in a particular age group is of the standardised death rate is approximately:

$$100 \times \frac{(d_a)^{\frac{1}{2}}/P_a}{S\,(P_a'/P' . d_a/P_a)} \times \left(1 - \frac{P_a'/P' . d_a/P_a - \frac{1}{2} d_a/P}{S\,(P_a'/P' . d_a/P_a)}\right),$$

where d_a = deaths at age a, P_a = exposed to risk at age a, P_a' = the standardised number exposed at a, and S is the symbol of summation for all values of a.

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A similar analysis has been made of the mortality at ages during the last sixty years for diphtheria. In Table III the death rates at each age in 1921–4 are expressed as a percentage of the corresponding rate in the earliest period

Table III. *Death rates per million. Diphtheria.*

	0–	5–	10–	15–	20–	25–	35–	45–	55–	65–	75 and up
Males											
1861–70	760	340	107	58	35	24	20	22	30	33	32
1921–4	523	340	86	17	5	5	3	2	3	4	2
1921–4 as percentage of 1861–70	68·8	100	80·4	29·3	14·3	20·8	15·0	9·1	10·0	12·1	6·3
Females											
1861–70	781	450	166	61	41	28	22	22	22	21	20
1921–4	496	416	93	18	9	5	4	5	3	3	4
1921–4 as percentage of 1861–70	63·5	92·4	56·0	29·5	22·0	17·9	18·2	22·7	13·6	14·3	20·0

1861–70. It is evident that although the age of maximum mortality was 0–5 in both periods, the age group showing the least change was 5–10 for both sexes. At this age the death rate for males was the same in the two periods and for females the death rate in 1921–4 was 92·4 per cent. of that in 1861–70.

In Table IV the relative mortalities are given from ages 0–5 to 20–25. The most important features of this table are the increases at ages 5–10 and the decreases at ages 15–20 and 20–25. With one exception the changes in the later period when compared with the earlier are significant with regard to the probable errors. Fatal diphtheria is concentrating on early school age

Table IV. *Diphtheria.*

Years	Standardised death rate per million	0–	5–	10–	15–	20–25
Males						
1861–70	(155)	490 ± 7·6	219 ± 6·4	69 ± 4·1	37 ± 3·2	23 ± 2·7
1871–80	(102)	465 ± 8·7	252 ± 7·7	71 ± 4·8	27 ± 3·1	20 ± 3·0
1881–90	(140)	491 ± 7·1	266 ± 6·3	60 ± 3·5	25 ± 2·4	14 ± 2·0
1891–1900	(248)	560 ± 6·0	248 ± 4·7	45 ± 2·5	15 ± 1·8	8 ± 1·3
1901–10	(178)	540 ± 5·7	277 ± 5·3	49 ± 2·6	11 ± 1·3	6 ± 1·0
1921–4	(109)	480 ± 7·1	312 ± 7·1	79 ± 4·1	16 ± 2·0	4 ± 1·0
Differences						
1861–70, 1901–10		+ *50* ± 9·5	+ *58* ± 8·3	− *20* ± 4·9	− *26* ± 3·5	− *17* ± 2·9
1861–70, 1921–4		− 10 ± 10·4	+ *93* ± 9·6	+ 10 ± 5·8	− *21* ± 3·8	− *19* ± 2·9
1871–80, 1901–10		+ *75* ± 10·4	+ 25 ± 9·3	− *22* ± 5·5	− *16* ± 3·4	− *14* ± 3·2
1871–80, 1921–4		+ 15 ± 11·2	+ *60* ± 10·5	+ 8 ± 6·3	− *11* ± 3·3	− *16* ± 3·2
Females						
1861–70	(176)	444 ± 7·2	256 ± 6·4	94 ± 4·4	35 ± 2·9	23 ± 2·4
1871–80	(114)	417 ± 8·2	287 ± 7·7	92 ± 5·1	33 ± 3·3	19 ± 2·5
1881–90	(156)	444 ± 6·7	304 ± 6·3	74 ± 3·7	24 ± 2·3	13 ± 1·7
1891–1900	(260)	514 ± 5·1	286 ± 4·6	53 ± 2·3	14 ± 1·2	8 ± 1·0
1901–10	(189)	498 ± 5·7	319 ± 5·4	50 ± 2·6	11 ± 1·3	5 ± 1·0
1921–4	(115)	431 ± 7·0	362 ± 7·2	81 ± 4·0	16 ± 1·9	8 ± 1·4
Differences						
1861–70, 1901–10		+ *54* ± 9·2	+ *63* ± 8·4	− *44* ± 5·1	− *24* ± 3·2	− *18* ± 2·5
1861–70, 1921–4		− 13 ± 10·0	+ *106* ± 9·6	− 13 ± 5·9	− *19* ± 3·5	− *15* ± 2·8
1871–80, 1901–10		+ *81* ± 10·0	+ *32* ± 9·4	− *42* ± 5·7	− *22* ± 3·5	− *14* ± 2·7
1871–80, 1921–4		+ 14 ± 10·8	+ *75* ± 10·5	− 11 ± 6·5	− *17* ± 3·8	− *11* ± 2·9

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and decreasing at older ages. Shirley Murphy's suggestion that the greater opportunity of infection by the attendance of children at the elementary schools has brought about this change is the hypothesis which best describes the facts.

The tendency of mortality from diphtheria to concentrate on early school age is a factor of particular importance with regard to the new methods of handling this disease. In a recent report, Forbes maintained with reference to the Schick test and toxin-antitoxin treatment that "there is now very little doubt that their systematic adoption would result in a great yearly saving of child life." The statistical evidence in support of this statement is perhaps ambiguous. To give one instance, the New York experience does not give any support to the contention that immunisation has had any effect upon either the death rate or the case rate, if one fits a straight line to the trend of mortality previous to 1918 and extrapolates for the years of treatment. The mortality falls very near the extended trend line; in other words, what has happened in New York since 1917 might have been expected to happen if there had been no new prophylaxis at all. The argument against this test is that the number of children treated up to the present is not large enough to show any effect on the total mortality. It is not intended here to dispute the efficacy of these prophylactic measures, only to suggest that some caution is necessary in accepting statements for which the statistical evidence is at present inadequate. There *is* other evidence as to the value of the immunisation methods. Take the experience of the nursing staffs in fever hospitals. In Little Bromwich Hospital, Birmingham, since 1922 and the City Fever Hospital, Edinburgh, since 1923 it has been the practice for the nursing staffs to be Schick tested on entry and those found susceptible to diphtheria to receive immunising doses of toxoid-antitoxin. In Little Bromwich Hospital the attack rate during the years 1922–4 was 3·7 per cent. per annum among an average nursing staff of 108. During the three years immediately preceding the introduction of immunisation the attack rate was 17·8 among an average nursing staff of 90. The difference between the attack rates for the two periods is more than four times its probable error, $14{\cdot}1 \pm 2{\cdot}98$—a greater difference than would be expected as a result of chance alone.

Further evidence is given by the Edinburgh experience. The attack rate in the pre-immunisation period 1919–22 was 9·5 per cent. among an average nursing staff of 147. In the post-immunisation period 1923–5 the attack rate was 3·5 per cent. and the average nursing staff 142. Here again there is a significant difference between the two attack rates $6{\cdot}0 \pm 1{\cdot}9$, and one is justified in concluding that in these two hospitals the protective measures have been successful.

If immunisation by means of the Schick test and toxin-antitoxin treatment is to be effective in reducing the incidence of and mortality from diphtheria among children, this analysis of the age distribution shows that the treatment must be given in the pre-school period or on entrance to school.

2. THE EFFECT OF ISOLATION UPON THE PREVALENCE AND MORTALITY FROM SCARLET FEVER AND DIPHTHERIA.

Although during the last twenty-five years scarlet fever has caused comparatively little loss of life, it has been responsible for much sickness. In 1926, over 81,000 cases were notified in England and Wales. A large proportion of the patients go to hospital and their treatment and isolation involves the expenditure of much public money.

Recently an enquiry was made by a special committee of the Ministry of Health into some administrative aspects of scarlet fever. Certain statistical analysis were made from the committee's data by Prof. Greenwood. The problem was to determine whether, from the statistics of cases and deaths, it could be shown that the practice of isolation had been effective in preventing the spread of scarlet fever and whether isolation had been an important factor in the decline of mortality from this disease. The process of analysis was this. Only districts were chosen which had either in the period 1906–10 or in 1911–15 returned at least 10 deaths from scarlet fever, the object being to exclude small districts greatly affected by random fluctuations. On this criterion 46 county boroughs and 48 urban districts were selected for the investigation. The towns dealt with provided a fair sample of the urban population of this country, from large manufacturing towns to seaside places and county towns. The data were divided into three periods: namely, 1906–10, 1911–15 and 1919–23. The isolation rate was measured as the average number of cases removed to hospital expressed as a percentage of total cases in each five year period, the attack rate was the number of cases per 1000 of the population, the death rate, the deaths per 100,000 population and the case mortality, the deaths per 1000 attacked.

In 1915 Prof. Karl Pearson and Miss Elderton published a statistical study of the effects of isolation on the attack rates and death rates from diphtheria. The scarlet fever data of the Ministry of Health were analysed on similar lines to those adopted for the diphtheria study so that the results might be compared for the two diseases. The data for the Pearson and Elderton study were supplied by Dr Snell, Medical Officer of Health for Coventry, and he obtained for a period of nine years, 1904–12 inclusive, for about eighty towns or districts of large populations, the annual number of diphtheria cases, the number removed to hospital and the number of deaths. The chief results of the Pearson and Elderton enquiry were that they were unable to demonstrate any important effect of isolation upon the prevalence or general mortality from diphtheria, but they were able to show that case mortality was usually negatively correlated with the proportion of cases isolated. The obvious interpretation is that the advantages of clinical handling, such as the use of anti-toxin tracheotomy etc., in special hospitals produced this result.

The different constants relating to scarlet fever for the three periods are shown in Table V. It will be seen that between 1906–10 and 1919–23 there has been some increase of the proportion of cases isolated, a decided decrease in both fatality and mortality and some decrease in the attack rate. If one finds a significant negative association between isolation and the case rate *and death rate from scarlet fever, that is to say that the incidence and death*

Table V. Scarlet Fever. Mean and Standard Deviations.

Variables	1906–10 Mean	1906–10 S.D.	1911–15 Mean	1911–15 S.D.	1919–23 Mean	1919–23 S.D.
Isolation rate per 100 cases	60·1	28·35	64·7	25·41	68·3	23·63
Case mortality per 1000 cases	26·9	13·51	17·98	8·48	11·49	6·96
Death rate per 100,000 population	11·0	6·79	7·21	4·78	3·27	2·45
Attack rate per 1000 population	4·1	1·63	3·87	1·56	2·85	1·12

	Mean	S.D.
% overcrowding 1911	8·49	8·07
% overcrowding 1921	9·77	8·59
Infant mortality 1911–15	114·47	23·72
Infant mortality 1919–23	75·96	15·32

rate are significantly lower in districts where isolation is higher, and the magnitude of this association has increased during the last twenty years, one may say there is substantial evidence that isolation has been effective. The correlation results are shown in Table VI together with those relating to the diphtheria study by Elderton and Pearson. The coefficients of correlation between isolation rate and attack rate are all negligibly small. There appears to be no general tendency for scarlet fever to be less prevalent in districts with a high proportion of isolated cases. Neither can one demonstrate that

Table VI. *Coefficients of Correlation.*

Variables		1906–10	1911–15	1919–23
Isolation rate and attack rate	Scarlet fever	−·043 ± ·069	+ ·049 ± ·069	−·108 ± ·069
	Diphtheria	+ ·427 ± ·063	+ ·290 ± ·069	
Isolation rate and death rate	Scarlet fever	−·156 ± ·068	+ ·010 ± ·070	+ ·063 ± ·069
	Diphtheria	+ ·153 ± ·075	−·012 ± ·075	
Isolation rate and death rate *Constant* attack rate	Scarlet fever	−·163 ± ·068	−·040 + ·069	+ ·159 ± ·068
	Diphtheria	−·204 ± ·074	−·305 ± ·068	
Isolation rate and case mortality	Scarlet fever	−·290 ± ·064	−·194 ± ·067	+ ·149 ± ·068
	Diphtheria	−·509 ± ·057	−·534 ± ·054	
Attack rate and case mortality	Scarlet fever	+ ·063 ± ·069	+ ·203 ± ·067	+ ·095 ± ·069
	Diphtheria	−·527 ± ·056	−·495 ± ·057	
Attack rate and death rate	Scarlet fever	+ ·599 ± ·045	+ ·749 ± ·031	+ ·594 ± ·045
	Diphtheria	+ ·677 ± ·042	+ ·688 ± ·040	
Isolation rate and case mortality *Constant* number attacked	Scarlet fever	−·295 ± ·064	−·216 ± ·066	+ ·153 ± ·068
	Diphtheria	−·474 ± ·056	−·512 ± ·057	

the death rate is lower when the isolation rate is higher. This result was further tested by ascertaining whether the correlation was significantly altered by holding constant both the number of cases of scarlet fever and the population, *i.e.* one only allowed to vary deaths from scarlet fever and number of isolated cases. The correlation was practically unchanged.

In the two earlier periods the association between isolation and case mortality is negative and significant, but for the later experience the relation is changed to an insignificant positive one. In the earlier experience there

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was a tendency for case mortality to be low where isolation was high, but one cannot on the 1919–23 experience assert that the fatality rate is really lower when the isolation rate is higher.

Dr McKinlay suggested the following explanation. He pointed out that the severity of any disease is a graded character which may or may not admit of quantitative definition, but a *qualitative* division is possible in every case. Suppose in scarlet fever we choose some arbitrary group, graded from extremely mild to very severe. The exact type of distribution cannot be determined, but in the disease considered (with at the present time a practically negligible fatality) it is fairly certain that the fractional area of the distribution corresponding to the very severe cases is very small. A hypothetical distribution which would seem to be reasonable is a skew-positive one. Considering the low case fatality of scarlet fever, the proportion of very severe cases would not exceed say 10 per cent. of the total. Now let us assume that selective admission occurs, only those cases likely to prove fatal being removed to hospital. Under such circumstances it follows that whether the proportion of isolated cases be 15, 20, or 100 per cent. is irrelevant from the point of view of fatality although not necessarily irrelevant in regard to other aspects, *e.g.* prevention of the spread of the disease by contact. There might in fact be a high correlation between (*a*) percentage isolated, and (*b*) case fatality; but if the factor (*a*) varies only *outside* the limits within which any sensible correlation is to be expected, the coefficient of correlation is meaningless for this purpose. The main argument against selective admission (on the basis of severity) as a possible explanation of the lack of correlation between fatality and isolation in scarlet fever is that the prognosis must often be obscure at the early stages when removal to hospital has to be decided.

It seemed desirable to test the possibility of any "spurious" association in the correlations due to variation in population. It was satisfactory to find that no spurious element was involved. All the correlations with population were small and insignificant. The next point discussed was whether the total number attacked, being a factor of both isolation rate and case mortality, produced "spurious" correlations. Here again the correlations were insignificant. In the earlier period the correlations between isolation rate and case mortality were slightly increased where there was no variation in the number attacked. For the last period the correlation was slightly lower and insignificant.

It was of some interest to consider the type of district in which isolation is most practised, and to ascertain the possible influence of general social conditions. Elderton and Pearson concluded that the more prosperous and healthy districts have the greater isolation and these are subject to somewhat greater incidence. The usual statistical measures of sanitary conditions, *i.e.* the infant mortality rate and the percentage of the population living more than two per room, were correlated with scarlet fever attack rate, death rate and isolation rate. (Table VII.)

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As far as these measures are concerned they do not in any way determine the attack rate of scarlet fever. The death rate is positively correlated with both indices and in every case the correlations are significant. One may therefore conclude, that towns with bad social conditions tend to have a higher death rate from scarlet fever. With regard to isolation the index of overcrowding is positively correlated with the amount of isolation with one exception, but the correlations are small and only that for the period 1919–23 is significant. The conclusion was that towns with more overcrowding and

Table VII. *Coefficients of Correlation.*

Variables		1906–10	1911–15	1919–23
Attack rate and % overcrowding	Scarlet fever	$-\cdot122\pm\cdot069$	$+\cdot102\pm\cdot069$	$+\cdot093\pm\cdot069$
	Diphtheria	$-\cdot153\pm\cdot075$	$-\cdot136\pm\cdot074$	
Death rate and % overcrowding	Scarlet fever	$+\cdot195\pm\cdot067$	$+\cdot283\pm\cdot064$	$+\cdot250\pm\cdot065$
	Diphtheria	$+\cdot061\pm\cdot079$	$+\cdot004\pm\cdot075$	
Isolation rate and % overcrowding	Scarlet fever	$-\cdot109\pm\cdot069$	$+\cdot106\pm\cdot069$	$+\cdot208\pm\cdot067$
	Diphtheria	$-\cdot236\pm\cdot073$	$-\cdot235\pm\cdot071$	
Attack rate and infant mortality	Scarlet fever		$+\cdot067\pm\cdot069$	$+\cdot004\pm\cdot070$
	Diphtheria		$-\cdot206\pm\cdot072$	
Death rate and infant mortality	Scarlet fever		$+\cdot289\pm\cdot064$	$+\cdot437\pm\cdot063$
	Diphtheria		$+\cdot118\pm\cdot074$	
Isolation rate and infant mortality	Scarlet fever		$-\cdot247\pm\cdot067$	$-\cdot066\pm\cdot069$
	Diphtheria		$-\cdot375\pm\cdot065$	

bad social conditions have a higher death rate from scarlet fever, but there is very little evidence that more isolation is practised in the overcrowded districts. As Prof. Greenwood pointed out in the Ministry of Health's report, this may mean that high or low proportions of admissions are much more determined by the variations of general policy of the health and medical authorities from place to place than from particular circumstances of the individual place.

The conclusions from this statistical analysis amounted to this. It could not be shown that during the period studied isolation has had any effect, good or bad, on the prevalence or mortality from scarlet fever. It is realised that the method of analysis is open to criticism from the statistical point of view. The distributions were asymmetrical but the data were too few to allow a more elaborate analysis, and owing to the low death rates from scarlet fever the rates themselves are subject to the chance errors of sampling. But against this criticism it may be pointed out that the results obtained were in general agreement with the tabulated opinions obtained by questionnaires from the Medical Officers.

In 1926, Chapin, from a study of scarlet fever in various countries, put forward the theory, that the present mild type of the disease may be due to the selective force of case isolation having eliminated the more virulent strains. He pointed out that the fatality rate had decreased more recently and less regularly in America than in England. The majority of American communities were slower in adopting isolation and less rigorous in enforcing it than English or Scandinavian peoples. Holst was of a different opinion. He examined the statistics of morbidity and fatality of scarlet fever in Norway and found that the decline of the fatality curve was greatest when isolation in hospital was still very incomplete. He considered the decline of scarlet fever was dependent upon an unknown factor and that it had not been influenced perceptibly by the measures of isolation. No figures are given of the amount of isolation in Norway, but Holst illustrates his point with a comparison of mortality in Norway and Sweden. The sharp decline in the mortality appeared in Norway ten years before Sweden, although the conditions as to isolation were the same. Again he shows that although in Bergen and Frondlijem, two principal towns of Norway, the practice of isolation almost ceased fifteen years ago, the disease has been less prevalent and less fatal than in Oslo where strict hospitalisation is still continued.

The practice of isolation is probably more stringently carried out in London than in other large towns of England. A special study has been made of the experience of the Metropolitan Boroughs. The data, which were obtained from the annual reports of the Metropolitan Asylums Board, were analysed in two periods, 1911–15 and 1923–6.

It will be seen that the attack rate, death rate and case mortality have declined considerably during the last fifteen years.

Scarlet fever in London	1911–15	1923–6
Isolation rate per 100 cases	89·2	83·0
Attack rate per 1000 population	3·5	2·5
Fatality rate per 1000 cases	15·1	9·4
Death rate per 100,000 population	5·3	2·4

Since 1911–15 the death rate has fallen to less than half, the incidence in 1923–6 was 28 per cent. less than in 1911–15 and the case mortality declined more than 35 per cent. during the two periods. Isolation was slightly lower in 1923–6 but still over 80 per cent.

Has the practice of isolating the majority of cases been an important factor in the decline of scarlet fever in London? Scarlet fever has changed continuously with time and as the present decline started in the early 'nineties before the practice of isolation was in full force even in London, it cannot be argued that isolation has been one of the *primary* causes of the decline.

The first test was to compare the London data with those for the large towns used in the first study, although the periods are not strictly comparable. The analysis for the towns was confined to the periods 1911–15 and 1919–23, the data for London related to 1911–15 and 1923–6. Of 93 towns supplying information for the two periods, 31 were isolating not less than 80 per cent. of the scarlet fever cases in 1911–15. It will be seen from Table VIII that the mean fatality rate and death rate were both appreciably higher in the 31 towns than in London. The decline in incidence was approximately the same in both areas, 29·1 per cent. against 28 per cent. The improvement in case mortality was greater in London, but relatively the decline in the death rate was only slightly greater in London than in the towns. So far it appears that a high degree of isolation is associated with a considerable improvement in incidence and mortality. What improvement was shown by towns with a rate of less than 80 per cent. isolation? There were 21 towns isolating between 70 and 80 per cent. of the cases in 1911–15. In this group the attack rate had declined 32 per cent., the fatality rate 34 per cent. and the death rate 60 per cent. in 1919–23. These towns were in a more favourable position both relatively and absolutely as regards the decline in fatality and death rate than towns isolating over 80 per cent. The 22 towns in the 50–70 per cent. isolation group had improved less in incidence but about the same in fatality and death

Table VIII.

		1911–15				1919–23 (London 1923–6)							
	No. of towns	Mean isolation rate	Attack rate per 1000	Fatality rate per 1000	Death rate per 100,000	Mean isolation rate	% increase or decrease	Attack rate per 1000	% increase or decrease	Fatality rate per 1000	% increase or decrease	Death rate per 100,000	% increase
London	—	89·2	3·47	15·1	5·3	83·0	– 7·0	2·5	–28·0	9·4	–37·7	2·39	–
County Boroughs and Urban Districts Isolation rate in 1911–15													
Over 80 %	(31)	86·8	3·81	17·9	7·2	85·4	– 1·6	2·7	–29·1	12·3	–31·3	3·43	–5
70–80 %	(21)	74·5	3·98	16·4	7·7	78·4	+ 5·2	2·7	–32·2	10·9	–33·5	3·06	–6
50–70 %	(22)	60·9	3·98	17·7	7·1	66·2	+ 8·7	3·0	–24·6	12·3	–30·5	3·55	–5
Under 50 %	(19)	19·6	4·04	19·2	7·2	32·5	+66·0	2·7	–33·2	9·6	–50·0	3·02	–5

rate as the 80 per cent. group. But the greatest contrast appeared in the last group, towns isolating less than 50 per cent.—actually the mean isolation rate was 19·6 per cent. in 1911–15 and 32·5 in 1919–23. This group recorded a higher attack rate and fatality rate than any other group in 1911–15, but in 1919–23 it recorded the greatest improvement. The attack rate declined 33 per cent., the fatality rate declined 50 per cent. and now occupied the lowest place among the groups while the death rate had declined to less than half. In other words, the improvement was as great in towns with little isolation as in those isolating most of the cases.

The next test was to see whether there was any relation between the amount of isolation in the Metropolitan Boroughs and incidence and fatality. The difficulty which arises in applying the method of correlation to the London data is that owing to the large proportion of cases isolated in each of the Boroughs and the consequent limitation of the possible range of variation of one factor, the meaning of the correlation is not always clear.

The zero order correlations between isolation and attack rate, death rate and fatality rate of scarlet fever are uniformly positive (Table IX), but the correlations for the later period are consistently lower than those for the earlier period, and are all insignificant with regard to their probable errors. The only significant correlation in the 1923–6 experience was that between the attack rate and death rate. When variations in the attack rate were eliminated, there was some reduction in the correlation between isolation and death rate but the relation, although insignificant, was still a positive one.

As Pearson and Elderton pointed out in their memoir, a positive correlation between isolation and the attack or death rates by no means justifies us in asserting that isolation is worse than non-effective. An attempt to throw further light on the problem was made by considering how much social environment as measured by infant mortality and the percentage living more than two in a room influenced the prevalence and mortality from scarlet fever in London.

Table IX. *Metropolitan Boroughs.*

Variables	Scarlet fever 1911–15	Scarlet fever 1923–6	Diphtheria 1923–6
Isolation rate and attack rate	·417 ± ·125	·341 ± ·115	·147 ± ·127
Isolation rate and death rate	·544 ± ·106	·327 ± ·116	·371 ± ·112
Isolation rate and case mortality	·388 ± ·128	·217 ± ·124	·374 ± ·112
Attack rate and case mortality	− ·131 ± ·148	·136 ± ·127	− ·213 ± ·111
Attack rate and death rate	·496 ± ·114	·469 ± ·101	·825 ± ·041
Isolation rate and death rate Attack rate constant	·431 ± ·138	·268 ± ·121	·448 ± ·104

It has been frequently pointed out that these indices are not absolute measures of the economic prosperity of a town and vary considerably from city to city. London has the advantage of greater statistical homogeneity. In the poorer districts of London it is well known that infant mortality is higher and there are more persons per room than in the districts mainly inhabited by the more prosperous classes. To quote Heron "where there is the greatest poverty, greatest drunkenness, least thrift, there the carelessness of child life is greatest and there the infantile mortality reaches its largest proportions." In 1923–6 the mean infant mortality rate in Hampstead was 53·3; in Shoreditch the rate was as high as 80·7 and it was 74·7 in Bethnal Green. The differences are more striking if one takes the amount of overcrowding. Hampstead is a residential area of the well-to-do and only 6·5 per cent. of its population in 1921 were living more than two per room. In Bethnal Green the percentage was 27·8 and in Shoreditch 32 per cent. It may be noted that these indices of social well-being are not perfectly related; the correlation between them in London is of the order of 0·8. Overcrowding is much more variable than infant mortality. The coefficient of variation is 12 per cent. for infant mortality and 46·4 for overcrowding. But infant mortality is dependent on many other factors than good environment and probably the proportion living under overcrowded conditions is a better index of poverty than infant mortality.

The following calculations show the possible influence of environment.

	Scarlet fever 1923–6
Isolation and infant mortality	+ ·043 ± ·130
Attack rate and infant mortality	+ ·284 ± ·119
Death rate and infant mortality	+ ·449 ± ·104
Fatality rate and infant mortality	+ ·418 ± ·107
Isolation and poverty (% overcrowding)	+ ·094 ± ·129
Attack rate and poverty ,,	+ ·562 ± ·089
Death rate and poverty ,,	+ ·302 ± ·188
Fatality rate and poverty ,,	+ ·143 ± ·127

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The death rate and fatality rate are positively and significantly correlated with infant mortality. Those districts with a higher infant death rate tend to have a higher death rate from scarlet fever. The correlations between isolation and these two indices are negligible. There is no relation between the amount of isolation and type of district. The attack rate appears to be highest in districts where there is most overcrowding, but overcrowding is not an important factor of the death rate or fatality rate.

It was suggested that a better measure of social environment might be obtained by taking the ratio of males in occupations graded by the Registrar-General into Social Classes I and II, to all occupied males in each of the London Boroughs. The scheme of grading in 1921 was essentially occupational. Social Classes I and II include managers, ship-owners, company directors, bankers, clergymen, physicians, barristers, engineers, clerks, etc. and may be taken as representative of the upper and middle or more prosperous classes. The results were as follows:

	Scarlet fever 1923–6
Isolation rate and prosperity (% Social Classes I and II)	$-\cdot 508 \pm \cdot 096$
Attack rate and prosperity	$-\cdot 692 \pm \cdot 068$
Death ,,	$-\cdot 219 \pm \cdot 124$
Fatality ,,	$-\cdot 007 \pm \cdot 130$

With the exception of the correlation involving isolation, the results are in agreement with those obtained from the index of poverty. All the correlations are reversed in sign. The attack rate is highest where prosperity is lowest, but in this instance there is a high negative correlation between prosperity and isolation. Isolation is less exclusively practised in the well-to-do districts.

When these social indices are held constant the correlations of isolation with attack rate, death rate or case mortality are practically unchanged. In no instance is there any evidence pointing to the advantageous result of isolation.

On the whole the results for diphtheria are not different from those for scarlet fever (Table VI). Isolation is positively correlated with the attack rate, death rate and case mortality; in the first case the correlation is not significant, in the last two only just significant.

The influence of social environment on the prevalence and mortality from diphtheria is specially interesting.

	Diphtheria 1923–6		
	Infant mortality	Poverty (% overcrowding)	Prosperity (% Social Class I and II)
Isolation and	$-\cdot 143 \pm \cdot 127$	$-\cdot 326 \pm \cdot 116$	$+\cdot 086 \pm \cdot 129$
Attack rate and	$+\cdot 443 \pm \cdot 104$	$+\cdot 573 \pm \cdot 087$	$-\cdot 716 \pm \cdot 063$
Death rate and	$+\cdot 261 \pm \cdot 121$	$+\cdot 284 \pm \cdot 119$	$-\cdot 447 \pm \cdot 104$
Fatality rate and	$-\cdot 294 \pm \cdot 119$	$-\cdot 415 \pm \cdot 107$	$+\cdot 386 \pm \cdot 110$

These correlation are all consistent and tell the same story. The attack rate is highest where unhealthy conditions are worst, but on the other hand the fatality rate is highest in the best social environment. This result does not seem reasonable. Is there some fallacy here? A possible explanation might be this. In epidemic times slight cases are less seldom overlooked than in inter-epidemic times. The suggestion might be advanced that in districts where the disease is actually most prevalent there is less tendency to overlook mild or atypical cases than in districts where the disease is not so prominent. The result of this would be to produce greater differences in incidence than might actually be true, and in places where the disease is most prevalent a larger proportion of mild and presumably non-fatal cases would be included. Consequently there might be a difference in the relationship between case incidence and case fatality with any other factor we are studying. If the above argument held, we should expect to find the correlation between case fatality to be lower or reversed in sign. This is what happens. The case incidence is lower in the upper than in the lower social classes, whereas with case fatality this relationship is reversed.

It is impossible from the available data to prove this explanation to be correct, but some evidence in support of it is given by studying the relationship of bacteriological cases with social factors. In the London County Council Schools great precautions are taken as regards school outbreaks, and bacteriological examinations are made of children in infected classes. In the Annual Report for 1925 the School Medical Officer pointed out that the notification figures were undoubtedly swollen by the inclusion of purely bacteriological cases. These cases may to some extent be taken as an index of the efficiency of medical supervision, and on the above hypothesis the proportion of bacteriological to total cases should be positively related to indices of poverty.

The correlations found were:

% bacteriological cases (1923–6) and %	overcrowding	$+\cdot479\pm\cdot100$
,, ,, ,,	infant mortality	$+\cdot533\pm\cdot093$
,, ,, ,,	"prosperity"	$-\cdot201\pm\cdot124$

The non-clinical cases appear to come mainly from the poorer districts. These results go some way towards supporting the above explanation of the correlations found.

CONCLUSIONS.

1. The mortality from scarlet fever has declined relatively most at ages 0–5 and there is a tendency for a greater proportion of the mortality to occur among older children and young adults.

2. The mortality from diphtheria appears to be concentrating on early school age and decreasing at older ages.

3. The decline in incidence and mortality from scarlet fever has been as great in towns with little isolation as in those where the majority of cases are hospitalised.

4. It cannot be shown that during the period studied isolation has had any effect good or bad on the prevalence or mortality from scarlet fever.

5. As far as the analysis goes, and the method of correlation can show, there is no evidence pointing to the advantageous results of isolation of diphtheria in London.

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