THE INFLUENCE OF THE AGE OF THE PARENT AT THE BIRTH OF OFFSPRING ON THE AGE AT WHICH THEY ARE ATTACKED BY SOME OF THE ZYMOTIC DISEASES, WITH SPECIAL REFERENCE TO THE EPIDEMIOLOGY OF SCARLET FEVER.

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(With 2 Charts.)

In a previous paper (1912) a rough analysis of certain statistical data was made which seemed to show that the age of the parent at the birth of the offspring was a factor in its susceptibility to the Zymotic Diseases.

In the present paper it is proposed to consider the existence of such a possibility in more detail with special reference to the fallacies that are likely to arise.

The official sources of information are twofold, firstly the Death Returns published by the Registrar General and secondly the Notification of Infectious Disease. Most of the data dealt with have been collected through the latter of these channels.

The first point is, to what extent do these returns fail to reflect the actual prevalence of the disease here considered? The question may be divided into errors of excess and defect, Scarlet Fever being taken as an example.

(*a*) *Errors of excess.*

The most comprehensive figures dealing with this point are to be found in the Metropolitan Asylums Board's Reports from the year 1902

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to the present. The actual data for the ten years 1903 to 1912 are as follows:

	Estimated population to middle of year	Notifications: Scarlet Fever	Notifications: Diphtheria (including membranous croup)	Notifications: Enteric Fever	Percentage of Notifications admitted to hospital: Scarlet Fever	Percentage of Notifications admitted to hospital: Diphtheria	Percentage of Notifications admitted to hospital: Enteric Fever	Cases notified as Scarlet but suffering from other diseases	Cases notified as Diphtheria but suffering from other diseases	Cases notified as Enteric but suffering from other diseases
1901	4,544,983	—	—	—	—	—	—	—	—	—
1903	4,613,812	12,531	7739	2339	83·8	80·3	51·8	701	873	308
1904	4,648,950	13,439	7219	1896	84·5	79·5	51·7	806	902	268
1905	4,684,794	19,461	6482	1552	88·6	82·1	51·4	975	908	247
1906	4,721,217	20,329	8045	1600	88·5	79·7	55·1	932	959	235
1907	4,758,218	25,925	8771	1394	89·4	83·2	51·5	1670	1180	222
1908	4,795,757	22,071	8002	1357	90·9	84·1	50·4	1202	1159	199
1909	4,833,938	17,254	6679	1043	90·2	85·7	49·3	1132	930	202
1910	4,872,702	10,509	5494	1284	88·9	84·8	51·7	918	599	168
1911	4,521,301	10,483	7385	1022	89·2	85·0	50·6	843	783	187
1912	4,519,754	11,321	7106	705	90·6	86·7	52·9	672	775	153

From these figures, it is seen that the discrepancies between the notifying Doctor and the Receiving Officer are:

	Scarlet Fever %	Diphtheria %	Enteric Fever %
1903	6·97	14·05	25·55
1904	7·10	15·71	27·34
1905	5·65	17·06	30·95
1906	5·18	14·96	26·64
1907	7·21	16·17	30·92
1908	5·99	17·22	29·29
1909	7·27	16·25	39·30
1910	9·83	12·86	25·30
1911	9·02	12·47	36·17
1912	6·55	12·58	40·02

In Scarlet Fever, the particular disease under consideration, the percentage varies from 5–9. As to whether this is a true error of excess cannot be decided in the absence of definite bacteriological tests, but it may be taken to represent it rather closely, for in those hospitals where little or no attempt is made to isolate doubtful cases, approximately 5 % of the total number of admissions develop the disease during the course of their stay.

If the numbers of cases said to be wrongly diagnosed are correlated with the total numbers, the population being made constant, the result is $r = -\cdot 2974 \pm \cdot 1248$ for Scarlet Fever, $-\cdot 0163 \pm \cdot 1349$ for Diphtheria, and $-\cdot 2513 \pm \cdot 1239$ for Enteric Fever.

That is to say, as the number of cases goes up, the percentage error goes down. It would seem to suggest that certain fairly constant numbers of cases are returned each year, suffering from other diseases than that with which they are labelled. It is obvious that if one takes samples of a universe and notes the frequencies of A's and B's and adds to both groups a certain number of C's in fairly equal proportions, then some correlation between A and B must exist depending on the proportion of C's. Hence if we correlate the prevalence of Scarlet Fever and Diphtheria in different areas for any year, counting along with each, other diseases, a relationship must exist. In effect, we find[1] that the correlation between Scarlet Fever and Diphtheria

in 1912 for the County Boroughs of England was $r = \cdot1067 \pm \cdot0831$
,, 1911 ,, ,, ,, ,, $r = \cdot1796 \pm \cdot0842$
,, 1912 Rural Counties of England ... $r = \cdot2454 \pm \cdot0875$
,, 1911 ,, ,, ,, ... $r = \cdot2644 \pm \cdot0808$
,, 1911 for the American Cities (Mass.) ... $r = \cdot0696 \pm \cdot1012$.

[1] The example was worked out in class at the Lister Institute.

TABLE I. *Theoretical distribution of Scarlet Fever, according to age of*

Age of attack	Age of parent at birth 17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32
0	·5	1	2	3	3·5	4·5	5·5	5·5	5·5	5·5	5·5	5	5	4·5	4·5	4
1	1	3	7	10·5	12·5	15	17·5	18	18·5	18	17·5	17	16	15·5	14·5	14
2	2	7·5	14·5	22	26	31	35·5	37	37·5	36·5	35·5	34·5	33	32	30	28·5
3	3	10·5	20·5	30·5	36	43·5	49·5	51·5	52	51	49·5	48	46	44	41·5	39·5
4	3·5	12·5	24	35·5	42	51	58	60·5	60·5	59·5	58	56	54	51·5	48·5	46
5	4	13	25	37	44	53	60·5	63	63	61·5	60·5	58	56	53·5	50·5	47·5
6	3·5	12	23·5	35	41	50	56·5	60	59	58	56·5	54·5	52·5	50	47	44·5
7	3	10·5	20	30	35	42·5	48	49·5	50·5	49·5	48	46·5	44·5	42·5	40	38
8	2·5	9	17·5	25·5	30·5	37·5	41·5	43·5	43·5	42·5	41·5	40	38·5	36·5	34·5	32·5
9	2	7·5	14·5	21·5	25·5	31	35	36·5	36·5	35·5	35	33·5	32·5	31	29	27·5
10	2	6·5	12·5	18	21·5	26	29·5	30·5	31	30	29·5	28	27	26	24·5	23
11	1·5	5	10	14·5	17·5	21	23·5	24·5	24·5	24	23·5	22·5	21·5	20·5	19·5	18·5
12	1	4	8	12	14	16·5	19	20	20	19·5	19	18	17·5	16·5	15·5	14·5
13	1	3·5	6	9·5	11	13·5	15·5	16	16	15·5	15	14·5	14	13·5	12·5	12
14	·5	2	4	6	7·5	8·5	10	10·5	10·5	10	10	9·5	9	8·5	8	7·5
15	·5	2	3·5	5	6	7	8	8·5	8·5	8·5	8	7·5	7·5	7	6·5	6·5
16	·5	1·5	3	4	5	6	6·5	7	7	6·5	6·5	6·5	6	5·5	5·5	5
17	·5	1	2·5	3·5	4	4·5	5·5	5·5	5·5	5·5	5·5	5	5	4·5	4·5	4
18	·5	1	2	3	3·5	4	4·5	5	5	4·5	4·5	4·5	4	4	4	3·5
19	·5	1	2	2·5	3	3·5	4	4·5	4	4	4	4	3·5	3·5	3·5	3
20	—	·5	1·5	2	2·5	3	3·5	3·5	3·5	3·5	3	3	3	3	2·5	2·5
Totals	33·5	114·5	223·5	330·5	391·5	472·5	537	560·5	562	549	536	516	496	473·5	446·5	422

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Thus in the American Cities (Mass.) there is no association, in the County Boroughs it is twice its probable error and in the Rural Districts highest of all. This would seem to suggest that in England some other diseases are indiscriminately returned as either Scarlet Fever or Diphtheria. The following figures taken from the Metropolitan Report for 1906 support this contention.

	Scarlet Fever	Diphtheria
Number of cases isolated ...	17,983	6319
Number found to be suffering from other diseases ...	932	959
The above include Measles ...	93	47
Tonsilitis, etc.	178	661

Thus a proportion of the rate in each case consists of conditions which might be included in either; hence the correlations found may be due to the excessive prevalence of simple inflammatory conditions of the respiratory passages so common in these Islands. There is no evidence to show in what way this error will distribute itself with respect to age at birth, and if it is assumed that it takes the form of

parent at birth and age of attack—the parent being alive—original number 10,000.

Age of parent at birth

33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	Totals
4	4	3·5	3	2·5	2·5	2	1·5	1·5	1	1	·5	·5	·5	—	—	93·0
13	12·5	11·5	10	8·5	8	6·5	5	4·5	3·5	2·5	2	1·5	1	·5	·5	306·5
27	25	23	21	17·5	16	13	10·5	9	7	5·5	4·5	2·5	1·5	1	·5	627·5
37·5	35	32	29	24·5	22	18	14·5	12·5	9·5	7·5	6	4	2·5	1·5	1	873·5
43·5	41	37·5	33·5	28·5	25·5	21	17	14·5	11	9	7	4·5	3	1·5	1	1019·0
45	42	39	35	29·5	26·5	22	17·5	15	11·5	9	7	4·5	3	1·5	1	1059·0
42	39·5	36	32·5	27·5	24·5	20·5	16	14	10·5	8·5	6·5	4	2·5	1·5	1	990·5
35·5	33·5	31	27·5	23·5	21	17·5	14	12	9	7	5·5	3·5	2	1·5	·5	842·5
30·5	28·5	26·5	23·5	20	18	15	12	10	7·5	6	4·5	3	2	1	·5	725·0
25·5	24	22	20	16·5	15	12·5	10	8·5	6·5	5	4	2·5	1·5	1	·5	609·0
21·5	20	18·5	16·5	14	12·5	10	8·5	7	5·5	4	3·5	2	1·5	·5	·5	511·5
17·5	16	15	13·5	11	10	8	6·5	6	4	3·5	2·5	1·5	1	·5	·5	409·0
14	13	12	10·5	9	8	6·5	5	4·5	3·5	2·5	2	1·5	1	·5	·5	329·0
11	10·5	9·5	8·5	7	6·5	5·5	4	3·5	2·5	2	1·5	1	·5	·5	—	263·0
7	6·5	6	5·5	4·5	4	3·5	2·5	2·5	2	1·5	1	·5	·5	—	—	169·5
6	5·5	5	4·5	3·5	3·5	2·5	2	2	1·5	1	1	·5	·5	—	—	139·5
4·5	4·5	4	3·5	3	2·5	2	2	1·5	1	1	·5	·5	·5	—	—	113·0
4	3·5	3	3	2·5	2	2	1·5	1	1	·5	·5	·5	—	—	—	91·5
3·5	3	3	2·5	2	2	1·5	1	1	1	·5	·5	·5	—	—	—	79·5
3	2·5	2·5	2	2	1·5	1·5	1	1	·5	·5	·5	—	—	—	—	69·0
2·5	2	2	1·5	1·5	1·5	1	1	·5	·5	·5	·5	—	—	—	—	55·5
398	372	342·5	306·5	258·5	233	192	153	132	100	78·5	61·5	39	25	13	8	9376

a dilution of material, then any correlation found will be reduced according to the formula

$$\frac{r_2}{r_1} = \frac{n_1}{n_1+n_2},$$

where n_1 = numbers of correlated pairs, n_2 = numbers of non-correlated pairs.

(*b*) *Errors of defect.*

Another source of fallacy arises from the manner in which the material is collected, as it is usual to obtain information only concerning the actual occupants of the house in which the disease occurs. Hence a child of 13 born by a woman of 45 should have a mother aged 58 if alive and it is obvious that there is a certain defect owing to the mothers of young adults born late in life having died. Some idea of this can be obtained by calculations based on the 1901–11 life table. The frequency that should be observed where the mother is living, is given on a basis of 10,000 cases of Scarlet Fever, in Table I.

The correlation which must necessarily occur between age of mother at birth and age of child when attacked is $-\cdot016$, that is to say, that any positive association in numbers over 1000 is probably significant of some bias. Of course no record was obtained of mothers who had deserted or left their children, this error is small and probably has no constant tendency.

(*c*) *Errors dependent on the source of infection.*

This source of fallacy is still more subtle and difficult to gauge and may be stated as follows:

Infection can be divided into two great sources:

(*a*) General; such as all are equally exposed to, and

(*b*) Family; that is, the risk that arises of one member of a family infecting another.

In Scarlet Fever, this source accounts for over 13 % if we assume that all cases other than the primary one are due to infection in this way.

Now it is obvious that home infection will vary according to the size of the family, their respective ages, and the extent of overcrowding. The necessity of considering these three points is fairly obvious. The following figures taken from Dr Chalmers' paper (1913) show that overcrowding may not only favour spread but may prejudice recovery.

Death rates per 1000 of similar ages, 1—5 years (Males).

	Measles	Whooping Cough	Scarlet Fever	Diphtheria
1 Apartment	8·6	4·36	1·26	2·62
2 Apartments	5·9	2·79	·97	1·56
3 "	2·85	1·42	·22	1·87
4 " and upwards	1·01	·67	—	1·01

The fall in the death rates is very apparent.

It is of interest to note, that although the same facts are fairly constant for Measles and Whooping Cough, some variation with respect to Scarlet Fever is noted when other age periods are considered.

Males—Death rates.

	0—1 years	1—5 years	6—10 years	All ages
1 Apartment	·28	1·26	·26	·23
2 Apartments	·32	·97	·36	·18
3 "	·32	·22	·19	·06
4 " and upwards	—	—	·77	·08

Females—Death rates.

	0—1 years	1—5 years	6—10 years	All ages
1 Apartment	·41	1·03	·51	·20
2 Apartments	·32	·95	·39	·19
3 "	·33	·72	·24	·08
4 " and upwards	—	·32	·10	·03

Hence overcrowding must be a factor in the spread of the disease.

The relationship is however more complex than appears from "a priori" reasoning. The following data were obtained in the Urban District of Barking Town with a population of 33,000 and give the size of family in which cases of Scarlet Fever occurred, when all are considered and when the initial case only is counted, that is to say, if several cases occur in one family, it is counted once only. These distributions are compared with (*a*) families which contain a child of school age, and (*b*) families which contain a child in its fifth year of age, the mean age being 5 years and 8 months. (Table II.)

It is seen that taking all cases the large families are unduly represented, but that taking each family once only, the distribution agrees very closely with that of families which contain a child in its 5th year. Now the mean age of attack for Scarlet Fever was 7·2 years. Hence this series of observations would seem to suggest that if the spread in the family itself be ignored, small families are more likely to be attacked than large ones. Such a conclusion might be explained in one of two ways, either small families are biologically different from large, or, in consequence of better medical supervision a smaller number of cases are overlooked. Pursuing this line of inquiry in more detail, and with the special object of examining the relationship of Scarlet Fever, and the mean size of families, the following data relative to the Rural districts of the Eastern Counties were collected.

TABLE II.

Scarlet Fever and size of family in Barking Town.

Size of family	Number in which a case of Scarlet Fever occurred: All cases	(1st invasion only)	Proportion	Number which contain a child in 6th, 9th or 13th year	Proportion	Number which contain a child in 6th year only	Proportion
1	11	11	·11579	70	·05414	33	·07174
2	19	16	·16842	117	·09049	97	·21087
3	21	16	·16842	239	·18484	105	·22826
4	32	22	·23158	193	·14927	67	·14564
5	21	11	·11579	186	·14385	60	·13043
6	10	6	·06316	121	·09358	31	·06739
7	9	6	·06316	75	·05800	23	·04999
8	2	1	·01053	77	·05955	16	·03478
9	10	4	·04211	60	·04640	8	·01739
10	1	1	·01053	34	·02630	7	·01522
11	—	—	—	25	·01933	7	·01522
12	—	—	—	10	·00774	4	·00870
13	—	—	—	9	·00696	2	·00435
14	—	—	—	13	·01005	—	—
15	3	1	·01053	3	·00232	—	—
16	—	—	—	1	·00077	—	—
	139	95	1·000	1293	1·000	460	1·000
Notation		X_1		X_2		X_3	

$X_{12}^2 = 80{\cdot}3181$, $P = {\cdot}000034$,

$X_{13}^2 = 22{\cdot}4014$, $P = {\cdot}6944$.

If 3 be raised from 460 to 1293

$X_{13}^2 = 35{\cdot}5324$ $P = {\cdot}1526$.

Hence 1 and 3 are similar distributions.

Mean age of attack for Scarlet Fever 7·22 years.

The Rural districts were chosen rather than the Urban, because the proportion of the rate dependent on spread in the family would presumably be greater owing to chances of infection from a general source being less. That such is the case, is borne out by the fact that taken as a whole the rate for a Rural population is less than for the Urban areas; it must also be remembered that medical attention is more expensive in sparsely populated districts than in the crowded centres.

The factors considered were as follows:

(1) Population. This is desirable as a spurious correlation is said to exist if indices are used and also it is desirable to give the proper significance to large and small districts.

(2) Acres per family. This is necessary because the chances of infection from a general source must be considered.

(3) Proportion under 10 years of age, because the incidence of Scarlet Fever is mainly on those below that age.

(4) Percentage, with more than two per room, because the greater the degree of overcrowding, the closer the contact between individual members of the family and the greater chance of spread in the family itself.

The data are as follows:

TABLE III.

Rural Districts of Eastern Counties and incidence of Scarlet Fever.

District	Population	Acres per family	Mean size of family	Proportion 10 years of age and under	Mean rates for years 1911-12-13 Scarlet Fever	Diphtheria	Percentage living more than two per room
Bedford							
Ampthill	19,540	13·56	3·91	19·19	2·01	0·43	3·2
Bedford	19,213	20·16	3·92	19·26	1·96	0·89	4·0
Biggleswade....	21,933	10·55	4·07	19·62	1·96	0·23	5·5
Eaton Bray ...	3,892	13·94	3·99	21·35	2·50	2·37	3·2
Eaton Socon ..	3,542	20·21	4·06	22·53	2·09	0·66	3·0
Luton	9,474	16·2	4·21	21·29	0·91	0·63	4·7
Cambridge							
Caxton	7,769	25·4	4·13	19·93	0·59	0·13	4·7
Linton	10,546	18·1	3·93	19·07	2·46	1·05	4·3
Melbourne	8,536	18·6	3·87	19·62	1·52	0·42	4·5
Newmarket	19,970	16·9	4·15	22·39	4·62	1·20	8·0
Swavesey	2,559	21·0	3·74	19·85	6·04	0·46	5·0
Essex							
Billericay	22,091	11·7	4·18	17·54	1·34	1·18	3·5
Braintree	18,510	13·2	3·86	17·55	1·68	0·53	3·7
Belchamp......	4 653	21·6	3·81	17·88	1·14	0·21	3·5
Bumpstead	2,601	18·1	3·92	20·68	0·90	5·86	6·4
Chelmsford	23,065	14·9	4·08	19·71	1·23	1·10	2·5
Dunmow	16,134	18·6	3·92	19·17	1·97	0·41	3·4
Epping	14,115	12·2	4·30	20·23	2·87	1·47	4·3
Halstead	10,353	14·8	3·92	19·23	0·90	0·26	2·9
Lexden	19,832	14·4	4·07	20·37	1·03	0·76	4·6
Maldon	16,367	20·4	4·02	21·03	1·60	0·91	2·8
Ongar	10,723	20·3	4·25	20·71	1·28	0·28	4·5
Orsett	18,938	7·7	4·45	22·89	3·87	0·78	6·6
Romford	26,194	5·43	4·47	22·62	1·81	0·68	4·6
Rochford	18,880	13·0	4·20	20·76	1·28	1·46	4·0
Saffron Walden	10,816	21·8	3·92	19·53	1·88	1·14	4·4
Stansted	7,090	13·4	4·12	20·38	0·23	0·24	3·6
Tendring	22,171	14·1	4·01	20·58	0·59	0·28	4·1

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TABLE III—(*continued*).

Rural Districts of Eastern Counties and incidence of Scarlet Fever.

District	Population	Acres per family	Mean size of family	Proportion 10 years of age and under	Mean rates for years 1911-12-13		Percentage living more than two per room
					Scarlet Fever	Diphtheria	
Huntingdon							
Huntingdon....	6,938	32·97	4·05	20·32	0·92	0·19	4·0
Norman Cross..	5,624	23·36	4·31	21·10	0·89	0·79	3·8
St Neots	7,227	27·78	3·95	18·78	2·35	0·56	3·5
St Ives........	9,701	18·29	3·85	20·0	0·62	0·38	2·8
Lincoln							
Bourne	13,391	25·57	4·15	20·80	1·19	0·71	4·6
Branston	14,913	21·97	4·24	19·50	1·04	0·85	3·0
Caistor	13,146	38·55	4·19	20·59	1·65	0·53	2·2
Glandford Brigg	29,895	17·99	4·34	23·67	1·20	0·56	3·2
Gainsborough ..	14,743	26·38	4·10	20·73	1·70	0·97	2·7
Grimsby.......	10,629	19·74	4·16	21·46	1·14	1·84	5·1
Grantham	12,257	30·59	4·23	21·14	1·44	1·41	4·8
Horncastle.....	13,102	35·83	4·13	20·88	1·35	0·56	3·2
Louth	18,285	34·03	4·02	19·64	0·60	0·45	2·4
Spilsby	21,012	24·45	3·94	19·43	1·51	0·90	2·5
Sleaford	17,269	31·65	4·23	20·38	1·95	0·64	4·1
Spalding.......	13,186	23·56	4·33	22·40	1·68	0·12	3·6
Welton	11,111	31·16	4·13	20·30	2·25	1·02	2·4
Norfolk							
Aylsham.......	17,383	16·88	4·13	20·92	2·55	0·62	5·8
Blofield........	12,201	17·3	4·10	17·95	2·02	1·09	3·9
Depwade	19,909	16·3	4·01	20·25	0·90	0·48	3·2
Docking	17,101	21·2	4·01	19·61	0·86	0·61	5·5
Downham	15,618	21·8	4·10	20·60	0·91	0·10	4·0
Forehoe	11,390	13·7	3·99	20·68	1·02	0·90	3·9
Flegg	10,027	12·1	4·13	23·06	1·73	0·87	3·2
Henstead	10,275	17·2	4·14	19·21	4·18	1·52	3·3
Freebridge, Lynn	12,140	25·4	4·07	19·53	1·13	0·33	4·4
Erpingham	17,272	15·5	4·16	20·24	1·28	1·20	4·8
Loddon	12,571	20·1	4·12	20·68	1·65	1·41	4·3
Marchland	12,518	18·0	4·05	21·01	1·10	0·51	3·6
Mitford........	18,733	22·0	3·9	20·37	1·00	0·86	4·1
Smallburgh	12,434	18·8	3·99	22·21	1·29	1·14	5·4
St Faith's	10,864	19·6	4·09	18·62	2·10	1·02	4·9
Swaffham......	7,561	39·5	3·99	21·00	0·92	0·31	2·9
Thetford.......	10,076	39·1	4·10	20·95	0·53	0·10	4·5
Wakingham....	17,266	19·4	4·15	23·87	3·11	1·91	5·3
Wayland	14,509	19·5	3·94	19·13	2·49	0·23	3·1
Mean..........	13,778	20·42	4·088	20·41	1·66	—	4·04
Standard deviation.........	57·7105	7·6553	0·1591	1·3510	1·0001	—	1·0856
Notation	r_6	r_4	r_2	r_3	r_1		r_5

Coefficients

$r_{12} = -\cdot 0383 \pm \cdot 0835$, $r_{24} = -\cdot 2971 \pm \cdot 0763$, $r_{16} = -\cdot 0412 \pm \cdot 0835$,
$r_{13} = \cdot 0823 \pm \cdot 0830$, $r_{25} = \cdot 5115 \pm \cdot 0618$, $r_{26} = \cdot 0251 \pm \cdot 0836$,
$r_{14} = -\cdot 1717 \pm \cdot 0811$, $r_{34} = -\cdot 2821 \pm \cdot 0770$, $r_{36} = \cdot 0971 \pm \cdot 0829$,
$r_{15} = \cdot 3531 \pm \cdot 0732$, $r_{35} = \cdot 3055 \pm \cdot 0758$, $r_{46} = -\cdot 2999 \pm \cdot 0761$,
$r_{23} = \cdot 2012 \pm \cdot 0803$, $r_{45} = -\cdot 0344 \pm \cdot 0836$, $r_{56} = \cdot 0918 \pm \cdot 0830$.

Partial coefficients

$r_{12} = -\cdot 0383 \pm \cdot 0835$, ${}_{3}r_{12} = -\cdot 0562 \pm \cdot 0834$, ${}_{34}r_{12} = -\cdot 1104 \pm \cdot 0826$,
${}_{345}r_{12} = -\cdot 3565 \pm \cdot 0730$,
${}_{234}r_{13} = \cdot 4819 \pm \cdot 0642$, ${}_{235}r_{14} = -\cdot 3013 \pm \cdot 0761$, ${}_{245}r_{13} = -\cdot 1034 \pm \cdot 0827$.

In two instances only do we find that the association between Scarlet Fever and these variables is significant, namely, with acres per family and overcrowding, that is, greater facilities for the spread of the disease, whether in the general or particular sense, increases the rate. In forming partial correlations, population can be ignored, as in one instance only, namely with acres per family, is the coefficient more than twice its error. Taking the remaining five we have:

(1) Scarlet Fever rate and mean size of family $r_{12} = -\cdot 0383 \pm \cdot 0835$.

(2) With proportion of children under 10 years constant

$$_{3}r_{12} = -\cdot 0562 \pm \cdot 0834.$$

(3) With proportion of children under 10 and acres per family constant

$$_{34}r_{12} = -\cdot 1104 \pm \cdot 0826.$$

(4) With proportion of children under 10, acres per family and proportion living more than two per room constant

$$_{345}r_{12} = -\cdot 3565 \pm \cdot 0730.$$

From these figures we can conclude that, with a population of constant susceptibility and constant chance of infection both at home and abroad, the smaller families are much more likely to be attacked than large ones. It is to be observed as each additional factor is taken into consideration the association becomes more marked.

If we take the Scarlet Fever rate with proportion of children under ten years, with chance of infection constant we have $_{45}r_{13} = -\cdot 0876 \pm \cdot 0829$ and with size of family under similar conditions $_{45}r_{12} = -\cdot 3518 \pm \cdot 0731$, which also suggests that size of family, irrespective of age or chance of infection, influences the rate. The remaining partial coefficients found are such as "a priori" reasoning would suggest. Thus both in Urban Districts, when the initial invasion, and in Rural Districts when all cases are considered, there is reason to believe that Scarlet Fever is likely to come to the notice of the authorities in small families rather than in large. In so far as Scarlet Fever has been for many years a mild disease and the symptoms very indefinite, the result found does suggest that an error of omission exists and is greatest when the financial position of the family is straitened. It must, however, be remembered that the mean age of the mother at birth of offspring does not vary materially with the size of completed families and that small families are more closely centred round the 28th year than large ones, hence if age at birth does influence susceptibility, that is, those born at maturity react more characteristically than those born at the extreme of the reproductive epoch, then we should expect the results that have already been found. Both of the explanations may be correct, though the weight of evidence is in favour of a large error of omission. The following data rather lend support to this view.

Inquiry through the Education Act (Administrative Provisions), 1907, was made from several areas as to the number of children found to be actually suffering or recently recovered from Scarlet Fever during the Routine Medical Inspection. (The criteria on which this opinion was based were desquamation with a recent history of illness.) The groups selected were those entering on or finishing their education, that is, approximately, the 5th and 13th years of age. The proportion of each was about equal. The figures were as follows:

Number examined, 58,936. Number found desquamating and with a history of a recent illness or actually suffering from Scarlet Fever 13. Number of cases of Scarlet Fever notified 5120. Number of same age as children examined 726.

Now if thirteen were actually found and the search conducted for two-thirds of the year (Saturdays, Sundays and Holidays omitted) the actual number for a complete year is 19·5. If we agree that the illness, or its subsequent desquamation, can be easily detected for an average period of fourteen days, then the number that must have existed will be $20 \times 26 = 520$. The actual number recorded was 726. From a practical knowledge of Medical Inspection of School Children and its deadening tendency, I think this calculation rather underestimates the actual error of omission. Hence an error of 40 % in defect will probably not be very far from the truth.

If we accept the hypothesis of a large number of missed cases, then it is fair to assume that the aggregation of children in school should be followed by a rise in the incidence. Such rises or rather variations in the seasonal curve have been shown to coincide with scholastic activities. The contention however arises that they may be dependent on the work of the School Attendance Officers and may really support the belief that there is a large error of omission. The fact that in the accompanying diagram the fatality curve is continuous, whilst the curve for incidence is disturbed in August and January, does suggest that the error of omission is larger at these periods.

Regarding Scarlet Fever as a disease with a short incubation period, we might expect the daily return of cases to be modified by the school closure on Saturday and Sunday;—few notifications are for obvious

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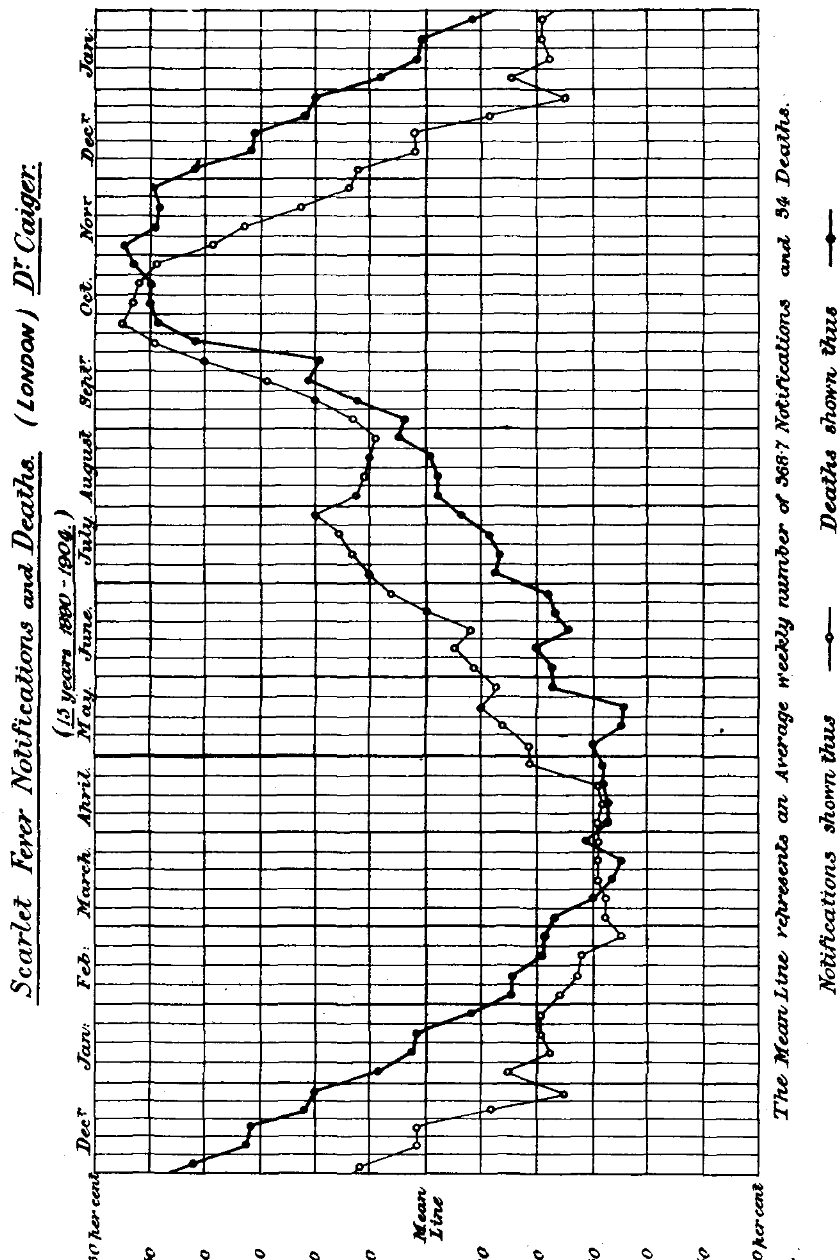

Curve 1.

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reasons received as dated on a Sunday. If, however, we divide our returns into those from 0 to 5 years and from 6 to 12 years and regard these as two random samples of a universe, we have two series that are comparable. The figures are as follows:

TABLE IV.

Ages	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday	Total
0 to 5 yrs.	54	50	59	42	40	55	31	331
Proportion	·1631	·1510	·1782	·1270	·1208	·1662	·0936	
6 to 12 yrs.	119	105	108	97	95	105	66	695
Proportion	·1722	·1511	·1554	·1395	·1367	·1511	·0950	
					Total	...	...	1026

$X^2 = 1{\cdot}3144$, $P = {\cdot}99989$.

Brownlee (1910) gives the following:

	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Actual number notified	124	143	117	134	120	143	126
Theoretical value	129·6	129·6	129·6	129·6	129·6	129·6	129·6

$X^2 = 5{\cdot}18$, $P = {\cdot}522$.

That is half the trials made would give as much divergence as actually found.

From these figures $X^2 = 1{\cdot}3144$ and $P = {\cdot}99989$, or the odds are 9 to 10 against the two distributions being dissimilar. This is smaller than the figure found by Brownlee. He also shows (1902 and 1904) that the same deductions can be made when the age incidence, before and after the introduction of compulsory elementary education, was introduced. We can conclude from this that a school distributes Scarlet Fever to approximately the same extent as the home and other outside influences. We are not justified in saying that the schools do not disseminate the disease.

Susceptibility and chance of infection.

From the point of view of our inquiry, namely the influence of age of parent at birth on susceptibility, it would greatly strengthen conclusions drawn from any bias that the figures may show, if we can assume that all persons of the population are uniformly exposed or that susceptibility is a more important factor than chance of infection.

If we assume the truth of the data already produced, it does seem probable that all are breathing a more or less diluted infection and that the factor which decides whether they will react or not is their susceptibility. To get some idea of the amount of infection that exists in the general population, we must take away a certain proportion and see what happens to the susceptible units, which are known to exist. This experiment has been done on a large scale owing to the provisions of the Act of 1899. We are able by this means to investigate, firstly the effect of removal on infection in the home, by comparing isolated and non-isolated cases, and secondly the effect on any given area, when the proportion isolated is variable.

TABLE V.

(1) *The effect of removal on the spread in the house.*

Arnold gives the following figures:

	Cases isolated (Hospital)	Cases not isolated (Home)
Total houses supplying cases	3213	405
Houses supplying more than one case ...	324	135
Number of children left after primary cases	8472 (2·6 %)	777 (1·9 %)
Number of these attacked	405 (4·8 %)	187 (24·1 %)
Number possibly due to failure of isolation etc.	201 (2·4 %)	124 (16 %)
Number of "return cases"	254 (3 %)	—

It can be said that the families of cases treated at home are under better medical supervision than those treated at hospital and hence a smaller error of omission may occur. Against this, the mean size of family of those isolated is larger and the chance of spread more likely (2·6 against 1·9). That isolation does however actually prevent the spread is shown by the infection of some of the susceptible units, after the primary case has returned from hospital.

As to whether 3 % really represents the amount of leakage from such institutions is open to some doubt. Newsholme gives the following data collected from Brighton:

Secondary cases as rate per cent. of population in immediate contact in the tenement.

	Attack rate per 1000 amongst those living in same family		Total persons in same house	
	Under 20	Over 20	Under 20	Over 20
Isolation carried out	32·7	4·1	28·8	2·8
Not isolated ...	50·2	5·2	46·3	4·3

which brings out the same point. Further it is seen that inclusion of others living in the same house tends to reduce the percentage infected.

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The following figures illustrate this point in another way:

TABLE VI.

Day of disease on which patient was removed	Number of cases of Scarlet Fever: One only		More than one		Rates
1	7		—		—
2	19		5		3·8
3	26		5		5·2
4	20	46	3	9	—
5	11		—		—
6	2		—		—
7	3		—		—
8	2		2		—
9	1		—		—
10	—		—		—
11	2		—		5·1
12	1		—		—
13	1		2		—
14	—		1		—
15	1		—		—
16	1		—		—
17	1		—		—
18	—		1		—

From the run of the figures, delay in removing the primary case tends to increase the number of secondary cases. It is possible that the larger the family, the greater the delay in sending for Medical Assistance, owing to financial and other circumstances (still the conclusion drawn may be safely inferred).

To make these comparisons more complete "return cases" should be included. Although many observers have held that they depend upon what is technically known as "Hospitalism," Newsholme has strongly dissented from this view. The following figures given by Sörensen show a sequence which suggests that a person leaving hospital does bring something with him which slowly diminishes either through time or the exhaustion of the susceptible material by means of which its presence is detected. The figures are as follows:

TABLE VII.

Interval between discharge of patient and return of another from same house.

2 to 10 days	163
11 „ 20 „	77
21 „ 30 „	30
31 „ 38 „	2
39 „ 70 „	2

On the other hand, Chapin has shown for the City of New York, where it is usual to keep the infected member at home and send the others away—a method contrary to ours, that out of 317 healthy children sent away, eighteen were attacked on their return, being a percentage of six. Arnold states that out of 8472 children remaining at home amongst whom 3213 were received from hospital, 254 were infected, or a percentage of 3·0. This would seem to negative the idea that patients collect infection in their systems whilst in a hospital ward, hence we are justified in grouping Neech's material in the following manner.

The figures are taken from the experience of Halifax, and relate to the length of time taken by a family to react to the introduction of infection and the influence of hospital isolation. They are of interest in showing to what extent infection may be present after considerable lapse of time and that the periods given must necessarily be the minimum as the susceptible material by means of which infection is detected soon becomes exhausted.

TABLE VIII.

	Years	Primary cases	Secondary cases after interval of: 1 week to 6	7	8	9	10	11	12	13	14
No hospital	1887 1888	1169	184 = 97 %	2	1	1	0	0	0	1	1
				6 = 3 %							
Hospital	1901 1902	1188	110 = 62 %	7	2	9	9	15	11	4	9
				66 = 37·4 %							

The question is, to what extent after an attack of Scarlet Fever does infection persist in the person attacked? To elucidate this problem we have taken the initial case away for a period of time, and then compared the spread of the disease in the family, with a period in all respects apparently similar, except that the initial case was not removed.

In Arnold's data already given, we have seen that the comparison of families in which cases were and were not isolated is not applicable, as the families are essentially different in social status, and in the medical supervision received. This does not apply to Neech's data and if we can assume that in Halifax the type of disease was similar in the years cited, the material is strictly comparable. Taking the first six weeks of the 1887 to 1888 period and adding to the corresponding weeks of the 1901 to 1902 period the cases that occurred from the 7th to the 12th weeks we have:

	Initial cases	Secondary cases					
		1st week	2nd week	3rd week	4th week	5th week	6th week
1887–1888	1167	75	60	24	16	4	5
		1st and 7th week	2nd and 8th week	3rd and 9th week	4th and 10th week	5th and 11th week	6th and 12th week
1901–1902	1188	71	24	23	16	17	12

The question is: what is the probability of these two series being samples of different universes?

$$X^2 = 26{\cdot}675 \quad \text{and} \quad P = {\cdot}017.$$

Hence the odds are about 50 to 1 against the distribution being taken from the same material. It must be borne in mind that it was assumed that all cases were discharged at the 6th week, which is not correct and it is probable that had we been able to place "return cases" in their appropriate weeks from the date the infecting case left hospital, some of the cases placed in the 5th and 11th weeks and 6th and 12th weeks would have found their way to the 2nd and 8th weeks, the fit being improved; still from the data already given it is justifiable to say firstly that removal of the primary case delays secondary infection and secondly reduces the number infected in the home, the actual reduction being probably small.

(2) *The effect of isolating different proportions on general prevalence.*

(*a*) *Different periods of same district.*

We have a useful series given by Dr Walford for the City of Bristol, though the difficulty in drawing a conclusion is that the type of disease varies from year to year. The figures are in the order of the percentage isolated.

TABLE IX.

Years	Attack rate 15 and under	Percentage isolated
1891	13·4	—
	32·1	13
↑	14·9	22
	10·3	31
	8·5	43
	21·4	47
to	21·7	48
	14·8	48
	13·1	50
↓	5·3	56
	14·1	63
	6·1	65
1903	2·7	66

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From this it will be seen that the greater the number isolated the smaller the attack rate. The association may however be spurious as the disease itself is a very variable factor.

The following series of data bear out the point in more detail. They are taken from the Metropolitan Asylums Board's records given by Parsons in a report on Isolation Hospitals to the Local Government Board 1910–1911, page 8.

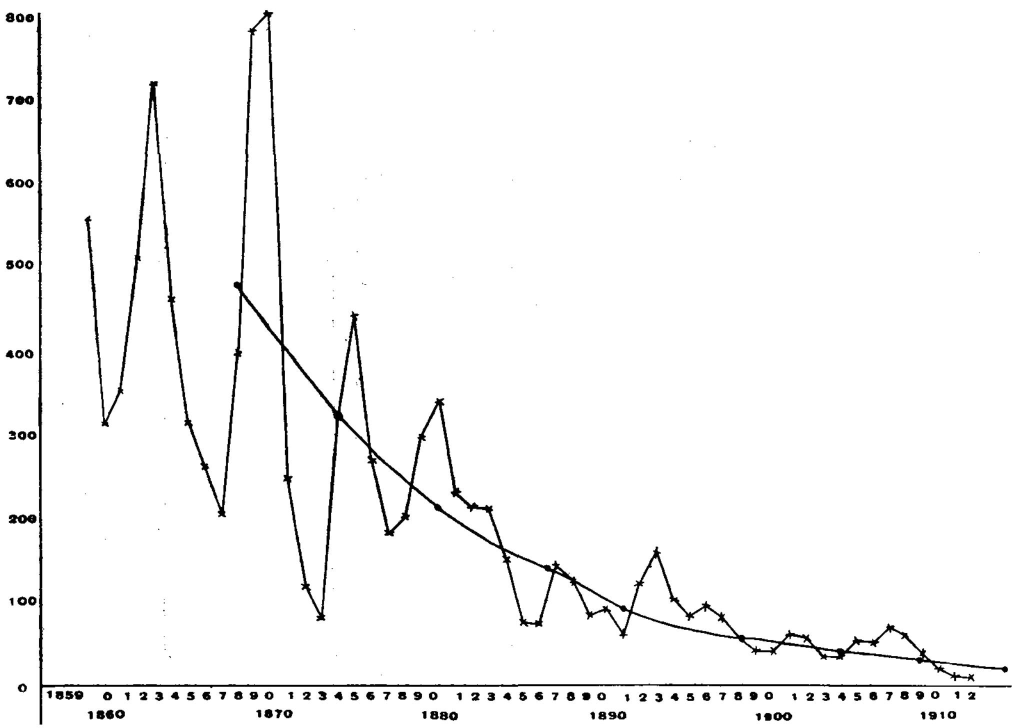
TABLE X.

Scarlet Fever in London. (H. Franklin Parsons, M.D.)

Year	Notifications per 1000 population		Deaths per 1000 population		Case Mortality per cent.		Percentage of cases removed to Hospital		Case Mortality per cent. in Hospitals	
1890	3·7		·21		5·6		42·8		7·9	
1891	2·7		·14		5·1		46·8		6·7	
1892	6·4		·27		4·3		48·8		7·3	
1893	8·6		·37		4·3		39·7		6·1	
1894	4·3	average	·22	average	5·2	average	63·9	average	5·9	average
1895	4·5	of 10	·19	of 10	4·2	of 10	58·2	of 10	5·4	of 10
1896	5·7	years	·21	years	3·7	years	62·6	years	4·3	years
1897	5·1	4·8	·18	·19	3·4	3·8	67·0	61·0	4·1	4·9
1898	3·8		·13		3·4		73·2		4·1	
1899	4·1		·09		2·2		74·3		2·6	
1900	3·1		·08		2·6		75·1		3·0	
1901	4·1		·13		3·2		78·9		3·8	
1902	3·9		·12		3·1		80·3		3·4	
1903	2·8		·08		2·9		83·8		3·1	
1904	3·0	average	·08	average	2·7	average	84·5	average	3·4	average
1905	4·3	of 10	·12	of 10	2·8	of 10	88·6	of 10	3·3	of 10
1906	4·4	years	·12	years	2·6	years	88·5	years	2·9	years
1907	5·8	3·8	·14	·10	2·5	2·7	89·4	86·1	2·8	3·0
1908	4·8		·12		2·5		90·9		2·6	
1909	3·8		·08		2·2		90·2		2·3	
1910	2·5		·05		2·0		85·6		2·3	

From these figures it is seen that the increase in the proportion of cases admitted to the Isolation Hospitals is associated with a fall in the number notified per 1000 population, in the death rate and in the case mortality. The rates are based on large numbers and can be taken as significant. Some doubt, however, is thrown upon the nature of the association when we consider the history of the Scarletinal death rate, previous to 1890, the year in which comprehensive Isolation of Scarlet Fever can be said to have begun in the Metropolitan Area. The following diagram is taken from a paper published by Dr Brownlee (1913) dealing with the periodicity of Infectious Diseases.

A curve has been fitted to the variations in the Scarletinal death rates from 1868 onwards, from which Dr Brownlee remarks, "The irregular curve of the epidemic waves, swings very evenly above and below the curve of the geometrical progression." "If the peak in 1875 is taken as the starting point it may be noticed that it is followed by a lower but broader epidemic wave culminating in 1880. The same phenomenon is repeated on a lower level beginning in 1887, and again in 1901. There is thus a complex fourteen year cycle in the epidemic wave."



Curve 2.

It will be noted that there is nothing in this curve which in any way demarcates the difference in the practice in the treatment of the disease in the neighbourhood of 1890. It would be of interest, therefore, to correlate the attack rate with the percentage isolated, the case mortality being kept constant. That is to say, what would the effect of isolation have been had the severity of the disease remained constant?

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The most useful series of figures that I have been able to find bearing on this point are those given in the Annual Reports for the City of Nottingham, in which we have the case rate per 1000 population, the percentage removed to hospital and the case mortality for the years 1882 to 1910. The Nottingham series are of especial value, for from the year around about 1894 the tendency has been for the number isolated to diminish. It would be, on this account, reasonable to expect some increase in the disease in the later years. The series includes three years, 1882–1884, which were prior to the establishment of a hospital.

The table is as follows:

TABLE XI.

Scarlet Fever in Nottingham. (P. Boobbyer, M.D.)

Year	Cases	Case rate per 1000 population	Death rate per 1000 population	Case Mortality per 100 cases	Percentage removed to hospital	Cases per household invaded	Return cases per 100 discharged from hospital
1882	1029	5·2	1·45	27·8	—	1·15	—
1883	428	2·2	·29	13·8	—	1·2	—
1884	384	1·8	·18	9·6	—	1·12	—
1885	390	1·8	·14	7·7	12	1·2	—
1886	351	1·6	·06	3·7	15	1·4	—
1887	615	2·9	·10	3·6	45	1·4	—
1888	643	3·0	·11	3·9	49	1·3	—
1889	1047	4·8	·13	3·2	71	1·2	—
1890	984	4·7	·15	3·3	81	1·3	—
1891	895	4·2	·13	3·2	86	1·39	—
1892	1163	5·4	·19	3·7	88	1·13	4·0
1893	1511	6·8	·37	5·4	70	1·2	5·0
1894	1164	5·3	·23	4·2	80	1·17	4·5
1895	1250	5·5	·23	4·1	93	1·3	5·1
1896	731	3·2	·11	3·7	86	1·4	2·3
1897	517	2·2	·15	6·6	90	1·2	3·0
1898	931	3·9	·14	3·5	71	1·5	3·4
1899	2500	10·8	·23	2·0	47	1·2	1·5
1900	1394	5·8	·23	4·0	49	1·2	3·2
1901	918	3·8	·05	1·2	47	1·1	5·5
1902	966	4·0	·10	2·1	52	1·1	3·68
1903	1420	5·8	·14	2·4	34	1·2	2·18
1904	1189	4·8	·11	2·3	39	1·2	3·48
1905	681	2·7	·07	2·8	56	1·35	1·28
1906	611	2·4	·07	2·8	57	1·26	1·17
1907	416	1·6	·02	1·2	69	1·2	1·76
1908	595	2·3	·04	1·85	52	1·1	2·27
1909	1036	3·9	·04	·96	54	1·1	2·56
1910	697	2·6	·06	2·0	60	1·3	2·6

Correlating these variables, the percentage number of cases isolated (1) and the attack rate per 1000 population (2), $r_{12} = \cdot 1024 \pm \cdot 1336$.

The percentage number isolated (1) and fatality rate (3)

$$r_{13} = -\cdot 2903 \pm \cdot 1228.$$

Note. If the years 1882–1884 where no cases were isolated be ignored, then $r_{13} = -\cdot 0031 \pm \cdot 1349$.

Case rate per 1000 population (2) and fatality rate per 100 attacked (3)

$$r_{23} = -\cdot 3064 \pm \cdot 1228.$$

From these figures it might be assumed that a decrease in the number isolated has been followed by the decrease in attack rate or in other words it might be said that the town has participated in the general fall of Scarlet Fever irrespective of hospital isolation. If we now make the case death rate constant then the correlation between the attack rate and the percentage removed will be ${}_3r_{12} = \cdot 0147 \pm \cdot 1340$.

Hence there is no legitimate evidence in these figures to believe that the practice of isolation has reduced the amount of floating infection in the community under consideration.

(*b*) *Towns isolating different proportions.*

If we assume that isolation affects the spread in the home and does not influence appreciably the amount of floating contagion in the community generally, it is possible to calculate, on the basis of the Croydon experience, what the rate would be in any group of towns isolating a varying proportion, supposing all were removed to hospital. A useful series has been collected by Dr Kaye and is as follows:

TABLE XII.

	Isolating less than 20 %	Isolating between 20 and 50 %	Isolating between 50 and 80 %	Isolating over 80 %
Number of towns in each group	25	42	17	9
Gross population	1,513,347	5,346,808	2,222,000	1,036,683
Total no. of cases of Scarlet Fever	7,037	22,831	9,235	3,815
Cases isolated	1,407	7,991	4,156	3,052
From the above we have:				
Cases not isolated	5,603	14,840	5,079	963
And on the basis of the Croydon figures the numbers of secondary cases will be	1,778	4,688	1,604	304
If all had been isolated the number of secondary cases would have been	789	2,082	712	135
Thus the total number of cases would have been if all had been isolated	5,048	20,225	8,343	3,646
Giving a rate of	3·34	3·78	3·76	3·51
The actual rate was	4·65	4·27	4·16	3·68

Thus the apparent effect of isolation disappears, an inference that Millard had already made when towns like Preston and Warrington were compared. To solve this problem, it should be handled in the same manner as has been already used in elucidating the influence of overcrowding, size of family, etc. As this paper does not concern itself with the utility of the isolation hospital, the rather laborious task of handling a problem with at least six variables has not been undertaken[1]. It can be concluded that the effect of removing cases from the home, even in spite of leakage from the hospital, through "return cases," has more effect on the production of secondary cases in the home than removal of all known cases has on the prevalence of the disease in the community. Hence there must be some other source from which infection arises, and it must be such as is hardly influenced by the isolation of known cases. This may arise through

(1) A large number being missed.

(2) A large proportion reacting atypically.

(3) Infection persisting in certain cases for a considerable period of time.

(4) Infection arising through other channels than personal contact.

Evidence of the large error of omission has been already given. That the second cause is an operation factor is also probable. Jürgensen, Johannessen and Thomas emphasise the fact that Angina directly consequent on Scarlet Fever need not be accompanied by a rash. Further, in various epidemics, instances of which are given in the literature quoted, outbreaks have either been preceded, or accompanied by a number of cases of sore throat. It has been observed in the Barking School Clinic that the autumnal rise is preceded by an increase in the number of throat ailments sent to the clinic from the schools for diagnosis and advice. The figures are as follows:

	Jan.—July	Aug.	Sept.	Oct.	Nov.	Dec.
Cases of Scarlet Fever	61	4	18	29	28	22
Cases of Angina and Tonsilitis ...	10	3	21	6	5	3

The same sequence has been observed each year, so that the figures cannot be said to be a chance happening.

[1] K. Pearson and E. Elderton in a paper on the Influence of Isolation on the Diphtheria attack and death rate (*Biometrika*, x. 1915, p. 549) have come to a similar conclusion, details of which are given later in the paper.

The following data, given by Butler, lend support to this view, and relate to the existence of sore throats previous to the occurrence of a definite case of Scarlet Fever in an individual house.

	Scarlet Fever	Other diseases
No. of houses infected	1266	1644
History of previous sore throats	395	47
Percentage	31·2	2·8

It is stated that adults were more frequently attacked, but such conditions in children are more likely to be overlooked.

In connection with the third factor concerned in the failure of isolation to modify the prevalence of the disease, it is of interest to examine whether the usual figure of 3–4 % of infecting cases (that is, cases which are definitely known to infect others in the same household after isolation), really represents the number that leave the hospital in that state.

The following figures show that the persistence of infection depends on the severity of the attack. They are taken from Sörensen's observations on Scarlet Fever in Copenhagen.

TABLE XIII.

Year	No. of cases isolated	Attack rate per 1000 population	Death rate	No. of return cases per 1000 discharged: Less than 10 days	Over 10 days	
1893	1,758	9·9	3·3	—	—	3·8
1894	2,137	16·4	4·2	—	—	3·1
1895	1,050	5·5	3·8	1·9	2·7	3·3
1896	781	4·5	2·3	2·0	3·7	4·0
1897	676	4·2	1·4	2·2	2·5	3·6
1898	913	5·9	2·2	1·8	2·7	2·4
1899	1,763	10·9	2·5	2·5	3·4	3·9
1900	1,408	6·5	2·4	2·7	3·8	4·5
1901	813	3·3	2·4	1·9	3·5	4·1
Total	11,299	3·6	—	—	—	—

Considering the same point with respect to the nature of the population to which cases discharged from hospital are sent, we have the following data taken from Barking. One hundred and ninety-eight cases discharged from hospital were followed by the recurrence of the disease in other members of the family in ten instances within one month. The age distributions of the families were as follows:

TABLE XIV.

Age	Number	Number said to have been previously attacked
No children at home	21	—
Under 1 year	26	—
1–2	15	—
2	28	—
3	27	—
4	24	1
5	33	—
6	28	—
7	32	2
8	23	3
9	28	4
10	22	4
11	19	1
12	23	1
13	26	4
14	20	3
15	22	2
16	11	1
17 and over	12	—
	440	26

Hence the attack rate is 10 in 440 or 22 per thousand in one month. The rate for the population 16 years and under in Barking, for a corresponding period, was 3·2 per 1000.

It is of interest to note that the attack rate based on "return cases" amongst such a population is seven times as great as that for the whole town. The actual number of cases leaving the hospital in an infective state must be fairly high, for it is unlikely that in every instance "return cases" will follow in the family to which an infective case is discharged.

Now it was found that during the same period 15 % of the above notifications were secondary cases, and if we assume that secondary cases are due to the primary one, then a large proportion (85 %) of the families which supplied one case only must be relatively insusceptible. Hence such a family when it again receives its infected member is not likely to furnish a return case. Should we assume that such cases as are discharged from hospital have the same infective power as "initial" cases, then the number leaving hospital in that state must be $\frac{85}{15} \times 5 = 28$ %. This would seem to indicate that every fourth child leaving hospital irrespective of discharges from nose or throat is capable of causing further cases even after six weeks isolation. Support is lent to this view that infection is very persistent in a large proportion of cases, by the frequently observed outbreaks of Scarlet Fever, after operation for chronic suppuration of the middle-ear amongst the inmates of a childrens' ward, even when the attack of Scarlet Fever upon which the condition was dependent had occurred many years before. Boeck gives an instance where the infection was apparently transmitted through the medium of hair, after twenty years, and Elliston, quoted by Murchison, gives instances of personal infection after two years.

The period of six weeks must be looked upon as a purely arbitrary standard and is based more on the demands of the general public than on the reasoned advice of the medical profession. The last of the series, namely whether infection may arise from other sources than personal contact, requires some attention, though the facts already given are sufficient to account for the endemic nature of the disease.

Milk as a possible source of infection.

Scarlet Fever has been associated with almost all articles of diet, though milk only has supplied sufficient evidence to make it worthy of consideration.

Up to 1885, milk was supposed to convey the infection in a passive manner, but Klein and others have thought that a micrococcus, transmitted from the cow, was the specific cause[1]. The active theory of the agency of milk has not received confirmation from later observers, so that the original position has been reverted to.

Kober collected instances of 330 milk epidemics of which 243 occurred in England, 52 in America, 11 in Sweden, 10 in France, 2 in Germany and 12 in other countries, and he suggests that in England and Sweden much milk is consumed in a raw state and might explain the differences in the proportion noted. Hall also shows that in Japan and China and India, Scarlet Fever is unknown and milk is not consumed. Neither of the statements is really accurate, for Ashmead has described a disease as Scarlet Fever in Japan which if not common is certainly distinct, and closely resembles Scarlet Fever.

Kober also shows that even if an undue proportion of cases fall upon a certain milk supply, the cause is not certain, as it is quite common for certain supplies to run in certain parts of a community where other

[1] The outbreak at Hendon in 1885 investigated by Klein and Power (see Rep. Med. Off. Local Gov. Board 1886–7, Klein, *Proc. Roy. Soc.* Vol. XLIII.) is well known in this connection.

means of contact are quite common. Hamilton after a close study of all available literature divides milk epidemics into two classes.

(1) The larger, which includes those which must be ignored, as the statistical evidence is not adequate, a class which arose from the erroneous belief that the cow suffered from a disease communicable to man.

(2) The smaller group, which present evidence which she regards as above suspicion, and can be attributed to the fact that under certain circumstances milk offers a suitable medium for the propagation of the virus.

Freeman gives the following as characters of a milk epidemic.

(1) *The disease appears suddenly and subsides equally suddenly.*

The actual occurrence of cases has been examined by Brownlee and he finds, in the case of an epidemic in Glasgow, that a "normal" curve gives a very good fit. The seasonal rise and fall also can be fitted in a similar way, so that the difference between a milk epidemic and ordinary incidence is one of degree and not of kind.

A group of cases due to milk infection may however be the beginning of an epidemic dependent on personal contact. The following figures are taken from an epidemic at Weymouth in 1901 where the first few cases appear to have been due to milk, though subsequent contact appears to have been responsible for the extensive spread. It is compared with the epidemic at Thorshavn in 1873, where the origin was from one case only. Weymouth had been fairly free from Scarlet Fever, whilst in Thorshavn no case had been observed during the generation then alive.

	Population	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	April	May
Weymouth	15,400	—	21	14	52	36	16	6	—
Thorshavn	930	4	118	72	21	5	12	2	2

It is seen that in the latter the rise is sudden, more so than in the former. Other examples could be given bearing on the same point. It would appear that the steepness of the curve may depend on the nature or distribution of the population rather than on the source of the infection. The curves of different epidemics are so variable that it would be hardly safe to draw any conclusion from the peculiarities of any particular one.

(2) *The houses invaded are quite distinct and not restricted.*

Generally speaking it is the exception, rather than the rule, to be able to trace the origin of infection in primary cases. This can hardly be a character of a milk epidemic.

(3) *The houses invaded belong to the rich rather than the poor.*

This is no peculiarity of a milk epidemic. The ubiquitous character of Scarlet Fever is noteworthy and, as has been shown, its diagnosis may be a measure of the ability of the family to procure medical assistance.

(4) *The incidence of a milk epidemic. It is said that* 78 % *of those attacked are milk drinkers, whilst in ordinary epidemics the figure is only* 27 %.

This is not a useful criterion, as the milk supply even of a small village is usually from several sources, and it does not take into account the alternatives of an epidemic being started by milk and spread by personal contact, or being wholly due to milk infection. It is plausible to suppose that in the latter case it should partake of the character of an epidemic of meat poisoning, such as occurred at Chesterfield, Derby and elsewhere. In any case such estimates are of little help in a decision.

(5) *It has been suggested that multiple cases are more frequent in milk epidemics than in endemic incidence.*

The following figures lend no support to this contention.

	Multiple cases (Weymouth) Milk epidemic, 1901 (Sept.—Jan.)	Multiple cases (Middlesbrough), 1910 (Sept.—Jan.)
Houses not invaded	4290	20,165
With 1 case	80	65
„ 2 cases	15	20
„ 3 „	5	9
„ 4 „	3	3
„ 5 „	5	—
Totals	108	97

There is nothing very different in these two series. In the latter the incidence is less, and the proportion of multiple cases is greater. If we compare the Autumn and Spring incidence in any town it is seen that multiple cases are more frequent in the latter than the former period. It would thus appear that they depend on the virulence of the infection rather than the agent by which it is spread.

(6) *It has also been thought that Milk Scarlet Fever is more prone to attack adults than children.*

Comparing the classic epidemic at Thorshavn and the milk epidemic at Weymouth, we see that age of attack is a factor dependent on the previous history of the disease. In any community which has been free for a considerable period, the incidence tends to be on adults.

TABLE XV.

Thorshavn.

Age	No. living	No. attacked	Rate	Milk epidemic (Weymouth) Age	Rate	
0–1	12	8	66·6	0–5	2·4	
1–5	65	44	67·1			
5–15	155	99	63·9	5–10	5·3	
15–20	56	42	75·0	10–15	3·2	
20–40	171	40	23·4	15–20	1·6	
40–60	105	3	2·9	20–30	2·1	3·5
over 60	55	1	1·8	over 30	1·4	

It is possible that more information would be obtained were care taken to separate primary cases, that is, the first case occurring in any household should only be considered. In no epidemic of any considerable size, as far as my search has gone, have I been able to separate the cases as described. With the information given in this manner, the only real statistical test can be applied and the chance calculated of an undue proportion falling to any particular milk supply. In the town of Barking there are twelve wholesale supplies. The problem is, what is the chance of 50 % or more of a series of 100 consecutive cases of Scarlet Fever falling to one milk vendor? By calculation it was found that this should happen about once in 25 years. In so far as approximately 100 cases are notified annually, and as such a grouping has not occurred in the last 25 years, though search has been made, milk cannot be said to be a cause of the disease in this district. Support is lent to this deduction by the following data.

Inquiry was made of 400 households, which contained a child of school age. This age period was chosen because such a sample would be a fair reflection of the households from which a case of Scarlet Fever was likely to occur; the mean age of attack of Scarlet Fever being a little over seven years. Comparing this with the source of the milk supply of these households where Scarlet Fever occurred we have:

	Random samples	Condensed milk and no milk	Fresh milk A	B	C	D	E
	357	92	31	23	46	48	117
Scarlet Fever cases	320	87	37	31	39	49	77

Classes A to D are definite, class E includes those where the source was indefinite or where the supply came from two or more dealers: it also includes those which had less than 20 customers.

From this $X^2 = 12{\cdot}8$ and $P = {\cdot}29$.

If we assume that condensed milk cannot convey infection (I have only come across one instance of a small outbreak of Scarlet Fever which was attributed to condensed milk and in that instance the evidence was very meagre), we see that those who take no milk are just as likely to be attacked as those who consume fresh milk, if anything, rather more so. Before any milk supply is blamed, some figures such as the above should be collected and the chance evaluated of any variation in the distributions being significant. In so far as the milk supply in this country is very carefully watched, some of the distributions reported may be due to chance variation, and as in all I have only been able to get references to fifty-seven, we should hardly be justified in saying that milk is a frequent source of infection. In thirty-seven of the epidemics in which the evidence seems good there was contact with a previous case, either at the milking or shortly afterwards. This seems to suggest that the time when milk will absorb the infection is from time of milking to a few hours afterwards, that is, whilst the milk is warm and comparatively sterile. Instances of contamination of milk with Scarlet Fever infection in retail shops with no traceable cases is a frequent occurrence in any district. It would thus appear that when milk is cold and the lactic fermentation well advanced, it is apparently not a suitable medium. I am unable to trace any instances of butter or butter milk being the source of infection, though the processes to which it is subjected should render it liable to contamination.

From the evidence that has been gathered we can conclude firstly, that the main factors concerned in the maintenance of the disease are (*a*) atypical cases, (*b*) missed cases, (*c*) persistence of infection (carriers) in a certain proportion, and secondly, that in so far as isolation of known cases does not materially influence the chance of infection outside the home, the amount of floating infection must be extremely large. All must in the ordinary course of events come into frequent, almost daily contact with one or other of the above classes. Hence we must assume that susceptibility is a much greater factor in reaction to the presence of this parasite, than chance of infection.

The next point that requires consideration, in relation to errors of excess and defect, is to what extent do these categories differ in age distribution from a population composed of cases of true Scarlet Fever. The mean ages for the group considered under errors of excess should be the greater, for a case returned erroneously might be selected from any age period.

The following figures bear this out:

Cases returned as Scarlet Fever and found to be suffering from other diseases. (Barking Town Isolation Hospital, 1913–1914.)

	0–5 years	6–10 years	11–15 years	16 and over	Mean age years
Not Scarlet Fever cases ...	8	9	6	3	9
Scarlet Fever cases ...	36	178		11	7·4
General population per 1000	136	128	120	636	—

It is obvious that errors of excess cannot be regarded as a random sample of the general population, nor do they appear to coincide with a true Scarlet Fever distribution. The numbers are too small to allow one to examine the point in any detail.

No data are obtainable with respect to the effect of the inclusion of "errors of defect" on the mean age of attack. It seems likely, however, that the period during which any disturbance in health is likely to be overlooked, is from the 7th to the 14th year, that is during this period when the child is changing from a dependent to an independent position. The point is of some importance in our subsequent inquiry and it is to be regretted that a more definite statement cannot be made.

It may be questioned as to whether data subject to such large errors be worthy of detailed examination, but as some questions of great interest have arisen, their analysis may not be without profit.

Before discussing the main theme it will be advisable to examine in what way the age curve of incidence is modified by susceptibility.

Age incidence and susceptibility.

To elucidate this, a group of children were obtained during the course of medical inspection, the selective factor being the presence of such parents as thought fit to attend the examination, and the point as to whether an inherited predisposition to the disease existed was examined. An ordinary fourfold table was formed, the figures being as follows:

	Children: Not had Scarlet Fever	Children: Had Scarlet Fever	Totals
Mothers not had Scarlet Fever	1042	388	1430
„ had Scarlet Fever ...	140	94	234
Totals	1182	482	1664

$r_1 = \cdot 152 \pm \cdot 0286.$

On the assumption that the above figures are diluted, as far as the children are concerned, with 50 % of uncorrelated data, then (notation as on p. 212)

$$\frac{r_1}{r_2} = \frac{n_1}{n_1 + n_2},$$

$$\therefore\ r_2 = \cdot 304.$$

This allows only for errors relative to children. It does not account for defects of memory, or ignorance with respect to parents. From this it can be safely assumed that there is a strong inherited predisposition not necessarily to the invasion of the parasite but certainly in reacting to its presence by the production of the symptoms which give the disease its name.

If heredity plays a part in susceptibility, we should expect certain families to be more frequently invaded on distinct and separate occasions than chance would lead us to anticipate.

The following figures given by Dr Butler with respect to the house are consistent with such a view. The approximation after a five years' interval may be due to the increasing number of removals, the house being no longer synonymous with the family.

Second notifications received from same address after varying intervals.

TABLE XVI.

Interval	Expected	Actual
3 weeks–3 mths	1·4	20·25
3 mths –6 ,,	1·7	6·75
6 ,, –12 ,,	3·5	6·1
1 yr –2 yrs	6·6	10·0
2 ,, –3 ,,	5·7	8·0
3 ,, –4 ,,	6·2	6·6
4 ,, –5 ,,	6·4	7·0

It is of course probable that the large percentage in the first three periods given is due to infection in the family itself. From the 12th month onward, the cause suggested above may be an operative factor, and in so far as some families will be entering and others leaving the danger zone, the excess of the actual over the expected should decrease as the interval gets longer. That heredity however is concerned in the manner in which the organism reacts to the presence of infection is borne out by Thomas (Ziemssen's *Handbuch*), Copeman, Harlin quoted by Trousseau, Johannessen and Seitz—all of whom cite instances of variations in the characteristic features of the disease peculiar to a particular family.

Hence we are justified in grouping our children into those who have, and those who have not, a history of the complaint, and comparing the age distribution of attack.

From this we should get some idea as to the way in which susceptibility alters the curve of age incidence. The following figures were obtained:

TABLE XVII.

Age of child when attacked	Mothers who have had Scarlet Fever	Mothers who have not had Scarlet Fever
0	2	0
1	1	11
2	16	13
3	11	19
4	13	35
5	18	40
6	17	44
7	13	36
8	13	16
9	6	10
10	0	15
11	6	10
12	6	6
13	—	9
14	1	5
15	2	3
16	2	2
17	—	—
18	1	1
19	4	—
20	2	—

	Number	Mean age	Standard deviation
Children of mothers said to have had Scarlet Fever	134	$6{\cdot}7686 \pm {\cdot}1508$	$2{\cdot}8195 \pm {\cdot}1161$
Children of mothers said not to have had Scarlet Fever	275	$6{\cdot}8509 \pm {\cdot}0729$	$2{\cdot}5356 \pm {\cdot}0729$

It is seen from this that the mean age of attack is not altered, but that in the case of children of mothers who have not had the disease the scatter is less but the difference is hardly significant. Hence we may conclude that susceptibility does not alter the position of the axes of the curve of age incidence.

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Age of parent at birth and age of attack.

We can now turn to the actual data with some hope of interpreting any trend they may show. The figures were obtained from the records of the County Borough of Middlesbrough 1904–1912 of such cases as were notified to the Health Department as suffering from Scarlet and other Fevers.

Close on 3000 were notified during this period and 1991 afforded the information required. The following points are to be noted.

(1) Only such cases where the mother was alive were taken.

(2) All over nineteen were ignored, as it was found that even before this age the person attacked was not living in the same house as the parents and hence could not be included.

(3) No correction is made for errors of diagnosis.

TABLE XVIII.

Age of mother at birth of offspring and age of attack of Scarlet Fever. All parents living.

	Age of mother at birth of offspring												
Age of attack	18—19	20—21	22—23	24—25	26—27	28—29	30—31	32—33	34—35	36—37	38—39	40—41	42 and over	Totals
0	—	2	0	3	2	4	1	0	2	0	1	2	1	18
1	—	4	6	7	6	8	4	6	4	3	2	2	—	52
2	—	7	7	31	23	14	13	10	6	7	6	3	2	129
3	2	11	23	30	31	27	19	8	6	5	10	3	3	178
4	—	11	27	33	42	35	23	17	15	10	6	9	7	235
5	3	28	27	34	41	42	25	20	18	8	12	4	6	268
6	2	18	34	37	23	25	25	22	6	7	4	6	4	213
7	1	19	30	17	21	33	19	10	9	7	6	6	10	188
8	2	12	12	22	20	19	16	10	10	8	6	6	4	147
9	5	18	16	18	24	9	13	8	7	5	5	3	2	133
10	1	10	13	18	14	14	11	7	12	4	3	5	4	116
11	2	12	9	12	11	13	12	2	8	4	2	4	1	92
12	—	8	7	6	8	5	2	7	2	1	4	1	2	53
13	—	6	3	3	4	1	1	1	2	1	0	0	3	25
14	—	3	9	9	7	4	2	0	4	—	—	—	—	38
15	—	4	3	1	6	3	3	2	2	6	1	1	1	33
16 to 20	2	4	4	15	7	14	9	3	6	3	2	1	3	73
Totals	20	177	230	296	290	270	198	133	119	79	70	56	53	1991

$\sigma_{\text{age of attack}} = 3{\cdot}38$, $\sigma_{\text{age at birth}} = 2{\cdot}96$,

$r = {\cdot}0206 \pm {\cdot}0142.$

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The coefficients found are:

Age of mother at birth of child and age of attack	$r = \cdot 0206 \pm \cdot 014$
Correlation ratio of means of age of attack for arrays of mother's age	$= \cdot 0966 \pm \cdot 012$
Corrected	$= \cdot 06$
Correlation ratio of means of mother's age for arrays of child's age ...	$= \cdot 1080 \pm \cdot 011$
Corrected	$= \cdot 04$
Coefficient of contingency	$= \cdot 2510 \pm \cdot 010$

The distribution, therefore, is not a random sample, though it does not indicate that a significant and continuous increase in age of attack accompanies a corresponding increase in age at birth. There is a suggestion that the regression line is non-linear and that the mean age of attack is lowest between the 24th and 25th year of the mother. This is more easily appreciated in the following series of figures.

Dividing the data into groups of approximately 200, the means are:

Age of mother at birth	Number	Age of child at attack
21 yrs and under	197	7·92 yrs ± ·14
22–23 yrs	230	7·37 „ ± ·13
24–25 „	296	7·07 „ ± ·12
26–27 „	290	6·99 „ ± ·12
28–29 „	270	7·00 „ ± ·12
30–31 „	198	7·21 „ ± ·14
32–35 „	252	7·38 „ ± ·13
36 and over	258	7·27 „ ± ·13

It has been shown, however, that owing, 1st, to the omission of children of parents who have died, and 2nd, to the fact that infection in the home is more likely to occur in large than in small families and hence those born late are likely to be attacked at a more immature age—that a negative correlation was to be expected. Hence, in a truly representative population the suggestion is that those born late in life are likely to be attacked at the more mature ages.

The fact that those born around the 25th year are attacked earlier than those at either extreme, may be explained by the fact that smaller families are more carefully watched than large, and a smaller number of cases missed, with the result that the mean age of attack falls.

It must necessarily be so if we assume that the error is greater from the 7th to the 14th year than from 0 to 7 years.

In view of the extremely complex nature of the problem, any conclusion must be drawn with extreme hesitation, still as alteration in susceptibility does not necessarily alter the mean age of attack, a slight increase in the mean age may be a reflection of a marked variation in the biological character of the group in question.

DIPHTHERIA.

The attempt made to estimate the amount of infection existing in a population at any time is not necessary in the case of Diphtheria, as the actual agent causing the disease can be isolated fairly easily. The difficulty however arises, that in many instances virulent bacilli can be found in the throat of contacts, who do not react, or only very slightly. It is probable that, should a comprehensive survey of a population be made, the numbers classed as free—infection only—slight reaction, etc. would form some type of curve, and the question arises, which is of importance to this statement, at what point should clinical Diphtheria be said to begin. It is obvious, therefore, that clinical and bacteriological Diphtheria will be very different. There is no doubt, moreover, that the organism is as widely spread as the infection of Scarlet Fever and hence all must at one time or another come in contact with infection. What the error of omission is, will obviously depend on what point is taken on the reaction curve, beyond which clinical Diphtheria begins. The error of commission has been already discussed and is larger than that of Scarlet Fever. It would therefore appear that the present observations are much more vague than those already discussed, and as no attempt to purify the returns has been undertaken, the point under investigation is the influence of age at birth on the age at which a reaction of a diphtheritic appearance occurs.

There is, however, one other relevant source of error, namely, the number of instances that were ignored owing to the mother having died. The same calculations will apply as with Scarlet Fever, that is, a negative correlation of about ·016 is to be expected.

Elderton and Pearson (1915), in a recent paper, have investigated the relationship between isolation and attack rates. The material was supplied by E. H. Snell from the records of the City of Coventry and other areas. They find the crude correlation between isolation rate and attack rate for years 1904-08, $r = \cdot 427 \pm \cdot 063$ and for the four years 1908–12, $r = \cdot 290 \pm \cdot 069$.

They show for the two periods that there is no significant relationship between the death rate from Diphtheria and isolation rate and that there is a significant association between the case mortality and attack rate and between case mortality and isolation rate; the figures are $r = - \cdot 509 \pm \cdot 057$ and $r = - \cdot 507 \pm \cdot 056$ respectively.

The influence of density of population and prosperity as judged by proportions of domestic servants are considered, and values are found which suggest that the latter is associated with an increased rate and that the former does not appear to have any influence. They draw the following conclusions. "They contain nothing to support the theory that isolation markedly limits the incidence of Diphtheria. The disease itself does not appear where overcrowding is greatest nor where the population is most dense; on the other hand isolation is most practised in those towns where domestic servants are most common and which may be supposed to be most prosperous. The chief argument which can be drawn from the present data is a smaller case mortality, but such mortality might be obtained in all probability by specialised medical care as apart from isolation."

The weak point is the assumption that Diphtheria is a uniform disease and that all cases returned as such by a certifying doctor are really suffering from that complaint. We have seen early in the present paper that difference of opinion between two medical men with respect to this disease is found in 26 % of the cases notified. Further, in those prosperous areas where there is an adequate medical staff backed by a well equipped laboratory, bacterial Diphtheria will be included with clinical Diphtheria, that is to say, that a large number of mild cases will appear in the returns and consequently the case mortality will be low. If correction were made for the type of disease prevalent, which could be done by making the case mortality constant, it is possible that the correlation between isolation rate and mortality per 1000 of population would be materially altered. The tacit assumption that sanitation in the popular sense of the word may be a factor in reducing the rate may in some cases be fallacious, as a well equipped sanitary organisation will include an adequate number of officials, suitable laboratory facilities, ample supply of beds for the isolation of doubtful cases and encouragement to local practitioners to notify them. In Districts of this type an increase in the attack rate with the fall in the death rate may have been produced. From these facts it can be concluded that Diphtheria is in much the same position as Scarlet Fever, namely that infection is extremely widely spread and that a large error of omission occurs. It is hardly likely that isolation of a proportion of the cases during a short period of time will materially affect the amount of floating contagion. Direct evidence bearing on the number of contacts infected with the organism and on its distribution amongst a school population will be found in Professor Nuttall's *Text Book*, pages 425–490.

Age of parent at birth and age of attack.

The data are as follows:

TABLE XIX.

Diphtheria. Age of parent at birth of offspring and age of attack—the parent being alive.

	Age of parent at birth													
Age of attack	18—19	20—21	22—23	24—25	26—27	28—29	30—31	32—33	34—35	36—37	38—39	40—41	42 and over	Totals
0	1	—	—	3	1	1	2	1	5	—	1	1	—	16
1	2	4	6	10	10	7	7	4	5	4	4	3	1	67
2	3	8	5	6	7	10	4	6	1	3	2	2	2	59
3	2	9	3	14	9	15	8	6	8	6	1	3	—	84
4	2	4	8	12	14	7	10	6	8	3	4	2	3	83
5	1	9	12	13	12	13	9	7	6	7	4	5	1	99
6	2	2	4	14	7	10	9	5	3	6	1	1	3	67
7	—	7	9	6	9	5	7	3	6	—	—	—	1	53
8	1	—	3	7	8	1	1	1	2	3	1	1	1	30
9	1	2	2	2	2	3	3	2	—	1	—	—	—	18
10	2	1	4	3	1	1	5	2	2	1	4	—	1	27
11	1	3	4	5	5	4	1	5	1	—	2	2	—	33
12	—	—	2	—	1	—	2	1	—	—	1	1	—	8
13	—	3	—	4	1	3	3	1	2	1	—	2	—	20
14	1	—	4	5	3	1	—	1	—	1	1	—	1	18
15	—	2	1	—	—	1	1	1	1	—	—	—	—	7
16	—	—	—	—	—	—	1	—	—	—	—	—	—	1
Totals	19	54	67	104	90	82	73	52	50	36	26	23	14	690

The coefficients found are:

Age of attack and age of mother at birth $r = \cdot 034 \pm \cdot 0272$.

σ Age at attack ... ... $= 3\cdot 632$.

σ Age at birth ... ... $= 2\cdot 913$.

m Age of attack for arrays of mother's age $= \cdot 143$.

Corrected ... ... $= \cdot 0173$.

The means are:

Age at birth	Number	Mean
18–21 yrs	63	5·96
22–23 ,,	64	6·87
24–25 ,,	104	5·93
26–27 ,,	90	5·91
28–29 ,,	82	5·59
30–31 ,,	73	6·21
32–35 ,,	102	5·67
36 and over	99	5·86

If we accept the correction for death of parent, the correlation between age of mother at birth and

$$\text{Age of attack of child } r = \cdot 05 \pm \cdot 03.$$

From this taken by itself no conclusion could be drawn, but in so far as the same trend has been observed in the case of Scarlet Fever the result is suggestive.

The sequences are so irregular that, beyond the slight trend for the age of attack on the average to become later with the late born, little can be said.

ENTERIC FEVER.

With respect to Enteric Fever, the data are even more doubtful, as the error of commission is, according to the Metropolitan Asylums Board returns, about 40 %. There is no information as to the error of omission. Practically our heading in this case should read, "The Influence of Age of Parent at Birth of Offspring and Age of Attack in certain disorders of an 'Intestinal Type.'"

As the data were obtained in the same manner as those for Diphtheria and Scarlet Fever, the same defects will occur amongst those attacked late and born of mature parents. Hence on a random basis a negative correlation is expected.

The following figures relative to the epidemic at Lincoln and Basingstoke exemplify the point that multiple cases occur more frequently than chance could account for[1].

	Lincoln.		*Basingstoke* (1905).	
	No. of Houses expected to contain	No. of Houses found to contain	No. of Houses expected to contain	No. of Houses found to contain
0 cases	11,233	11,358	1864	1839·5
1 case	905	706	139	151·2
2 cases	36	79	11	6·2
3 ,,	1	27	1	·2
4 ,, and over	1	7	—	—
	12,176	12,177	1997	1997

Goodness in fit, $P = \cdot 045$.

[1] The example was worked out in class at the Lister Institute. It gives the first five terms of the binomial expansion of $12176\left(\frac{1}{12176}+\frac{12175}{12176}\right)^{1006}$. Naturally the method must be used with reserve owing to variation in size and number of inhabitants of houses.

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The features of the distribution are similar to those found in the case of Scarlet Fever, dependent on either milk or spread in the family itself. It must be also admitted that an inherited tendency running in particular families associated with infection from a general source would produce a similar result. The much longer incubation period of Enteric Fever and the sharp rise in the epidemic under consideration, and other reasons mentioned in the official account, leave little doubt that the spread was mainly due to the water supply. To what extent the errors already considered in the case of Scarlet Fever will affect the mean age of attack, can hardly be conjectured. In any case the indefinite nature of the material renders any detailed analysis of little value.

The data are as follows:

TABLE XX.

Age of mother at birth of offspring and age of attack of Enteric Fever. Mother still living.

	Age of parent at birth													
Age of attack	20and under	21—22	23—24	25—26	27—28	29—30	31—32	33—34	35—36	37—38	39—40	41—42	43—44	Total
0	—	—	—	—	—	—	—	—	—	—	—	—	—	—
1	—	—	—	1	1	—	1	—	—	1	—	—	—	4
2	1	—	1	—	2	—	—	—	—	—	—	—	—	4
3	—	—	1	1	2	2	1	—	—	—	1	1	—	9
4	—	2	1	4	8	1	1	—	1	—	1	1	1	21
5	1	—	3	3	3	1	1	2	—	—	1	—	—	15
6	2	4	3	2	1	4	1	—	1	1	—	1	—	20
7	1	4	2	3	2	3	1	—	—	1	—	—	—	17
8	1	2	2	1	3	2	2	1	—	1	1	1	—	17
9	—	2	—	2	1	—	1	—	—	—	—	1	—	7
10	1	—	1	2	2	1	—	—	—	—	—	1	—	8
11	—	—	2	2	3	2	—	—	1	—	—	—	—	10
12	—	2	2	—	2	1	—	—	1	—	—	—	—	8
13	2	—	1	1	—	2	1	2	2	—	—	3	—	14
14	1	—	1	1	—	—	1	—	1	—	—	—	—	5
15	—	1	—	—	2	—	—	2	1	2	—	—	—	8
16	—	1	—	1	1	1	—	—	—	—	—	—	—	4
17 & over	4	5	6	11	4	5	7	3	1	—	6	1	—	53
Totals	14	23	26	35	37	25	18	10	9	6	10	10	1	224

The constants found were:

$$\sigma_{\text{age of attack}} = 6{\cdot}1404. \qquad \sigma_{\text{age at birth}} = 5{\cdot}8485.$$

$$r = {\cdot}0293 \pm {\cdot}0472.$$

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In view of the fact that a negative correlation was expected it seems likely that the earlier born are attacked at a more immature age, or react more characteristically, and are recorded whilst the others are missed.

SMALL-POX AND TUBERCULOSIS.

The following diseases, namely Small-pox and Tuberculosis, have only been introduced on account of their intrinsic interest. It should be clearly understood that, owing to the small number of observations available, the results at best can be taken as suggestions only.

(1) *Small-pox.*

These data were obtained through the courtesy of Drs Hamer and Millard, under the same conditions as the Scarlet Fever material already described, and hence a negative correlation was to be expected. Small-pox being a more infectious disease than Scarlet Fever, home infection is very probable if the members have not been previously vaccinated. The chances of infection in the later born will be more marked than in the earlier born, and a negative association produced.

The actual data are as follows for father:

TABLE XXI.

Age of father at birth of offspring and age of attack of Small-pox. Father living at time of attack.

Age of attack	Age of father at birth: 20 and under	21—24	25—28	29—32	33—36	37—40	41—44	45—48	Totals
0–1	0	5	5	11	5	4	0	1	31
2–3	0	5	11	10	9	6	0	2	43
4–5	0	6	9	10	5	5	2	0	37
6–7	1	5	6	10	7	2	2	0	33
8–9	0	5	8	11	4	7	3	0	38
10–11	1	7	6	9	8	2	0	1	34
12–13	1	4	4	8	3	2	2	0	24
14–15	4	3	11	6	4	3	2	0	33
16–17	0	0	8	7	5	3	2	0	25
18–19	0	2	7	9	6	3	0	0	27
Totals	7	42	75	91	56	37	13	4	325

The constants obtained were:

$$\sigma_{\text{age at birth}} = 1{\cdot}7. \qquad \sigma_{\text{age of attack}} = 2{\cdot}8.$$

Age of father at birth and age of attack $r = -\cdot067 \pm \cdot034$.

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The data for the mother are:

TABLE XXII.

Age of mother at birth of offspring and age of attack of Small-pox.

Age of attack	Age of mother at birth: 20 and under	21—24	25—28	29—32	33—36	37—40	41—44	45—48	Totals
0–1	1	5	6	8	4	2	0	1	27
2–3	1	6	12	7	4	3	0	1	34
4–5	1	3	9	7	7	2	1	0	30
6–7	2	7	12	3	2	3	0	0	29
8–9	1	8	5	9	4	4	0	0	31
10–11	3	6	8	8	2	1	0	0	28
12–13	1	3	2	5	2	0	0	0	13
14–15	4	3	9	5	3	1	0	0	25
16–17	0	6	3	5	3	3	1	0	21
18–19	0	2	7	7	1	1	1	0	19
Totals	14	49	73	64	32	20	3	2	257

The constants were:

$$\sigma_{\text{age of attack}} = 2{\cdot}77. \qquad \sigma_{\text{age at birth}} = 1{\cdot}54.$$

$$r = -\cdot092 \pm \cdot034.$$

$$\eta_{\text{age of attack for arrays of mother's age}} = \cdot0924 \pm \cdot035.$$

The regression is effectively linear.

Taking the following coefficients,

Age of father at birth (1) and age of attack (2)

$$r_{12} = -\cdot0672.$$

Age of father at birth (3) and age of attack (2)

$$r_{23} = -\cdot0921.$$

Age of father at birth (1) and age of mother at birth (3)

$$r_{13} = -\cdot7214.$$

Making age of mother constant, the correlation between age of father at birth and age of attack approximates to zero. The same for age of mother at birth and the father being constant,

$$_1r_{23} = -\cdot058 \pm \cdot032.$$

It would be decidedly unsafe to draw any definite conclusion until more is known relative to the value of the correlation to be expected dependent on home infection, in a population where all families independent of size are grouped together.

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(2) *Tuberculosis.*

Turning now to Pulmonary Tuberculosis the data are scanty. It should be noted that in 112 instances given, the Tubercle Bacillus was found in the sputum.

No corrections,such as have been described in the previous cases are necessary in these, firstly because information relative to age of parents at birth was obtained irrespective of the fact of the parents being alive or dead, and secondly, there is no evidence as to the relative parts played by general and home infection in the spread of this disease.

In the present state of our knowledge it can be assumed for our purposes that all are equally exposed to risk.

The data are as follows:

TABLE XXIII.

Age of mother at birth of offspring and age at which Pulmonary Tuberculosis becomes recognisable clinically.

	Age of mother at birth of offspring															
Age of attack	17—18	19—20	21—22	23—24	25—26	27—28	29—30	31—32	33—34	35—36	37—38	39—40	41—42	43—44	45 and over	Totals
0–8	1	—	—	2	1	1	4	1	—	2	1	1	—	—	—	14
9–12	—	—	1	1	1	2	1	—	—	—	—	—	1	—	—	7
13–16	—	—	1	2	1	2	3	2	—	2	—	—	—	—	—	13
17–20	—	1	1	1	4	2	2	7	—	1	2	1	—	—	—	22
21–24	—	—	1	4	1	3	1	2	2	1	—	2	1	—	1	19
25–28	—	2	1	5	1	3	1	1	3	2	—	1	—	1	—	21
29–32	—	1	1	3	4	1	4	1	4	—	1	1	—	—	—	21
33–36	—	1	1	4	5	4	1	2	1	3	2	2	1	1	1	29
37–40	—	—	1	—	—	2	1	3	2	3	—	1	1	1	—	15
41–44	—	—	1	—	3	—	—	—	1	—	1	—	—	—	—	6
45–48	—	—	—	—	—	1	—	1	—	—	1	—	—	—	—	3
49–52	—	—	—	—	1	—	1	—	—	—	—	—	—	—	—	2
53–56	—	—	—	—	—	1	—	—	—	—	—	—	—	—	—	1
57–60	—	—	1	—	—	1	—	—	—	—	—	1	—	—	—	3
Totals	1	5	10	22	22	23	19	20	13	14	8	10	4	3	2	176

The constants obtained were:

$$\sigma_{\text{age of attack}} = 2{\cdot}87. \qquad \sigma_{\text{age at birth}} = 3{\cdot}02.$$

Correlation between age of mother at birth and age of attack

$$r = {\cdot}09 \pm {\cdot}05.$$

That is to say, the younger born are probably attacked earlier. If we take Hansen's data as quoted by Dr Greenwood, and fit a straight line to the number attacked with Tuberculosis and the number expected, in respect to order of birth,

$$r = \cdot 0172 \pm \cdot 0084.$$

$$\text{Mean order expected} = 3\cdot 4236.$$

$$\text{Mean order Tuberculous} = 3\cdot 2817.$$

Hence, on the average, the earlier born are either attacked at younger ages or more frequently than the elder born. The former seems the more likely explanation.

Now bearing in mind that the association between age of mother at birth and age of attack by Tuberculosis is small but positive ($r = \cdot 09$) and for Small-Pox is negative $r = - \cdot 09$, it suggests that these two diseases are dissimilar in their incidence. Even should it be supposed that the negative association for Small-pox is dependent on infection in large families, it would still have the same effect on the prevalence of the former disease.

The possibility that the fall in the Phthisis rate from 1840 to the present day may be due to the survival of certain units that would have been killed by Small-pox if prevalent, does seem to be a question worthy of further investigation.

Minor infectious diseases.

The following table drawn from inquiries of such mothers as attended the examination of children under the Education Act 1898 (Administrative Provisions) leads to conclusions similar to those already drawn from the more serious infectious ailments.

All children were in their 7th year at the time of inquiry and were born in 1903. Each mother was asked whether the child had or had not had the complaints under inquiry.

The data are as follows:

Incidence of Measles and other diseases on children in the first seven years of life (*born in* 1903) *according to the age of the mother at birth.*

Age of mother at birth of child	Number of inquiries	Number of illnesses per child	Number attacked with measles per 100	Number attacked with whooping cough per 100	Number attacked with chicken-pox per 100
20 and under	21	2·05	97	63	35
21–25	143	2·25	89	59	45
26–30	182	2·1	88	54	41
31–35	92	2·1	82	48	38
36–40	54	1·9	82	40	25
40 and over	41	1·7	80	43	44

NOTE.—The column "illnesses per child" included pneumonia, vague febrile attacks, and other ill-defined conditions.

With the exception of Chicken-pox the percentage incidence falls steadily in all cases as the age of the mother at birth advances. As the age taken was the 7th year, some susceptible children will be attacked at later ages. Hence it is not unfair to assume that for these diseases the later born are attacked at more mature ages or not at all.

GENERAL CONCLUSIONS.

Although in many of the instances given the correlations are very small, the concordance does suggest that, with the exception of Small-pox and possibly Chicken-pox, infectious diseases attack the earlier born at younger ages than the later born.

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