PERIODICITY IN INFECTIOUS DISEASE.

BY

JOHN BROWNLEE, M.D., D.Sc.

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ROYAL PHILOSOPHICAL SOCIETY OF GLASGOW,

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Periodicity in Infectious Disease.

By John Brownlee, M.D., D.Sc., President of the Sanitary and Social Economy Section.

[Read before the Society, 25th March, 1914.]

In investigating the periodicity of disease there is one factor which is immediately evident, and that is the action of the seasons in producing epidemic waves. Thus scarlet fever and enteric fever are diseases having a well marked maximum nearly every autumn. Whooping-cough is a disease of the winter. Measles has two maxima, one in November and one in May. These curves need not be reproduced here, as they are shown in any good text book of vital statistics or of public health, or in the reports of the medical officers of health of any of the large towns. This periodicity is well known and depends on climatic variations, though how these act is at present not understood. The periodicities to be investigated here, however, are of quite different origin; they seem to depend on some cycle in the life history of the infecting organism, and are quite independent of the solar year. Sometimes they so nearly correspond with it as to lead the belief that the seasonal influence is the chief one, but that is not the rule.

As a result of these two factors interference curves are frequent in epidemiology. Often the organism seems to waken into activity at a season of the year which is not suitable for the rise of an epidemic, and the outburst is then small; whereas if in the course of its life history the wakening of the organism to activity corresponds with the season of the year suitable for its development a large outbreak is the result. The period of the life history of the organism seems in general to be from one to three years, but on account of the interference between periods of the year and that of the organism longer waves of disease can often be demonstrated.

The method by which periodicity of disease is here investigated is that known as the periodogram. This method has been applied by Professor Schuster and others to the discovery of the periods of sun spots, weather phenomena, etc., but it has not so far as I know been hitherto applied in the field of epidemiology. In its application it is simple but laborious. If any series of figures be taken which show periodic phenomena the method is to write the first n of the figures in a row, the next succeeding n figures are placed under the first and so on till we have p rows of n figures written in sequence. The columns are then summed. One of two things happens: if a period has been guessed correctly, or nearly correctly, then as each additional row is added to the sum the progress from a maximum to a minimum tends to become more apparent, other accidental variations tending to become eliminated. If on the other hand a period has not been guessed the periodic variations tend to cancel each other, and the sums of the columns approach more and more nearly the same value the more rows which are taken. If a period has only been approximately guessed, the true period can be obtained by taking first a series of q rows and summing. Second, third and fourth series of q rows are summed in a like manner if the statistics are sufficiently numerous to supply such a number. A maximum will appear in each of these series, but not at the same place. By considering the amount which this maximum moves forwards and backwards in succeeding sums the real period can be approximately evaluated. By further developments of the theory the probability of an apparent period being the result of a true periodicity, or the result of chance variations in the figures can be estimated. This part of the theory does not concern us here, because the differences found are so great as not to require the application of such a process, and secondly, because I do not think the theory of chance can be immediately applied to the numbers of cases of epidemic disease occurring in definite periods of time. It is not necessary to give examples of the method of working in this place. Numerous examples are given later, and in addition any one who wishes to try the method can easily write out a series of obviously periodic figures and sum them in different ways.

The first example of periodicity which I will consider is that of measles. This disease is commonly supposed to have a two-years' period, and a first glance at the figures seems to justify this view. On investigation, however, it is found to be erroneous. Some times in some places a two-years' period has held for a considerable series of years, but this period is far from universal. The figures which give the key to the whole subject are those of London. In this case we have a series of figures giving the number of deaths from measles for seventy-two years. These are published by the Registrar General both for quarter-year periods and for the weeks of each year. It was found that for the purposes of this investigation the deaths in each quarter year afforded a sufficient fineness of gradation to determine the periods. A clue to the period was suggested by the method in which the two-yearly period changed. It was noticed that from 1838 till 1853 the number of deaths in the first alternate year was less than that in the second; thus there were more deaths from measles in 1839 than in 1838, and so on to 1853. With 1854 a change took place, and from 1854 till 1871 the excess was the other way, that is, in 1854 there were more deaths than in 1855, and so on. With 1872 the change again took place, again in 1890, and lastly in 1908. The exact determination of the period of change was difficult, but it was approximately eighteen years. It was thought first that as two and a quarter years is an eighth of eighteen, and as a two-years' approximate period existed that the former might be the true period. It was found, however, on forming the sums on that supposition for each successive period of nine years that the maximum moved steadily backwards, and in the eight periods available made almost a complete revolution. A rough calculation thus decided that the two-and-a-quarter-year period was approximately three-eighths of a year too long, and a new summation was made on that basis. This turned out to be almost absolutely correct. The figures of each eighth of a year not being directly available an approximation to them was obtained by halving the number in each quarter. As this example is of very considerable importance the whole figures are printed in Table A.

A complete period consists of fifteen years, so that the table contains four complete cycles and seven periods of the next cycle. When the sums of the first four periods taken in pairs and of the part of the last period are examined it is seen that there exists an almost perfectly symmetrical distribution of the series, rising from the minimum to the maximum smoothly for both cycles, but that the maximum in the second pair of periods has moved about half a division backwards from that in the first. This amounts in thirty years to one-sixteenth of a year, so that the actual average period of

TABLE A.

DEATHS FROM MEASLES LONDON, 1840 - 1912 IN EACH EIGHTH OF A YEAR.

10	10	14	14	15	15	18	18	8	8	7	7	13	13	20
20	15	15	17	17	15	15	17	17	13	13	18	18	18	18
23	23	17	17	10	10	13	13	19	19	19	19	16	16	34
34	46	46	20	20	8	8	4	4	5	5	5	5	14	14
26	26	44	44	23	23	15	15	8	8	11	11	9	9	18
18	14	14	17	17	15	15	12	12	9	9	13	13	18	18
25	25	13	13	10	10	7	7	10	10	6	6	6	6	9
9	13	13	11	11	17	17	17	17	24	24	10	10	18	18
16	16	9	9	5	5	13	13	13	13	21	21	20	20	19
19	17	17	18	18	13	13	20	20	36	36	34	34	23	23
26	26	18	18	15	15	12	12	20	20	14	14	28	28	29
29	32	32	22	22	14	14	10	10	9	9	12	12	25	25
32	32	45	45	29	29	30	30	11	11	15	15	21	21	42
42	43	43	32	32	17	17	10	10	13	13	25	25	28	28
41	41	26	26	18	18	12	12	10	10	9	9	25	25	23
23	37	37	20	20	19	19	15	15	16	16	17	17	24	24

17	17	25	15	15	15	15	15	10	10	11	11	13	13	38
38	32	32	33	33	12	12	7	7	6	6	15	15	18	18
71	71	41	41	23	23	10	10	8	8	9	9	15	15	17
17	31	31	33	33	28	28	11	11	14	14	18	18	34	34
22	22	44	44	35	35	17	17	8	8	15	15	14	14	42
42	33	33	34	34	17	17	18	18	15	15	25	25	24	24
45	45	29	29	28	28	27	27	31	31	20	20	38	38	24
24	40	40	33	33	24	24	27	27	51	51	21	21	15	15
24	24	59	59	30	30	32	32	25	25	27	27	19	19	32
32	43	43	61	61	24	24	16	16	12	12	12	12	21	21
74	74	55	55	33	33	11	11	16	16	17	17	49	49	47
47	51	51	22	22	23	23	12	12	32	32	41	41	80	80
29	29	19	19	16	16	22	22	23	23	22	22	38	38	87
87	23	23	15	15	15	15	28	28	38	38	51	51	69	69
81	81	25	25	9	9	8	8	15	15	15	15	58	58	75
75	54	54	12	12	13	13	19	19	35	35	26	26	26	26

	30	30	38	38	16	16	12	12	22	22	27	27	22	22	27
	27	36	36	36	36	17	17	28	28	33	33	38	38	12	12
	19	19	33	33	46	46	18	18	14	14	18	18	27	27	13
	13	28	28	34	34	38	38	13	13	10	10	23	23	33	33
	20	20	14	14	17	17	24	24	13	13	23	23	57	57	42
	42	10	10	7	7	12	12	27	27	17	17	42	42	79	79
	35	35	8	8	7	7	10	10	21	21	18	18	39	39	43
Total 1st Group	393	416	403	343	282	243	238	225	204	224	227	236	272	306	362
2nd "	725	670	604	539	432	345	298	280	274	339	339	345	453	531	649
3rd "	186	178	167	170	163	153	131	132	138	130	146	189	248	269	249
TOTAL	1,304	1,264	1,174	1,052	877	741	667	637	616	693	712	770	973	1,106	1,260

Totals corrected for increase of population at the different periods.

Total 1st Group	393	416	403	343	282	243	238	225	204	224	227	236	272	306	362
2nd "	487	450	405	367	290	232	200	188	184	228	228	232	304	356	436
3rd "	126	121	113	115	110	104	89	89	93	88	99	128	168	182	169
TOTAL	1,006	987	921	825	682	579	527	502	481	540	554	596	744	844	967

one and seven-eights of a year shown in the table is one-thirtieth multiplied by one-sixteenth of a year in excess, that being approximately three-quarters of a day. The same phenomena observed in the two cycles are observable in the part of the third cycle, when, however, the maximum falls a little further back. In the lowest part of the table these figures are adjusted to the varying populations present at the different dates and summed. The same regular progression may be noted in this sum as in each of the individual cycles. The curve has been fitted to a Fourier series. It is found to be almost a pure cosine curve: the only coefficient of cosine terms of any importance being that of cosine $2x$. This indicates a close approach to normality on the part of the curve, the equation of the normal curve in the Fourier series being given in terms of cosines.

In the case considered the coefficient of cosine$x$ is equal to about six times six of cosine$2x$ in place of 4·5 times required by the normal curve. Certain other phenomena stand to be noted in this table. The first column of Table A represents closely the maximum point of the curve. This column is seen to have a very marked four-period period throughout. This has an obvious meaning. The organism has an average life history of one and seven-eighth years, sometimes shorter, sometimes longer, but varying within very moderate limits of that period. The season of the year, as has been indicated in an earlier part of the paper, has a considerable amount of effect in determining whether an epidemic can take place or not. November and May are the two months of choice for the height of an epidemic. As there are two suitable periods in the year, and as the cycle of the organism's life history moves round the cycle of the year by eighths of a year, periods suitable and unsuitable for the rise of an epidemic will alternate in fours. If the May epidemic is consistently larger than that of December, as is the case in London, or vice versa, one of double the length will result. In the former case we have a period of seven and a half years, in the latter of fifteen. The former corresponds to four periods, and the latter to eight.

When the earlier figures for measles in London are considered, it is found that from 1740 to 1820 a seven and a half years' period also exists, so it may be taken that for nearly two centuries in London the type of epidemic prevalence of measles has been one

TABLE B.

DEATHS FROM MEASLES IN QUARTER YEARS. ABERDEEN

Thirty and one quarter years 1856-1885¼ in two and three quarter year periods.

	-	1	1	-	23	44	2	1	2	-	-
	-	-	-	-	7	76	36	5	15	8	1
	4	-	-	-	10	150	27	7	1	-	-
	1	1	2	1	-	1	-	44	8	2	3
	-	-	1	1	5	92	34	3	-	3	1
	2	-	1	-	1	-	-	4	94	49	4
	-	3	-	-	-	22	58	7	1	2	-
	-	-	-	-	4	18	40	5	1	-	4
	-	-	1	-	9	31	5	-	-	4	5
	10	18	4	6	3	6	38	8	2	-	-
	1	-	-	-	12	83	9	1	3	-	-
TOTALS	18	23	10	8	74	543	249	85	127	68	16

Intermediate period 1885½-1891.

2 1 8 125 100 2 1 - - - 1 5 65 41 23 14 25
11 4 1 - 1 -

Eighteen years 1892-1909 in two year periods.

	1	1	17	126	15	2	-	6
	4	10	9	44	139	36	5	1
	-	-	-	29	17	7	-	-
	1	-	-	25	103	9	-	2
	-	1	4	51	56	24	2	1
	-	-	-	18	97	13	1	2
	1	6	9	78	27	4	-	-
	-	-	8	66	25	2	1	6
	34	17	9	6	15	10	4	4
TOTALS	41	35	56	443	494	107	13	22

for which the organism has a life history averaging in duration one and seven-eighth years with little tendency to depart therefrom. Unfortunately the total figures for years are only available so that the result cannot be said to be definitely proved. An example of the difficulty of determining short periods when the annual number of deaths alone is know is given later in this paper when the figures relating to smallpox are discussed.

The example just given for London is the most perfect at our disposal. In completeness it cannot be matched elsewhere, and it clearly illustrates the method by which statistics at first sight presenting little obvious periodicity may be made to yield their secrets. The figures for four towns in Scotland, Glasgow, Aberdeen, Perth and Dundee, from 1855 till 1912, have also been investigated. In addition the statistics of Glasgow between 1773 and 1812 have been examined. The result of this is to show that the periodicity of measles epidemics varies from fifteen and a half months to three years.

In Aberdeen (Table B) for the thirty years 1856 to 1885, epidemics of measles occur with regularity every two and three-quarter years. The only aberrant epidemics are two. An inter-period of some five years then occurred in which no regular epidemic type is present but apparently as the result of the introduction of a new infection in the year 1892, a two-years' period became established which has lasted up to the present date. On only one occasion in this latter period was there anything approaching an epidemic except at the expected time. Aberdeen also affords the means of showing that the periodicity of cases is well paralleled by that of deaths in as much as notification of measles was in existence for a considerable time. In Table I. the case rate is given in the first line, and in the second the number of deaths. The correspondence is sufficiently close to justify the acceptance of the death figures as giving the essential periodicity.

TABLE I.

Case Rate,	20	49	75	781	818	137	23	22
Deaths, -	6	12	30	275	330	78	7	10

Dundee (Table C) falls into line with Aberdeen. From 1855 till 1873 two separate series of these years' epidemics run more or less

Table C.

DEATHS FROM MEASLES IN QUARTER YEARS. DUNDEE.

Eighteen years 1856-1873 in three year periods

	17	106	47	2	2	-	1	-	-	5	10	78
	103	12	2	1	2	13	35	29	9	2	4	18
	118	97	29	12	8	4	46	43	16	7	2	-
	1	71	103	15	6	1	-	2	1	2	1	1
	75	104	6	-	1	-	1	-	-	1	5	20
	11	8	-	2	3	42	76	12	8	9	7	1
TOTALS	325	398	187	30	9	1	2	2	1	8	22	118
	-	-	-	2	13	59	157	84	33	18	7	-

Thirty-eight years 1874-1911 in two year periods.

	11	17	6	3	-	3	-	1
	28	50	5	-	5	8	9	10
	58	49	8	-	-	-	-	1
	94	64	1	-	-	-	-	1
	1	15	62	21	4	3	-	-
	1	37	17	36	18	4	-	-
	-	1	-	-	1	-	1	40
	17	-	-	-	15	10	-	-
	7	124	31	1	-	1	-	-
	-	1	2	55	203	25	5	-
	6	22	32	21	11	11	2	9
	7	29	7	5	1	1	-	-
	-	73	62	4	7	3	1	33
	44	17	5	-	10	17	31	43
	43	32	6	1	-	2	-	2
	47	23	2	-	1	-	3	83
	44	16	2	3	-	-	1	139
	15	-	-	-	2	-	-	2
	33	246	11	-	-	1	1	1
TOTALS	454	763	178	38	53	57	47	365
	2	53	81	114	225	32	5	-
	456	816	259	252	278	89	52	365

alternately, the second series indicated in the table by the numbers of the cases being underlined. From 1874 a two years' period has been constant with these exceptions shown in the same way. Further remarks seem unnecessary.

Perth furnishes an example of great interest. For the last forty years the epidemics have occurred regularly every sixteen months. Only twice in that period was there any variation from this law. It does not seem necessary to reproduce the whole figures, but the totals are given in Table II.

TABLE II.

38	23	20	15	17	8	8	6	4	1	5	3	5	5	15	23
									7	7	7	3	2		
38,	23,	20,	15,	17,	8,	8,	6,	4,	8,	12,	10,	8,	7,	15,	23

In the first line of the table the total deaths are given excluding the aberrant epidemics. In the second line the totals of the aberrant epidemics, and in the third line the total of all the deaths. It is to be noted that even when the aberrant epidemics are added no marked difference is made in the periodicity. It is further of interest to note that though measles may be absent sometimes for more than a year, in which case a period is missed, the next period turns up true to time. It is of course possible that a small epidemic has occurred in the interval which was unaccompanied by any deaths.

With regard to Glasgow there are some specially interesting points. The earliest figures, these from 1773 to 1812, are contained in the celebrated "Treatise on the Chincough," by Dr Watt. In this Dr Watt develops the theory that one disease may take the place of another. Thus in the earlier part of that period smallpox caused a large number of deaths among the children of Glasgow. With the coming of vaccination this cause of death was greatly lessened. As concurrent facts Dr Watt notes that in the earlier period deaths from measles were few, but in the latter period they greatly increased. These facts he correlates, developing his "substitution" theory. Examined, however, in the light of the present method another explanation is possible. Till 1800 there was present in Glasgow a type of measles having an approximate period of fifteen and a half months, a figure

Table D.

DEATHS FROM MEASLES GLASGOW 1856 - 1910.

HALF CALENDAR MONTHS.

7	7	2	2	4	4	5	5	10	10	7	7	12	12	10	10	11	11	8	8	23	23	40	40	38	38	28	28	51	51	50	50	44	44	39	39	36	36	34	34	12	12	10	10	6	6	6	6	10
10	18	18	28	28	34	34	41	41	66	66	66	66	55	55	50	50	29	29	42	42	32	32	36	36	27	27	16	16	8	8	12	12	8	8	16	16	8	8	8	8	7	7	6	6	6	6	20	20
17	17	26	26	45	45	74	74	115	115	123	123	59	59	37	37	16	16	22	22	21	21	25	25	12	12	15	15	10	10	11	11	28	28	22	22	11	11	6	6	5	5	14	14	9	9	18	18	7
7	14	14	19	19	17	17	19	19	26	26	17	17	19	19	24	24	44	44	60	60	47	47	39	39	29	29	36	36	50	50	70	70	63	63	41	41	29	29	11	11	21	21	19	19	21	21	16	16
40	40	27	27	20	20	26	26	30	30	30	30	36	36	42	42	84	84	89	89	83	83	45	45	26	26	28	28	26	26	11	11	27	27	25	25	10	10	11	11	21	21	29	29	29	29	23	23	28
28	36	36	47	47	47	47	49	49	21	21	15	15	17	17	23	23	21	21	40	40	37	37	45	45	42	42	47	47	36	36	52	52	32	32	21	21	19	19	10	10	12	12	17	17	36	36	24	24
27	27	36	36	52	52	50	50	33	33	24	24	22	22	18	18	26	26	50	50	73	73	71	71	65	65	98	98	92	92	86	86	49	49	25	25	19	19	18	18	8	8	10	10	6	6	1	1	2
2	4	4	1	1	2	2	6	6	1	1	12	12	21	21	57	57	42	42	27	27	44	44	68	68	162	162	202	202	223	223	94	94	55	55	27	27	13	13	8	8	12	12	6	6	8	8	12	12
10	10	8	8	3	3	2	2	3	3	6	6	18	18	22	22	19	19	42	42	82	82	77	77	140	140	115	115	75	75	44	44	15	15	12	12	2	2	5	5	6	6	7	7	16	16	17	17	26
26	36	36	53	53	29	29	20	20	20	20	17	17	25	25	22	22	16	16	44	44	49	49	47	47	55	55	44	44	27	27	16	16	12	12	11	11	10	10	20	20	35	35	39	39	42	42	39	39
37	37	34	34	17	17	15	15	7	7	14	14	13	13	17	17	21	21	29	29	41	41	69	69	62	62	46	46	25	25	14	14	17	17	14	14	15	15	14	14	6	6	9	9	23	23	30	30	31
31	39	39	29	29	9	9	20	20	26	26	49	49	26	26	17	17	18	18	10	10	27	27	23	23	15	15	5	5	3	3	5	5	3	3	9	9	5	5	8	8	23	23	33	33	36	36	60	60
59	59	21	21	20	20	13	13	28	28	22	22	31	31	20	20	22	22	27	27	28	28	33	33	40	40	22	22	17	17	21	21	39	39	54	54	48	48	23	23	21	21	22	22	27	27	17	17	5
301	344	301	331	338	299	323	340	381	386	386	402	367	354	329	359	392	369	437	490	574	587	596	618	641	713	682	702	646	643	584	486	468	392	364	316	266	225	195	176	144	189	211	221	236	265	261	283	280

5	6	6	2	2	10	10	12	12	45	45	39	39	20	20	74	74	105	105	167	167	131	131	62	62	10	10	12	12	9	9	5	5	7	7	-	-	11	11	12	12	15	15	23	23	24	24	23	23
19	19	24	24	37	37	63	63	102	102	70	70	62	62	92	92	84	84	52	52	45	45	14	14	5	5	5	5	3	3	4	4	3	3	2	2	2	2	1	1	2	2	5	5	8	8	5	5	8
8	3	3	5	5	12	12	45	45	50	50	48	48	64	64	46	46	41	41	30	30	11	11	2	2	2	2	3	3	5	5	2	2	6	6	6	6	18	18	18	18	41	41	43	43	23	23	8	8
10	10	5	5	16	16	22	22	48	48	78	78	133	133	126	126	74	74	53	53	35	35	9	9	14	14	13	13	19	19	42	42	58	58	39	39	68	68	84	84	97	97	99	99	65	65	14	14	22
22	21	21	37	37	27	27	28	28	18	18	53	53	60	60	53	53	68	68	30	30	17	17	19	19	29	29	37	37	26	26	28	28	33	33	58	58	65	65	131	131	128	128	71	71	53	53	13	13
20	20	54	54	118	118	136	136	69	69	116	116	155	155	155	155	130	130	59	59	21	21	9	9	1	1	3	3	1	1	6	6	-	-	8	8	4	4	3	3	17	17	19	19	9	9	5	5	22
22	55	55	102	102	101	101	65	65	47	47	21	21	18	18	20	20	21	21	12	12	5	5	2	2	1	1	17	17	17	17	11	11	28	28	29	29	53	53	113	113	137	137	64	64	36	36	52	52
105	105	169	169	134	134	110	110	84	84	61	61	53	53	21	21	8	8	6	6	6	6	20	20	30	30	41	41	45	45	51	51	81	81	91	91	89	89	69	69	39	39	11	11	9	9	13	13	11
11	26	26	17	17	20	20	41	41	54	54	65	65	65	65	61	61	51	51	12	12	49	49	48	48	65	65	84	84	51	51	49	49	56	56	44	44	55	55	57	57	35	35	8	8	8	8	4	4
10	10	4	4	9	9	8	8	18	18	37	37	54	54	62	62	45	45	26	26	50	50	86	86	98	98	86	86	38	38	31	31	21	21	16	16	28	28	12	12	8	8	4	4	6	6	2	2	10
10	4	4	4	4	9	9	6	6	21	21	19	19	18	18	15	15	19	19	46	46	60	60	126	126	53	53	50	50	53	53	55	55	35	35	23	23	7	7	10	10	9	9	8	8	11	11	18	18
15	15	16	16	24	24	52	52	103	103	56	56	42	42	32	32	15	15	50	50	81	81	78	78	90	90	75	75	58	58	40	40	43	43	41	41	19	19	10	10	7	7	7	7	2	2	2	2	8
8	2	2	10	10	21	21	14	14	12	12	24	24	12	12	9	9	25	25	80	80	182	182	298	298	175	175	155	155	102	102	49	49	20	20	5	5	11	11	6	6	3	3	4	4	2	2	1	1
-	-	1	1	1	1	2	2	3	3	8	8	11	11	8	8	21	21	142	142	202	202	178	178	128	128	97	97	57	57	41	41	15	15	10	10	5	5	1	1	1	1	1	1	1	1	2	2	3
266	296	390	450	516	539	593	604	638	674	673	695	779	767	753	774	655	707	718	765	817	895	849	951	923	701	655	678	579	484	478	414	420	406	392	372	380	435	400	527	518	539	514	367	321	257	200	162	203

closely allied to that seen to occur at present in Perth. This apparently was a non-virulent measles. Bearing no relation to this period two great epidemics of measles occurred in 1808-1810 which can be explained by the introduction of a new organism of much more fatal type. The latter explanation seems to me the more probable. Unfortunately data for the further investigation are lacking till the year 1855. From this time the chief period has been twenty-four and a half months (Table D). With a period so nearly two years as this the motion round the solar year is exceedingly slow. It thus follows that the period when the organism wakens to activity will be at an unsuitable season of the year in a large number of years in succession. This is what is seen to occur on examining the tables, but the defect of epidemic is supplied by an epidemic having a period of twenty-three and a half months. This is shown in the table by the oblique line drawn through the middle portion of the succeeding epidemics. It almost looks as if there had been introduced an organism of a two-years' period which had split into variants, of periods one slightly less and one slightly more than two years. The figures since 1855 have also been examined for the fifteen-and-a-half-months' period and for the longer period of the 1808-1810 epidemics without any trace of either being discovered. It is therefore probable that these are quite extinct.

The periodicity of smallpox resembles that of measles and varies apparently within the same limits. It is, however, specially difficult to obtain statistics of smallpox in sufficient detail to permit of the periodicity being accurately ascertained, and this is made more difficult in as much as the introduction of vaccination has so much lessened the mortality from smallpox that the figures are rarely sufficiently great to permit of any accurate investigation. For the eighteenth century the only figures which give the monthly deaths which I have had access to are those given by Dr Watt in his book already referred to. In this the monthly deaths from smallpox from 1773 till 1812 are tabulated among others. In the accompanying table (Table E), these are arranged in groups of quarter years and in periods of seven quarters of a year. The totals are given in two rows, the first for fifteen and three-quarter years from 1773, and the next group for the next fourteen years. It will be noticed that the maximum has moved forward slightly in these two groups, indicating that the period is very slightly more than a year and three-quarters, but that a very well defined maximum and minimum exists. For comparison with this the deaths from smallpox in Glasgow have been taken out from 1856 to 1872, these being years in which there was a considerable amount of smallpox in Glasgow. Here we have an example of a very much shorter period, namely, one of fifteen and a half months. The maximum value of the ordinate of this curve is in this case about four times the minimum value, and the curve is fairly regular. The same variation in epidemic periodicity is thus found to exist in the case of smallpox as was previously found in the case of measles due probably to the presence of a different strain of organism.

With regard to short periods it is to be specially noted that these though perfectly definite and quite easily ascertained if statistics of sufficient fineness are obtainable appear only doubtfully if annual death rates alone can be obtained. The example just given illustrates this. The periodicity is perfectly definitely one and three-quarter years as has been seen. If, however, the annual deaths are taken, and the one-and-three-quarter-year period sought on the assumption that during each year the prevalence of the disease is uniform, then, though the period appears, yet the difference between the minimum and maximum is quite small. The sums for each quarter of a year are as follows :—

382, 370, 368, 349, 382, 392, and 397.

Thus taking the minimum as 350, and the maximum as 400, the amount of rise and fall above and below the mean is only one-fifteenth part of the mean; this is very different from what has been shown when the quarterly periods are taken. There, the difference between the minimum and the maximum is not far short of the mean itself. As a last example the epidemics of whooping cough in London (Table F) have been analysed, hence the average periodicity is $1\frac{14}{13}$ years, very approximately. As the statistics give the figures in thirteenths of a year there are only twenty five columns in the table, but position of the columns is kept accurate by the omission of single numbers at the appropriate places.

In the preceding pages it has, I think, been made quite evident that there are periods in the epidemicity of disease dependent on the life history of the organism and not on the weather. The two

TABLE E.

DEATHS IN QUARTER YEARS FROM SMALLPOX, GLASGOW 1773 - 1812.

	108	34	13	2	12	40	188	146	159	82	64	65	77	42
	185	52	22	57	85	65	37	67	91	71	40	37	97	70
	89	139	137	69	61	133	123	15	33	38	26	28	46	96
	96	124	56	54	83	101	118	90	69	30	24	7	2	12
	117	103	90	26	30	74	182	25	10	5	6	7	15	12
	321	83	14	25	90	59	53	28	42	11	15	10	5	7
	113	174	147	36	18	34	46	20	54	78	17	6	1	4
	85	148	123	89	43	40	25	10	14	57	28	17	26	25
	67	132	88	57	44	48	71							
1st Group	1,181	989	690	415	466	614	843	401	472	372	220	177	269	268
2nd "	401	472	372	220	177	269	268							
	1,582	1,461	1,062	635	643	883	1,111							

periods, the one due to the life of the organism and the other to the seasonal variations of climate, present together a curve which shows interference phenomena. I have not illustrated these phenomena specially. They can more or less easily be observed by anyone examining the diagrams published in the reports of the Medical Officers of Health. Nor have I illustrated the secondary interference phenomena which must give rise to spurious periods, as I have not had time to go through the arithmetical work necessary to exhibit these without doubt. The instances which have been given are all comparatively simple. There is in addition, however, a much more complex series of instances, where not merely two but probably three factors take part in the causation of the epidemic wave. Such is almost certainly the case in scarlet fever. How this disease is spread is at present quite unknown, the form of the epidemic wave is not such as can be immediately explained on the basis used in the calculations in this paper. The epidemic course of malarial fever must certainly belong to this type, for here we have three definitely known factors—the season, the plasmodium of malaria, and the mosquito. I have not, however, been able to obtain a series of figures which is of sufficient length to warrant conclusions being drawn.

Nor has anything been said about the longer waves of disease. I propose to consider this subject at some future time, but it may be here remarked that the statistics of typhus fever show that, as that disease has declined, the rate of decline has closely approximated to what would be expected on the theory of epidemic which I have developed in the previous papers, namely, that the infectivity of the organism decreases in the geometrical law.

In applying these principles of epidemiology to higher animals data are far from numerous. Such data as exist I have not had time to systematically examine, but there is one example of considerable interest, namely, that concerning the periodicity of the outbursts of genius in English literature during the last thirteen hundred years. All the names of authors who have been considered by Professor Nichol as worthy of distinctive remark in his tables of history have been tabulated. The table is not printed but it can easily be verified that there are six cycles of two hundred and thirty years. The date of birth of each author has been chosen as the epoch of classification, that being the only biological fact, as it seems to me, of importance in fixing such a cycle. The cycles are represented as follows :—

(1) Caedmon, etc.
(2) Alfred and the Anglo-Saxon Chronicle.
(3) William of Malmesbury, Geoffrey of Monmouth, etc.
(4) Chaucer, Wycliffe, Langlands, Gower, etc.
(5) Shakespeare, Bacon, Spencer, etc.
(6) Wordsworth, Bryon, Scott, Shelley, Keats, etc.

It will be noticed that in each cycle a period of sixty years out of each two hundred and thirty years, the middle point of each period being exactly two hundred and thirty years from the preceding middle point, includes almost all the really great names in English literature. I do not wish to base too much on this table, but I think that the coincidence is too surprising to be accidental.

[Table F.

Table F.

DEATHS FROM WHOOPING-COUGH, LONDON 1840 - 1900.

11	8	9	10	9	9	7	7	5	7	6	8	13	16	23	22	21	17	14	13	14	13	18	18	21
20	25	24	18	16	13	12	8	6	4	7	9	8	12	14	15	18	17	20	18	18	11	8	10	15
13	15	11	15	18	16	13	8	6	6	4	6	6	8	12	10	12	15	17	14	13	12	13	10	12
15	19	19	23	24	23	22	19	15	14	14	8	9	9	11	15	18	16	17	14	13	11	9	7	7
8	6	11	20	13	10	10	17	14	12	12	10	9	12	11	14	19	24	28	30	26	24	21	19	14
12	11	8	8	12	13	14	14	14	12	9	9	9	10	8	11	21	19	22	31	23	26	27	17	13
10	8	6	10	11	16	15	18	17	15	13	11	7	7	8	10	9	12	16	22	26	30	26	24	21
15	10	11	16	18	24	29	32	26	29	24	23	17	11	9	8	11	13	16	27	32	30	26	20	16
14	14	12	10	10	12	19	21	19	21	19	17	18	17	13	8	11	10	16	18	23	26	25	24	21
22	19	16	14	9	12	20	19	20	21	28	30	28	24	23	18	13	11	13	21	20	23	23	20	19
14	13	9	10	7	5	6	9	14	20	19	24	18	11	10	11	9	13	13	17	22	35	34	32	36
39	35	27	22	18	17	14	21	21	29	24	23	19	18	14	11	20	9	7	10	16	21	24	24	24
27	21	18	12	11	11	11	8	12	15	28	27	29	26	21	18	12	14	13	10	10	14	17	27	30
35	39	25	20	19	16	11	12	16	17	26	25	25	27	33	42	36	20	17	13	9	14	14	19	28
27	28	23	16	16	12	12	9	9	12	12	22	23	24	22	23	24	24	21	16	11	9	9	12	15

	26	27	28	36	36	37	31	27	29	22	25	27	26	25	28	23	24	17	11	11	10	7	6	7	10
	16	17	21	22	20	15	14	12	12	11	12	14	21	38	42	40	42	41	32	25	20	20	14	13	13
	11	13	16	23	24	27	28	23	18	21	18	15	13	16	21	18	24	24	21	16	13	11	7	8	6
	5	14	19	20	24	23	25	35	26	23	23	25	19	18	22	31	35	43	34	38	31	54	13	14	10
	6	6	10	11	13	16	14	21	19	15	14	11	7	9	8	10	21	37	43	42	58	46	50	40	37
	24	17	14	15	27	24	29	31	29	19	14	14	16	14	13	16	38	57	75	50	42	30	24	15	13
	9	8	6	6	9	13	13	12	14	12	12	16	13	10	10	14	20	37	51	65	71	63	49	39	31
	22	15	12	9	7	11	12	14	15	16	12	10	12	10	10	10	8	11	17	28	33	38	49	45	31
	26	21	12	8	5	8	11	19	18	19	21	22	18	23	18	16	11	13	19	32	43	51	49	39	31
	15	12	10	9	5	5	6	8	11	15	15	17	26	29	33	33	19	16	15	23	41	58	58	37	38
	28	17	12	12	10	7	7	7	13	13	14	19	18	16	11	9	9	8	8	14	22	40	38	35	37
	36	30	24	20	16	12	11	9	15	24	18	22	22	27	23	20	17	18	17	14	26	40	64	41	34
	28	23	15	11	8	4	4	2	4	9	12	16	18	22	17	15	21	21	17	17	12	17	27	37	26
	24	24	24	16	10	14	9	7	6	6	9	11	15	21	19	15	11	9	9	7	7	6	7	12	20
	32	36	42	43	32	22	20	12	8	7	7	8	15	17	17	20	14	14	11	13	11	10	8	13	22
1st Group	282	271	229	224	211	209	215	222	214	234	245	252	238	232	232	236	254	234	250	274	276	299	294	283	292
2nd "	308	280	265	261	246	238	234	239	237	232	226	247	259	295	292	290	314	366	380	415	440	491	463	395	359
TOTALS	590	551	494	485	457	447	449	461	451	466	471	499	497	527	524	526	568	600	630	689	716	790	757	678	651