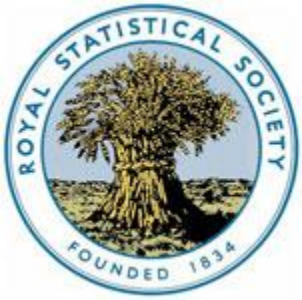

The Interpretation of Periodicity in Disease Prevalence
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The Interpretation of Periodicity in Disease Prevalence.

By H. E. Soper, M.A., of the Statistical Department of the National Institute for Medical Research.

[Read before the Royal Statistical Society, December 18, 1928, the President, Mr. A. W. Flux, in the Chair.]

Introductory.

Perhaps no events of human experience interest us so continuously, from generation to generation, as those which are, or seem to be, periodic. Whether it is the return of a comet, sunspots, wet weather or business "cycles," the interest of the man in the street and the assiduity of the mathematician—amateur or professional—is always stimulated. Since periodic, or at least oscillatory, secular trends are very common indeed in the experience of those who deal with the records of sickness and mortality—in fact, in the ordinary use of language an epidemic which never varied in its demands for victims would be something of a contradiction in terms—medical literature is full of discussions of waves, cycles and periods, even if the definition of their vague words has sometimes been to seek. Perhaps no epidemic disease has had so much attention of this kind paid to it as measles. Nearly fifty years ago, August Hirsch laid down the law upon the matter very firmly. He began by remarking coldly that, "as in the case of smallpox, many observers think they have discovered a *periodicity* in the recurrence of these local epidemics (of measles)." He then catalogued the people who, as he said, thought they had discovered periodicities, those who plumped for two to three years, those who found three to four years, and so on. He then catalogued the places where the recurrences had been, as it appeared, quite irregular, and finally pronounced judgment as follows:—"The recurrence of the epidemics of measles at one particular place is connected neither with an unknown something (the mystical number of the Pythagoreans), nor with 'general constitutional vicissitudes,' as Köstlin thinks; but it depends solely on two factors, the time of importation of the morbid poison, and the number of persons susceptible of it. The same law, accordingly, applies here as in smallpox" * This, even for the time at which it was written, was perhaps a little too magisterial, particularly as there might be some doubt whether the "law" of

* *Handbook of Geographical and Historical Pathology*, by A. Hirsch. Vol. I. (1883), p. 161.

smallpox epidemics *were* so simple. But that the accumulation of susceptibles—since more than 90 per cent. of all children born in Western Europe and surviving infancy pass through an attack of measles—is an important factor of the oscillations or periods of epidemics has been adopted by the great majority of epidemiologists. Indeed, the probability of that hypothesis has always been, implicitly or explicitly, the greatest obstacle to the acceptance of the interpretation placed by the late Dr. John Brownlee upon the striking results which the method of periodogram analysis yielded in his hands. Very few people would entertain any explanation, however ingenious, which had no place for the variations in numbers of susceptible children imposed by the " laws " of natality.

In the course of an examination of possible methods of forecasting the incidence of the common zymotics which I undertook at the suggestion of Professor Greenwood, I was led to re-examine this problem of measles and, with the view of obtaining numerical results, was led to adopt the simplest mathematical postulate that would describe in a first measure the generally accepted mechanism of epidemic measles, if the accumulation of susceptibles were really the prime factor : to compare the deduced results with the observed facts and then to modify the primary hypothesis. In this research I was merely following up the trail blazed by Sir William Hamer more than twenty years ago, only in detail departing from his methods, and I am not without hope that the endeavour now to be described may prompt others to push parallel lines of attack and incidentally bring about helpful discussion.

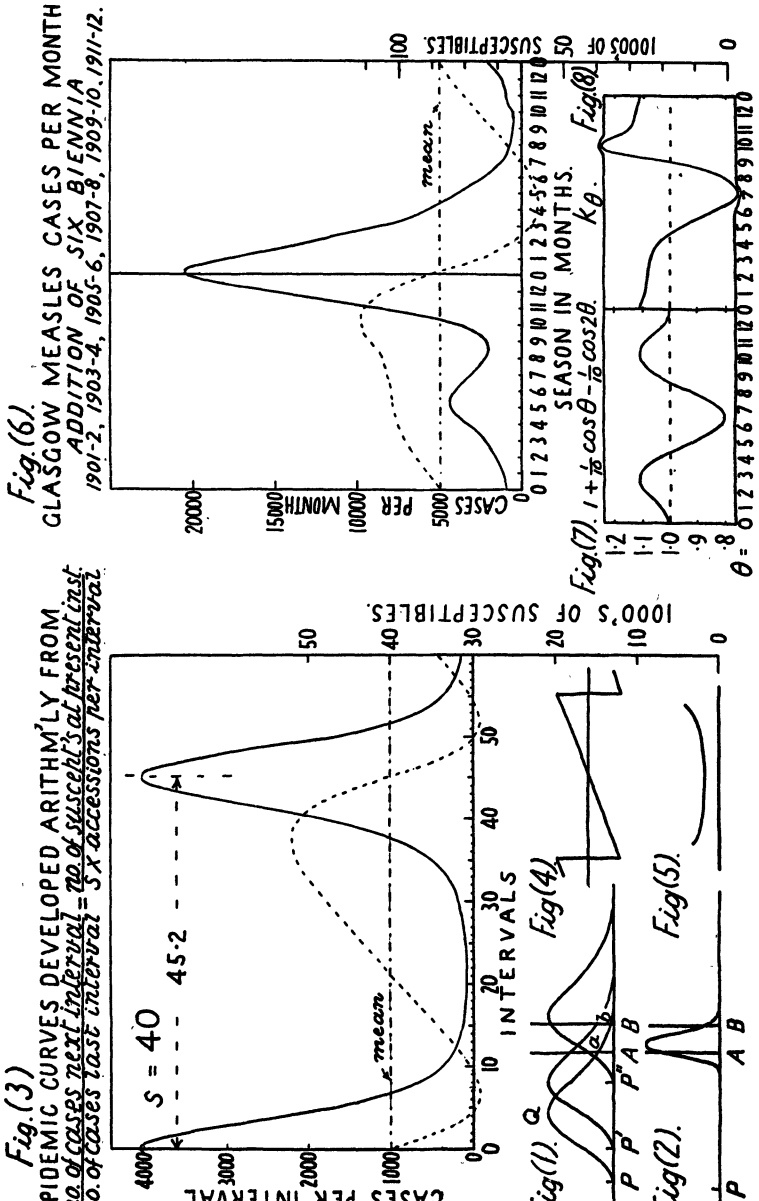
§ 1. *Infection Interval. Mass Action. Periods.*

The mathematical picture intended as a first approximation to a continuous measles epidemic is formed thus.

Conceive a community into which is drafted a perpetual flow *adt* of susceptibles possessing three characteristics, viz. (1) an equal susceptibility to a disease prevalent in the community, (2) an equal capacity to transmit the disease according to a law, when infected, and (3) the property of passing out of observation when the transmitting period is over.

Then the course of the epidemic will depend upon the law of infection assumed.

We may suppose, for example, that the disease is acquired as the result of an over-accumulation of doses of infection above what can be dealt with by the resisting powers of the body, or, on the other hand, that it is acquired instantaneously. We may suppose, again, that after acquisition the disease has powers of infecting



others according to some law of intensity with lapse of time, or we may suppose, in the opposite extreme, that there is a certain incubation period at the definite end of which all infecting power is concentrated.

If the power of transmitting infection is some function of the lapse of time from a definite infection instant, then the matter would have to be treated in this wise. Let the ordinates of the curve, *PQab*, Fig. 1, whose area is unity, be proportional to the power of infecting at instants after the instant *P* when infection was taken. Then if *AB* is the interval for which we desire to estimate the number of new "cases," the previous "case" at *P* would for the reckoning count a certain fraction of an entire case, namely, the area *ABba*. Other cases, at *P'P''* . . ., would, as the curve is moved, count differently, and thus it is seen how the infective material governing the number of cases during *AB* is to be reckoned as a certain integral of the prior cases.

If, as is probably true for measles, the power of infecting others is concentrated within narrow limits about the end of an incubation period, then the graph will show as Fig. 2, and we are approaching a condition in which the number of cases between *A* and *B* will depend on the number of cases in an equal interval removed from *AB* by the incubation period.

It is probable that, although the picture of a precise interval and an instantaneous power of reinfecting at the end cannot be argued to portray any known disease, yet the interval from "taking" to "mean giving" is so much of the essence of the course of an epidemic like measles that many of its features can be reproduced by making the "instant" hypothesis, that would not be greatly modified by supposing infectings to be grouped either side of the mean "instant" or "point of time" terminating the "interval."

The instant or point infection law being accepted, it is next assumed that a process analogous to "mass action" governs the operations of transmission and that, other things equal, the number of cases infected by one case is proportional to the number of susceptibles in the community at the instant, and that, if this is x, whilst m is the "steady state" number of susceptibles, when "one infects one," then $\frac{x}{m}$ cases will arise from one case at the end of the interval.

Since the synthetic epidemics to be made do not depend on absolute sizes of communities, we relate m and a by the quotient s defined by

$$m = sa,$$

and think of a community as characterized by a time element s,

the time the accessions a must accumulate to give m, the steady state charge of susceptibles. The space of time s is a measure of the "seclusion" of the community, a large s arguing few interminglings of the sort that conduce to infection, and it will be shown that if the incubation interval is τ and the repletion time is s, then the period of small epidemics is, under the laws taken, $2\pi \times$ the geometric mean of s and τ.

If, then, zdt are the cases and a suffix is employed with the meaning of advancing the time, and the incubation period is taken as unit of time measurement, we have, in the simple case,

$$z = \frac{x}{m} \times z_{-1}$$

and, since the change in x (number of susceptibles) is usually small in the unit interval (about a fortnight for measles), we write this,

$$\frac{z_{\frac{1}{2}}}{z_{-\frac{1}{2}}} = \frac{x}{m}, \text{ or } \frac{z_{\frac{1}{2}}}{z_{-\frac{1}{2}}} = \frac{x}{sa} \quad . \quad . \quad . \quad . \quad . \quad (1)$$

and interpret $z_{\frac{1}{2}}$ as the number of cases in the unit interval succeeding the present instant, and $z_{-\frac{1}{2}}$ as the number of cases in the unit interval preceding the present instant, and read it,

$$\frac{\text{no. of cases next interval}}{\text{no. of cases last interval}} = \frac{\text{no. of susceptibles at present instant}}{s \times \text{accessions per interval}}.$$

The epidemic curves, as Fig. 3, *e.g.*, were drawn from machine calculations made step by step by this formula, supposing 1000 susceptibles added each interval, or step, and taking $s = 20$, 30, 40, 50, so that the steady state numbers of susceptibles are 20,000, 30,000, 40,000 and 50,000. A start was made at a peak, with $z_{\frac{1}{2}}$ equal to $z_{-\frac{1}{2}}$, and consequently $x = m$. The successive values of x are obtained by adding 1,000 susceptibles each time and subtracting the number of cases in the last or preceding interval.

The result is a series of epidemic curves showing all the features found by Sir William Hamer for his composite London measles curve,* among them the asymmetry. I do not find any damping,† and the curves appear to repeat themselves precisely.

A rather serious epidemic starting-point was taken, namely, when the cases were four times the accessions (that is, four times the number of cases characterizing a steady state, without oscilla-

* Roy. Coll. of Physicians, Milroy Lecture, 1906. Hamer analyses his observational curve, and his theory and method are followed in this investigation.

† Damping or lowering of successive peaks is a feature to be expected when infecting power is supposed to last for a finite time, but on a point infection hypothesis there can be no damping. See Appendix III.

tions), and under these conditions, with epidemics repeating at each period, of a fourfold height, the periodic times were found to be,

s =	20	30	40	50	intervals,
period =	31·9	39·1	45·2	50·3	intervals.

From the analogy of pendulum swings it is to be expected that the more serious epidemics will swing slower than the lighter ones, and it is possible to obtain the periods of infinitesimal epidemics, that is, small disturbances from a uniform equality of cases and accessions, under conditions approximating to those experienced, to test this point.

Periods. If the incubation interval is τ, the equation of the epidemic curve of the kind presupposed is,

$$\frac{z_{\frac{1}{2}\tau}}{z_{-\frac{1}{2}\tau}} = \frac{x}{m} \text{ and, } \because x = m + \int_0^t (a - z)dt, \therefore \frac{dx}{dt} = a - z \quad . \quad (2)$$

where z = cases per unit time,
x = number of susceptibles,
a = accessions of susceptibles per unit time,
m = steady state, or level, number of susceptibles, when one infects one,

and the time t is taken from an instant when susceptibles were level.

Let $z = ae^u$, so that u is an index measure of cases, . (3)

$$\therefore e^{u_{\frac{1}{2}\tau} - u_{-\frac{1}{2}\tau}} = \frac{x}{m}, \text{ or } e^{\delta_\tau u} = \frac{x}{m}, \text{ in the usual notation} \quad . \quad (4)$$

If the changes are small in the interval and $(\delta_\tau u)^2$ and $\delta^2_\tau u$ can be neglected beside $\delta_\tau u$, then the equation reduces to

$$1 + \delta_\tau u = \frac{x}{m} \text{ and this to } 1 + \tau \frac{du}{dt} = \frac{x}{m};$$

$\therefore$, differentiating,

$$\tau \frac{d^2u}{dt^2} = \frac{1}{m}\frac{dx}{dt} = \frac{a - z}{m} \text{ by (2)} = \frac{a(1 - e^u)}{m} \text{ by (3).}$$

Hence, since we have put s for $\frac{m}{a}$, the equation of the epidemic curve under the conditions stated is,

$$\frac{d^2u}{dt^2} = \frac{1 - e^u}{s\tau} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

If the oscillations of z from its level value a are small, then u is small and the equation becomes

$$\frac{d^2u}{dt^2} + \frac{u}{s\tau} = 0 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

Thus small epidemics under the conditions assumed are cyclic and

$$period = 2\pi\sqrt{s\tau} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

If $\sqrt{s\tau}$ is taken as unit of time, equation (5) assumes its simplest form,

$$\frac{d^2u}{dt^2} = 1 - e^u \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

and the period of small oscillations is 2π.

If, as already done, we choose the incubation interval τ as our unit of time, the equation is,

$$\frac{d^2u}{dt^2} = \frac{1}{s}(1 - e^u) . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

and small oscillations have period measured as $2\pi\sqrt{s}$.

For small epidemic oscillations, then, we should have

$s =$	20	30	40	50	intervals,
Period $= 2\pi\sqrt{s} =$	28·1	34·4	39·8	44·4	intervals.

Hence we find that fourfold epidemics increase the period,

$$+13{\cdot}5,\ +13{\cdot}7,\ +13{\cdot}6,\ +13{\cdot}3 \text{ per cent.},$$

and, pending further investigation, may, perhaps, expect that each addition of inflow number a to height of peak will add $4\frac{1}{2}$ per cent. to the period. The result may be stated :

> In an epidemic in which attack follows attack at incubation interval τ and cases next interval are to cases last interval as susceptibles at mid instant are to steady state susceptibles, if adt are the steady accessions and m is the steady state number of susceptibles, when one infects one, an initial disturbance from the steady state is followed by oscillations, which are perpetuated. The period of a small oscillation is,
>
> $$2\pi\sqrt{s\tau},\ (s = m/a), \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$
>
> that is, 2π times the geometric mean of the incubation and repletion intervals, and period lengthens with amplitude of peaks and is about $13\frac{1}{2}$ per cent. longer when the peak cases outnumber the accessions fourfold.

A few features of the curves obtained on the above simple assumptions may be noted, some already pointed out and explained by Hamer for this class of epidemic eventuation.

The cases curve follows behind the susceptibles curve, and cases are peak and bottom when susceptibles are level coming down and level going up. For small oscillations the lag is quarter period. For small and large oscillations the susceptibles are peak when the

cases cross the accessions level going up and are bottom when the cases cross the same level coming down.

The susceptibles rise slow and fall quick unless, of course, the oscillations are minute. When the peaks are immense, that is, the epidemic is explosive, there follows a long intermission, when cases remain few; and the susceptibles rise uniformly, at the rate of the accessions, during this stage. Later on, during the next explosive peak they fall extremely rapidly. The curve of susceptibles in the limit is saw-shaped as in Fig. 4. Whilst the susceptibles are rising at a uniform rate the curve of cases is $\frac{z_{\frac{1}{2}}}{z_{-\frac{1}{2}}} = \frac{m + at}{m}$, and is therefore shaped like the inverse of a *poisson* and as shown in Fig. 5.

§ 2. *The Point Infection Curve modified by Seasonal Change in Infectivity. Analysis of a Glasgow Composite Measles Curve. Synthetic Curves of Epidemic Measles.*

The Glasgow curve of measles cases 1888–1927 examined for the purposes of this inquiry did not show anywhere the simple form of a single repeated wave, and Glasgow appears to be rather different from London (Hamer's composite curve) in the course taken by its measles epidemics. The nearest approach to a repetition of a curve was found in the six consecutive biennia '01–'12, and these biennia were, in the first analysis, compounded, and the result is shown in Fig. 6. This curve was integrated for area below the mean to get the curve of susceptibles, which is also drawn in and scaled from an origin to be explained.

It appears that in Glasgow the simple law that gives a single undulation at some period of recurrence cannot be postulated. The curves of cases at this epoch show, sensibly, the two-yearly repetition assumed in superposing, but show a large winter peak and small summer forepeak. It would be easy to suppose a two-year cycle in infecting agencies to account for the two-yearly effects, but this would be a little unhappy. Can we get the biennial phenomenon by applying the point infection law and merely presupposing an *annual*, that is, *seasonal*, change in perturbing influences, such as might be brought about by school break-up and reassembling, or other annual recurrences?

This was attempted as follows. Hamer, assuming a like law of infectivity, but with no seasonal coefficient, and assuming a fortnight the incubation interval, deduces from his composite curve a level number of susceptibles equivalent to 70 weeks' accumulation of inflow. The present endeavour, to arrive at a suitable season factor, was made antecedently to that connecting number of sus-

ceptibles with period, and it was assumed that Hamer's finding for London, in this matter, would sufficiently serve the purpose. Since Glasgow's inflow, as given by mean cases, was 208 per week during these six biennia, or 1,250 for the composite curve, the level number of susceptibles, when cases are peak (at the commencement of the year) was taken as $1{,}250 \times 70 = 87{,}500$, and the curve of susceptibles scaled from an origin to give this figure.

The data give cases per month, and if i is the incubation interval in months and k_θ the factor representing influence of season θ, the epidemic curve will take the form

$$\left(\frac{z_{\frac{1}{2}}}{z_{-\frac{1}{2}}}\right)^i = k_\theta \frac{x}{m} \quad . \quad . \quad . \quad . \quad . \quad (11)$$

or $$i\delta \log z = \log k_\theta + \log x - \log m.$$

Plotting $\delta \log z$ against $\log x$ and joining the points having the same season and having regard to the errors that "cases" are subject to in the deep trough in the second year of the pair, the value of $i = \frac{1}{2}$ appeared to be justified, and the errors from the line $i\delta \log z = \log x - \log m$ appeared to call for a factor of the form,

$$k_\theta = 1 + \tfrac{1}{10} \cos \theta - \tfrac{1}{10} \cos 2\theta \quad . \quad . \quad . \quad . \quad (12)$$

The season factor k_θ, plotted in Fig. 7, argues a great reduction in infection carrying power in the summer and a smaller reduction in the winter, the latter being 10 per cent. below and the former 28 per cent. below the values at spring and autumn maxima. It thus roughly represents changes of concentration, such as are brought about by school and holidays, that are generally held to be answerable in some measure for the changes in infectivity.

It will be of interest to make an experiment to see how far this rounded form of season factor pulling with the susceptibles factor will modify the shape of the curve and the periods between peaks.

In order, at first, to avoid the possible effects of resonance, the factor was applied to a community, for which $s = 40$, and the natural period of peaks therefore in the neighbourhood of 45 fortnights, or 90 weeks, and not too near two years or 104 weeks for which resonance effects might be expected. The curve traced is therefore (fortnight units),

$$\frac{z_{\frac{1}{2}}}{z_{-\frac{1}{2}}} = (1 + \tfrac{1}{10} \cos \theta - \tfrac{1}{10} \cos 2\theta) \frac{x}{40a} \quad . \quad . \quad (13)$$

and a was taken = 1,000 susceptibles added per fortnight, so that the number of susceptibles when one infects one at season = 0 is 40,000. A start was made at the beginning of the year with a twofold strength of epidemic peak in the last fortnight of the old year

and the first fortnight of the new year, and therefore an accumulation of the level number of 40,000 susceptibles to begin the year, and the numerical computations of numbers of susceptibles and numbers of cases were machine calculated alternately to unfold the course of the epidemic for ten years.*

The graph is drawn out in Fig. 9, and the following points may be noted :

(i) The peaks still show but are often double.
(ii) The period of 45 fortnights, expected when no seasonal change in infectivity is introduced, is still discernible. The arrows drawn point to peaks or mean peaks.
(iii) No resonance effect is discernible up to the point taken, and peaks (and troughs therefore) are of about the same content at the end as at the beginning of the ten-year period.
(iv) The curve does not repeat, but is likely to do so, or very nearly repeat, in time.
(v) The curve very nearly reached "steady-state" conditions at the end of the fourth year, with cases nearly a thousand and susceptibles nearly 40,000, yet the season stimulus sent the cases up two-and-a-half-fold in little over a year.

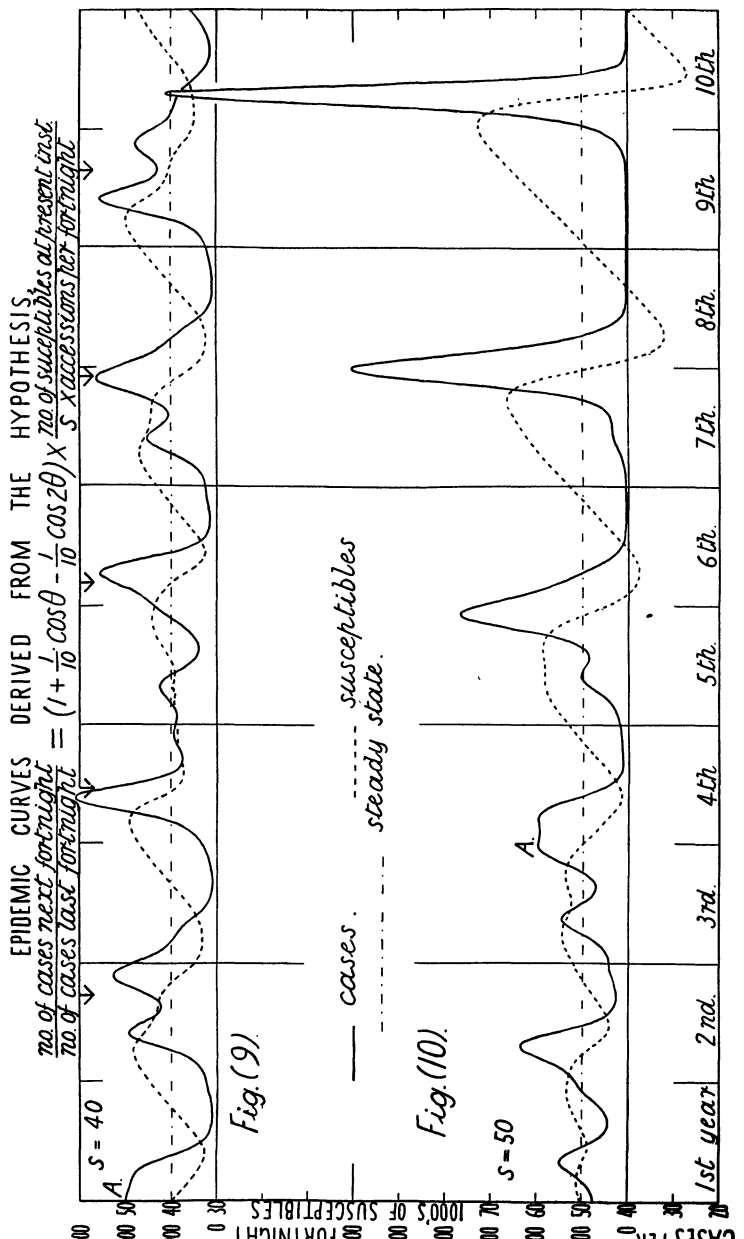
It appears to follow, then, that if a period can be seen with some security in any series of epidemic curves of the character of measles, this, in spite of seasonal disturbance, should yield an approximation to s and the level number of susceptibles.

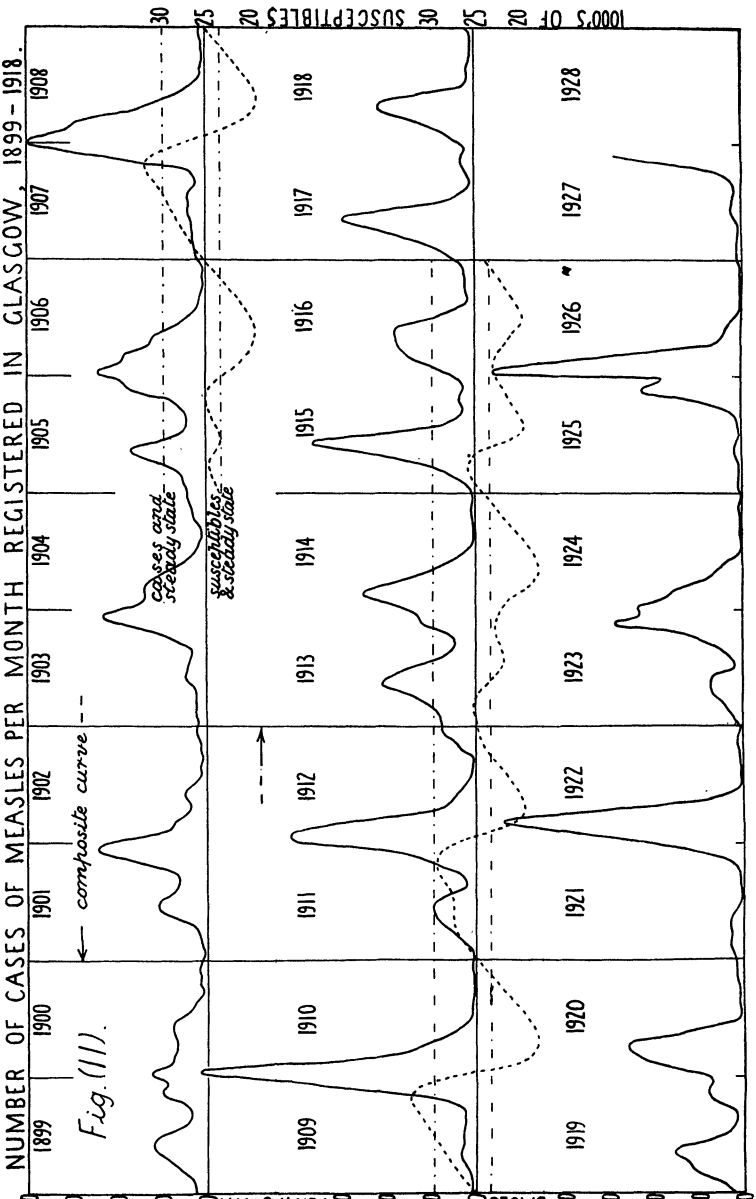
If, for instance, an 87-week period is discerned, as assuredly found by Brownlee for a part of London, an easy interpolation shows that the same recurrence period will be given as the result of supposing a point infection epidemic development, and a community so constructed in its inter-communications that one will infect one when the charge of susceptibles is equal to about 74 weeks' inflow of susceptibles.

The experiment seems to justify a new assessment of the number of susceptibles for Glasgow, previously conjectured at 70 weeks' accumulation, and this is next done, using the information thought to be afforded by considerations of periods. The rough fitted season factor is not changed and an attempt is made to reproduce the Glasgow type of curves, using this factor found from the compound curve and applying it to a bettered valuation of s, found from periods.

Now the period appears to be short of two years, but so nearly two years that, for the experiment, we take $s = 50$, which we should

* The commencement of this computation is shown in the Appendix.





expect to produce fourfold peaks succeeding one another at intermissions of 50·3 incubation intervals, taken as fortnights, or 100·6 weeks, which may very well represent the facts as to period more nearly than 104 weeks. For this epidemic series, then, are step by step calculated (fortnight units),

$$\frac{z_{\frac{1}{2}}}{z_{-\frac{1}{2}}} = (1 + \tfrac{1}{10}\cos 0 - \tfrac{1}{10}\cos 2\theta)\frac{x}{50a}. \quad . \quad . \quad (14)$$

and, as before, a start is made with a twofold peak, so that the calculations commence, as before, with

$$0 = 0,\ z_{-\frac{1}{2}} = 2{,}000,\ z_{\frac{1}{2}} = 2{,}000,$$

but in this instance $x = 50{,}000$ in place of 40,000.

The development is shown in the graph Fig. 10, *A* being the start, and the course of the epidemic was traced for nine years * forward and was retraced for three years backward, the numerical calculations for tracing the past being merely the reverse of those for unfolding the future. From this curve the following observations are suggested :—

(i) Starting the fourth year at a twofold peak, the fifth and sixth years very nearly reproduce the composite picture of the Glasgow epidemics '01–'12, and in particular the years '01–'02, '11–'12 (see Fig. 11). The seventh and eighth years reproduce Glasgow's great peak of '09–'10 and the diminishing forepeak. Thereafter Glasgow actually falls a little, but the fabricated curve continues to rise, and at the twelfth and thirteenth years has soared 13-fold, due to "resonance."

(ii) The first period from *A* is 101 weeks. The next is 106 weeks, the next 121 weeks, and the last is 133 weeks, so that these are much as to be expected between peaks of heights 2-, $3\frac{3}{4}$-, 6-, 10-, and 13-fold the steady state numbers of cases.† The precise periods are a little risky.

(iii) Continuing back from *A* the epidemic becomes more level. The forepeak has beginnings that might with the main peak be held to form an *annual* epidemic progression, later on to move up to and subside down into the main peak. The annual early summer peak is evidenced many times in the Glasgow curves prior to and subsequent to the forepeak phase '01–'12 used for compounding.

(iv) There is not sufficient evidence to prove that the theoretical

* The graph here given omits the last two years.

† For small oscillations we expect period $2\pi\sqrt{50} = 44\frac{1}{2}$ fortn's = 89 weeks. For 2-fold epidemics we expect period (add $4\frac{1}{2}\% = 4$) = 93 weeks.

For 2-, 3-, 4-, 5-, 6-, 7-, 8-, 9-, 10-, 11-, 12-, 13-fold epidemics we expect

93, 97, 101, 105, 109, 113, 117, 121, 125, 129, 133, 137-week periods (15)

epidemics will go on soaring, but probably they will. When the cases are at bottom level the numbers have gone down to half a child a fortnight, and although decimalizing enables the theoretical curve to go on, practically any law has ceased to operate. This must happen in some measure also after every large epidemic. The cases reach a low level, when propagation depends upon a few occurrences, and on the events of these will, when the susceptibles have accumulated, depend the future course and whether the almost geometric progression will be a few intervals in advance or a few intervals behind their time.

In this section, then, from a composite curve of Glasgow measles a roughly approximating season factor of infectivity has been deduced formed of two Fourier terms, and this forced oscillation has been supposed to work with the natural oscillations to discover what kind of changes are made in the epidemic course as developed arithmetically from the formula.

In the next section, instead of compounding epidemic curves, which is clearly a risky proceeding where unrepetitive detail is to seek, I have taken twelve individual consecutive years, choosing the years '05–'16 in place of '01–'12, as giving steadier biennial "case" figures (on which the inflow of susceptibles is based) at the expense of unrepetitive shape of curve, which is now immaterial, and tried from these limited data to get answers to the questions, whether a month, fortnight, or week is better taken as the infection interval and, when a fortnight is shown to be a little the better of the three (when no season factor is assumed), whether the steady state number of susceptibles can again be taken as approximately 50 fortnights' inflow, as suggested by the period investigation, and, when this appears to be justified, whether a better season factor than the cosine formula can be found; and lastly, when the factor is chosen, what are its month by month errors and what statistical value can be put upon the formula used for prediction. The result is not very telling and seems to argue conditions in operation not taken account of in the simple theory.

§ 3. *Analysis of a Sequence of Years. Prediction.*

The figures * of the Glasgow monthly measles cases 1888–1927 are plotted on the chart Fig. 11,† and the curves seem to warrant

* The figures for '88–'16 were obtained from fortnightly figures supplied some time back to the late Dr. Brownlee. The figures for '17– were obtained by readings of the chart given on p. 100, Glasgow M.O.H. Report, 1926, and by interpolation of the calendar month figures in the subsequent Reports.

† Only years 1899–1927 are reproduced. 1918 in heading should read 1927.

the division of the whole period of 40 years into an initial five " even-odd " biennia showing peaks (where existing) near the middle of the space, an interjected peak year (1898) and a subsequent fifteen " odd-even " biennia (the last one, '27–'28, incompleted) having similar characteristics of inwardly disposed peakiness.

In order to estimate in some measure the varying inflow of susceptible persons, taken here to mean those who are going to be registered as contracting the disease, the actual numbers of measles cases annually and in the above biennial groupings are set out as follows :—

Cases of Measles registered in Glasgow.

1888	3,127	10,019	1901	10,719	16,289	1915	13,593	24,708
89	6,892		02	5,570		16	11,115	
90	4,837	8,225	03	8,768	17,175	17	12,670	21,190
91	3,388		04	8,407		18	8,520	
92	6,864	14,699	05	12,445	22,642	19	9,210	20,700
93	7,835		06	10,197		20	11,490	
94	4,890	10,470	07	9,821	24,443	21	4,030	21,810
95	5,580		08	14,622		22	17,780	
96	9,022	17,152	09	10,088	24,600	23	11,330	18,520
97	8,130		10	14,512		24	7,190	
98	9,623		11	9,503	24,310	25	6,830	22,580
			12	14,807		26	15,750	
99	9,186	15,922	13	14,745	25,078	27	8,980	
1900	6,736		14	10,333		28	—	

Since measles is a disease of early childhood, the great changes in the figures of cases, which appear to double in 40 years, preclude the supposition of an even inflow of susceptibles throughout the period. In place of attempting to estimate the changes of inflow from the changes in cases, a part period was taken, namely, that from '05 to '16, comprising six biennia in which the registered cases were fairly equal and at the average rate of 12,148 per annum. Moreover, an examination of the ends of the '04 and '16 curves give assurance that the initial and final conditions of the period are much alike as regards the numbers of susceptibles in the community; for the cases were minimum about $4\frac{1}{2}$ months prior to each end, and the excess of susceptibles will be the subsequent accumulation, which must be about the same in both instances, since the cases are about the same.

We take then for detail analysis the twelve years' experience '05–'16 and take as the accessions of susceptible subjects to measles, male and female, the steady figure of 234 per week, or 468 per fortnight, or 936 per four-week month making a figure of 12,168 per annum, a trifle in excess of the average of registered cases of no consequence.

If it is desired to compare this figure with the births in Glasgow, these have been comparatively steady from '98 to '27, averaging

25,500 per annum, so that less than one-half of the births will come into our counts although the period was a heavy one in measles. Since it is a wide experience that some 90 per cent. of children reaching the age of 10 years have already had measles, there is clearly a serious discrepancy between "cases" and "registered cases," and it is not possible to say to what extent the existence of a large number of unregistered cases will invalidate any analysis based upon registered cases.

The number of susceptibles, then, according to our supposition, will increase by 936, the inflow, in any month and diminish by the number of cases. It will be known throughout when the commencing number is known. Since one purpose of the investigation is to find this number, we will only estimate it so that the integrals may be tabulated with least requirement of zero adjustment.

The curves seem to call a period of a little under two years, and, if a fortnight is the infection interval, this period would, by what has gone before, be given by supposing the steady state number of susceptibles equal to 50 fortnights' accessions. This number is 23,400 and, making allowances for the stage of the epidemic process reached, the initial number of susceptibles was reckoned at 23,500. Calling x' the numbers based on this commencing number, the adjusted numbers of susceptibles will be,

$$x = x' + A$$

where x' is observed and A is to be found.

The problem proposed is now to be stated thus. If, as before written, $z_{\frac{1}{2}}$ is the number of cases next month and $z_{-\frac{1}{2}}$ is the number of cases last month, and x is the present number of susceptibles, and if m is the steady state number of susceptibles and k_θ a seasonal disturbing factor, and if i is the transmission interval in months from infected to infecting, to find A, m, k_θ and i so that the data for the 12 years taken are best fitted by the formula,

$$\left(\frac{z_{\frac{1}{2}}}{z_{-\frac{1}{2}}}\right)^i = k_\theta \frac{x' + A}{m} \quad . \quad . \quad . \quad . \quad . \quad (16)$$

As a practicable way of approach i was given the values 1, $\frac{1}{2}$ and $\frac{1}{4}$ and the left side calculated by slide rule and Barlow's tables for each month succession and the best fit linear relation with x' found, k_θ being put unity, that is, season ignored. When i was selected k_θ was found to best correct the errors of each season. The procedure is plainly makeshift.*

* If i is found $= \frac{1}{2}$ and we call $\left(\frac{z_{\frac{1}{2}}}{z_{-\frac{1}{2}}}\right)^{\frac{1}{2}} = v$, the "infectivity," then to form the best relation $v = h(x' + A)$, where h is a constant for each season, θ, we should rightly make sum $\{v - h(x' + A)\}^2$ min., or sum$_\theta$ sum $\{v - h_\theta(x' + A)\}^2$

The results and their interpretations are as follows, and one of the three correlation tables, that for Case (ii), is shown.

(i) $i = 1$.

That is, if we take a month to be the step in the infection process,

the steady-state number of susceptibles is . . . . 10,277 = 936 × 11
and represents 11 months' accumulation of inflow . . . . (0·85 yr.)
and we expect sm. epidemics in pds. of $2\pi\sqrt{11}$ or 21 mths. (1·60 yrs.)
and large 4-fold epidemics to have periods $13\frac{1}{2}\%$ greater (1·82 yrs.).

(ii) $i = \frac{1}{2}$.

Or, if we take a fortnight as the infection interval,

the steady-state number of susceptibles is . . . . 22,700 = 468 × $48\frac{1}{2}$
and represents $48\frac{1}{2}$ fortnights' accumulation of inflow . . . (1·87 yrs.)
and we expect sm. epidemics in pds. of $2\pi\sqrt{48\frac{1}{2}}$ or $43\frac{3}{4}$ fortnts. (1·68 yrs.)
and large 4-fold epidemics to have periods $13\frac{1}{2}\%$ greater (1·91 yrs.).

Correlation of $(z_{\frac{1}{2}}/z_{-\frac{1}{2}})^{\frac{1}{2}}$ *with* x'.

Values of x' in 1000's.

$(z_{\frac{1}{2}}/z_{-\frac{1}{2}})^{\frac{1}{2}}$	17-	18-	19-	20-	21-	22-	23-	24-	25-	26-	27-	28-	29-	30-	31-	32-
·2							1									
·1																
2																
·9																
·8								1							1	
·7									1							1
·6									1				1			1
·5										1					1	
·4						1	1		1							
·3					1	1		2	3		1		1	1		
·2						2	2	4		1	3	1	1	2		
·1				2	2	2	2	5	1		1	1				
1					2	7	4	3	3	1	4	1	1	1	1	
·9			3	3		5	1	2			1	1	2	1		
·8	1	2	4	4	5		1	1								
·7	2	1	7	2	7		3	1	1		1			1		
·6		3	2	1							1					
·5		1	1	2												

(iii) $i = \frac{1}{4}$.

If, lastly, we take a week to represent the interval, the finding is that

the steady-state number of susceptibles is . . . . 44,900 = 234 × 192
and represents 192 weeks' accumulation of inflow . . . . (3·69 yrs.)
and we expect sm. epidemics in pds. of $2\pi\sqrt{192}$ or 87 wks. (1·67 yrs.)
and large 4-fold epidemics to have periods $13\frac{1}{2}\%$ greater (1·90 yrs.).

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min. Hence, varying h_θ, for each θ: $(vx')_\theta + (v_\theta)A - h_\theta\{(x'^2)_\theta + 2(x'_\theta)A + (1)_\theta.1^2\} = 0$, where $(\ )_\theta$ sums for all observations, season θ; and, varying A,

$$\text{sum}_\theta\{(v_\theta)h_\theta - (x')_\theta h_\theta^2 - (1)_\theta h_\theta^2 A\} = 0$$

yielding, for 13 seasons, an equation of the 51st degree to find A.

The standard errors of the predictions,

$$\frac{\text{next month's cases}}{\text{last month's cases}} =, \text{ (i) } \frac{\text{susceps.}}{10{,}277}, \text{ (ii) } \left(\frac{\text{susceps.}}{22{,}700}\right)^2, \text{ (iii) } \left(\frac{\text{susceps.}}{44{,}900}\right)^4,$$

will be about (i) 0·58, (ii) 0·47, (iii) 0·49, and thus no very firm answer is given to the question put to the data, What is the interval from passage to passage of the infection? The errors, ignoring the influence of season, are least for (ii) a fortnight, but are not much greater for (iii) a week, whilst both findings will give susceptibles in number such as to give periodic surges a little less than two years in separation, such as is observed.

Although (iii) argues a susceptible population of 3·7 years' accumulation, or life, and this might be thought to accord better with the observed ages of cases, which were found to have a mean of $4\frac{1}{2}$ years in the great '25–'26 Glasgow epidemic, whilst (ii) offers a susceptible life of 1·9 years only, yet other considerations, such as, for instance, a varying susceptibility in the young unaffected population, would have to be brought into consideration to fill out the already dismembered picture, and since a fortnight is the usually accepted interval, this interval will be taken, as best supported by the somewhat uncertain evidence here presented.*

We take then (ii), $i = \frac{1}{2}$, as the best formula (disregarding seasons) to represent the progressive features of the Glasgow '05–'16 epidemics of measles. The regression line gives not only the denominator, 22,700, but also the unknown constant to be added to all the tabulated numbers of susceptibles. This constant A is given as 120. Thus the steady-state number of susceptibles and the initial number, as given by the statistical regression, are both very near what had been reckoned by periods and phases, and in the next investigation relating to the values of the season constant k_0, the previously reckoned constants were left unchanged.

The formula taken, then, is,

$$\left(\frac{z_{\frac{1}{2}}}{z_{-\frac{1}{2}}}\right)^{\frac{1}{2}} = k_0\frac{x}{23{,}400}, \text{ (23,400 = 50 } \times \text{ fortnight's inflow),}$$

with a commencing number of susceptibles equal to 23,500 and is calculated for each monthly sequence. It is clear that good agreement with a law cannot be expected when the cases number, say only 100 a month, and better values of k_0 will be evidenced when

* It is clear that, if the variations from steady conditions are small, one formula will be functionally derivable from another, and halving the interval will in effect be similar to doubling the susceptibles. If ξ is small, $\frac{z_{\frac{1}{2}}}{z_{-\frac{1}{2}}} = \frac{m+\xi}{m}$ is the same as $\left(\frac{z_{\frac{1}{2}}}{z_{-\frac{1}{2}}}\right)^{\frac{1}{2}} = \frac{2m+\xi}{2m}$.

the cases number over 1,000. The table below gives the calculated values, and against each is put a number, the number (1) indicating that the lesser of the monthly cases ratioed is between 44 and 100, (2) between 101 and 500, (3) between 501 and 1,000, (4) that both exceed 1,000. Season 0 is the commencement of the year and is cyclically the same as season 13.

The means are those of the values numbered (2), (3) and (4), *i.e.* neglecting (1), and the third mean is adjusted from 1·087 and the fourth from 1·052, the remainder being nearest figures.

The curve of seasonal coefficient of infectivity so given is shown in Fig. 8, but it must be admitted that the actual ratios diverge at times very much from this mean curve. The curve as it stands differs from the symmetrical sine curve previously fitted in having an enhanced autumn peak at $\theta = 10$, followed by a gradual descent instead of by a dip and rise. To put a statistical value upon the result, as a portrayal of what has actually happened in the twelve years that have been analysed for fitting the law taken, we may examine the values of $\left(\frac{z_{\frac{1}{2}}}{z_{-\frac{1}{2}}}\right)^{\frac{1}{2}}$, which measures to some approximation the numbers infected a fortnight hence by each present case, at the several dates, or the " manifest " infectivity. These figures, already calculated and shown in the correlation table, range round about 1, and, taking the 126 monthly experiences, namely, the $12 \times 13 = 156$ total less 30 marked (1), and rejected because one of the two months reported less than 100 cases, the mean divergence from 1 is 0·211. The mean error of a forecast of precise unity for the present infectivity is thus 21 per cent. If, on the other hand, we estimate as done and allow for the changing numbers of susceptibles and allow for the season factor, whose mean is 1·02, the figures for the errors in this, by the foregoing table, will have mean 0·107 or 10·5 per cent. It appears then that the application of the process may be expected to remove one-half of the error assumed in merely predicting the infectivity at its steady-state value of unity, that is, in predicting next fortnight's cases equal to last fortnight's cases.

In effect, then, the result is much the same as saying that infectivity has correlation $\sqrt{1 - (\frac{1}{2})^2} = 0{\cdot}87$ with susceptibles and season, as formulated.

The law of propagation of the disease of measles, as disclosed in the twelve years' data from Glasgow, is therefore not quite so simple that we can get good forecasts merely by premising a uniform inflow of susceptibles, who will all take the disease, and an infectivity depending on the accumulation of such susceptibles and on a season

Values of k_θ.

Season ...	0	1	2	3	4	5	6	7	8	9	10	11	12
Year, '05 ...	1·04 (2)	1·04 (2)	1·10 (3)	1·25 (3)	1·14 (4)	0·87 (4)	0·72 (3)	0·79 (2)	0·99 (2)	1·10 (2)	1·16 (3)	1·29 (3)	1·03 (4)
'06 ...	1·11 (4)	0·96 (4)	1·10 (4)	0·97 (4)	1·15 (4)	0·94 (3)	0·94 (2)	0·77 (2)	0·94 (2)	0·78 (1)	0·99 (1)	1·07 (1)	0·96 (1)
'07 ...	1·65 (1)	0·93 (2)	0·93 (2)	0·89 (2)	0·87 (2)	0·91 (2)	0·79 (2)	0·78 (2)	0·57 (2)	0·90 (2)	1·34 (2)	1·07 (3)	0·96 (4)
'08 ...	0·89 (4)	0·86 (4)	1·00 (4)	1·02 (4)	0·98 (4)	0·93 (3)	0·85 (2)	0·68 (2)	1·03 (2)	0·84 (1)	1·39 (1)	1·09 (1)	1·25 (1)
'09 ...	0·74 (1)	0·96 (1)	1·12 (1)	1·14 (2)	0·88 (2)	0·74 (2)	0·82 (2)	0·72 (2)	0·76 (2)	0·79 (2)	1·27 (2)	1·23 (3)	1·02 (4)
'10 ...	1·01 (4)	0·85 (4)	0·83 (4)	1·03 (4)	0·99 (3)	0·92 (2)	0·76 (2)	1·06 (1)	0·98 (1)	0·84 (1)	1·08 (1)	1·23 (1)	1·16 (1)
'11 ...	0·72 (1)	1·54 (1)	1·33 (2)	1·08 (2)	1·03 (3)	0·90 (3)	0·84 (3)	0·65 (3)	0·51 (2)	1·03 (2)	1·31 (2)	1·01 (3)	1·12 (4)
'12 ...	1·09 (4)	0·94 (4)	0·90 (4)	0·78 (4)	0·86 (3)	1·00 (2)	0·84 (2)	0·78 (2)	0·86 (1)	0·98 (1)	2·25 (1)	1·21 (2)	1·15 (3)
'13 ...	0·93 (3)	0·99 (3)	1·05 (3)	1·08 (4)	1·14 (4)	0·97 (4)	0·94 (4)	0·83 (3)	0·84 (3)	0·96 (2)	1·25 (3)	1·36 (3)	1·43 (4)
'14 ...	1·24 (4)	1·26 (4)	1·15 (4)	1·04 (4)	1·05 (4)	0·98 (3)	0·82 (2)	0·67 (1)	1·14 (1)	0·98 (1)	1·44 (1)	1·12 (1)	0·79 (1)
'15 ...	1·30 (1)	1·72 (2)	1·36 (2)	1·24 (3)	1·23 (4)	1·19 (4)	0·92 (4)	0·68 (3)	0·84 (2)	0·96 (2)	1·30 (2)	0·97 (2)	1·14 (2)
'16 ...	1·49 (2)	1·32 (3)	1·21 (4)	1·11 (4)	1·11 (4)	1·14 (4)	0·88 (3)	0·82 (2)	0·69 (2)	1·25 (2)	1·09 (2)	1·07 (2)	1·19 (2)
Means	1·11	1·09	1·08	1·07	1·04	0·96	0·84	0·75	0·80	1·00	1·25	1·15	1·13

factor. This may be said to give half the picture * in a selected period. Beyond the period taken the biennial cases are subject to great changes, in that a quarter instead of a half of the births may become registered cases, and a further difficulty will therefore be met, here, in prescribing what are to be laid down as the larger movements in "births" and level "populations" of supposed susceptible persons upon which the epidemic upheavals are raised. Indeed, the difficulty, perhaps, has been evaded only in the period chosen, and an even biennial inflow of registered cases cannot be held to justify the assumption of an even inflow of susceptible persons who will become registered cases.

In many other respects the model must be liable to wide differences from the actual phenomenon, and the observed discord between formula and event may be thought as due to many possible reasons above and beyond that already commented upon, the want of parity between actual and registered cases.

Most cogent of these is, perhaps, a false analogy between infection in disease and the mechanism understood under the name of chemical mass-action which is premised when the cases at any instant are put equal to the cases one infection interval back multiplied by the number of susceptibles and some constant. Apart from the great differences in the statistical numbers dealt with in the two fields, in a liquid the intimate uniformity of the mixture and the conditions of intermingling and collision are likely to be more law-abiding than are the similar traits in a community of persons. After all, the contacts are comparatively few and are subject to volition as well as to chance, and, in addition, a single community may be quite differently constituted in respect to its seclusion or minglings in one part and another. The school long recess and reopenings will be a common feature, and this change in concentration seems to be reflected in the great dip in the curve of the seasonal factor k in the seventh month and rise in the tenth month, of the thirteen months. But even if a general factor can be accepted to take care of the degrees of mingling in the several seasons, and whatever influences may be attributable to temperature and weather, and if, in each section of the community having intercourse, something approaching the mass action law of infection is followed, yet it is still questionable how far the different curves with their different phases and, perhaps, different periods will unite into a single curve

* Of course the prediction, next fortnight's cases/last fortnight's cases = 1 is a great advance upon the prediction of the crude statistical mean of cases. It is the errors in $\left(\frac{z_{\frac{1}{2}}}{z_{-\frac{1}{2}}}\right)^{\frac{1}{2}} = 1$ that have been halved in $\left(\frac{z_{\frac{1}{2}}}{z_{-\frac{1}{2}}}\right)^{\frac{1}{2}} = k\theta\frac{x}{m}$, *i.e.* in allowing for season factor and estimate of susceptibles.

having the same characteristics, and perhaps it is the imperfect mixture and the imperfect tuning of the parts that are responsible for the apparent discord in the whole.

In another respect the outline is drawn free-hand, for susceptibility cannot be thought of as a unitary character, but certainly varies with age and probably with constitution and with occasion. Under these conditions a " number of susceptibles " can only be a mathematical figment to represent the result of such a division of the community into naughts and ones as will nearest reproduce the effect observed under the law pronounced. Here, then, may lurk another source of error. It may, perhaps, not be true that the numbers counted as " having taken the disease " is the correct depletion from this fictitious number of " susceptibles " that governs the count of attacks.

The examination has been confined to a series of measles epidemics where the kind of process premised is already known to be operative, and it might be asked whether *any* disease of variable prevalence could not be analysed in the same way to show " exhaustion " and " replenishment " of susceptibles, should contagion and immunisation of susceptibles exist in fact or not. The process is a physical one and is very similar to that governing the alternations of two forms of energy seen in many periodic phenomena, as, for instance, in the swing of the pendulum, where, in fact, our equation would be $\frac{d^2\theta}{dt^2} = -\sin\theta$ in place of $\frac{d^2u}{dt^2} = 1 - e^u$. The argument for the alternation of states rests upon the fit of the facts to the physical law proposed, and chief of the facts must be periodicity. If in an epidemic curve periodicity can be discerned through such disturbing influences as forced seasonal impulses and the lawlessness of small numbers, then the pendulum action can be argued, and the phenomenon admits interpretation in rough analogy as the exchange of the potential energy of susceptibles for the kinetic energy of cases (in their departures from steady-state values). If the oscillations are large, additional argument can be adduced by bringing to bear a more minute analysis and the law can be better defined and additional constants inferred. Naturally the oscillations could be supposed produced in other ways, and the logic only says that they might or might not reasonably be supposed to be produced in the manner put forward.

An instance in point will be the chart of weekly cases of diphtheria in London 1914 to 1927 shown in Fig. 12. There is clearly a seasonal impulse and cases are more numerous in the fourth quarter of the year. But, apart from this (which is a forced oscillation) no pendulum effect is in clear evidence. The epidemic was at a steady level

during the war years, and the season factor was not able to create oscillations of increasing magnitude. Upon this steady state was impressed in the winter of 1919 a great impulse and cases were high, that is, the pendulum was swinging fast, say to right, during '20, '21, '22 and until the summer of '23. Had there been, as a consequence of this increase in cases for $3\frac{1}{2}$ years, a reduction in the normal number of susceptibles and had the disease been of the kind in large measure propagated by case to case infection, then we should expect the fast swing to right to be followed by a fast swing to left, during which cases were below their steady-state value. But the cases descend only to their former steady level and not perceptibly below it, and, moreover, there is no very evident swing-swang in the subsequent course as far as the data are available.

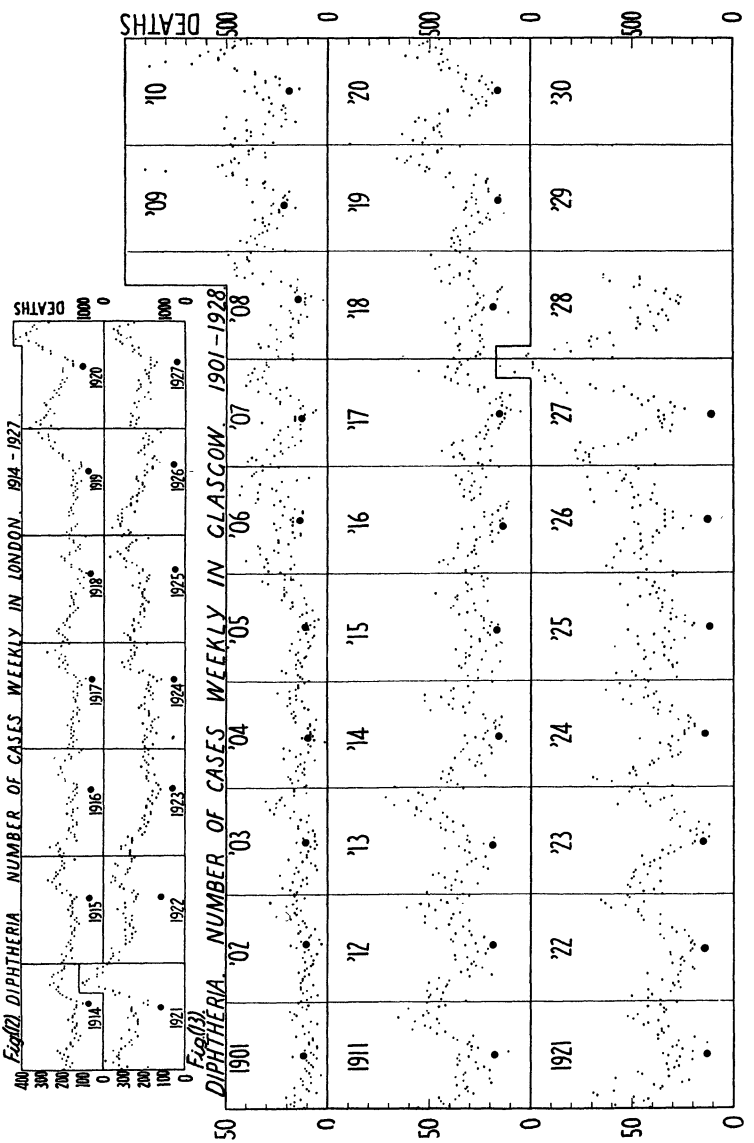
It does not appear then that such a chart as this could be subjected to any analysis that would show evidence of the existence of an underlying duality of phases taken up by the community alternately with a natural period of recurrence and which calls for a physical explanation.

The picture that would suffice for the London diphtheria series here presented is a mere multiplication of the annual phenomenon, in numbers, for a few years, followed by no reversal of the portrait. It does not follow, of course, that the action is not taking place, but that, if it does, either for other reasons or for the reason that London has too many pendulums and too loose a beam, the simple phenomenon cannot be disengaged.

A second instance is the like plot of diphtheria weekly cases in Glasgow for 1901–28 shown in Fig. 13.* Although a smaller city and, it might be thought, more self-contained, yet no more in Glasgow than in London do we find, at least upon eye evidence, the phenomenon of higher crest followed by deeper trough, necessary to justify the postulate of an exhaustion of susceptibles and deduce pendulum action. It may perhaps be, as some think, that diphtheria is propagated largely by subclinical cases, or carriers, and that, in the wider action, immunity is very imperfect, and, if this is so, then the equations must be reconstructed, and perhaps it would appear that a high degree of damping precludes the sustenance of waves.

In both the London and Glasgow data there is a great discrepancy between notified cases of diphtheria and deaths as shown for each year by the large dots. One expects a proportionality between cases and deaths if both are like occurrences in a like process following a natural course. The cases have advanced out of all proportionality, and in Glasgow, for instance, comparing 1927 with 1898, the cases are multiplied by 7 whilst the deaths are the same, viz. 113.

* From figures kindly supplied by the Medical Officer of Health, Glasgow.



Perhaps here may await further troubles for those who would digest the presented figures, this time a surfeit in place of a dearth of cases, and as part explanation the Medical Officer of Health (Glasgow Report, 1908, p. 64) states that "the practice which has been followed for some time of examining the throats of contacts in houses whenever a second case occurs, and the consequent registration of cases which by reason of their mildness would have escaped observation altogether but for the recovery of the organism of the disease, has undoubtedly tended to reduce the ratio of fatal attacks." Clearly, then, a "case" has changed its meaning and we cannot postulate a continuity of the readings of the instruments in this series representing the prevalence of diphtheria.

Although the course of epidemic measles in Glasgow during forty years is far from yielding obedience to the simple law of infection that is modelled on mass action in a perfect mixture, yet the overriding waves possess features similar to those shown proper to such an action, characterized, let us say, by delayed instant activation in a uniformly replenished motile mass. By study of these short-timed waves some representative constants can be found, susceptible of interpretation, and with help of these the epidemic process can to some extent be followed and foreshadowed.

I wish to acknowledge the invaluable help that I have received from Professor Greenwood in carrying out and presenting this investigation.

APPENDIX.

I. Number of cases per month (4 weeks) registered in Glasgow, 1901–16.

II. Calculation for ten years (26 fortnights) of synthetic epidemic,

$$\frac{\text{cases next fortnight}}{\text{cases last fortnight}} = (1 + \tfrac{1}{16}\cos\theta - \tfrac{1}{16}\cos 2\theta) \times \frac{\text{no. of susceps. at present instant}}{40 \times \text{accessions per fortnight}}$$

III. Conditions leading to damped oscillations (and example worked out).

III.—*Hypothesis of diminishing Infective Power. Damped Oscillations.*

In the foregoing theory, intended to be a first approximation to the transmission of a disease such as measles, infecting power was supposed to be instant, at the termination of a certain incubation period, and it appears that, with such a law in operation, an initial upset of steady conditions of prevalence will be followed by epidemic

I.—*Cases of Measles registered in Glasgow in Four-week Periods*, 1901–16.

Month.	'01.	'02.	'03.	'04.	'05.	'06.	'07.	'08.	'09.	'10.	'11.	'12.	'13.	'14.	'15.	'16.
1	65	1674	191	1532	452	2416	224	3911	84	6133	53	4107	749	1808	103	682
2	92	824	220	1354	512	1906	240	3159	96	3914	151	3888	843	2421	344	1141
3	124	679	212	1387	679	1804	275	2897	158	1782	366	2621	1078	2319	756	1568
4	190	410	206	1185	1176	1238	298	1803	285	1145	575	1123	1440	1566	1407	1712
5	523	357	281	813	1672	1136	325	1224	324	660	841	582	2060	1008	2470	1770
6	1023	503	463	449	1290	690	401	709	271	339	941	409	1910	565	3610	1751
7	1076	296	404	238	661	425	383	353	289	126	922	219	1549	232	2489	960
8	757	108	364	163	418	183	368	121	246	99	536	109	915	68	794	452
9	607	126	325	95	441	128	197	102	249	72	195	71	561	63	391	161
10	644	91	677	141	588	68	285	62	285	42	313	64	462	47	265	201
11	1169	120	1164	297	895	61	927	67	861	44	813	331	679	83	356	205
12	2036	160	1974	341	1707	71	2314	80	2483	65	1298	519	1203	96	282	215
13	2413	223	2287	412	1954	71	3584	134	4457	91	2499	764	1296	57	326	297

II.—*Calculation of Synthetic Epidemic* $\dfrac{\textit{Cases next fortnight}}{\textit{Cases last fortnight}} = c \times \dfrac{\textit{susceps. at present instant}}{40 \times \textit{accessions per fortnight.}}$

(Accessions = 1000.)

$c = 1 + \frac{1}{16}\cos\theta - \frac{1}{16}\cos 2\theta =$	1·0000	1·0086	1·0317	1·0628	1·0923	1·1104	1·1092	1·0851	1·0394	0·9787	0·9130	0·8547	0·8144	0·8000
when $\theta =$	0,26	1,25	2,24	3,23	4,22	5,21	6,20	7,19	8,18	9,17	10,16	11,15	12,14	13

			First year									Tenth year	
θ.	c.	$\frac{40,000}{c}$.	susceps.	cases.								susceps.	cases.
				2,000	...	...	...	...	...	...	...		1,499
0	1·0000	40,000	40,000									35,380	
				2,000	...	...	...	...	...	...	...		1,326
1	1·0086	39,660	39,000									35,054	
				1,967	...	...	...	...	...	...	...		1,172
2	1·0317	38,770	38,033									34,882	
				1,930	...	...	...	...	...	...	...		1,054
...	...	...	...	...	...	...	...	...	...	...	...	...	...
				217	...	...	...	...	...	...	...		550
26	1·0000	40,000	44,778									47,187	

waves that propagate themselves indefinitely, without diminution of amplitude.

To illustrate how a modification of the "instant" hypothesis may affect the result and, in this case, introduce a damping down of the oscillations, let us make the supposition that infecting power is possessed immediately infection is taken and is exercised without loss until the moment of recovery and passage out of the statistics. Let us also suppose that this may happen with equal chance $\frac{dt}{\tau}$ at any instant, so that τ is the mean "life" in the infecting condition; then if y stand for the number of infected individuals at any moment, $\frac{ydt}{\tau}$ is the depletion of y in time dt due to "recoveries." We may regard τ as the equivalent, here, of the incubation period, before, and shall put it = 2 weeks for the arithmetical example.

Let a, as before, stand for the accessions of susceptibles per unit of time. Then, in the steady-state, a is also the number of new cases, since we suppose no deaths amongst the x's. In the steady state, therefore, $y = a\tau$. Let $x = as$ under the same circumstances, that is, let the steady-state susceptibles be the accumulation of accessions for time s (following our former connotation). Then at any moment the cases per unit time are $a\frac{x}{as}\frac{y}{a\tau}$. Hence the equations for developing the epidemic form are,

$$\left.\begin{aligned} \frac{dx}{dt} &= a - a\frac{x}{as}\frac{y}{a\tau} \\ \frac{dy}{dt} &= a\frac{x}{as}\frac{y}{a\tau} - a\frac{y}{a\tau} \end{aligned}\right\} \quad . \quad . \quad . \quad . \quad . \quad (i)$$

To obtain an arithmetical result the data found by Sir William Hamer for London measles were taken, viz. a = 2,200 susceptibles added per week, as = steady-state susceptibles = 150,000 ($\therefore$ s = 68·2 weeks), and putting τ = 2 weeks and finite differences for differential coefficients, the equations are,

$$\left.\begin{aligned} x_1 &= x + 2{,}200 - \frac{xy}{300{,}000} \\ y_1 &= y + \frac{xy}{300{,}000} - \tfrac{1}{2}y \end{aligned}\right\} \quad . \quad . \quad . \quad (ii)$$

The week by week numbers of susceptibles x and infected y and new cases xy/300,000 were calculated, commencing with a peak of 6,500 cases, or nearly threefold, and the curve of cases proved to be periodic, with period 77 weeks (very near the 78 weeks assumed by Hamer for compounding). The form of the curve was very similar to Fig. 3 found on the previous hypothesis, but now the peaks are

successively lowered and the second peak is only 5,168 cases, or 80 per cent. of the first.

Damping down of oscillations is therefore to be expected on the theory that infecting power, instead of being "instant" after an "interval" is prolonged from the time infection was taken for a "chance" space of time.

The values found for period and damping for this epidemic wave, commencing with a threefold peak, may be compared with values that can be computed for small oscillations.

If u, v are small fractional departures in x and y from their steady-state values, as, $a\tau$, then, putting $x/as = 1 + u$, $y/a\tau = 1 + v$ in (i) and neglecting products of u, v, the equations become,

$$\left.\begin{aligned} s\frac{du}{dt} &= -u - v \\ \tau\frac{dv}{dt} &= u \end{aligned}\right\},$$

$$\therefore \frac{d^2u}{dt^2} + \frac{1}{s}\frac{du}{dt} + \frac{1}{s\tau}u = 0,$$

with like equation for v. Hence, solving the quadratic,

$$u = \hat{u}\, e^{-\frac{t}{2s}} \cos\left\{\sqrt{1 - \frac{\tau}{4s}}\,\frac{t}{\sqrt{s\tau}}\right\} \qquad \text{(iii)}$$

Thus the period is now $\dfrac{2\pi\sqrt{s\tau}}{\sqrt{1 - \dfrac{\tau}{4s}}}$, and will be a trifle longer than the period $2\pi\sqrt{s\tau}$ found for the "point" hypothesis, whilst damping has time-modulus $2s$.

Putting $\tau = 2$ weeks and $s = 68{\cdot}2$ weeks, we get for small oscillations a period of 73·7 weeks and damping to the extent in one period of $exp. - 73{\cdot}7/2 \times 68{\cdot}2 = 0{\cdot}58$.

It appears, then, that if this kind of infectivity is supposed to follow a case of measles, namely, if we suppose infective power maintained without loss for a term whose chance of end is dt/τ, or, what amounts to the same thing, if we suppose the power to suffer geometrical diminution with time in each attacked individual at rate dt/τ, then, if in the steady-state susceptibles are = accessions accumulated for time s, small oscillations have

$$\text{period} = \frac{2\pi\sqrt{s\tau}}{\sqrt{1 - \dfrac{\tau}{4s}}}; \text{ time modulus of damping} = 2s.$$

For the case, studied arithmetically, in which $\tau = 2$, $s = 68{\cdot}2$ and first peak was threefold, the period was found 77 weeks in place of 73·7, calculated for small oscillations, and the second peak was found to be 0·80 of the first peak in place of 0·58 so calculated.

DISCUSSION ON MR. SOPER'S PAPER.

SIR WILLIAM HAMER: I am very glad to have an opportunity of thanking Mr. Soper for the far too generous terms in which he has referred to my London measles-curve of twenty-two years ago. It was just the outcome of realizing—as Professor Boycott told us the other day we ought to do—that " we must not be too shy of drawing general conclusions from such specially easy and demonstrative examples as Providence has provided for our learning and pushes under our noses "—and such an instance is unquestionably that which was singled out half a century ago by Ransome, and was later studied by Whitelegge, Campbell Munro and others, viz. the example presented by the insistent invariability of the measles organism coupled with the lasting protection afforded by one attack of the disease.

Professor Boycott, it is true, pointed out on the same occasion " the danger of cultivating thoughts and reading books to which we are not equal." At the same time he did not entirely discountenance the " putting together of some sort of lay figure on which we can hang the facts which interest us and see how they fit," and " of getting rid of some of our imaginings and sketching the Jemima on which they seem to look fairly presentable." My poor little Jemima has grown beyond all recognition, if she be in any way related to the lady whose portrait Mr. Soper has unveiled for us this evening. The transformation he has effected can only be compared with that accomplished by Mr. Bernard Shaw's Pygmalion—the Professor of Phonetics—who fashioned the Covent Garden flower-girl, Eliza Doolittle, into one of the most peerless Galateas that ever stepped off a pedestal. Mr. Soper's analysis is extraordinarily interesting. He favours a point of infection law in measles, and so enlarges our sense of " the importance of *annual*, that is, *seasonal* change in perturbing epidemics, such as might be brought about by school break-ups and assembling, and other annual occurrences." These influences were all very clearly discussed by Power and Shirley Murphy forty years ago. Again, Mr. Soper deplores the existence of evidence showing the number of unregistered cases in Glasgow, and here too London experience bears him out. German measles, moreover, is a great trouble when it becomes epidemic. And then, as Mr. Soper says, " a single community may be quite differently constituted in respect to its seclusion or mingling in one part or another." Allowing for all this, the fact clearly emerges that Mr. Soper is *really* " blazing a trail," and not merely peeping into the jungle, as I did twenty-two years ago, and just scuttling away on discerning the presence there of forbidding shapes in the form of theoretical measles waves. Realizing as I now do how fearsome these monsters are, I rejoice to find a much more intrepid, and withal fully equipped, explorer now describing his adventures in these practically unexplored, but most intriguing happy hunting grounds.

DR. ISSERLIS: I welcome the opportunity of congratulating the Society on this excellent paper that Mr. Soper has read this evening.

I had rather thought that Sir William Hamer would speak from his particular knowledge of the subject, and that as Mr. Soper has treated the subject from the point of view of mathematics, the pure mathematician would be asked to speak about the mathematical aspects of the case. I feel, however, that we have had sufficient mathematics to follow without the aid of pencil and paper, and I prefer to confine myself to making the general statement that it is in my opinion a very important thing to lay down a hypothesis—a simple hypothesis if you like, but a definite hypothesis—and to follow it out to its mathematical conclusions in this way; to confront the results of that hypothesis with the facts or the results of experiment. In treating the problem in this way, Sir William Hamer and Mr. Soper have followed a totally different trail from that followed by the late Dr. Brownlee, who followed the astronomers in their analysis of sun-spots in order to observe periods in them.

The result of Mr. Soper's analysis has been this :—He says that a simple hypothesis is, in the case of the observations to which he has applied it, sufficient to account rightly for about one-half of the observed phenomena, and that is a very great deal. The question now is, how soon will Mr. Soper undertake to clear up the remaining half of the phenomena? There was one paragraph in the paper that Mr. Soper did not read to us; that is, the paragraph in which he draws our attention to the fact that the underlying assumption of the whole mathematical analysis is the constancy of the quantity A, which is the number of oscillations per unit of time. That is obviously an important simple case, but it is more likely to be the state of affairs in a large town like London than in a smaller town like Glasgow, and still less likely to be the case in a small community like Beacontree, in which the immigration year after year of young persons results not exactly in an addition to the birth-rate, but in a steady increase in Mr. Soper's A; and I dare say one could imagine a Welsh mining village under prevailing conditions, in which the steady emigration of young men and women would result in an increase of A.

I would throw out the suggestion that if Mr. Soper treated his A as, first, a slowly increasing function of the time, and, second, a slowly decreasing function of time—that is, combined with his hypothesis, a variable infectivity period—he might be able to clear up some part of the remaining phenomena.

Of course to ask Mr. Soper to do more is obviously at the same time to express one's satisfaction with what he has done.

I do not wish at this stage to enter into any discussion of the mathematical part of the theory, and I simply ask you to receive from me my expression of appreciation of Mr. Soper's paper.

Dr. Crookshank said that when asked by the Honorary Secretary to attend the meeting and to intervene in the discussion, he had replied by saying that he would only speak if he could do so intelligently, and he had hoped that, having said so much, he would have been protected! But Dr. Greenwood had told him a few minutes

before the meeting that he would be showing a lack of appreciation of the courtesy extended to him if he did not make *some* remarks, and that, in the circumstances, remarks he might make would be considered relevant that might not be so considered otherwise.

He had the profoundest admiration for the mathematical part of the paper; truly, he did not understand anything about it, and perhaps that was why he had such an admiration for it. But he had to confess to a profound distrust of statistical method on all occasions excepting when applied to the examination of a particular theory, or of particular data. As to the supposed value of the " numerical method " as a method of finding out " what really happens," he shared the constitutional antipathy of the late Professor Trousseau, who was as great a clinical physician as he himself was a very obscure one.

It was only from the point of view of the clinical physician or epidemiologist that he could say anything on the subject.

So far as Mr. Soper's paper was to be considered as an examination of the theory put forward by Sir William Hamer, Dr. Crookshank said that he must admit that for many years he had had a profound distrust of Sir William's views on this particular subject, though not on any other. So far as Mr. Soper's remarks were to be considered as elucidatory of the general theory of epidemiology, Dr. Crookshank distrusted his analysis. But there were several points in the paper about which he felt bound to speak because they hit him in weak spots and gave him occasion to bring out what friends called his " King Charles's head." At the bottom of page 35, Mr. Soper said: " We may suppose, again, that after acquisition the *disease* has *powers* of infecting others according to some law of intensity with lapse of time." That was the kind of phrase that, as a clinical physician, he strongly objected to, because he could not understand what people meant when they spoke about " *a* " *disease* which could be *acquired* and which itself *had powers* of infecting others. It seemed to him that this speaking about a disease as a separate entity with specific powers let us in for scholastic realism of the worst possible kind.

One important question, from the point of view of the clinical physician, was whether one should ever talk in this kind of way about the phenomena with which one had to deal, as if due to the actual acquisition or powers of some kind of entity. On the other hand, the tactical advantage of speaking in this way about a *disease* which had *powers* of this kind was that one did get out of a certain amount of awkwardness in controversy. Truly one might suppose that after acquisition of the *bacillus* the *bacillus* had powers of infecting other people, but it was not yet determined what the virus of measles was, and although it was assumed that measles could be dealt with as if it were a question of dealing with a bacillus, there was still an element of doubt. He could not help feeling that these mathematical analyses of the so-called phenomena of epidemic diseases were too often analyses of the particular views or notions of a particular person, rather than of *what actually did happen*, and

before one went much further in the way of mathematical analysis of epidemiological *statistics* there ought to be some better hypotheses than at present concerning epidemic disease and so forth, on which the mathematician should get to work on the lines indicated by Dr. Isserlis.

Dr. Crookshank said he deprecated mathematical discussion at the present stage so long as only those theories of Sir William Hamer were available. After all, Sir William Hamer had put forward his notions in 1906 and the author of the present paper spoke as if no other theories had been put forward since. He (Mr. Soper) had evidently forgotten the clear-cut and well-stated notions regarding epidemic disease—he referred here to work done by himself, Dr. Crookshank—of which no notice had ever been taken. It was because no notice had been taken that he began to feel there was something in them, and that they evidently did not afford matter for destructive criticism. Some of his original work on this subject was done in 1908, two years after Sir William Hamer's, and his own tentative " Jemima " was put forward at Sir William's own request and had been ignored by everybody ever since.

One of his difficulties was what was meant by the term " susceptible." Up to the present he had never heard any other meaning than what was implied when we say that susceptibles were the people who got the disease, and the non-susceptibles were those who did not get it. By this reasoning, certainly, the epidemic came to an end because the susceptibles were exhausted and only the non-susceptibles left.

As he had pointed out, Sir William Hamer's work was done over twenty years ago, and there did seem to have been a certain amount of work done on the subject since, and some attention should be paid to it. The writer who should be nameless had made an attempt to get round the difficulty, but instead of dividing the population into

A—susceptibles (people who took the disease),
B—non-susceptibles (people who did not take the disease),

he divided them into three classes :

A—susceptibles,
B—non-susceptibles,
C—an intermediate group—people who did not get the *disease* but who were transformed from susceptibles to non-susceptibles.

An interesting point about such a theory was that there were three categories instead of two, and it was much easier to indulge in a satisfactory *petitio principii* when one had three terms to juggle with instead of two.

To proceed a little further, supposing the question of susceptibility *were* examined mathematically, there were so many constants, and susceptibility was such an extraordinarily relative thing. One might be susceptible in the morning but not susceptible in the afternoon. One was susceptible if one went out to see a case in the

middle of the night on an empty stomach, but not susceptible if one saw a case after a meal, and Dr. Crookshank could not see how mathematicians were going to deal with that kind of variation.

There was another factor mentioned by someone—if not Professor Chadwick it should have been—that besides the seed and the soil, one had to deal with *occasion*. There seemed to be something intervening besides soil and seed before the thing "clicked." Speaking as a worker in the field, he felt that that "occasion" business had to be recognized. Mr. Soper spoke about the discrepancy between registered and unregistered cases. Few people realized how great that was; it was colossal, and in saying so he was speaking with feeling, because of what he experienced years ago when he was occupying three positions at once—engaged in general practice, as a Medical Officer of Health, and as a Superintendent of an Isolation Hospital. (A curve should be constructed to show how rare such a thing was.) It meant that one had remarkable opportunities for observation, and he used to know that scarlet fever and measles were prevalent in the district long before his colleagues in practice started notifying them as such, so that the curves he constructed from the notified cases had no relation to the curves he could construct from his own observations.

On one occasion he saw two little children in one day who were suffering from a form of diarrhœa. That day one of his colleagues notified a case as one of typhoid fever. He (Dr. Crookshank) asked for the usual enquiries to be made as to the milk-supply, found it was supplied by a certain dairy, and ascertained that his own two cases had been supplied by the same milkman, which caused him to wonder whether they also were not typhoid. The following day the bacteriologist's report said that his colleague's case was not typhoid fever, but Dr. Crookshank disregarded this finding in the same way that he would a mathematical report. In the course of the afternoon he heard of another child with diarrhœa after taking milk from the same dairy. He then sent out a questionnaire to the medical men in the district to ask if they had had any cases of diarrhœa within the last fortnight, and he received fifty replies in the affirmative. The next district also had no typhoid but many cases of diarrhœa. In forty-eight hours the milk-supply of all the cases was traced to a dairy farm in Wiltshire, where the farmer's child had mild typhoid fever that had been diagnosed as meningitis, and her clothing had been washed in the milk churn.

Ultimately about one hundred and twenty cases of typhoid were traced to this milk-supply, but if he had waited for notification in the ordinary way, it would have taken two or three weeks, and then half the cases would have been missed. That was only one instance of what commonly happened. Experience of this kind rather went to show that these statistical enquiries did not represent what actually happened in the field, but what happened in the bureau of the Medical Officer of Health.

Dr. Crookshank said he would like briefly to refer to the advisability of not entirely discarding the miasmatic theory in dealing

with epidemics. He did not want to set it up in opposition to the theory of infection, but to show that there was room for both. There might be some atmospheric changes which allowed a certain number of people to become at a given time simultaneously susceptible to certain organisms, and then once they had developed the disease, they might then transmit the virus directly to other people. Unfortunately people argued as to which of the two theories was right; only a few people realized there was room for *both* theories. There would only be progress when proper attention was paid to the miasmatic side as well as to the theory of infection.

Last summer when there was hot weather due to cosmic change, people who were over-clothed suddenly changed their garments. This was due to some common cause. Later, other people did the same thing by way of imitation or "infection"! About the month of March or April, small boys suddenly began to play with tops all over the street. Why did that happen? They were people of a particular age, and only this particular population seemed to be susceptible to this epidemic of top-spinning. Was it "infectivity"? Did one boy infect another? Might it not be that there was some common impulse that brought boys forward at one time to play tops?

If one kept to the *facts* in the first place and then tried to get a better *theory* than Sir William Hamer's, Mr. Soper might be given material for a most delightful investigation, which Dr. Crookshank would support because it would be on his side.

Mr. Udny Yule said he did not feel competent at present to discuss the paper, as he had not had time thoroughly to follow it, but, with all respect to Dr. Crookshank, he would say that this was a very valuable paper. The only way of testing a theory was to see how far it could interpret such knowledge concerning facts as was available. It was unfortunate from that standpoint that there was so great a discrepancy between the facts available and those that were needed. At present there existed only facts concerning cases notified, whereas facts were required concerning cases occurring.

Mr. Soper had carried out a very capable and interesting piece of analysis that showed in detail what the consequences of Sir William Hamer's theory might be, and his conclusions did reproduce in a remarkable way many of the features of the statistics. How far that agreement in effect supported the theory must necessarily be a matter for persons better qualified than himself to discuss, but he thanked Mr. Soper for an extremely interesting paper which must have cost far more labour than appeared, because a great deal of labour had often been condensed into a mere table or a graph.

Dr. Halliday said that Mr. Soper had dealt at length in his paper with the Glasgow figures for measles, and it happened that he also had been working at them. At one time he had thought that he might be able to do something to them on the lines taken by Mr. Soper, but, as the mathematical processes involved were so intricate, he could not have accomplished the work so deftly. However,

the work was never undertaken because he found out that the result for Glasgow would apply only to that city, and entirely different calculations would be needed for other cities, such as Greenock, Edinburgh, and Aberdeen.

There was no time to go into all the epidemiological issues involved, but he might mention that one of the points that had been so far omitted in consideration of the subject of measles epidemicity was the nature of the topographical unit to be studied. This was very important, as every unit presented different features and the periodicity of measles took a different course in each. This diversity was associated with the fact that measles as outbreak did not develop simultaneously throughout a community. In Glasgow it began in September in one or more foci, and, if conditions were favourable, measles as outbreak spread from these foci in a radial manner along the lines of communication. If, however, conditions were not favourable, it did not spread as outbreak until January, February, or March.

Now, measles as outbreak takes time to move through a community. In Glasgow, when an outbreak began in September, it was found that it took twenty-four weeks to pass over the thirty-seven sections or wards of the city. On the other hand, if measles did not begin in the form of outbreak until January, February or March, it followed that the whole city would not be covered until June, July or August. But this did not happen because, owing to the interposition of another factor, the progression of the outbreak in space was frustrated in May or June. This other factor might be called the refractory period because it was found that, as far as Glasgow was concerned, all late epidemics collapse suddenly at the end of May, often leaving large tracts of the city unaffected.

To sum up, when measles began as outbreak in September or October, and conditions for its spread were favourable, there was time for it to travel throughout all sections of a city of the size of Glasgow. By covering the whole population a considerable increase in the immunity of the population resulted. Such early outbreaks reached their peaks in the late winter or early spring, and in the following annual period, owing to the high immunity produced, no epidemic occurred. If, however, measles as outbreak began late, *e.g.* in January or February, it had not sufficient time to cover the whole population before the onset of the refractory period in May, and consequently the city was only partially immunized. As a result of this partial immunization, measles again appeared as outbreak in the following annual period.

In Glasgow, as Mr. Soper's figures had shown, measles as outbreak occurred at two-yearly intervals for a number of years; then it had a phase of annual appearance, and recently it has reverted to the biennial type. When biennial, the outbreak was always considerable in extent and reached a peak in winter or spring; when annual, the outbreaks were smaller and reached a peak in May or early June.

In units smaller than Glasgow, measles as an outbreak could

rapidly cover the population and thus bring about a high immunity, even when the outbreak started somewhat late in the annual period. In the majority of smaller units examined it was found—as was expected—that measles would appear mainly in its biennial form. Such was the case for Greenock, Aberdeen and Dundee.

If the population was large, or if it was well dispersed throughout space, measles in the form of outbreak had seldom time to traverse the whole area before the Refractory Period set in in May, the result being that annual outbreaks predominated. Such was the case for towns like Paris and Edinburgh.

The best example of an extreme biennial appearance was to be found in Greenock, and of an extreme annual appearance in Paris. The majority of cities examined were intermediate in type. In Glasgow, biennial outbreaks predominated over annual. In London, annual outbreaks predominated over biennial.

The subject of measles epidemicity was, in Dr. Halliday's opinion, one that required further epidemiological investigation on a topographical basis, and only secondarily, if at all, should an approach be made mathematically. Mr. Soper was to be congratulated on a very fine piece of mathematical work.

Mr. Connor said he would like to associate himself with Mr. Isserlis and Mr. Yule in their remarks upon the mathematical aspects of the paper, and to express his appreciation of the remarkable skill and clearness, and of the ingenuity with which Mr. Soper had found his constant.

Professor Greenwood said he would like to add a word of appreciation of the beautiful work that Mr. Soper had done. Not only, as Mr. Yule had pointed out, was there an enormous amount of labour behind the single figures, but he ventured to suggest that the mathematical expression of the results was singularly elegant. He knew that he had had the advantage of reading the paper more than once, and that a method of presentation which on first reading might not seem simple, often proved, when mastered, enormously helpful. Mr. Soper's admirable work on Frequency Averages was an example. He suggested that Mr. Soper's plan in this paper of taking an epidemiological hypothesis, expressing that hypothesis arithmetically and determining how nearly it described the observations of others, was the one way in which one could hope to render more precise the description of epidemiological phenomena.

Mr. Flux said he would like to associate himself with Professor Greenwood and other speakers, but particularly with Professor Greenwood in his remarks upon the neatness of the mathematical work put before the Society by Mr. Soper. Unfortunately he had not had a copy of the paper until he arrived at the meeting that afternoon, and there had naturally been insufficient time for him to do more than glance superficially at it, but that aspect of the work struck him forcibly.

He would put to the meeting the Vote of Thanks proposed by Sir William Hamer, seconded by Dr. Isserlis and supported by other speakers.

Mr. Soper intimated that he did not wish to make any attempt that evening to meet criticisms upon the paper, but would do his best if the editors of the *Journal* would allow him space for that purpose in due course.

The following written reply was received from him latter :—

I wonder if Dr. Crookshank's professed inability to understand mathematics is only a dark glass assumed that he may administer a destructive ray upon my use of the word disease? When I say " The mathematical picture is formed (so, and) we may suppose . . . the disease has powers of infecting," the disease is neither the " real occurrence," whatever those who use the term may mean, nor is it a " mental construct " involving " a single person manifesting a defined group of symptoms correlated with a single intra-corporeal cause," as has been said. It is the picture of a passed ball and the mental construct is shorn of particularizing features as in the familiar bags of balls. The tactical advantage of the mathematics is admittedly taken, and I hope here at any rate gets me out of awkward controversy.

This mathematical process of naming and numbering and relating is surely the sole means we have of understanding complex things, and no statistician would surely cavil at the taking of a quotient, as a death-rate, to eliminate numbers. Some have thought that they could discern a relation between a quotient called infectivity and a difference called number of susceptibles, and there is no harm in carrying the argument through a succession of arithmetical repetitions to see what happens. The result is wrong, and now come in many helpful suggestions to show reason why.

Dr. Isserlis makes the valuable suggestion that the accessions of " susceptibles " might with more truth be made variable, and the consequence of this supposition should certainly be followed up.

Dr. Crookshank offers the mathematical notion (to my view) of a by-pass flow of susceptibles to the insusceptible state without going through " case," and this again should be examined, and if not a cogent factor in measles might be of dominating importance in such a disease as diphtheria. The miasmatic theory that connects infectivity with atmospheric conditions, in greater or less degree, may also have to be reckoned with to narrow down the unexplained balances. The further complexities of a changing susceptibility and " occasion " can perhaps be thought of as belonging to that class of determinants which have no statistical balances in the main account.

From Dr. Halliday, who has made a detailed study of measles epidemics in Glasgow, comes perhaps the most instructive criticism. Apart from the domestic heterogeneity characterizing the different wards and parts of a city, the fact that the parts are not going together, but that a case, or glut of cases, arising here or there

after the refractory period, intensify round the foci and propagate as waves over the remainder of the city is a phenomenon that may sadly upset the results of the simple hypothesis, especially if it takes, as he says, some twenty-four weeks for a wave to traverse the city. True, a mass action law pretends to eliminate local actions, their joint consequence being statistically ascertainable, but it may be that, when cases are few, the after development of the epidemics may depend materially upon their distribution upon the map, and for a statistical presentment, besides errors of number, there would have to be brought in error of spatial distribution, from norms.

Some synoptic charts of the topographical course of an epidemic in a large city like Glasgow would be of great interest in this connection, and perhaps an arithmetical propagation could be devised to simulate the demonstrated waves and strengthen the verbal explanations, always, of course, with the purpose of finding out how much can be explained and how much is left for explanation by less puissant agents and chance.

I wish to express my thanks for the criticisms offered and remarks made upon this attempt to continue a trail on a hastily chosen line, and to ask those who scent "mathematics" to see in the paper only a piece of simple arithmetic.

Dr. A. Salusbury MacNalty, of the Ministry of Health, who was prevented at the last moment from attending the meeting, has since sent the following commentary on the paper:—

I should like to express my appreciation of Mr. Soper's mathematical interpretation of periodicity in disease prevalence, a welcome contribution to a complex and obscure subject.

As Mr. Soper has observed, the periodicity of epidemics of measles has been long recognized, and I would refer especially to Whitelegge's work in this connection. We know that there is a seasonal maximum prevalence of measles, and also that in large centres of population epidemics of measles occur, usually about every two or three years. A graphic record will show for measles biennial or triennial excesses of mortality.

Whitelegge terms these outbreaks "minor epidemics," and gives as their causes in urban centres—

(1) The persistence of measles always ready to spread.
(2) The accumulation of susceptible children getting nearer and nearer to the degree of density required for epidemic extension.
(3) Climatic influences which from time to time (usually once but sometimes twice a year) afford in some way maximum facilities for the outbreak.

But Whitelegge in 1892 also drew attention to a cyclical change in the manifestations of measles; occasionally over wide or narrow areas. Successive minor epidemics become more and more virulent and destructive, owing, as he suggests, to progressive intensification of the measles virus; and these long waves, built up of many successive

minor epidemics, in his opinion, may fittingly be termed major epidemics. When the crest of the epidemic wave begins to rise a greatly increased mortality from measles may be anticipated, such as occurred in the " eighties " and the " nineties."

The causes of these major epidemics are obscure; they occur at long intervals. Whitelegge states their advent may be recognized by a progressive intensification of virulence of the biennial minor epidemics. At all events they cannot be entirely explained by the inflow of susceptibles.

Mr. Soper has found some difficulty in applying the equations to measles epidemics in Glasgow and also to outbreaks of diphtheria. He has, I think, anticipated criticism by putting his finger upon certain discrepancies. There is perhaps a false analogy between infection in disease and the mechanism known as chemical mass-action. The notification figures of measles in a district are, of course, unreliable with regard to the true incidence of cases of the disease in an epidemic. So many cases are nursed at home and remain unnotified. The registered deaths from measles furnish the best available statistical evidence.

Then in regard to the question of susceptibility in disease we have still much to learn.

In selecting measles for a trial essay of his hypothesis, Mr. Soper has chosen a disease in which there is a high degree of susceptibility. Nearly every child gets measles, and the inflow of susceptibles indubitably is reflected in the periodicity of minor epidemics.

It must be remembered, however, that the age at which susceptibles contract measles is to some extent variable and therefore disturbs the mathematical forecast. Certainly among the well-to-do it is the exception and not the rule for children in this social class to contract measles under five year of age. Because measles is most fatal to children in this age-period, all our public health efforts are directed to educating parents of all classes to guard young children under five years from exposure to infection. If this campaign has met with any success it will have postponed the onset of measles to a later age-period.

Halliday, in a recent report to the Medical Research Council, has shown that the period of child-life in which an attack takes place differs considerably according as circumstances vary.

He writes: " Among crowded tenement quarters housing a working-class population such as are to be found in Glasgow, the disease is essentially one of children under school-age. In the working-class and middle-class families of Birmingham and Willesden who live in houses of the single-entry type, the disease is predominantly one of scholars of ages five to ten. In country districts also the disease tends to be one of school-children of ages five to ten. Among the public-school class the age of attack seems to be postponed to a still later period of life. At the other extreme from the Glasgow tenements are to be found the very remote districts, such as the Highland glen mentioned by Brownlee, where all the inhabitants were attacked irrespective of age."

Halliday also found that a large number of the children in the

tenements of Glasgow did not contract measles although they were all presumably exposed to infection. He suggests that the conditions of exposure are such that susceptible children may respond either by acquiring the disease or by developing a partial and probably temporary immunity to it. This immunity on the part of a proportion of susceptibles may be one of the causes of the natural decline of an epidemic before it has reached the theoretically possible limits of its spread in the population.

I am especially interested in these findings of Halliday in relation to measles because this view is one I have advanced in regard to epidemic diseases of the central nervous system, although many would hold that only a limited number of susceptibles contract these diseases. It is also in accord with the theory of the " velocity of infection " elaborated by Surgeon-Commander S. F. Dudley.

I should be much interested to see Mr. Soper's formulæ applied to the interpretation of periodicity in the prevalence of epidemic poliomyelitis.

In these remarks I have merely endeavoured to sketch some of the epidemiological circumstances which may interfere with, but do not detract from, the value of his mathematical interpretation of periodicity in disease prevalence.

During the meeting the PRESIDENT announced that the Frances Wood Memorial Prize for the encouragement of work in social statistics, which had been offered for competition in 1928, had been awarded by the Council to Mr. C. G. Clark, for his essay, " A Graphical Analysis of the Unemployment Position during the period 1920–28." The President then handed Mr. Clark the cheque for thirty pounds which formed the prize, at the same time expressing his congratulations, and his satisfaction, which would be shared by the Fellows, that the Society was in a position to stimulate work of this kind.

The President then reminded the meeting of his reference, in November, to a Fellow of the Society, Mr. J. Russell Sowray, whose Fellowship extended over seventy-three years, and expressed his regret at the news received within the last week, that of Mr. Sowray's death at the age of ninety-eight, a regret which he felt would be shared by all present.

As a result of the ballot taken during the meeting, the five candidates named below were elected Fellows of the Society :—

Alistair McBride Armour, B.Com.
Howard Granville Borden.
Sir Atul Chandra Chatterjee.
Henry Vincent Hodson.
Peter Laird McKinlay, M.D., D.Ph.