

An Investigation into the Periodicity of Measles Epidemics in the Different Districts of London for the Years 1890-1912

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III.—An Investigation into the Periodicity of Measles Epidemics in the Different Districts of London for the Years 1890–1912.

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Communicated by Dr. W. M. Fletcher, F.R.S.

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II. Distribution of Epidemics of different Periodicities in the City of London.

In a recent contribution to the 'Transactions' of this Society I discussed the periodicity of the epidemics of measles in the City of London during the period of 200 years for which statistics exist. The most important part of the investigation was that referring to the last 70 years, and this showed, among other things, that numerous quite definite periodicities existed. The chief of these was 97 weeks in length, but several other periods, especially in the latter part of the epoch considered, were found to have high amplitudes, namely, those of 87, $109\frac{1}{2}$, and 114 weeks.

One result of the discovery of these periods has been to bring the investigation of the spatial distributions of epidemics within the range of practical calculation. Hitherto, except for large solitary epidemics, such as the epidemic of smallpox in London in 1902—an instance in which the problem appears in its simplest aspect—the study of spatial distribution of zymotic disease has been almost impracticable. There was no method of disentangling the different strands of infection which together contributed to the total number of infections in a definite district. A phenomenon which one observer might explain as a spread of a disease from one district to another, a second observer might often, with equal probability, consider to be due to the occurrence of an independent outburst of the disease. In such cases some method of averaging is necessary, and the application of any such method must not be subject to the caprice of the investigator. In the absence of a rigid mathematic the results deduced can only at best be received with a measure of thanks for the work done. No certainty can come on such lines.

Once, however, it had been discovered that definite periodic phenomena exist in a given series of figures then it was obvious that a method of averaging nearly independent of the manipulation of the investigator was ready for the purpose of this kind of research. The following pages contain a first study based on these lines.

The data for London are extraordinarily complete, as the statistics of the number of deaths from measles and other infectious diseases in each week for each registration sub-district have been published by the Registrar-General for the last 70 years.

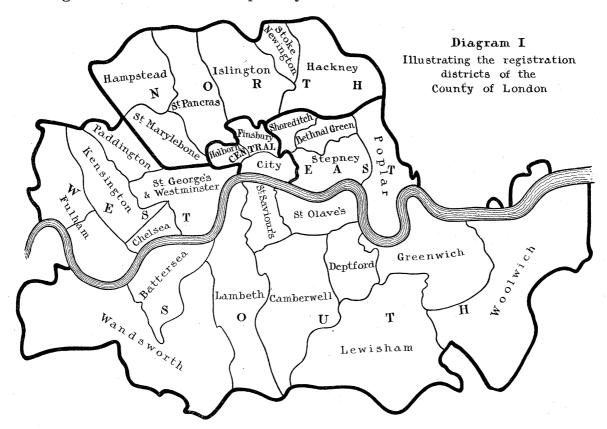
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These sub-districts are again grouped together into districts and finally into five large divisions, the North, the South, the East, the West, and the Central. Four of these divisions are situated on the north side of the river, the south side of the river constituting the South division. As frequent reference will be made to these districts and divisions, and as part of the argument depends on their geographical relation, a sketch map has been prepared which shows their chief features (Diagram I).

In the course of the investigation, in the first place, the weekly number of deaths from measles were extracted from the Registrar-General's returns for each of the five large divisions of London separately. The statistics selected referred to the



23 years, 1890–1912, this being nearly equivalent to ten times the period of 114 weeks. Secondly, the figures for each division and for each of the four periods 87, 97, 109½, and 114 weeks were added in the customary manner, and the results of the additions graphed. It is not necessary to reproduce these graphs, a brief account of the phenomena observed being sufficient for the present purpose. Thus it is found that the epidemic of 87 weeks' period is wholly confined to the south of the Thames, there being no evidence of its presence to any but a very slight extent in any other part of London. The fact that this epidemic is confined in area gives it very great local importance, the amplitude of the graph in its own district being greater than that of the period of 97 weeks for the County of London as a whole.

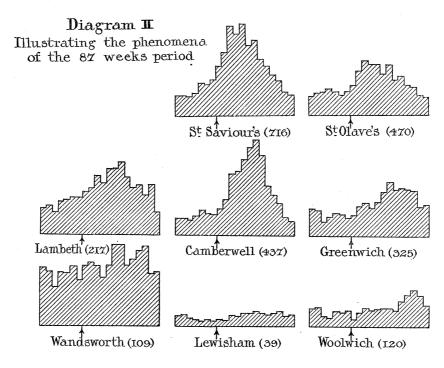
Quite a different distribution is found for the epidemic of 97 weeks' period. This epidemic is well marked in all the divisions of London, but very specially marked in the Western division in which it is present as the dominant epidemic. In the Southern division it is as prominent as that of the 87 weeks' period; in the Northern as important as in the Southern; least marked in the Central and Eastern. With regard to the epidemic of $109\frac{1}{2}$ weeks, this is found specially prominent in the Central and Western districts, fairly conspicuous in the Northern, less so in the Southern, and nearly absent from the Eastern district. The epidemic period of 114 weeks is found well marked in the Northern and Central districts, but much less so in the other districts of London. A Table of the values of the amplitudes (Table I) is given to illustrate these points.

Table I.—Showing the Values of the Amplitudes of the First Harmonics of the Epidemics of different Periodicity in the different Divisions of London.

								Period.			
	_							97 weeks.	$109\frac{1}{2}$ weeks.	114 weeks.	
Northern		•	•	•	•		•	520	388	309	
Western			• .					913	569	239	
Central .								$\boldsymbol{322}$	497	437	
Eastern .		٠.		•.				349	167	161	
Southern								506	282	218	

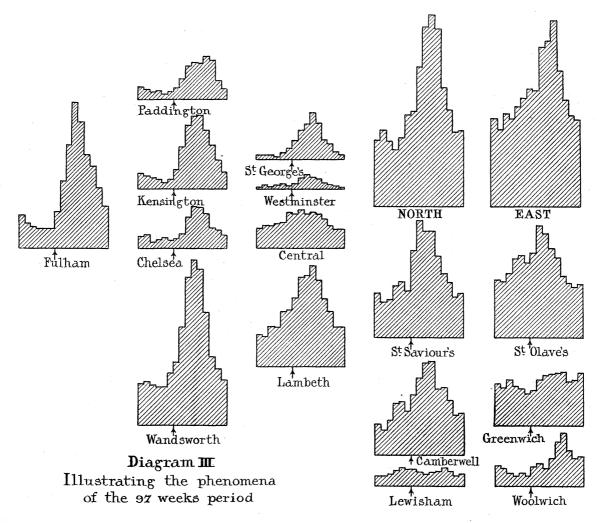
When these facts had been ascertained the obvious line of further research was to investigate how far the sub-districts in the Western and Southern divisions showed the same characteristics as the districts themselves. These districts are in the case of the West six in number, and in the case of the South eight. It would be very laborious to make the necessary investigation among the weekly number of deaths for so many different districts. Fortunately this detail is not necessary. Certain arithmetical simplifications are possible. Thus 87 weeks is almost exactly one and two-third years; 97 weeks one and seven-eighth years; and $109\frac{1}{2}$ weeks two and one-tenth years. latter figure differs by only one-fortieth of a year or approximately one-eightieth of a period from two and one-eighth years. As the data contain only 10 periods this is not a difference sufficient to introduce any serious error, and in addition the error is the same in effect in all the sub-districts so that any differences found between the different sub-districts will be independent of this simplification. The subsequent investigation is confined to these three periods. The method pursued has been as follows:—The numbers of deaths in each sub-district were taken out in quarter years. In the period of 87 weeks each of these quarter years was used three times in the writing out of the sums and in the case of the 97 week and $109\frac{1}{2}$ week periods twice.

As has been stated the 87 weeks' epidemic is confined to the southern side of the Thames. This area is divided by the Registrar-General into eight districts, St. Saviour's or Southwark, St. Olave's or Bermondsey, Lambeth, Camberwell, Greenwich including Deptford, Wandsworth including Battersea, Lewisham, and Woolwich. To illustrate the phenomena which exist the course of the epidemic in time has been graphed for each of the different districts, and the different graphs arranged in a diagram in such a way as to roughly represent the relative geographical distribution of the different districts. To permit comparison in time the same zero in time is indicated in each graph by an arrow. Certain points must be remembered in studying such a diagram. Where there is a mixture of epidemics the graph of any period consists of two parts. One part, which may be taken as expressed



by a straight line, represents the sum of the cases belonging to the epidemics of all other periods, the variations of the periods which differ in length from that at the moment discussed neutralizing themselves over a series of years. The second part consists of the variation of the number of cases in time due to the period itself. The proportion which the number of deaths, corresponding to the epidemic period, bears to the total number of deaths or better still to the population of the district at susceptible ages, indicates roughly the extent of the epidemic prevalence due to the period in question in each district. The number of deaths from measles associated in each district with the special period has been obtained from the total number of deaths by subtracting the average number of deaths occurring in the inter-epidemic period, this number being associated with epidemics of the other periods. The number of deaths thus found has been compared with the number of children living under five

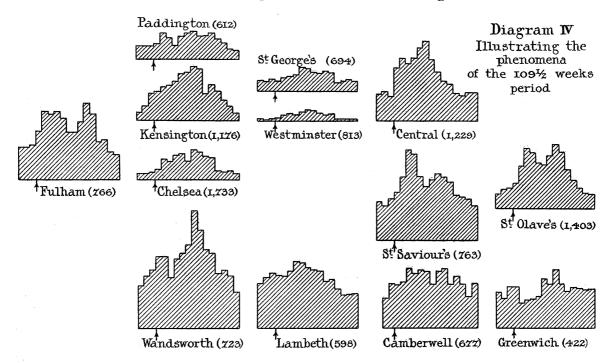
years of age in each district and the ratio between the two calculated. These figures are shown in brackets in the diagram under the corresponding graph. It can at once be observed that in St. Saviour's the proportion which the epidemic wave bears to the total number of deaths is much greater than in any of the other districts. The adjacent districts of St. Olave's and Camberwell follow in order, then Greenwich, Lambeth, Woolwich, Wandsworth and Lewisham. It is also to be observed in the diagram that the epidemic wave begins earliest in St. Saviour's, later in St. Olave's



and Camberwell, later still in Lambeth and Greenwich and still later in the three remaining districts. It is to be noted that the later the epidemic occurs, the smaller the proportion of the number of deaths associated with the period bears to the number of children susceptible to the disease. Further, the epidemic ends in all the districts approximately at the same time. It would be difficult, I think, to find a better example of the spread of an epidemic from a central focus.

When the statistics relating to the main epidemic of London, namely, that of 97 weeks, are investigated a different state of affairs is observed (Diagram III). There

is no evidence of spread from any centre in the manner shown to exist for the epidemic which has a period of 87 weeks. The epidemic begins practically at the same time all over London, except in the Eastern division where it is definitely later. Its chief seat is in the Western division in which it is much the most extensive epidemic present, but it also markedly affects the Northern and Southern divisions, especially in the latter, affecting Wandsworth, Lambeth, Camberwell, St. Saviour's and St. Olave's, while in Greenwich, Woolwich and Lewisham it is hardly present. Woolwich, it is true, has an apparent epidemic of this period, but the variation in the number of cases is almost solely due to one large epidemic. In this instance the epidemic is obviously due to the introduction of infection from without, the date of the maximum of the epidemic in Woolwich being about 15 weeks later



than in St. Saviour's or St. Olave's. It would appear, therefore, that all over London the epidemic of the period of 97 weeks begins about the same time. If anything the maximum of the epidemic is earlier south of the river than in the west, though the difference does not amount at most to six weeks, a period quite insufficient to permit of the extensive spread of the disease when the phenomena of the epidemic of 87 weeks' period are examined.

The cases just discussed are comparatively simple. A less simple case is that of the 109½ weeks' period (Diagram IV). The epidemic of this period occurs in the Central, Northern, and Western divisions, and to a less extent in the Southern division as well. It would seem that in this case it exhibits some of the qualities of both the epidemics of the 87 week and of the 97 week periods.

It apparently starts in the Central, Northern, and Western districts at the same

time. From the Central it seems to spread to St. Saviour's, and then through the eastern part of the Southern district. Apparently, Wandsworth is infected from Chelsea and Fulham. There is, however, none of the simplicity in the mode of spread that exists with regard to the epidemics of the shorter period. The figures representing the attack rate in each district, calculated in the same way as for the epidemic of 87 weeks' period, do not show the same ease of interpretation, but on the whole it may be said that in those districts into which the epidemic is introduced later, the number of deaths is proportionately low.

As a point subsidiary in importance, it may be noted that in the diagrams relating to Woolwich and Greenwich the amplitude corresponding to the chief London epidemics are never large. Greenwich has epidemic periods of its own approximating to 78 weeks, and Woolwich apparently has similar epidemic periods, but the data in neither district are suitable for the investigation of periodicities, as the presence of one or two large epidemics dominates the rest of the figures, and if in the investigation of any period two or more of these large epidemics come into the same column, an amplitude is obtained quite out of proportion to any real amplitude in that region. Statistics such as these are insufficient to furnish accurate information of the presence of periodicities.

The varieties of the spatial distribution in time being thus determined, it remains to inquire into the light these throw on the principles of epidemiology.

Of periodicities in infectious diseases two explanations are possible. hypothesis the periodicity may be due to causes depending on the variation of infecting power of the causal organism, multiplicity of period depending on different strains of the organism having somewhat different life properties; on the other the varying local conditions in different parts of a city might be sufficient to account for the phenomena found, as the method of the spread of a disease and the number of persons infected in any epidemic must depend to some extent on the number of susceptible persons, on the density of population, on the season of the year, and on other similar These two explanations have very different bases. In the one case the infecting organism is the main factor. In the second the conditions of the population. On both hypotheses epidemic periodicities can be explained.* Further, both give rise to forms of epidemic waves in time so much alike that it is doubtful if examination of the form of this wave in view of the complicated nature of the measles epidemics will be sufficient alone to decide which view is correct. On the other hand, the manner in which the disease spreads when introduced into a suitable locality will be different. On the hypothesis that an epidemic ends because the organism has lost its infecting power, the method of spread of the disease is roughly as follows. Cases of disease will occur first in the immediate neighbourhood of the centre of infection, and from this a peripheral spread will take place. As the disease spreads, a larger

^{*} Of course these theories are not mutually exclusive; the point to be determined is their relative importance. My opinion is strongly in favour of the first hypothesis.

and larger amount of infectible material becomes available, but as the infecting power of the organism is decreasing the epidemic comes to an end in spite of this extra supply of infectible material. I have already shown that this is what takes place with regard to a number of epidemics, and specially with regard to the cases of the epidemics of smallpox in Liverpool and in London in the years 1901–1902, and of relapsing fever in Glasgow in the year 1872.*

On the second hypothesis, namely, that an epidemic ends from lack of susceptible material, a quite different series of phenomena must result. The epidemic will die out in the centre of the district while spreading peripherally, and in the periphery will continue to spread till the number of susceptible persons becomes too few to furnish new cases of disease.

As a first approximation, I showed in my first paper† that the loss of infectivity might be assumed to obey the law of a mono-molecular reaction, that is to say, that the infectivity might be measured at equal intervals of time by the successive terms of a decreasing geometrical progression. On this hypothesis, and with the further assumption that the infecting power at any time is proportional to the actual number of infected persons, I showed that the distribution in time of an epidemic is given by the normal curve of error, and the distribution in space by a symmetrical normal surface of error. The expression, which may be taken to represent the spatial distribution of the epidemic at any time, is thus of the form

$$z = ce^{\frac{x^2 + y}{2\sigma^2 a^t}}$$

when z is the number of cases at the point (x, y) at time t and σ , c, α are constants; the course of the epidemic in time can thus be easily studied for any region.

In the accompanying diagram (Diagram V, a) the time distributions of cases in a central and two peripheral zones are shown. The diagram refers to the number of persons infected in each area proportionately to the whole susceptible population. It will be observed that, with each increase of distance from the centre of the epidemic in space, the maximum point in time is later, but that the end of the epidemic is nearly synchronous in all. In the centre the increase in the number of cases is more rapid than the decline, and in the periphery the curve is nearly symmetrical.

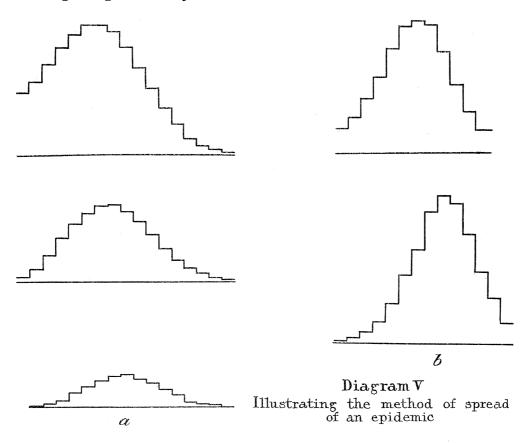
On the second hypothesis the integration is much more difficult. The form of the wave in successive regions has therefore been traced arithmetically to save labour. The solution has been made for a two-dimensional problem, but the result for a three-dimensional problem will not be essentially different. It will be noted, on examining the diagram (Diagram V, b), that, as the epidemic spreads from the centre, the form of the wave in each case is essentially the same, and that the end of the epidemic in the periphery is as much later as its maximum, the curve of the epidemic wave being translated in time. If, then, typical examples of epidemics

^{* &}quot;The Theory of an Epidemic," 'Roy. Soc. Proc. Edin., 1905, vol. 26, p. 511 et seq.

[†] Loc. cit., p. 502.

spreading from centres can be found, these should furnish sufficient evidence to determine which theory is most likely to be correct.

The different epidemics of measles have been disentangled by a study of their periodicities, and the characteristics of these epidemics, as observed in different districts and divisions of the city, furnish in different ways, each a quota of its own to the solution of the problem. From the statistics of the great epidemic of 97 weeks' period, it is seen that an epidemic can begin at essentially the same time over a very large area, and this is a point of great importance. It unfortunately, however, throws no light on the question of the cause of the periodicity. An epidemic, beginning essentially at the same time all over the district, will run its



course and recur on both the theories of causation considered, and, though the epidemic form in time is found actually to be represented very closely by the normal curve of error, the form which arises necessarily from the law of loss of infective power postulated, yet this evidence is not sufficient to distinguish the right of the two theories from the wrong.

When, however, an epidemic spreads from a well-defined centre, this objection does not hold, and of this type the epidemic of 87 weeks' periodicity seems to furnish an excellent example. In this case a central focus is found to exist in the district of St. Saviour's, and from this focus the disease spreads into the surrounding districts.

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On the theory that an epidemic ceases because the number of susceptible persons is exhausted, the course and the severity of the secondary epidemics in the districts surrounding the central focus should not be essentially different from that in the central area itself. On certain occasions, it is true, it might happen that in one or other of these surrounding districts an independent epidemic of measles might have recently taken place, and the spread of a new infection thus rendered impossible on account of the lack of susceptible persons, but, when a series of years is taken, as has been done in this case, and when the series of years contains at least ten periods of each epidemic studied, this possibility must be dismissed as not probable on the average considered. It must be remembered that the kind of disturbance suggested in the peripheral districts is just as likely to affect the central focus, so that the effect will be equalised. The facts relating to the epidemic of 87 weeks' period are thus wholly in favour of the theory that the power of infection of the causal organism plays a large part in determining the course of the epidemic. The data referring to the epidemic of $109\frac{1}{2}$ weeks' period do not offer an equally clear interpretation, but such evidence as they present is read by me in the same light.

One point of great interest, if it be admitted that the different periodicities are due to the action of different strains of organisms, refers to the degree of protection which one strain of organism may afford against another. The facts seem to indicate that this degree of protection is high, but it is certainly not absolute. Second infections from measles within the short period of three weeks were far from uncommon in the wards of the city of Glasgow hospitals set apart for the treatment of that disease. Further, as the frequency of such second infections varied with different epidemics, the phenomenon being at times absent, it is probable that, on the occasions when the frequency was high, the epidemic in the city was not a single epidemic due to one strain of organism, but to the accidental concurrence of epidemics due to independent infecting agents.