Measles Periodicity and Community Size

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Professor E. S. Pearson, C.B.E., in the Chair]

Contents

1. Retrospect

A CRITIQUE of the statistical theory of epidemics arising from the transmission of infection from person to person, with particular reference to the theory of recurrent epidemics, was attempted in a recent paper presented at Berkeley in 1955 (Bartlett, 1956). Explicit consideration was given to measles epidemics, on which a good deal of previous investigation, both theoretical and observational, has been made (see References). It was suggested in my paper that the simple assumptions made in the Hamer-Soper model (see Soper, 1929) of measles, while leading to gross discrepancies with observed statistics, might be rehabilitated if formulated in proper stochastic (i.e. probabilistic) terms. It should be explained that statistics in a fairly large-scale sense, as obtained, for example, from the Registrar-General's reports, are being referred to. The detailed study of infection is also important in elucidating the values of constants occurring in theoretical models, but this problem, which has been studied by R. E. Hope Simpson (1948, 1952), N. T. J. Bailey (1955, 1956) and others, is not being considered here.

The two chief theoretical points may be recapitulated as follows:

(i) The deterministic form of the Hamer-Soper model leads to damping of the epidemic oscillations (this damping is reduced but not eliminated by a shorter period of infectivity), in contrast with the quasi-stationary character of observed epidemics (cf. Wilson and Worcester (1945a)). On the other hand, the stochastic formulation leads to a stationary time-series with a pattern of oscillations depending on the community size. The theoretical size of these oscillations depends in a complicated way on the "fade-out" effect referred to in (ii) below, especially when the extension of the community in space is included in the model.

(ii) The recurrence of epidemics is made possible by the continual influx of susceptibles (in the case of measles, the continual growing-up of children into the critical age-period), but in the absence of "carriers" may be prevented by random extinction or "fade-out" of the infection. This is the more likely the smaller the community. This seems well-known to field epidemiologists, at least in the case of measles epidemics for small village or island communities, but a more quantitative observational study, linked to predicted theoretical relationships, seems desirable, and is one of the main objects of this paper.

It is perhaps some justification of the present approach that, in spite of the inevitable idealization of the mathematical model, preventing any exact quantitative comparison, two important characteristics of the pattern of measles epidemics were surmised theoretically and then checked observationally. The first was a statistical relation between the mean period between epidemics and the size of the community, the second was the existence of a critical community size above which "fade-out" of infection was unlikely. In order to assist the theoretical discussion of the latter phenomenon in the absence of detailed mathematical solutions, artificial realizations of

epidemic series for fair-sized communities have been generated with the aid of the Manchester electronic computer, and (while this part of the investigation is still incomplete) may be compared with actual epidemic statistics.

2. *Observational Material*

It has been common in previous studies of the periodicity of measles epidemics to quote the statistics for large urban areas, London, Glasgow or Manchester, and the biennial measles period-dicity often observed (in times of population stability) thus merely refers to such large units. It has been noted, for example, by Hope Simpson (in the discussion following Bailey (1955)) and by Bartlett (1956), that much longer periods are observed for smaller communities. A typical small town epidemic series, for Ffestiniog in Wales, was shown in my 1956 paper. In order to study the dependence of the epidemic pattern on town size more systematically, twenty towns of varying sizes were chosen from an A.A. handbook. The important requirement for the smaller towns was reasonable isolation, for obviously a satellite district near a larger town would merely reflect the characteristics of the larger community.

TABLE 1

Nineteen Towns in England and Wales Ranked According to Population (Average from 1940)*

Town	Population (Thousands)	Town	Population (Thousands)
(1) Birmingham	1,046·0	(11) Carmarthen	11·7
(2) Manchester	658·0	(12) Penrith	10·5
(3) Bristol	415·2	(13) Ffestiniog	7·14
(4) Hull	269·4	(14) Brecon	5·62
(5) Plymouth	180·0	(15) Okehampton	4·02
(6) Norwich	113·2	(16) Cardigan	3·51
(7) Barrow-in-Furness	66·4	(17) South Molton	3·07
(8) Carlisle	65·0	(18) Llanrwst	2·59
(9) Bridgwater	21·8	(19) Appleby	1·74
(10) Newbury	18·1		

* London was originally also included, but was dropped owing to the inconvenience of no over-all figures for London (except for the Administrative County) being quoted in the Registrar-General's weekly return.

The weekly measles notifications for the towns in Table 1 were then extracted from the Registrar-General's weekly returns of births, deaths and infectious diseases in England and Wales. It is hardly feasible to reproduce such statistics, or graphs of them, here* in full, but their chief charac-teristics will be summarized. The gradual change in the epidemic pattern from the continuous epidemic peaks and troughs in the case of the large towns like Birmingham and Manchester to the more spasmodic and of course smaller epidemics in the smaller towns was quite apparent. Two of the smallest towns considered, Cardigan and Llanrwst, were especially remarkable in experiencing only two epidemics each over the entire period for which statistics were available, 1940 to the beginning of 1956. A further feature, which is not unexpected if the greater spatial extent of the bigger towns is borne in mind, was the more "drawn-out" character of some of the epidemics in the large towns.

In order to investigate the time between epidemics, a precise definition of an epidemic is re-quired. This is rather arbitrary, but it is advisable to adopt a definite rule throughout. In the one adopted, weekly notifications had to rise above one case per 4,000 population, except in small towns for which just a few notifications would give this frequency. In the latter case, a minimum of 8 notifications in at least one week were required, with some further cases in previous or suc-ceeding weeks. (This last rule is perhaps rather too stringent and might tend to introduce a slight spurious relation between community size and epidemic period, but from inspection of the complete series of notifications no genuine epidemics seemed excluded by this rule in the smaller towns.)

* That is, in this paper. A complete set of graphs was displayed at the meeting.

It is known that epidemics in different towns, while necessarily having some linkage, do not always remain in phase. Some subsidiary investigation of this point was made by a deliberate choice of four further Welsh towns situated roughly on the rim and centre of a "wheel", with Ffestiniog and Llanrwst forming two of the towns on the rim. The remaining towns were Bala, Bethesda, Dolgelly and Portmadoc. These towns are too small for any very systematic epidemic pattern to be discernible, and some tendency to remain in phase and some tendency to get out of phase both seemed to be present. Thus in 1942 all towns were in phase except for Llanrwst, which missed altogether. Beginning in 1946, phase differences were considerable, Bethesda and Ffestiniog being in phase, Portmadoc not getting an epidemic until 1947, and Bala and Dolgelly until the beginning of 1948. Llanrwst again missed. The next general outbreak began with Llanrwst at the end of 1950, occurred in Bethesda, Portmadoc and Dolgelly in the middle of 1951, in Ffestiniog at the beginning of 1952, and again latest in Bala, at the beginning of 1953. Some of these phase differences are of course much too large to be compatible with direct infection from one town to another, and a much more detailed tracing of individual infections would be needed before a complete picture was available. This is rarely feasible except for very small communities.

3. *The Observed and Theoretical Relation between Measles Periodicity and Community Size*

A rough theoretical model of the distribution of times between epidemics when fade-out of infection occurs after major epidemics was referred to in my Berkeley paper. From equation (5.7) of that paper it was noted that the mode of this distribution is of the form $a + b/\sqrt{\varepsilon}$, where ε is the immigration rate for new infection. The mean of the distribution has a less simple mathematical expression, but may be taken approximately to be of the same form. If we now make the further rough assumption that immigration of infected persons will tend to be proportional to the town size N, it follows that the mean period between epidemics should for small towns be roughly of the form $a + c/\sqrt{N}$. This relation will, however, be inapplicable to large towns, for when a town is large enough for fade-out to be negligible, the mean period should conform more to the value given by the deterministic Hamer-Soper model, and in so far as the characteristics and communicability of the disease remain constant from town to town, the period will be constant within this range.

To compare the observed times between epidemics with these theoretical predictions, it was first necessary to obtain estimates of the mean periods. In the case of towns for which the weekly notifications formed an unbroken series, separate outbreaks were required to have an intervening "trough" of less than 1 notification per 20,000 for two consecutive weeks. The mean period was calculated from the complete periods observed in all cases, except in the case of the smallest towns, for which only one or two epidemics occurred. In such cases the evidence on the mean period provided by the time intervals at the beginning and end of the total time of the available records was important, for an alternative estimate is obtained by taking this total time and dividing by two more than the observed number of epidemics. Such an estimate is obviously biased, but *negatively*. When such an estimate still exceeded the first estimate, it was substituted.

It was interesting to find that the evidence for fade-out, judged by three or more consecutive weeks showing no notifications, went strictly with the order of towns given in Table 1, Birmingham and Manchester showing no fade-out, Bristol, Hull and Plymouth occasional fade-out, and all the smaller towns listed invariable fade-out. These three groups are divided by the vertical dotted lines shown in Fig. 1, in which a plot of mean period against $1/\sqrt{N}$ has been made. The mean periods there depicted are recorded in Table 2 and of course are subject to greater error in the case of the smaller towns, as both the dispersion of the individual periods is greater and there are less observed periods to calculate the average from. With this *caveat*, the observed relation, while naturally imprecise, seems entirely compatible with the predicted relation. For completeness the "linked" Welsh towns were also added, and again these fitted with the broad relation observed from the original nineteen towns chosen.

It would be possible to discuss to what extent apparent departures from a strict relation between mean period and town size might be real. For example, Cardigan gives a somewhat large period for its size, and Carmarthen a somewhat small one. This may well reflect a higher
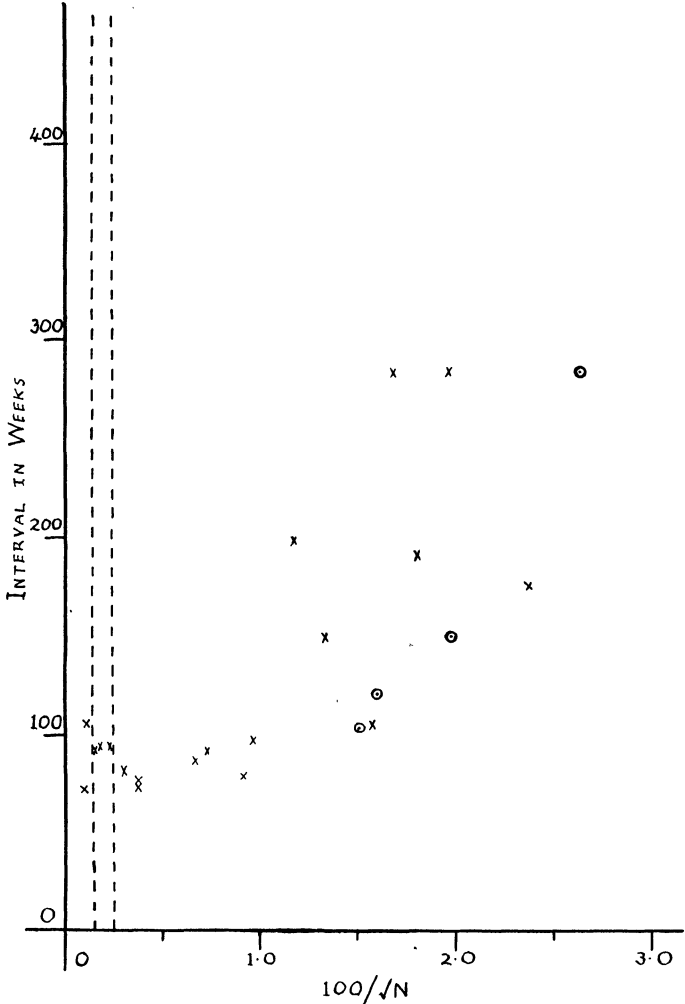
FIG. 1.—Observed relation between epidemic period and population (N).

TABLE 2

Mean Period Between Epidemics

Town			Period	Town			Period
(1) Birmingham	.	.	.	72·7	(13) Ffestiniog	.	.	.	199·0
(2) Manchester	.	.	.	106·0	(14) Brecon .	.	.	.	149·0
(3) Bristol	.	.	.	92·1	(15) Okehampton .	.	.	104·6
(4) Hull	.	.	.	93·0	(16) Cardigan	.	.	.	284·3*
(5) Plymouth .	.	.	.	94·3	(17) South Molton	.	.	191·3
(6) Norwich .	.	.	.	80·4	(18) Llanrwst	.	.	.	284·3*
(7) Barrow-in-Furness	.	.	74·0	(19) Appleby	.	.	.	175·2
(8) Carlisle .	.	.	.	75·2	(20) Bala .	.	.	.	284·3*
(9) Bridgwater	.	.	.	86·4	(21) Bethesda	.	.	.	104·0*
(10) Newbury .	.	.	.	91·6	(22) Dolgelly	.	.	.	150·0
(11) Carmarthen	.	.	.	79·0	(23) Portmadoc	.	.	.	121·9*
(12) Penrith .	.	.	.	97·6				

* Based on total time interval.

relative immigration rate for Carmarthen than Cardigan; but a discussion of such possible local differences was not intended. If it were attempted, further appraisal of the proximity of other towns would also be necessary.

4. *The Artificial Series Generated on the Manchester Electronic Computer*

Some discussion was given in my Berkeley paper of the likely effect on an epidemic series of the movement of infection over an extended area; but in the absence of a theoretical solution it is hardly possible to proceed very far without generating some artificial realizations based on the assumed model. A convenient way of allowing for spatial diffusion is to set up a "grid" of cells or "wards", such that movement of infectives from contiguous cells is possible.

Even on an electronic computer the number of events taking place increases very rapidly with the number of cells. While it was important to have enough cells to give a reasonable statistical picture, it was reckoned that a 6×6 grid was perhaps the largest that was feasible. The basic model used and the method of generating the artificial series were indicated in my previous paper, the only modification here being due to the spatial grid. Some of the simplifications may be felt to make the model academic, such as the use of transition probabilities homogeneous in space and time, and the use of a continuous removal rate of an infected person giving an average infectious "lifetime" of a fortnight. No seasonal variation in infectivity has been inserted. It should be recalled that observed seasonal variation may be a secondary aspect of school assembly and dispersal, and it may be argued that the effect of such heterogeneities in space and time should be allowed for (cf. Hope Simpson, in discussion following Bailey (1955)). However, it is again stressed that it is the large-scale features that are under investigation in a semi-quantitative way, and that if these appear promising these further elaborations can always be considered if required.

The use of a migration coefficient ε of infectives between cells separated by a common boundary was preferred to the use of a non-localized infectivity function (corresponding to movement of an infective to another cell and then returning), and for simplicity no movement of susceptibles was allowed (cf. Bartlett, 1956).

In view of the desirability of not making the community size larger than necessary, a size expected to be small enough to give invariable extinction of infection after one epidemic cycle (starting with a reasonable amplitude) was first tried. The scheme of coefficients and initial conditions, referred to as Scheme I, was as follows:

$\lambda = 0 \cdot 01$ (rate of infection per week per infected person per susceptible person in one cell);

$\nu = 0 \cdot 75$ (rate of entry in one cell per week of new susceptibles);

$\mu = 0 \cdot 5$ (rate of removal or recovery of infectives per week per infected person);

$\varepsilon = 0 \cdot 25^*$ (rate of migration per week per infected person in one cell to any one neighbouring cell with common boundary).

1	2	3	10	11	12
4	5	6	13	14	15
7	8	9	16	17	18
19	20	21	28	29	30
22	23	24	31	32	33
25	26	27	34	35	36

A ... B (left/right labels), C ... D (lower labels)

∗ is believed to be reasonably representative (corresponding to the rough diffusion /week suggested in Bartlett (1956) p. 103, provided the population density is that hester); but it would be of interest to investigate the effect of changes in ε.

In cells 1 to 9 (A quarter) and 28 to 36 (D quarter), each cell had 3 infected persons initially and 75 susceptible persons. The other two quarters B and C also began with 75 susceptibles per cell, but had no infectives initially. This choice was of course somewhat arbitrary, but for the infectives was intended to reflect some initial heterogeneity. As the mean number of susceptibles in the deterministic Hamer-Soper model is $\mu/\lambda = 50$, it will be seen that the initial value of "f", the factor I have used elsewhere (Bartlett, 1956) to indicate the size of the epidemic swing, was of the order of $\frac{1}{2}$*. The value of $\sigma = \lambda\nu/\mu$, which largely determines the period in the deterministic model, was $66\frac{2}{3}$, and was sufficiently near the value of $68\cdot2$ used by Soper and adopted in my Berkeley paper.

Over a long period of time the mean number of susceptibles for the entire grid under Scheme I should be about $50 \times 36 = 1,800$, and the mean number of infectives 54. If we note that for Manchester the mean number of weekly notifications was about 170 from 1917–51, and the mean number m of infectives in the model is twice this figure, i.e. 340, we find a ratio of m to total population size of about 1 : 2,000 for Manchester. Using the same ratio, an equivalent total population size is obtained of about 100,000 for Scheme I. With this size (as is discussed more fully in §5) infection faded out after one epidemic cycle, as expected both from the actual measles statistics and from the rough theoretical calculations in my previous paper.

In Scheme II the population size was doubled by doubling ν. The value of λ had then to be halved in order to keep constant $\sigma \equiv \lambda\nu/\mu$. In order not to increase the number of cells, the value of ε was halved; this implies the same population density in a community double the size, or $\sqrt{2}$ times the linear dimensions, as the diffusion or migration standard deviation is proportional to $\sqrt{\varepsilon}$. With Scheme II the equivalent population size is of the order of 200,000, which is getting into the observed critical region. On the non-spatial model assumed for previous rough calculations, it was still not large enough to maintain recurrent epidemics (at least for $f = \frac{1}{2}$), but it was suspected that differences in phase within the community would help to avoid infection fade-out. It was thus hoped that Scheme II, which corresponded to about the maximum population size that could be tolerated on the present basis,† even with an electronic computer, would begin to display the continuity of epidemics characteristic of very large communities.

In Scheme II the average number of susceptibles is 100 per cell, so the initial number was put at 150. The initial infected were as before. (It should be mentioned that owing to an oversight Scheme II was first started with only 75 susceptibles per cell. As this is below the threshold density, of course no major epidemic resulted and the infection began to fade out straightaway.)

The "weekly" numbers of infected and susceptibles in each cell, together with the weekly notifications, constituted the output of the computer. In addition to the total numbers for the whole community, the totals per quarter were summarized. The total weekly notifications, and those for each quarter of the grid, are shown in Figs. 2 and 3. The notifications for quarter D showed a somewhat anomalous drop before finally rising, so much so that the epidemics in B and C caught up with D. This seemed due to some peculiarity in the pseudo-random sequence used to generate the Monte Carlo sequence. Again, owing to an oversight, the sequence of "random" numbers used in Scheme II was begun as in Scheme I. This led to some similarity in behaviour at first, but this connection of the same numbers with the stages of the epidemic sequence finally disappeared of course as the sequence progressed. The notifications for Scheme II are recorded, as far as they were available when this paper was prepared, in Figs. 4 and 5.

5. *The Observed and Theoretical Critical Community Size*

The immediate and rather gratifying property with Scheme II is the tendency to avoid fadeout, manifested by the persistence of infection during the aftermath of the first epidemic. This is clearly sufficient, from the results recorded in Figs. 4 and 5, to begin a new epidemic,‡ even although infection at one stage faded out of all three quarters B, C, D and persisted only in A. It

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* A more relevant value of f is calculated at the "trough" of the epidemic; this turned out to be $\frac{2}{3}$.

† It is likely that the use of further approximations, in which the numbers of susceptibles and infectives are treated as continuous variables except at critical stages, would enable larger community sizes to be handled more efficiently, but the present scheme was most direct and was preferred at this stage.

‡ A graph showing the latest results available, including a substantial part of the second epidemic, was displayed at the meeting.

FIG. 2.—Artificial epidemic series, Scheme I.   Total notifications per week until "fade-out".

FIG. 3.—Artificial epidemic series, Scheme I.   Weekly notifications separately for each quarter of the total area.
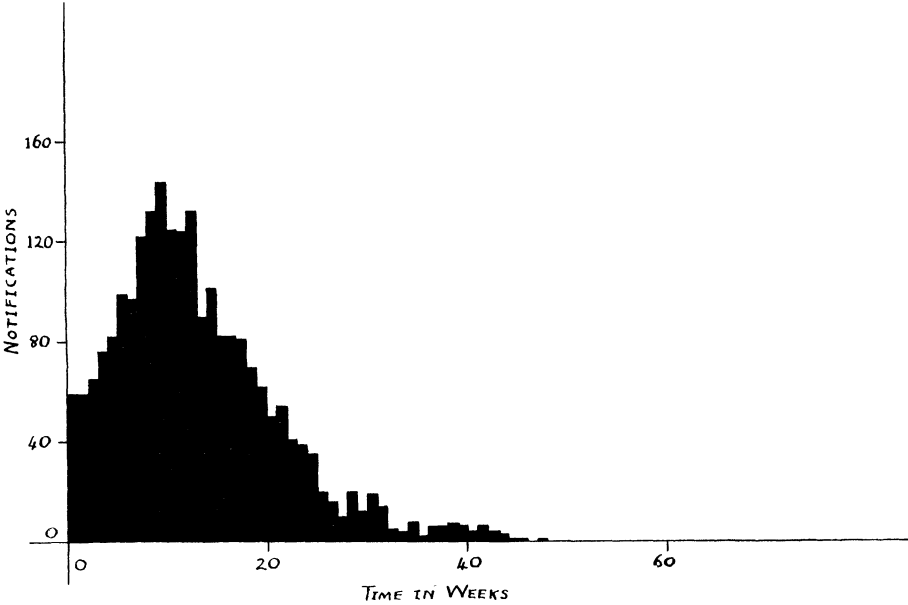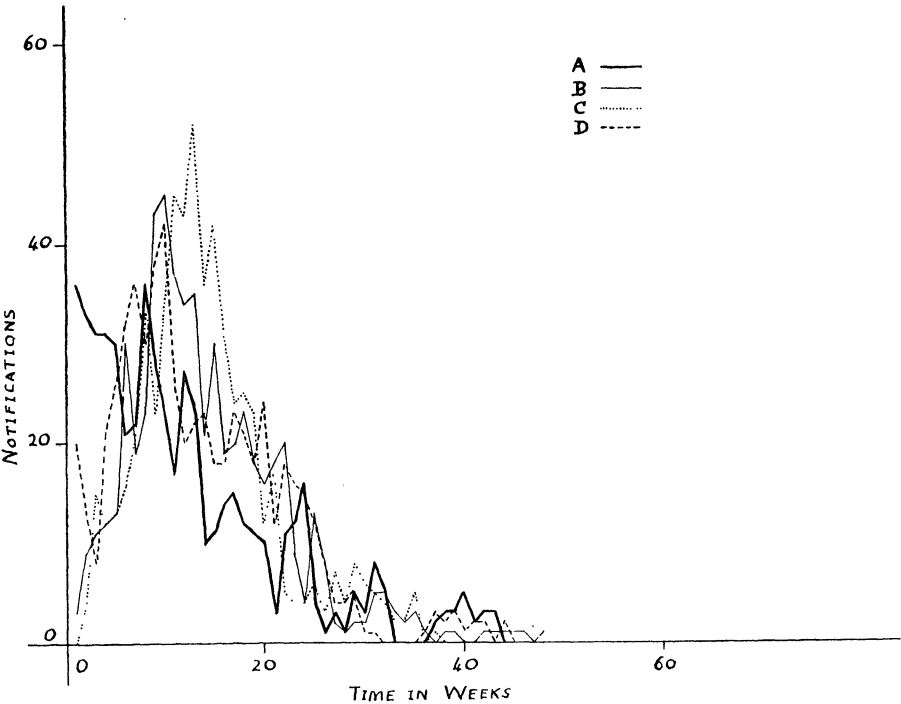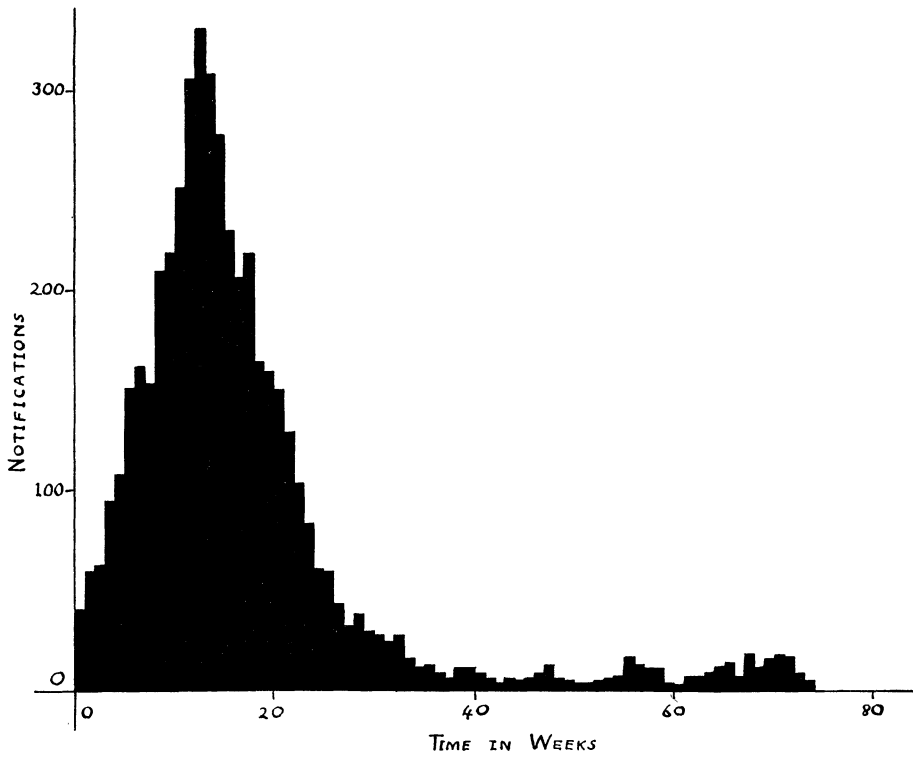
FIG. 4.—Artificial epidemic series, Scheme II.   Total notifications per week (to be continued).
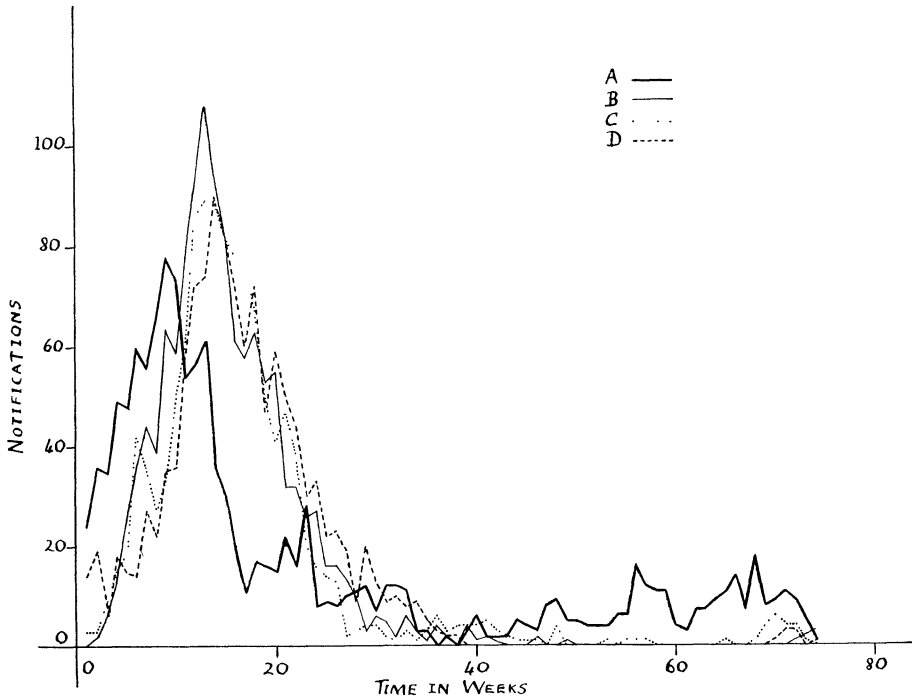

FIG. 5.—Artificial epidemic series, Scheme II.   Weekly notifications separately for each quarter of the total area.

is probable that the simplification of a continuous removal rate of infectives tends to favour persistence, partly owing to the increased deterministic damping to an equilibrium level, and partly because fade-out of infection can be less abrupt. There is also the difficulty that the stochastic "equilibrium" level of fluctuations is not known (the occurrence of local fade-out certainly complicates the theoretical picture, and no satisfactory method of calculating the amplitude of oscillations allowing for this fade-out effect is yet available); the artificial sequence should be allowed to continue, to see whether in the absence of fade-out a reaonsably stable series has been reached, and this point is being checked as soon as practicable. It should be recalled that the critical average number of infectives as calculated in my Berkeley paper dropped by a factor of 10 when the f factor was increased from $\frac{1}{2}$ to $\frac{2}{3}$; and a higher effective f in actual communities could reduce the critical size considerably.
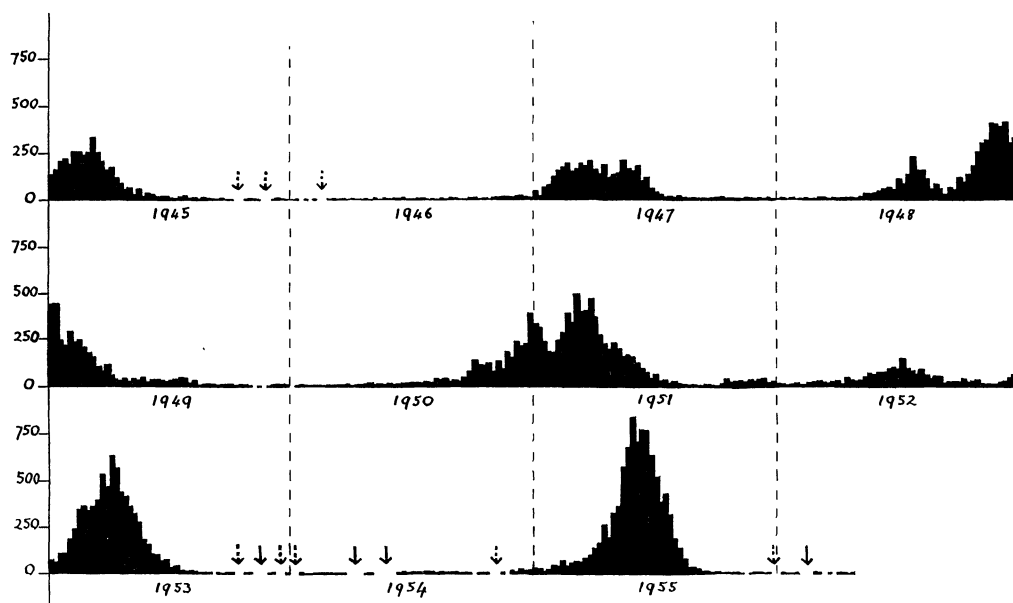
FIG. 6.—Observed weekly measles notifications for Bristol from 1945. Arrows (unbroken) denote absence of notifications for three or more weeks (broken arrows denote absence for exactly two weeks).

The community size of about 200,000 for Scheme II, while in the critical range for the sequence generated, must thus not be used as more than a pointer to the theoretical critical size which would result if all such factors were properly allowed for. Nevertheless, it is encouraging that it appears to be of the same order of magnitude as the observed critical size. It was noted in §3 that the three towns showing occasional fade-out were Bristol, Hull and Plymouth (the Bristol series from 1945 is shown in Fig. 6). If we define the critical size as one for which the chance of fade-out after a major epidemic is 50 per cent., then the two towns in the relevant range are Bristol and Hull (Plymouth giving rather a higher chance than this). The *observed* critical size is thus of the order of 300,000. It is of some interest that the average weekly notifications for Bristol and Hull were 67·0 and 57·0 respectively, rather nearer together than the corresponding total populations would have suggested. The corresponding critical size arrived at via the Manchester statistics would be 62 × 2 × 2,000, i.e. about 250,000, somewhat closer to the corresponding figure for the sequence of Scheme II.

It was considered whether an independent empirical estimate would be available from the weekly notifications for individual Manchester wards from 1925 (Linnert, 1954). By the pooling of contiguous wards, a decreasing probability of fade-out should be obtained. Unfortunately,

the theoretical functional form of the fade-out probability with the community size N (if the effect of size on the factor f is ignored) is e^{-aN}, and as the pooled wards are still unsegregated from the remaining wards, a further probability factor arising from the chance of immigration of infectives should be allowed for, as this can hardly be negligible. If the assumption made previously is retained, that the immigration rate is proportional to N, this extra factor would also be of the form e^{-bN}. Hence it would not be possible without independent information on the immigration rate to obtain by this means an estimate of the critical size of an *isolated* community. Of course the same effect must operate to some extent for entire towns like Bristol and Hull, giving an observed critical size somewhat less than the correct value for an entirely isolated town, but the effect here is probably not very great.
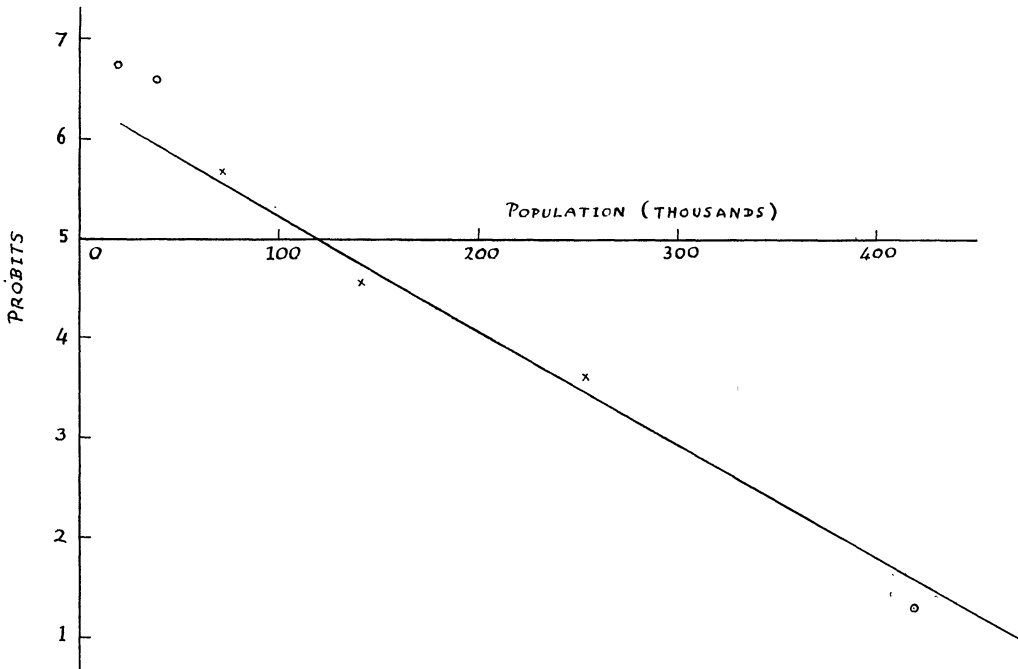
FIG. 7.—Observed relation between "fade-out" for area of Manchester and population of area.

However, in spite of the above limitation it was thought worth-while summarizing the information in the Manchester records. A cumulative set of wards was accordingly selected, with total populations ranging from about 20,000 for the smallest group (one ward only) to about 400,000 for the entire set available. In the period 1925–50 inclusive*, thirteen major epidemics occurred in Manchester, the first at the beginning of 1926 and the last at the end of 1950. Hence we have twelve epidemics (omitting the last) for checking fade-out effects. The information so obtained is shown in Table 3. In spite of the suggested theoretical form of the extinction probability, it was empirically more convenient to use a rough probit analysis to obtain the 50 per cent. point for fade-out. The successive observed probabilities are of course not independent, and no fit beyond the first visual line was attempted (except to note that the "working probits" for 0 per cent. or 100 per cent. probabilities would not greatly affect the estimate of where this first line cuts the 50 per cent. probability, this being at about $N = 120{,}000$—see Fig. 7). Remembering that this is necessarily an underestimate of the critical size of an isolated community, owing to immigration effects, we have reasonable consistency with the previous estimate from separate towns, of about 250,000. The difference suggests a rather high "immigration" effect between the Manchester

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* Although measles notifications were made compulsory in Manchester from 1917, alterations in ward boundaries make the year 1925 a preferable starting point.

wards, though the figures are too roughly determined to justify any more elaborate discussion of this point. It might be remembered that any investigation on observed fade-out must be affected by notification omissions.* Moreover, no attempt has been made to obtain figures for the populations at risk, and information on the numbers of susceptible children would have been useful. In the absence of such information no indication of the size of the f factor is available. Evidence from other sources suggests that for large towns at least the swing in numbers of susceptibles may be relatively low; Hedrich (1933), for example, gives an estimated range for Baltimore (U.S.A.) of 30–50 per cent. of the total child population under 15, equivalent to an f factor of 30 per cent./40 per cent. or $\frac{3}{4}$. If this were a representative figure, the theoretical critical population size would be comparatively small (cf. p. 53). However, the complication that the peak incidence occurs not in the youngest children, but in children of early school age (see Wilson *et al.*, 1939) stresses that the availability of the total susceptible population is not uniform, and may imply a smaller "effective" population of susceptibles. This may be perceived from the extreme case when, say, all children under 5 are supposed completely protected from infection.

TABLE 3

Observed (Aggregate) Fade-out Effect in Manchester Wards

Ward	Population (Thousands)	Cumulative Population	Number of Epidemics followed by Fade-out	Probability of Fade-out
Ardwick	18·4	18·4	12	100%
St. Mark's	19·8	38·2	12	100%
St. Luke's	20·6			
New Cross	13·0	71·8	9	75%
All Saints	13·1			
Beswick	22·1			
Miles Platting	14·9	140·8	4	33%
Openshaw	18·9			
Longsight	26·1			
Gorton North	22·4			
Gorton South	27·0			
Bradford	26·0			
St. Michaels	11·8	254·1	1	8%
St. George's	16·5			
Medlock Street	15·8			
Moss Side West	19·8			
Moss Side East	17·1			
Rusholme	20·6			
Newton Heath	21·3			
Collyhurst	12·6			
Harpurhey	18·9			
Cheetham	22·6	419·3	0	0%

As a further check on the "fade-out" estimate for non-isolated urban areas, the detailed measles figures for St. Pancras given by Stocks and Karn (1928) were examined. A similar analysis was made as with the Manchester wards, aggregating the squares into which these authors divided the total area they were studying. As, however, only two major epidemics occurred during the three year period available, March, 1924–March, 1927, no more than a very crude check was possible. The results are summarized below, two consecutive 10-day periods without further notifications being taken as the fade-out criterion.

TABLE 4

Aggregate area* . . .	H16	+J16	+H15 +K16	+G15, 16 +J17	Total area†
Total number of notifications .	787	1,616	2,834	4,628	6,468
Number of epidemics followed by fade-out	2	1	1	1	0

* For key, see Table 9, Stocks and Karn (1928).
† Excluding "fringe" squares where less than 50 notifications occurred, viz. D15, F14, 17, K15, L17.

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* For statistics of notification omissions, see, for example, Chope (1940). [I am indebted to Dr. Hope Simpson for this reference.]

It will be seen that the median area giving 50 per cent. fade-out had 2,834 notifications, compared with the figure 6,547 for the St. Pancras district, or 43 per cent. The total child population (under 15) was 54,600 in 1924, so for the median area it was about 23,500. Using the Manchester conversion ration of child to total population of $4 \cdot 43$ (Linnert, 1954), the equivalent (Manchester) total population was 110,000, compared with the critical figure of 120,000 obtained from the Manchester wards. (The agreement is closer than we have any right to expect, bearing in mind the 3 : 1 population range in the middle three entries of Table 4.)

Summary and Conclusion

To sum up the results presented in this paper, these have been concerned with the confirmation of two phenomena predicted from the stochastic model for measles previously put forward The first is a relation between measles periodicity and community size, provided the communities are comparatively isolated and do not exceed a certain critical size. The second is the existence of such a critical size. For the model this has been demonstrated, by means of an artificial series generated on an electronic computer, to be of the order of magnitude of 200,000 total population (in terms of Manchester figures), at least if the initial swing of susceptibles proves sufficiently representative of the quasi-equilibrium amplitude of such swings. The observed critical size (again in terms of Manchester figures) appears to be about 250,000. For non-isolated urban areas, the critical size is less, due to the immigration of infection from surrounding districts, and appears to be only about half the critical figure for entire towns.

Provided the main features of the present model appear reasonable, one of the points requiring further study is the effective swing of susceptibles, in both theory and practice. Admittedly the idealized model put forward still contains various limitations, some of which have been noted. It is, however, suggested that no previous (e.g. deterministic) model of measles could cope with the large-scale type of data collected and here presented, whereas by contrast characteristic properties of these data were predicted by means of the model. Such predictions have been broadly confirmed from the statistics.

Acknowledgments

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DISCUSSION ON PROFESSOR BARTLETT'S PAPER

Dr. REID: It gives me great pleasure to propose a vote of thanks to Professor Bartlett for this important contribution to theoretical epidemiology. In the discussion after a paper by the late Professor Greenwood, Professor Kendall asked whether this sort of approach to epidemiology was better made by a doctor with some taste for mathematics or a mathematician more fully competent to deal with the analytical complexities involved. As a medical teacher of epidemiology who lacks that competence, I for one welcome Professor Bartlett to this field. Although Jonathan Swift in his book published in 1720 on *Precedence between Physicians and Civilians* described himself as "a master of the stochastic art" he did not say it was a distinguishing feature of the professional; and I shall be singularly relieved if others deal with the mathematics and leave me with the measles.

Measles has always had obvious attractions for the epidemiological theorists. Diagnosis is reasonably certain and the disease is generally notifiable throughout the country. But here we come at once to the question which haunts these theoretical studies—are the basic assumptions reasonable? I hope that Professor Bartlett's illusions about the noblest profession will not be shattered by the cynical comment in a recent *Lancet* leader. Discussing age differences in reported measles attack rates the *Lancet* points out that the trends observed "might be related in some way with the 1948 increase in the fee from 1s. to 2s. 6d. for notifying measles. It is not an uncommon experience elsewhere to find that both measles and whooping cough notifications showed a definite increase as practitioners realized the advantage. Many said quite frankly that they would not bother to write out and post a certificate for a shilling, when all the other diseases were worth half a crown". As Mr. Bailey has shown by his demonstration of the positive correlation between tonsillectomy and circumcision rates in Cambridge undergraduates and the fees of the public schools they attended, the dollar sign has not yet been taken out of medicine. My point is not entirely frivolous, for the decision of what to call an epidemic in small towns of less than 5,000 population may be affected by considerations of practitioner habits and pressure of work and the probability of under-reporting. A Poisson expectation may not be entirely appropriate to a localized outbreak of an infectious illness but it would seem to me that if the standard rate is 1 case per 4,000 population Professor Bartlett has been unduly strict in demanding at least 8 notifications in a week in small towns of 5,000 or less before counting the end of an inter-epidemic interval. Since under-reporting is a serious risk, the spurious correlation between community size and inter-epidemic period may be even greater than Professor Bartlett fears.

In section 3 of his paper, Professor Bartlett shows, however, that even in the large town the mean period between epidemics is negatively associated with population size. In his discussion of this result, he rather implies that any inconsistencies observed may be the result of differences in the rates of migration into these communities. Certainly a good fit is obtained between observation and expectation based on the theory expressed in the formula (5.7) of his Berkeley paper which gives the mode of the distribution of intervals as $a + b/\sqrt{\varepsilon}$ when ε is the immigration rate for new infection. But in practice this rate is not estimated directly but simply taken as proportional to N, the size of the population. This in turn means that, as far as migration is concerned, the goodness of fit may be almost entirely coincidental. In Frost's original formulation of the measles epidemic problem, frequency and effectiveness of contact between infective case and susceptible plays a dominant role in determining the epidemic pattern. In larger towns then, differences in the manner of life with multiple opportunities for contact might well prevent "fade-out" quite apart from any immigration of infective cases and immunes from outside. I suggest, therefore, that the term "migration" should, in the present state of our knowledge, be interpreted in the widest possible sense.

The problem of movement into and within populations comes up again in the study of the spatial distribution of disease incidence. In some early work on the spread of infection from smallpox hospitals, the occurrence of cases outside but close to the hospitals raised the possibility

of widespread aerial dissemination from the hospitals. Field studies soon showed, however, that such cases were more likely to arise from contact with patients who refreshed themselves at one of the local hostelries just before admission to the hospital. The realities of the situation should not be too lightly dismissed. In measles epidemics in circumscribed urban areas, the relative importance of chance factors in contact makes stochastic models even more appropriate than in the study of epidemic behaviour in time in large populations, but it is in just these circumstances that the heterogeneities in space and time pointed out by Hope Simpson may bulk so large. A diagram of the epidemic spread in an outbreak among children in 6 Southall schools some years ago may make these points clear. Infection spread from area to area largely through the movement of susceptible children from neighbouring sectors to the corresponding schools and at school the duration of infectious exposure before removal is inevitably much shorter than a fortnight. For the larger sectors which Professor Bartlett had in mind, such considerations may not be so apposite, but he might earn the gratitude of epidemiologists if he would return to the attack on the problems of small-scale investigations such as the recent survey by Dr. Nicol in the parishes of the Isle of Wight.

A few days ago I was gratified and flattered to receive a request from Professor Kendall's department for any reprints which I might still have available. The sting was in the tail: "papers on the practical aspects of statistics", it said "are not required". Professor Bartlett may wish to be reassured that his paper is not going to be dismissed on the score of immediate application in epidemiological practice; but he should be warned that if he continues in this way the value of the stochastic outlook in epidemiological forecasting will be appreciated by practical men sooner than he now anticipates.

Mr. N. T. J. BAILEY: It gives me great pleasure to have the privilege of seconding the vote of thanks to Professor Bartlett.

The application of stochastic processes to the mathematical theory of epidemics gives rise to several inter-related difficulties. In the first place there is the purely mathematical aspect: one is liable to arrive very quickly at an intractable mass of algebra. Indeed, merely to write down the equations for a continuous-infection process in a two-dimensional continuum uses up quite a lot of paper. Secondly, there is the difficulty of hitting on a model that is sufficiently close to the epidemiological realities, without being too complicated to handle either verbally or mathematically.

Professor Bartlett's previous work has already contributed considerably to our understanding of the behaviour of recurrent epidemics. When the spatial element is absent considerable progress can be made along purely mathematical lines; but in the extension to planar processes the difficulties are formidable. One way out is to use the Monte Carlo method of building up mock epidemics in the way that Professor Bartlett has done. The work described in this paper is undoubtedly a landmark of major importance in the advancement of epidemic theory.

As with all good applied mathematics, the purely abstract development must be constantly checked against experiment and observation. It is therefore particularly gratifying to see how Professor Bartlett has managed to establish a broad correspondence between his theoretical results and actual epidemiological data. This is a particularly difficult thing to do in the field of large-scale phenomena; the corresponding procedure is much easier when we deal with epidemic processes in small groups like families or school classrooms.

One of the signs of the times is the use of an electronic computer to handle the Monte Carlo experiments. Provided they are not made an excuse for avoiding difficult mathematics, I think there is great scope for such computers in biometrical work. To speak only of the epidemiological field, there are several applications that come to mind, apart from the one made here. In this one wants to study the large-scale behaviour of epidemic processes in time and space under a wide variety of conditions.

In small-scale studies, on the other hand, we are more concerned to fit theoretical models in detail. We want to deal with the distributions of latent periods and infectious periods, and this involves the estimation of several parameters—not less than four in the simplest case, and appreciably more in models that are only slightly more realistic. We may before long, especially if further data become available, be faced with the problem of estimation on a considerably increased scale. It will certainly be worth seeing what help can be obtained from electronic methods of computation in applying, say, standard maximum-likelihood scoring techniques.

Another aspect I should like to mention is the perennial dream of epidemiologists, mathematical and otherwise, of being able to predict the course of an epidemic from its initial stages. Statistically speaking, this is in general likely to be unsatisfactory because of the inherent lack of information in the data. Nevertheless, when records for the first few weeks, of, say, a polio epidemic have been accumulated, the kind of predictions *potentially* available must become more precise. If there were sufficient knowledge of the epidemiological state of a community when an epidemic

started it should be possible to specify the course of the outbreak in terms of probability statements, which became progressively more accurate. It would, of course, be necessary to utilize a great deal of detailed social, clinical and epidemiological information, but such a procedure would, if it could be developed, be of considerable value to Medical Officers of Health, for instance.

I look forward to the development of these and many other applications suggested by the contents of Professor Bartlett's paper.

The vote of thanks was put to the meeting and carried unanimously.

Colonel W. BUTLER: Measles more than any other disease has been the plaything of the statistician. Perhaps this is due largely to the fact that its events, long recognized as in some way periodic, recur frequently and in high numbers.

I am not quite clear—beyond what is inferential from known facts—what Professor Bartlett's thesis is as to the effect of size of population upon the periodicity of measles epidemics. Certainly of far greater effect upon the character and periodicity of measles outbreaks than the size of the community attacked is the susceptibility-immunity constitution of any such unit of population. When measles attacks primitive races which for generations have been insulated nearly everyone succumbs; it is virtually universal in its incidence and it kills at a rate which is never experienced among inured peoples. Whole native tribes have in the past been completely eliminated by epidemics of measles. From that extreme of virtually universal susceptibility to the immunity constitution of population, such as is represented in this country, is a wide range mainly, but not wholly, determined by this circumstance. Of varying immunity and age-constitution, small and sheltered communities, isolated villages and sleepy towns will, of course, give developmental and periodicity patterns of epidemicity different from those of larger groups of population, densely packed and with a higher degree of intercommunication and commingling of persons.

Some 50 years ago I had during a number of years the opportunity of observing the incidence of measles in a suburban population in relation to its immunity constitution.* Out of 14,000 or so persons definitely exposed to infection by its outbreak in the home it was found that about 78 per cent. at all ages and 97 per cent. of persons aged 15 and upward had already suffered the disease. Of those at all ages who were exposed who had already suffered from it less than 1 per cent. were attacked; of those who gave no history of previous attack 66 per cent. succumbed. That of those not already protected by a previous attack 66 per cent. only failed and 34 per cent. escaped when exposed to the infection, contrasts with the almost universal incidence where infection is first introduced among aboriginal peoples, or returns only after a long interval, as in the Faroes, where in 1846 it reappeared after an absence of 65 years.

If you have already suffered from measles you have had conferred upon you in nearly all cases, a protection from future attack. If you have not had measles after six months of age—under six months you do not get it—until the end of life you are susceptible to attack if exposed.

Over 5 years of age, as the years advance the liability to attack gets rather less. I have suggested, and it has since become an almost accepted theory, that those not observed previously to have suffered, who have not, when known to have been exposed, been attacked, have acquired an active immunity by minor non-critical doses of the infection and, have built up at least a temporary mmunity.

Passing from the observed facts determinant of the nature of measles prevalence to description of its incidence and the periodicity of its recurrences in a population habitually subject to its presence, we enter a field of observation obscured in the past by lack of statutory notification.

As Professor Bartlett rightly says, "in order to investigate the time between epidemics", precise definition of what we mean by epidemic is required. Epidemic incidence is sharply defined when identified with "weekly notifications [which] had to rise above one case per 4,000 population except in small towns". But the definition, admittedly arbitrary, is *sui generis* and so inapplicable to the epidemicity of other diseases of markedly lower prevalence. Above all, it is fundamentally defective in that it fails to include commencing and ending phases of epidemic incidence, essential data, obviously, in any statement of inter-epidemic periodicity.

In an investigation of the epidemic features disclosed by statutory notification of measles, I examined at the time the returns of the first 8 years of its operation, 1940–47. As defining epidemic I took "the succession of phases in a continuum of growing, enduring and declining incidence which from a commencing rise develops a prevalence, for a time, above the mean of its weekly serial incidence and thereafter from its peak declines to sustained low levels or, it may be, an enduring zero".

* "Measles", *Proc. Roy. Soc. Med.* (1913), **6**, Sect., Epidemiology and State Medicine.

From the analysis of 8 years of measles notification, there emerged repetitive patterns of incidence the cycles of which conformed generally to well defined types.

Graphs* of the continuous incidence of measles, epidemic and sub-epidemic, during this period when for the first time this was possible, showed 4 completed epidemics, each of some 20 months duration and separated by a low level of sub-epidemicity in the intervening four months before commencement of another epidemic. Each succeeding cycle occupied completely the 24 months of the respective two-yearly periods. Beginning in January of one year, an epidemic reached its peak in March of the next and by September following had fallen to low levels definitely sub-epidemic and virtually of uniform incidence until the commencing rise in January of the following year. The duration of each phase of incidence is very different from what formerly was taken to be the case, and from what would be given by graphs of epidemic incidence as defined by Professor Bartlett. Instead of brief inter-epidemic periods of some 4 months, sub-epidemicity of over a year's duration would be shown and in lieu of the lengthy periods of developing, mature and declining epidemicity, high peaks of an intensive shortened incidence would alone be shown. The cycle of biennial periodicity would be apparent in either graph, but the recurrencies would be of wholly different phenomena.

In the more inclusive survey, the periodicity disclosed is richer in repetitive coincidences. Characteristic phases, the summer hump and the autumn notch, in the first year of developing epidemicity and other features throughout share in the rhythmic recurrences of now modified major events and their inter-relations. Generally the pattern was the same for England and Wales, London and the Great Towns, counties such as the West Riding, Durham and Middlesex, and great cities such as London and Manchester.

As in a composite photograph, composite graphs of two or more epidemics emphasized the more periodic and outstanding features.

Examination on similar lines of smaller communities was not undertaken, but it is assumed that in them only the most rudimentary, if any, conformity to type would be detected.

Dr. J. O. IRWIN: I should like to express my admiration, not only for this paper, but for all that lies behind it. Professor Bartlett seems to me to be the only person who has got near to accounting on theoretical grounds for the observed features of measles epidemics. In this particular paper he has concentrated on two points; a relation between measles periodicity and community size and the critical size below which this relation holds.

This particular work encouraged me to look at the paper which he read to the Symposium at Berkeley in California on the theory of recurrent epidemics and I was amazed to see how much had been done. For the first time I felt I really understood the relation between Soper's original deterministic model for measles epidemics and the new stochastic model and how the newer theory can account for the limitations of the old. The difficulty is best described in the quotation from Wilson and Worcester made by Professor Bartlett himself in the Berkeley paper: "It must be admitted that the phenomenon of recurrent measles epidemics gives no clear evidence of any damping. This creates something of a difficulty with the theory in respect to the prediction of damping and throws some doubt on the reality of periods; it is possible that measles simply dies out and then returns and under such a hypothesis there would seem to be no reason to expect either definite periods or damping to be observable by comparing successive epidemics."

Bartlett has got us out of this difficulty by analysing the effect of the more complete stochastic formulation and considering the spatial or topographical factor, that is, allowing for the fact that communities are not in fact closed. I have not yet fully understood all the intricate mathematical technique connected with the spatial problem, I hope to do so in time; but I did understand, I think, his treatment of the extinction problem and I did realize the skill with which his mathematics is directed to practical ends.

I was stimulated to a few general reflections on statistical method. There is always a tendency for statisticians to become slaves of their own techniques. It does not matter, provided we have the ability, how apparently recondite are the mathematical methods, if they are directed towards ends which are important and are finally put to the test of comparison with observation. It is very easy to overestimate the importance of significance tests; after all, it matters little if an effect is significant if because of its magnitude say, or on other grounds, it is unimportant. Too great an obsession with significance tests is apt to empty out the baby with the bath. This work on measles illustrates the point very well. It is to understanding the nature of the epidemic phenomenon that all this work is directed and tests of goodness of fit might only impede progress at this stage.

* *Bulletin of the Ministry of Health*, April 1946, April 1947, May 1948, and paper on "Whooping cough and measles", *Proc. Roy. Soc. Med.* (1947), **40**, Sect. Epidemiology and State Medicine.

I had the curiosity to turn up the discussion on Soper's original paper, read to this Society in 1929, at which I was present. Sir William Hamer proposed the vote of thanks. Among other things he said: "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 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." My imagination boggles at trying to suggest what Sir William Hamer would have said Bartlett had done with Galatea.

Mr. J. C. Gower: I should like to describe in a little more detail the programme for the Manchester computer which has produced the results that Professor Bartlett has been discussing.

A description of the computing procedure required in this type of problem can be found in Bartlett, *Applied Statistics*, 2, No. 1, 1955. The epidemic model investigated there is much less elaborate, but is similar in principle to the model discussed to-day. The basic computing cycle is divided into two parts, first to calculate the time to the next event, which is assumed exponentially distributed, and secondly to decide which of the 228 possible events has occurred and to act accordingly. For both of these steps a random number is required. Owing to the fact that the computer makes not infrequent mistakes and in view of the apparent impossibility of getting an overall check on the accuracy of this type of calculation, it is necessary to repeat the calculations. For this purpose it is convenient to use one of the methods for producing pseudo-random numbers. In addition, the calculation is programmed in steps taking about a minute each which are then repeated and checked automatically. If the check fails the previous minute's calculation is repeated again, and checked and so on until two consecutive repeats agree.

Some difficulty was experienced in deciding which of the many available methods for producing pseudo-random number sequences would be the most suitable. In fact I carried out an investigation into three of the more simple methods, paying particular attention to the dependence of the successive groups of digits in the resulting sequences. Any undue bias of this sort could lead to rather peculiar results, in extreme cases probably producing an epidemic only in the lower right hand ward. These investigations indicated that the well known mid-product process was adequate for the purpose. In this method two numbers N_1 and N_2 are chosen at random, both of d digits. The product N_1N_2 is found and N_3 is equated to the middle d digits of the resulting $2d$ digits. The process is then repeated on N_2 and N_3 etc. The method has the disadvantage that it can get into a loop, repeating the same numbers in sequence, and in particular of looping on zero. To minimize this danger I adopted the following scheme:

The random numbers are produced in batches of 64. Each batch is tested for divergence from the expected number of unit digits. If the test fails a new batch is produced and tested. If three successive batches fail the machine stops and hoots continuously. As a further precaution for each run of the programme, a new pair of random numbers is used to start off the mid-product process.

Only once in the sixteen months during which the programme has been running have three successive batches of numbers failed. The random numbers x produced are assumed uniformly distributed between 0 and 1 and the exponential time interval t is obtained by the formula

$$t = -\log x,$$

allowance being made for the mean of the distribution.

Finally some figures concerning the time taken to carry out the calculations. It should be remembered that the computer at Manchester is quite old for an electronic machine and more modern equipment would be considerably faster. Furthermore some improvement could probably be obtained by re-coding parts of the programme.

				Epidemic Time	*Machine Time*
Scheme I	.	.	.	49 weeks	40 hours
Scheme II	.	.	.	105 ,,	159 ,,

These figures are possibly a little inaccurate as I have not been running the programme myself and have had to estimate them from the number of occasions when I have received results. In an hour's computing time the machine can deal with some 2,000 events.

Mr. D. G. Kendall (amplified in writing): Professor Bartlett's fascinating study of the development of an epidemic in space and time has encouraged me to collect some fragmentary results on the behaviour of a similar but much simpler deterministic system. Consider an infinite uniform two-dimensional population for which σ denotes the number of persons per unit area.

We shall count as members of the population only those individuals who are old enough to catch and transmit the disease (thus, if the "disease" is a rumour, we shall exclude those children who have not yet learnt to talk), and the problem will be further simplified by neglecting the effects of spatial migration, the recruitment of fresh susceptibles from lower age-groups and mortality from other causes.   There will accordingly be no question of the epidemic's recurrence in time, but it is still possible to ask non-trivial questions about its spatial development, the extent to which an initially local infection can ultimately leave its mark on the whole population, and so forth. These are questions which must necessarily be asked in any thorough study of spatio-temporal epidemic behaviour although they are rather different in character from the questions with which Professor Bartlett has been concerned in his present paper.

If dS denotes an element of area then we may follow Kermack and McKendrick* and classify the σdS individuals resident in dS as follows:

$$x \, \sigma \, dS \quad \text{``susceptibles''},$$
$$y \, \sigma \, dS \quad \text{``infected-and-infectious''},$$
$$z \, \sigma \, dS \quad \text{``removed''},$$

where as usual the third class (of "z-men") contains isolated infected cases, persons who have died from the disease and persons who have recovered from it and are now immune.   (It is the separation of the second and third classes which distinguishes the present model from that of Rushton and Mautner.†)   The classification is supposed exclusive and exhaustive, so that

$$x + y + z = 1 \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

at all times and at all places (each term on the left-hand side of this equation can vary with the time t and with the position P in the plane).   We now write down a set of differential equations analogous to and modelled on those of Kermack and McKendrick.   They will represent the joint effects of (i) *removal* (converting y-men into z-men) acting at a rate proportional to y and (ii) *infection* (converting x-men into y-men) acting at a rate jointly proportional to x and to a (spatial) moving average of y :

$$\left. \begin{aligned} \frac{\partial x}{\partial t} &= - \beta \sigma x \tilde{y}, \\[6pt] \frac{\partial y}{\partial t} &= \beta \sigma x \tilde{y} - \gamma y, \\[6pt] \frac{\partial z}{\partial t} &= \gamma y. \end{aligned} \right\} \quad . \quad . \quad . \quad . \quad . \quad (2)$$

Here β and γ are constants; β is an intrinsic infection rate and γ an intrinsic removal rate, and the explicit factor σ in the term $\beta \sigma x \tilde{y}$ is needed to keep β free from density-dependence.   The quantity $\tilde{y}$ is obtained from y as follows:

$$\tilde{y}(P, t) = \iint \lambda(PQ) \, y(Q, t) \, dS. \quad . \quad . \quad . \quad . \quad (3)$$

Here dS is an element of area located at Q, and the non-negative coefficient $\lambda(PQ)$ weights the contributions of the y-men at Q to the infection of susceptibles at P.   The integration at (3) is to be extended over the whole plane and by the suitable adjustment of β we can arrange that‡

$$\lambda(r) \geqslant 0; \iint \lambda(PQ) \, dS \equiv 2\pi \int_0^\infty \lambda(r) r \, dr = 1. \quad . \quad . \quad . \quad (4)$$

Let us now apply the operation "$\sim$" to the third of equations (2) to get

$$\frac{\partial \tilde{z}}{\partial t} = \gamma \tilde{y},$$

* For a summary of their work see my paper in the *Third Berkeley Symposium*.
† *Biometrika*, **42**, 126–132.
‡ It is reasonable to require the integral at (3) to converge when y is a constant, and this makes it possible to effect the normalization (4).

and divide this into the first of equations (2). It will then follow that, for a fixed point P of the plane,

$$\frac{dx}{d\tilde{z}} = -\sigma x/\rho \qquad . \qquad . \qquad . \qquad . \qquad . \qquad . \qquad (5)$$

where $\rho \equiv \gamma/\beta$. Thus, if initially

$$x(P, 0) = 1 - \varepsilon, \qquad y(P, 0) = \varepsilon, \qquad z(P, 0) = 0 \qquad . \qquad . \qquad . \qquad (6)$$

(when ε is a function of P), we shall have

$$x(P, t) = \{1 - \varepsilon(P)\} \, e^{-\sigma \tilde{z}(P, t)/\rho}. \qquad . \qquad . \qquad . \qquad . \qquad (7)$$

On combining this with (1) and with the last of equations (2) we get the equation

$$\frac{1}{\gamma} \frac{\partial z}{\partial t} = \varepsilon + (1 - \varepsilon)(1 - e^{-\sigma \tilde{z}/\rho}) - z \qquad . \qquad . \qquad . \qquad . \qquad (8)$$

which, with the initial condition $z(P, 0) \equiv 0$, is to determine z for all P and t. The other dependent variables x and y will then be determined by (7) and (1).

An adequate treatment of the equation (8) presents some difficulty, even if (as we shall) we choose a very simple initial condition such as

$$\begin{aligned}\varepsilon(P) &\equiv \alpha > 0 \qquad (OP < a), \\ \varepsilon(P) &\equiv 0 \qquad\quad (OP > a).\end{aligned} \Big\} \qquad . \qquad . \qquad . \qquad . \qquad (9)$$

Some progress can be made if we assume that the λ-function satisfies the condition,

$$\begin{aligned}\lambda(r) &> 0 \qquad (0 \leqslant r < b), \\ \lambda(r) &\equiv 0 \qquad\quad (r \geqslant b).\end{aligned} \Big\} \qquad . \qquad . \qquad . \qquad . \qquad (10)$$

It is clear from (2) that x decreases and z increases when $t \to \infty$, and both are bounded so that (using (1)) we must have $x \downarrow X$, $y \to Y$ and $z \uparrow Z$, where $X + Y + Z = 1$. Again, (2) shows that $Y \equiv 0$ and so $X \equiv 1 - Z$; thus only $Z(P)$ need be found if we wish to study the ultimate effect of the epidemic. Now, from (8),

$$Z = \varepsilon + (1 - \varepsilon)(1 - e^{-\sigma \tilde{Z}/\rho}) \qquad . \qquad . \qquad . \qquad . \qquad (11)$$

and

$$\tilde{Z} = \frac{\rho}{\sigma} \log \frac{1}{1 - Z} \qquad (OP > a). \qquad . \qquad . \qquad . \qquad . \qquad (12)$$

It is clear that $Z(P) > 0$ whenever $\varepsilon(P) > 0$ and so, in particular, Z is positive when $OP < a$. Suppose *if possible* that $Z(A) = 0$ for some point A of the plane; then $\varepsilon(A) = 0$ and $\tilde{Z}(A) = 0$. But now (10) implies that $Z(P) \equiv 0$ almost everywhere inside the circle centred at A and of radius b, and on continuing this argument in the direction AO we should arrive at a contradiction in finitely many steps. We conclude therefore that $Z(P) > 0$ for all points P; that is, *the effects of the epidemic ultimately extend over the whole plane.*

To make further progress let us *assume* (*this ought to be studied further*) that $Z(P)$ decreases steadily as OP tends to infinity, at least so long as P is sufficiently far removed from the "focus", O, of infection. Then $Z(P) \to \zeta \geqslant 0$ as $OP \to \infty$ and

$$\zeta = 1 - e^{-\sigma \zeta/\rho}. \qquad . \qquad . \qquad . \qquad . \qquad . \qquad (13)$$

Now (13) always has the root $\zeta = 0$; it has a (unique) positive root if and only if $\sigma > \rho$. The quantity

$$\zeta \equiv \lim_{OP \to \infty} \lim_{t \to \infty} z(P, t) \qquad . \qquad . \qquad . \qquad . \qquad . \qquad (14)$$

is obviously of considerable interest; we shall say that there is a *pandemic* when $\zeta > 0$; this will mean that ultimately the fraction of individuals succumbing to the disease will be ζ or greater, even at indefinitely great distances from the focus. It will be convenient to call ζ the *severity of*

the pandemic. If we accept the assumption of the ultimate monotony of the Z-function we now have the following "Pandemic Threshold Theorem":

> (i) There will be a pandemic if and only if the population density σ *exceeds* the threshold density $\rho \equiv \gamma/\beta$.
>
> (ii) If there is a pandemic then its severity ζ will be the (unique) positive root of the equation (13).

For example, the severity ζ will be 10 per cent. if $\sigma = 1\cdot05\rho$ and 90 per cent. if $\sigma = 2\cdot56\rho$.

The proof is quite trivial save for the demonstration that $\zeta \neq 0$ when $\sigma > \rho$. This is shown as follows. Suppose $\zeta = 0$ and choose θ so that $\rho/\sigma < \theta < 1$; then from (12) we know that

$$\tilde{Z}(P) \leqslant \theta\, Z(P)$$

for all sufficiently large values of OP, say for $OP \geqslant c$. Iteration now gives

$$\tilde{Z}^n(P) \leqslant \theta^n\, Z(P)$$

provided that $OP \geqslant c + (n-1)\,b$, where $\tilde{Z}^n$ denotes the effect of applying the operation "$\sim$" n times to Z. Choose n so that $\theta^n < \frac{1}{8}$ and then fix it. We now consider the two circles

$$\Gamma_1: \text{ centre } O, \text{ radius } OP;$$
$$\Gamma_2: \text{ centre } P, \text{ radius } nb.$$

If OP is large enough then their region of overlap will be almost a semicircle of Γ_2 and it will at least include a quadrant of Γ_2; also, in this region of overlap, $Z \geqslant Z(P)$. Thus

$$\tilde{Z}^n(P) \geqslant \tfrac{1}{4}\, Z(P) \text{ for all sufficiently large } OP$$

and yet

$$\tilde{Z}^n(P) \leqslant \tfrac{1}{8}\, Z(P) \text{ if } OP \geqslant c + (n-1)\,b,$$

and $Z(P) \neq 0$. The desired contradiction has now been obtained, and it follows that $Z(P)$ must converge to the *positive* root of (13) when $\sigma > \rho$.

The threshold theorem just described presents a close similarity to the threshold theorem of Kermack and McKendrick for epidemics in closed populations. The stochastic equivalent of the older threshold theorem is now well known,[*] even if it has still to receive an exact formulation, and it is tempting to speculate about the stochastic analogue of the pandemic threshold theorem. In doing so one new feature deserves to be treated with special caution. As soon as a large epidemic has got under way in a closed population it is quite reasonable to expect the deterministic model to yield a good qualitative approximation to its stochastic equivalent. With the "open" population considered here this is no longer true; even in conditions of pandemicity the y-frequency will be small in a critical annular region advancing with the pandemic wave and so stochastic fluctuations in amplitude will continue to be of importance throughout the whole history of the pandemic. At first one may think in terms of a critical annulus of active y-ness surrounding a disc of passive z-ness and expanding into an infinite sea of susceptibles with a velocity which can be calculated (at least on a deterministic basis). A little reflection suggests, however, that the critical annulus will eventually break up into an increasing number of disjoint arcs (because of spatial "fade-out"), and an important question is whether some one of these arcs will escape fade-out altogether.

I have already indicated that this analysis may be applicable to the spreading of rumours, and in conclusion it may be of interest to note as a third example the obvious application to forest fires.

Dr. P. G. MOORE: I found Professor Bartlett's paper extremely illuminating in the light that it throws on the periodicity of epidemics, although to savour it to the full I found it necessary to make some study of the previous paper given at the Berkeley symposium. I should like to make a few comments on the relationship between periodicity and community size discussed on p. 50. The mode and the mean of the period given there are derived from (5.7) of the 1955 paper which is

$$f(T) = r(T-1)\,T^{r-1}\,e^{-r(T-1)}$$

where

$$r = \varepsilon\mu/\lambda v$$

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[*] See the contributions by Bartlett and myself to the discussion following Bailey's recent *Journal of the Royal Statistical Society* paper and to the *Third Berkeley Symposium*. See also P. Whittle, *Biometrika*, **42**, 116–122.

the symbols being defined on p. 52. The mode of this distribution is $1 + 1/\sqrt{r}$ and the mean a little greater. In plotting, as Professor Bartlett has done in Fig. 1, the average period between epidemics against the value of $100/\sqrt{N}$, N being the size of town, we are assuming that $\varepsilon\mu/\lambda v \propto N$ or if we say that $\varepsilon \propto N$ we assume that $\mu/\lambda v$ is constant for all the towns. This would seem to be a strong assumption if we compare, say, an isolated inland town and a seaside resort. It is difficult to see from Fig. 1 that there is a linear relationship, and experiments with other functions, such as $100/N$, give better straight lines so that more information would be needed to establish the relationship conclusively.

The distribution of T, for small r especially, is very skew and not at all symmetrical. There are large variations in the observed periods about the mean period, particularly on the positive side. Any tests employed would have to bear this form of departure from normality in mind. A few specimen calculations give

$r = 2$	Mean (ξ) = 2·2500	Standard deviation (σ) = 0·8292	$V = \dfrac{\sigma}{\xi} = 0\cdot37$
3	1·9630	0·6174	0·31
4	1·8047	0·5049	0·28
6	1·6291	0·3838	0·24

and the coefficients of variation are fairly large by everyday standards. To examine the agreement between theory and observation it would be interesting to compare the observed and theoretical standard deviations of the periods between epidemics. At present there do not seem to be enough data available for such a comparison although the data from Ffestiniog from 1940–55 give a value of V of 0·38 which is reasonable. However, as this period contains only three epidemics it is clearly too few on which to base any firm conclusions, but as data accumulate various tests could be made to test agreement between theory and observation apart from the mean.

Dr. FINNEY (read in his absence by the Honorary Secretary): How reliable are the figures for notifications? For the last two months there have been many cases in Aberdeen. For several weeks, my daughter's school class was reduced to about 4 children, the absentees being mostly cases of true and German measles. My medical colleagues tell me that differentiation between the two diseases is far from easy, but I know of cases of reputedly true measles in families of at least two members of the medical profession. Yet, in the middle of this period, our local daily paper contained a list of notifications of infectious diseases for the previous week including "Measles: 1". I have not attempted to check for a possible printer's error, but suggest that a *prima facie* case for questioning realiability of records exists.

Professor BARTLETT (in reply): While I am gratified that people have on the whole been rather kind, I think it fair to say that the more theoretical have been somewhat kinder than the medical people. This is as it should be. The actual facts and data and the assumptions made in the theory obviously need very careful consideration from the medical point of view.

Dr. Reid and Colonel Butler raised the question of the definition of an epidemic. I agree that my own definition was quite arbitrary, and no doubt could be improved, but I would reiterate a point I made in my introductory remarks at the beginning of the meeting. I should be the last to deny the importance of the medical aspects in all this work, but one cannot ignore the statistical aspects, and in particular the definition of an epidemic does seem to me to be essentially one that must be put in statistical terms, that is in "crowd" terms. It is not, I think, out of the question that the actual statistical theory will help in suggesting what one does. In the case of simple and closed populations where there is an epidemic, one knows from recent theoretical work that there may be a minor outbreak if the level of susceptibles is below the threshold, or a minor outbreak *or* epidemic if the level is above the threshold, and there may be something in between which one may not know whether to call an epidemic or not. There is an essential arbitrariness about it.

Again on the formula for measles periodicity and community size I hope I did not give a wrong impression in claiming I was establishing very precise results. Whatever the fate of the theory that is being put forward, it has certainly helped me to try to understand what is going on, if only to encourage me to look at the data to see how they conform with the theory. Any data put forward in the paper should be considered on their own merits, quite apart from the theory. Take the existence of a critical size. If one does not accept the theoretical reasons suggested, one has still to explain the phenomenon in terms of some other theory one may wish to put forward.

All this is perhaps a little relevant to some remarks made by Colonel Butler. For example, the question of virulence of an attack in a place where measles has not existed for a long time is quite undeniable; but, coming to less extreme cases, one finds that a certain proportion of the

population is attacked and then the epidemic will die down. The percentage of attacked is not determined necessarily because the rest of the population are more immune but because that is the statistical consequence in that sort of population.

I was interested in the detailed map which Dr. Reid displayed; it seemed to me to be something intermediate between the detailed work Mr. Bailey has been interested in and the sort of large-scale work I have been interested in here. Perhaps at some time I might have a closer look at the data.

Again in answer to Colonel Butler, I think I would agree with what Dr. Irwin suggested, that the object of this work was primarily to understand, or to try to understand, what was going on. We have a long way to go, but I submit that study from this angle, as well as from the medical angle, is at any rate of some relevance to the understanding of epidemiological phenomena.

Professor BARTLETT subsequently replied in writing as follows:

To add a little more to my reply to Col. Butler, I hope that he and I will not remain too much at cross-purposes in our approaches to epidemic theory. In my verbal reply I suggested that the data should at least be considered on their own merits, quite apart from any explanatory theory. However, I would not wish one general theoretical point to be ignored—namely, that complex, and certainly not obvious, consequences flow from even the simplest model. This means that observational data often cannot be adequately considered without the investigator having some awareness of these complexities. As a possible example (not perhaps a very good one, but it happens to arise from the discussion), consider the estimates by Dr. Nicol, referred to by Dr. Reid, of the percentage of children in the Isle of Wight ultimately succumbing to measles. In addition to the more obvious questions such as the completeness of notifications, the theoretical concept of critical size seems to me to have some relevance to such investigations; for if semi-isolated populations are below the critical size, the chance of a child being attacked at some stage must (though it is not immediately obvious to what extent) be affected.

There seems to me no incompatibility of such theoretical points with detailed studies of actual epidemic patterns and recurrences. Dr. Reid has noted the more extended and variegated interpretation of simple epidemiological concepts and assumptions that may be necessary before they can be very relevant to real life; and certainly there was no implication that my simple model was complete. To recall a complication noted in my paper, assembly and dispersal in schools is an important aspect contributing to seasonal variation in incidence, and even sometimes disrupting an epidemic and starting it up again after the summer holidays. (Should such an interrupted epidemic count as one epidemic or two?)

At one point in Col. Butler's remarks, he raised another possible complication of "at least a temporary immunity". This kind of hypothesis is also found in the 1928 measles study by Stocks and Karn. That I have not included any such assumption in my own model does not preclude its inclusion later if found necessary, but its importance, even if it has some medical basis, seems limited. It does not appear any longer helpful as an "explanation" of measles' biennial periodicity, nor do the observed attack-rates of 80 per cent. or so in some schools allow the production of such immunes to be anything like the three or four to one ratio of new cases that Stocks and Karn suggested at first. In a letter to me in 1954, Dr. Stocks modified the hypothesis to one of a differential immunization, with less effect in cases of close contact and heavy infection; in this more complex form, the hypothesis will unfortunately be even more difficult to verify.

The problem of incomplete notifications was mentioned both by Dr. Reid and by Dr. Finney (and also, as noted in my paper, by Dr. Hope Simpson, who I regret was unable to be present at the meeting). Some quantitative adjustment for this might be attempted, but it could hardly disturb my main thesis. It would have the effect of making the critical size estimated from actual data somewhat smaller, to allow for the chance of apparent "fade-out" being a consequence of incomplete notifications. The rather rudimentary quantitative estimates given in my paper are, however, in my opinion still too crude for such adjustment yet to be worth while.

Dr. Moore noted that the information available was hardly sufficient to establish my proposed linear relation between measles periodicity and $1/\sqrt{N}$. I quite agree. But bearing in mind that I was using the simplest assumptions, I consider the absence of contradiction encouraging enough. I would point out that my relation (for towns below the critical size) was augmented by the critical size concept, and the broad compatibility of theory and observation over the whole range of town size is by no means trivial.

Mr. David Kendall's (amplified) remarks represent a valuable contribution to the spatial theory of epidemics, and I hope its mathematical precision (coming at the end of a paper which, in spite of its theoretical flavour, was largely concerned with observed phenomena) will not be overlooked by serious students of epidemic theory. Mr. Kendall has given the spatial generaliza-

tion of his own exact solution (see his Berkeley paper) of the Kermack and McKendrick model of an epidemic in a closed population. Perhaps, regarding the associated stochastic problem raised at the end of his contribution, I might draw attention to the relevance of equation (9.5), and the immediately ensuing equations, in my own Berkeley paper.

Finally, I should like to record my grateful thanks to all the speakers for their various contributions.

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

Jane Frances Arnold.
Henry Moore Baker.
William John Fox Benton.
Derek Thomas Beeston.
Allan Birnbaum.
Frederick Ernest Bonner.
Robert George Bradley.
Leslie Brown.
Maude Caudwell.
William Horace Chapman.
John Welham Clarke.
Derek Edward Cook.
Reginald James Williams Crabbe.
Oliver Douglas Cumming.
Paul Omodara-Adeniyi Dada.
Dennis John Gerald Farlie.
Peter Raphael Francis.
Dennis Frank Gilley.

Joseph Hamilton-Jones.
Philip Horace Hammon.
Carola Herbert.
Percy Francis Hooker.
David Frank Kerridge.
Peter Thomas McIntosh.
Pinhas Paul Naor.
Emmanuel Noi Omaboe.
Alan Rowland Rogers.
Brian Frederick Sagar.
Norman Havelock Shears.
Arthur Gribble Simons.
Joseph Andrew George Taylor.
Sridhar Tripathy.
Charles Frederick Trustam.
Francis Herbest Wales.
Leonard Ainslie Williams.