NOTES ON THE SPREAD OF BACTERIAL INFECTION.

By E. C. RHODES.

(With 2 Charts.)

In a paper on "The Spread of Bacterial Infection" (*Journal of Hygiene*, XIX. No. 4, March 22, 1921) Dr W. W. C. Topley has shown the results of many months' observation of the progress of an epidemic in a population of mice. The author thus describes the experiment: "This experiment lasted from May 21, 1919, until June 11, 1920....The epidemic started about the middle of October, 1919, and continued in the manner to be described until the conclusion of the experiment....The period May 21 to September 17 is omitted....During this time there was no indication of the active spread of infection....The whole experiment may be divided roughly into four periods. The first extends from May 21 to Sept. 17, and has been referred to already. From Sept. 18 and onwards, only normal mice were added to the cage. From this date until Jan. 5, 1920, the mice were added in such a way as to keep the total number in the cage roughly constant. From Jan. 6 to April 27, 1920, three normal mice were added each day, except on two occasions when none was added. The number of mice in the cage during this period varied from day to day, reaching a maximum immediately before each considerable wave of mortality, and falling to a minimum just before its cessation. During the final period from April 28 to June 11, 1920, two normal mice were added daily instead of three."

The author then shows that during the period when constant daily additions of normal mice are made to the population, the form of the population curve (population against time) is wavy, and exhibits a periodicity of about 40 days. He further shows that those mice introduced into the cage, when the cage population is at a maximum, have a small survival time, and those mice introduced when the cage population is at a minimum have a large survival time. The paper proceeds to discuss other experiments.

The present writer has been concerned with the first experiment and in particular with that part of this experiment from Jan. 6 to April 27, 1920, when three normal mice were added daily to the cage. He has endeavoured to get some indication of the variations in the power of the population to infect new mice, by considering the actual daily constitution of the population, according to the number of days' residence in the cage of individual mice of the population. Fortunately, in Topley's paper there is a complete history of

each mouse forming part of the population of the cage; that is to say, we know its date of entry and its date of death. This statement is true, with the exception of a few cases, cases where mice have disappeared, probably eaten by the others. Thus when one actually traces the progress of individual mice, one finds a certain number whose death is not recorded. For this reason certain figures which will be given here for the cage population will be found to differ from Topley's figures, but the *sequence* of the figures is the same as with those of Topley. When the mice are shown in a distribution according to survival time it is seen that the mode of the distribution is at ten days, and the range of the distribution is about 30 days. Actually there are one or two cases of mice who have survived much more than 30 days, and Topley in his work rejects these cases; the present writer will do the same.

To get the number of mice alive on any day of the period under discussion, and the number of days each mouse had formed part of the population the writer traced, through the records given by Topley, all the mice who were in the cage previous to this day, with the exceptions mentioned above. In this way the cage population, distributed according to the time of sojourn in the cage, was obtained for each day from Jan. 26 to April 28 inclusive. In forming these totals, the deaths in the cage reported as on April 27, say, are supposed to have occurred during that day, and the population given for April 28 is supposed to be that at the beginning of the day. Similarly, for the other days in the series. The series starts at Jan. 26, because previous to that date there are alive in the cage, mice which had been put in before the three-per-day manner of addition commenced on Jan. 6.

Table I.

No. of days in cage	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	Total
Feb. 10	3	3	3	3	3	3	3	2	.	2	.	1	1	.	2	.	.	.	.	.	.	.	.	.	.	.	.	29
Apr. 9	3	3	3	3	3	3	3	3	2	3	3	.	.	1	.	3	1	.	1	.	.	1	1	.	1	.	1	42

Table I shows the distribution of the population at the beginning of two days (Feb. 10 and April 9) according to the length of time the mice had been in the cage. Thus on Feb. 10 there were three mice which had been in the cage one day, three had been in two days, three three days, and so on.

Chart 1 shows the alteration in the total population with time. The periodic character of the curve is indicated in this figure. For purposes of showing the alteration in the constitution of the population, it was thought better to group those days with 24 and 25 mice together; similarly, 26, 27; 28, 29; and so on. In this way we should get a better idea of the average constitution of the population when this population was a minimum, when it was increasing and decreasing, and when it was a maximum. A typical example will illustrate what was done.

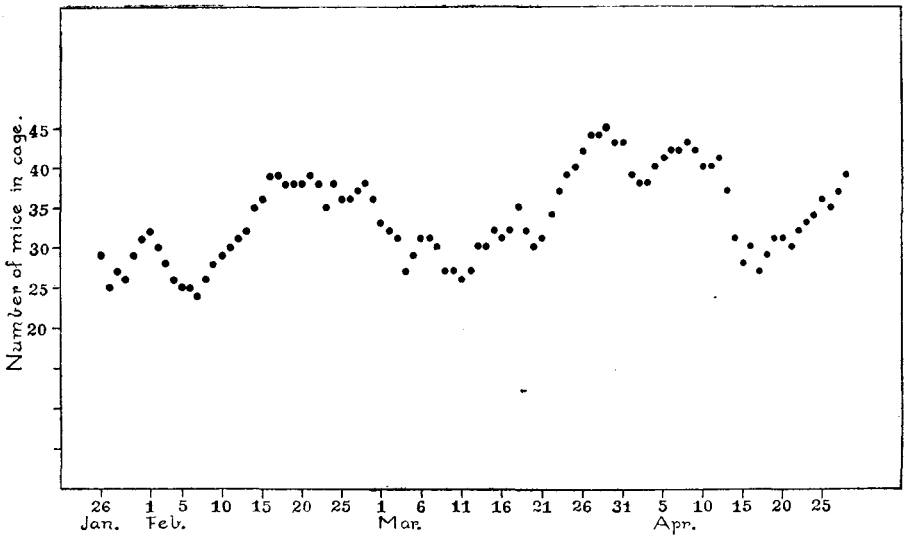

Chart 1. Population change with time.

Table II. *Population* 26 *and* 27 *mice.*

Number of days in cage

No. of Mice	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
0	.	.	.	.	.	.	.	1	1	2	2	7	5	7	8	9	10	10	9	10	10	9	10	10	9	10	10	10	10	10
1	.	.	.	.	.	.	1	2	2	5	6	1	3	2	2	1	.	.	1	.	.	1	.	.	1	.	.	.	.	.
2	.	.	.	2	1	2	1	3	4	2	1	2	1	1	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
3	10	9	8	7	8	8	7	4	2	1	1	.	1	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

Table II shows that on each of the ten days when the population was 26 or 27, three of the mice had been in the cage one day; on one day there were three mice which had been in the cage ten days; on two days there were two mice which had been ten days; on five days there was one mouse which had been in the cage ten days; on two days there were no mice which had been in the cage exactly ten days; on all ten days there were no mice which had been in the cage 20 days, and so on. The fact that the vertical totals in this table are not always ten, is due to the two days during the period considered when no mice at all were added to the cage.

From this table we may obtain the average number of mice of 1, 2, 3... days' sojourn in the cage contributing to a total of 26·5 mice. Similar tables made up for other populations will lead finally to Table III, where the results are shown. This table gives the constitution of the cage for totals ranging from 24 to 45, in groups 24, 25; 26, 27; 28, 29; etc., as indicated. Looking at this table, we seen that roughly all the populations on different days have the same number of mice which have been in the cage 1, 2, 3, 4, 5, 6 days, and that the difference between the total populations on two days is caused by differences in the numbers which have been in the cage seven or more days. This fact is brought out more easily in Table IV, formed from Table III, by grouping the various items together.

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Table III. *Showing the Mice forming part of the population according to the length of time they have been in the cage.*

Number of days in cage	24, 25	26, 27	28, 29	30, 31	32, 33	34, 35	36, 37	38, 39	40, 41	42, 43	44, 45
1	3·00	3·00	3·00	2·94	3·00	3·00	3·00	3·00	3·00	3·00	3·00
2	3·00	3·00	3·00	2·94	2·78	3·00	3·00	2·93	3·00	3·00	3·00
3	3·00	3·00	3·00	2·89	2·78	2·83	2·89	2·93	3·00	2·86	3·00
4	2·67	2·78	2·88	2·83	2·67	2·67	3·00	2·86	3·00	2·86	3·00
5	2·67	2·89	2·12	2·78	3·00	2·67	2·67	2·79	3·00	2·71	3·00
6	2·33	2·80	3·00	2·41	2·67	2·83	2·78	2·50	2·83	2·86	3·00
7	1·75	2·67	2·50	2·59	2·78	2·33	2·89	2·43	2·33	3·00	3·00
8	1·25	2·00	2·14	2·50	2·62	2·67	2·56	2·36	2·00	3·00	3·00
9	1·50	1·60	1·43	2·29	2·00	2·67	2·44	2·36	2·67	2·43	3·00
10	1·50	1·20	1·38	1·59	2·00	1·83	2·56	2·43	2·17	2·28	2·67
11	1·00	1·10	·75	1·24	2·00	2·20	1·89	2·00	2·00	1·86	2·67
12	1·75	·50	·88	·61	1·57	1·83	1·67	1·64	2·50	1·28	2·33
13	·50	·80	·88	1·00	·78	1·20	1·33	1·57	1·83	1·86	1·67
14	·75	·40	·75	·59	·56	·67	1·12	1·57	1·00	1·71	1·33
15	.	·20	·62	·50	·33	1·00	1·11	1·00	·83	1·28	1·33
16	.	·10	·12	·44	·78	1·00	·12	1·31	·17	1·14	1·33
17	.	.	.	·44	·22	·33	·67	·92	1·00	·86	·33
18	.	.	.	·17	·33	·17	·11	·77	1·00	·71	.
19	.	·10	.	·11	.	·33	·11	·46	1·00	·50	·33
20	.	.	·38	.	.	·33	·11	·31	·50	·86	·50
21	.	.	.	·11	.	.	·11	·38	·33	·43	2·00
22	.	·10	.	·11	.	.	·11	·14	·17	·57	1·00
23	.	.	·25	·06	.	.	·11	·08	·17	·33	1·00
24	.	.	.	·11	.	.	·12	.	·17	·50	.
25	.	·10	.	·06	.	.	.	·08	·17	·43	.
26	.	.	·12	·06	.	.	·12	·08	·33	·14	.
27	.	.	.	·06	·11	.	.	.	.	·14	.
28	.	.	.	·06	.	.	.	.	·20	.	.
29	.	.	.	·06	.	.	.	.	·20	.	.
30	.	.	.	.	·11	.	.	.	.	.	.
No. of days	4	10	8	18	9	6	9	14	6	7	3

Table IV.

Population	24, 25	26, 27	28, 29	30, 31	32, 33	34, 35	36, 37	38, 39	40, 41	42, 43	44, 45
No. of mice: less than 7 days	16·67	17·47	17·00	16·09	16·89	17·00	17·34	17·00	17·83	17·29	18·00
No. of mice: 7 days and more	10·00	10·87	12·20	14·76	16·19	18·56	19·25	21·89	22·74	24·67	27·50

This table shows that the increase in the number of mice (or the decrease) in the cage at any time, is roughly due to an increase (or a decrease) in the number of those which have been in the cage seven days or more. Now Topley observed that mice added to the cage survived longer or shorter periods according to the time they were introduced. We can confirm this fact for the period we are considering, in a rough manner, by means of the following table (V):

Table V. *Showing the alterations of average survival time of mice added to the cage, according to the time of addition.*

Week commencing	Jan. 28	Feb. 4	Feb. 11	Feb. 18	Feb. 25	Mar. 3	Mar. 10	Mar. 17	Mar. 24	Mar. 31	Apr. 7	Apr. 14	Apr. 21
Average survival time (days)	11·6	12·2	11·6	10·6	9·7	14·0	13·3	14·8	11·6	11·0	9·9	20·0	14·8
Average number in cage	29·0	26·1	34·6	37·7	35·4	29·4	29·0	33·0	42·4	40·1	40·7	29·4	33·9

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This table was obtained by taking the average time of survival of mice added in the weeks, Jan. 28 to Feb. 3, Feb. 4 to Feb. 10, and so on, during the period under review. Similarly, the bottom row indicates the average daily population in these weeks. Chart 2 shows the variation in the average survival

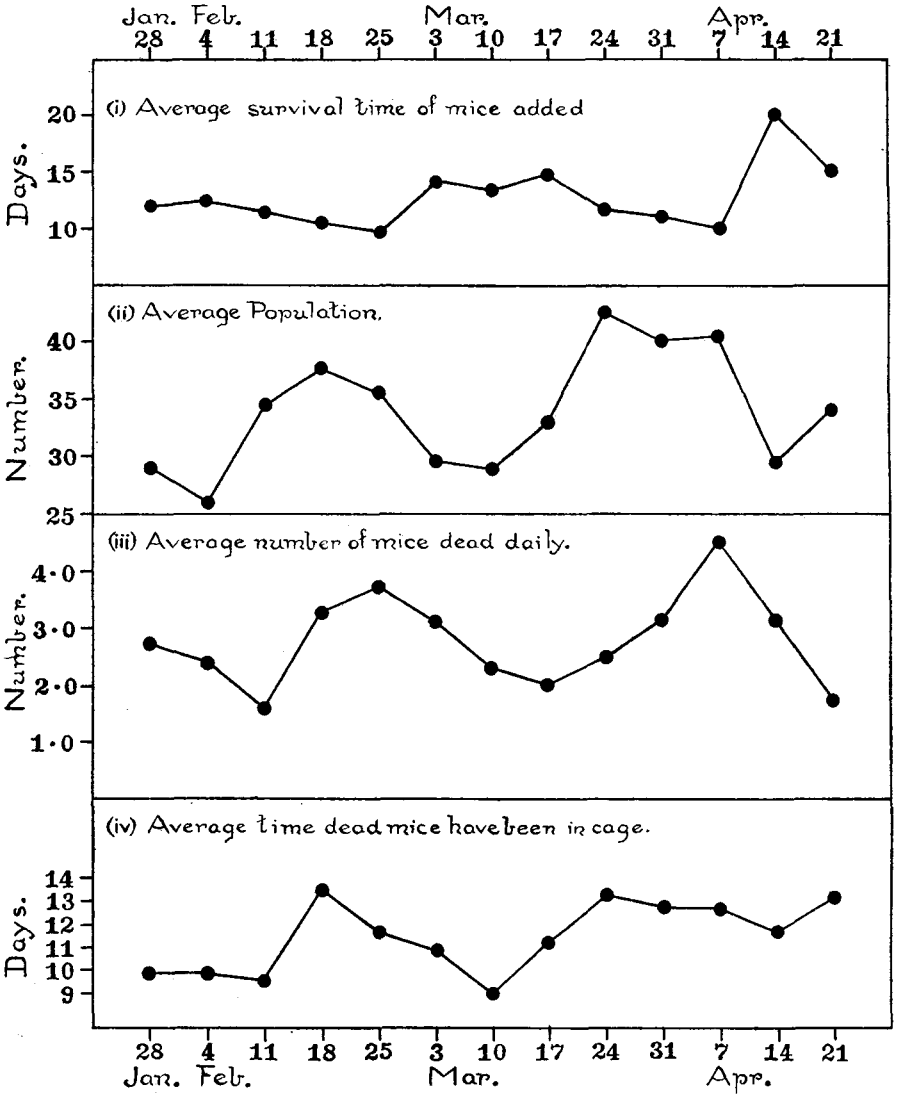

Chart 2.

time of mice added to the cage, and three other diagrams for comparison, all of which bring out the periodicity, viz.: The average daily population, the average daily deaths, and the average time in the cage of the daily batches of dead. At present, all we are concerned with are the two upper diagrams, which clearly indicate the fact that the average survival time introduced on any day

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bears some relationship to the number in the cage at or about the time when the mice form part of the population. Thus we conclude that when the number of mice forming the population is large there is some peculiarity appertaining to the population, which causes mice introduced at that time to die quickly; and when the number of mice is small this quality is missing and the mice live longer. We have observed that the difference between the constitutions of the populations when maximum and minimum lies in the presence of many or few mice who have been in the cage seven or more days, and this fact suggests the possibility that the quality to convey the disease to new mice in a virulent form is related to the presence of many mice which have themselves been exposed to infection seven or more days.

This fact may also be presented in another way, thus: Since the number of mice which have formed part of the population for 1, 2, 3, 4, 5, 6 days is practically the same during the whole time of the experiment, we may say that the variations in the survival times which are observed, are not related to the presence of mice in the cage of less than seven days' sojourn therein.

It would naturally be expected that in this experiment where the same number of new mice are added to the population each day, there would be more "older" mice when the total population is large than when the total population is small; but the writer is desirous of emphasising that there is always practically the same number of mice which have formed part of the population for periods ranging from one to six days.

In Chart 2, (iii) and (iv) have been given, because they help to bear out the conclusions obtained as to periodicity by Topley, and (iv) in addition supports Table III. From this table, we see that when the daily total changes from (say) 42 to 43, the dead mice on the day of the change will come from that part of the population whose time of sojourn is from 7 to 25 days (roughly); and when the daily total changes amongst the smaller numbers (24–25), the dead will be of those whose time in the cage has been 7 to 14 days. This is borne out by Chart 2 (iv) which shows that the average time of sojourn in the cage of the daily dead is greatest when the population is greatest, and least when the latter is least.

It was not thought of advantage to pursue the investigations further—it would be of interest to compare exactly the constituent populations day by day with the survival times of the mice introduced, but the numbers involved are so few, that there is danger of obtaining results which are really worthless, if finer methods of treatment are used.