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THE CHEMISTRY OF CELL DIVISION

I. THE EFFECT OF GLUTATHIONE ON CELL DIVISION IN AMOEBA PROTEUS

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Introduction

Cell division is a fundamental process in the normal growth of organisms and, in its pathological aspect, is one of the outstanding characteristics of neoplastic growth. All problems, therefore, which in their solution will tend to increase knowledge of the factors, physical or chemical, which initiate or control cell division, are of great importance to biology, medicine, and particularly to progress in the solution of the cancer problem.

As is well known, the morphological changes incident to cell division have been studied in great detail on a great variety of different cells; but there can be no doubt that morphological evidence alone, while of great importance, will never lead to an adequate understanding of cell division. It is obvious that the chemical phase of the problem is quite as important, if not more so, than the morphological side.

A review of the literature dealing with cell division reveals that several hypothetical and more or less vague views have been put forward in attempts to explain cell division on a chemical basis.

A brief glance at some of the more influential concepts as to the causal agencies in cell division may not be amiss at this point. R. Hertwig (1903) proposed his theory of "Kern-plasma Verhältniss." This theory, foreshadowed by Verworn (1899, p. 529-31), postulated that for a given cell there exists a size ratio between cytoplasm and nucleus, which if exceeded by reason of an increase in nuclear material as regards the cytoplasm, produces metabolic changes that result in cell division. The best evidence for the validity of this view is probably that adduced by Popoff (1909) for the ciliate *Frontonia*, and by Hegner (1920) for the rhizopod *Arcella*. Calkins (1926), however, notes that in *Uroleptus* and other forms, the many nuclei ordinarily present fuse to form a single compact nucleus of relatively small

volume just prior to division, and he therefore concludes that "it would seem that such changes in the relative volume of nucleus and cytoplasm are better interpreted as the effects of underlying conditions which cause division rather than as a cause of division themselves." Conklin (1912) reaches a similar conclusion as a result of his extensive research on the nucleo-plasmic ratio in developing echinoderm eggs.

Of recent years Robertson (1921) championed the theory that the living cell secretes and releases into the surrounding medium a substance of unknown chemical composition that stimulates neighboring cells to divide. His conclusions in this respect are contested by Woodruff (1911), Cutler and Crump (1923-1925), Greenleaf (1924-1926), Peskett (1925), Myers (1927), and Darby (1930). Finally, a recent theory is that of Gurwitsch (1923) based on extensive research by himself and his coworkers, which lead him to postulate the emission by living cells of ultra-violet light of definite wave length, which light impinging upon other cells acts as a stimulant to division. The validity of this theory is still a matter of controversy.

Hammett (1929) has advanced the theory that substances containing the sulphydril group play a specific rôle in cell division, and in the production of neoplasms. He goes as far as to claim that the sulphydril group is *the only specific* chemical factor controlling cell division.

A priori Hammett's hypothesis seems likely to err on the side of simplicity in view of the multiplicity of factors involved, and particularly in view of the partial independence in division of nucleus and cytoplasm. It must be constantly kept in mind that the division of a cell is not the division of a homogeneity, but a division of a heterogeneous system, the several parts of which are themselves divided (in some cases probably quantitatively, as in chloroplasts) prior to the division of the cell, and this view is extended by some to practically all morphological cell components. Wilson (1923) assumes this attitude, for he says:

For my part I am disposed to accept the probability that many of these particles, as if they were submicroscopical plastids, may have a persistent identity perpetuating themselves by growth and multiplication without loss of their specific individual type.

The fact that this mass of heterogeneous particulate protoplasm, the cell, is quantitatively divided is sufficient to show that the study of cell division is, from any viewpoint, a task of enormous complexity.

Calkins (1926, p. 204) well describes the present situation. He says:

In order to understand the relation of division to the chain of metabolic activities we should know more about the conditions under which division occurs and the causes of division.

However, no matter what view is taken as to the causes or control of cell division in terms of cell activity, it would seem certain that underlying any such action definite chemical substances must play an important if not a unique rôle. Hence, attempts to initiate or control cell division by chemical means, either by alteration of the chemical environment or direct introduction of chemicals into the cell, is a logical procedure. Alteration of the environment is simple and has already yielded results in at least one direction in that it has made possible the separation of certain chemical factors.

Cytoplasmic division may be inhibited by lowered oxygen tension, as shown by Demoor (1894) in experiments on plants (*Tradescantia*), and by Loeb (1899) with sea urchin eggs. The same result was also obtained with narcotics (chloroform and ether) by Demoor (1894) on *Tradescantia*, and on sea urchin eggs by Wilson (1901) and Chambers (1924). Under the conditions imposed by these workers nuclear division was not immediately prevented, proving that a certain degree of independence exists, in respect to division, between cytoplasm and nucleus. Further references will be found in a recent summary by Prät and Malkovsky (1927).

Increase in the rate of cell division has been claimed by Shumway (1917) to result in *Paramecium* from treatment with crude thyroid extract. Recently, Hammett (1929) found that substances containing the sulphydryl group accelerated the rate of division of certain plant root cells and *Paramecium*.

Formulation of Problem

As we are primarily interested in neoplastic growth in animals, we shall deal here exclusively with the chemistry of cell division in animal cells.

What is meant by the "chemistry of cell division"? What experimental procedures will yield valuable information in the study of this problem? We believe that it is essential to formulate our views with respect to these two questions before proceeding any further.

When a cell divides the daughter cells obviously are smaller than the parent cell. Under proper physiological conditions the daughter cells will take up from the environment nutrient material and grow in size. Cell division again occurs, and so on. *Growth of cells* (increase in mass of protoplasm) and *cell division* (increase in cell number), therefore proceed continually under these conditions.

Normal *cellular growth* over an extended period of several generations of cells unquestionably requires an adequate supply of food, which fulfills the energy requirements of the cells and contains, in sufficient amounts, *all* the different chemical substances needed for the building up of new protoplasm. Hence it is obvious that the continued growth of protoplasm is conditioned by a great variety of

chemical factors. Now, it is a fact that under all conditions of growth there is a limit to the size of cells beyond which they can not grow; and in order to increase the total mass of protoplasm, the cells must divide before growth can again proceed. *The chemistry of cell division, therefore, concerns itself with the chemical factors which control any one of the different phases of the division of cells, as distinguished from those chemical factors controlling the increase in the mass of protoplasm; for there is good reason to believe that a cell may go through the division process without an accompanying increase in the mass of protoplasm. Taking into account the great chemical and morphological complexity of all cells and the complicated morphological changes involved in cell division, it would seem a priori, that more than one chemical factor would control this process in its different phases.*

As to the *experimental procedures* to be used, it would appear from the above considerations, that conditions should be chosen which eliminate, as far as possible, the chemical factors operating in the increase in mass of protoplasm. This is of great importance in work with animal cells, as it is impossible at present to devise a "synthetic" medium of *known* and *exactly reproducible* chemical composition, which will support continued growth of protoplasm and cell division. If this were possible, it would obviously offer a splendid opportunity for the analytical determination of the components of this medium, which are specifically essential for cell division. We have chosen, therefore, *Amoeba proteus* as a suitable organism for the reason that it can be put for a number of days into a simple chemically reproducible, nonnutritive medium, without changing the organism sufficiently so as to prevent cell division.

Under these conditions it should be possible to ascertain the action of chemicals added to this medium upon cell division, as compared with the division in control animals. The question now arises as to what chemicals should be studied. In order to make progress, it would appear to us reasonable to begin with a study of those chemical components of cells which occur normally in relatively small amounts and to test the effect of very low concentrations of these substances on the rate of cell division of *Amoeba* under well-controlled conditions.

In choosing such substances we are guided by experimental evidence indicating that the metabolism of living organisms is *regulated* by chemical components, which normally occur in relatively *small amounts*. As examples, we may mention enzymes, certain hormones (Thyroxin), traces of certain heavy metals (Warburg's respiration enzyme), and vitamins. However, we do not mean to infer that the components occurring in relatively *large amounts*, such as proteins, fats, carbohydrates, and inorganic salts, are nonessential factors in the chemistry of cell division, but rather that these factors are *primarily* sources of chemical energy and that they furnish the chemical

building stones of protoplasm. There are indeed partial exceptions as in the regulation of the acid-base equilibrium, where major components exercise important regulatory functions. The concentration of the hydrogen ion in living protoplasm, however, is very low, and for this reason the hydrogen ion may be included in the class of minor components.

In view of Hammett's claims that sulphydril compounds increase the rate of cell division, we selected glutathione for the present investigation. This substance is of particular interest, as previous work has indicated that the glutathione content of rat embryos declines with the age of the embryo (Thompson and Voegtlin, 1926). Similar findings were published by Murray (1926) for chick embryos of different stages of development. Furthermore, Voegtlin and Thompson (1926) found that glutathione is present in malignant tumors in amounts as large as those in the liver, one of the normal organs richest in this substance. This finding was confirmed by Lecloux, Vivario, and Firket (1927). Finally, Baker (1929) found that the addition of small amounts of amorphous glutathione to certain culture media of sarcomatous fibroblasts of the rat exerted an accelerating effect on the growth of this tissue *in vitro*.

Chemically, SH glutathione is a tripeptide, composed of glycine, cysteine, and glutamic acid. The relation between SH glutathione and S-S glutathione can be presented as follows: $2 \text{ R-SH} \rightleftharpoons \text{R-S-S-R}$, where R represents the complex organic radical linked to sulphur. The arrows indicate the possibility of converting one form into the other by oxidation and reduction respectively. It has been established that this transformation is catalyzed by certain heavy metal salts and compounds.

Material and Method

Amoeba proteus is a unicellular rhizopod. It is relatively simple in structure, and is great enough (about 0.0008 to 0.006 cu. mm.) in volume and slow enough in locomotion to make handling and observation simple. It will live for several days (8-14) in the absence of food, and division has been observed under such conditions, personally and by Mast (1930). Culture of the organisms, however, can not as yet be made on synthetic media. This amoeba is not normally a bacterial feeder (Greenwood, 1886); therefore in excluding food it is not necessary entirely to exclude bacteria, but simply to wash the organism to remove larger forms, other protozoa, etc., which constitute the normal food. This is of considerable importance, as it obviates the need for an aseptic procedure.

The amoebae used were from a strain secured from Johns Hopkins University and conformed closely to the form *Amoeba proteus* (Schaeffer 1916). They were cultured in hard glass crystallizing dishes in 200

to 250 c. c. of saline solution made up as follows: 0.1 gram NaCl, 0.04 gram KCl, 0.06 gram CaCl₂, glass distilled H₂O to make 1,000 c. c. This solution is hereafter referred to as standard saline. To each dish was added 4 whole grains of polished rice. The pH of these cultures, when vigorous, was approximately 6.8. Addition of rice, as needed, served to keep the pH at about this figure.

All solutions used were made from C. P. chemicals and doubly glass distilled water. These chemicals undoubtedly contained minute traces of heavy metals; but as this is also true for the amoebae themselves, it did not appear that any end would be served by extreme precautions, especially as such traces would be common to both control and glutathione solutions.

We are indebted to Dr. J. M. Johnson for the glutathione used in this investigation. The crystalline SH glutathione was prepared according to Hopkins (1929), the final crystals being rapidly washed with cold glacial acetic acid to remove, as far as possible, traces of any heavy metals remaining in the product. The substance contained 13.65 per cent N (theory 13.68) and 10.69 per cent S (theory 10.40). The oxidized S-S glutathione was prepared from the crystalline SH glutathione by dissolving the crystals in a small amount of water, adding sufficient Ba(OH)₂ solution to make the solution faintly alkaline, and a drop of very dilute FeCl₃ solution. A rapid current of oxygen was then run through the solution at room temperature until the solution no longer gave the nitroprussid test. After removal of barium and concentration *in vacuo* at low temperature, the S-S glutathione was precipitated by absolute alcohol, filtered off, and dried to constant weight in a desiccator. The product contained 13.10 per cent N (theory 13.68) and 10.43 per cent S (theory 10.40). This product is evidently not absolutely pure, but yields better S and N figures than any oxidized glutathione described in the literature.

All solutions were buffered by addition of a small amount (2 to 3 c. c.) M/20 buffer to the liter of solution with Clark and Lubs phosphate buffers and the pH checked colorimetrically before and after each experiment.

It is evident that under conditions precluding feeding we could not expect to deal with comparisons of division rates. But it seems obvious that under such conditions if divisions can be evoked, differences in the per cents that divide in relatively large control and experimental groups can be considered as significant. The data then are presented in terms of percentages of division in the control and experimental groups.

Further, in view of the fact that deaths will occur during the experimental period, it was imperative that each cell be isolated and followed separately, since only in that way could the actual number

of divisions be accurately ascertained. Our procedure was then substantially as follows:

The amoebae were removed from the culture medium with a capillary pipette and washed twice in standard saline and placed singly on depression slides in a drop of the same saline. Examination of each amoeba, using a compound microscope with 20X ocular and 8 m. apochromat objective, was then made to insure that only mononuclear cells were used and the approximate volume of each cell in arbitrary units was ascertained. This was accomplished by stimulating the cell by repeatedly drawing it up into and ejecting it from a capillary pipette until it had assumed a spherical shape, and then measuring its diameter by use of the compound microscope and an ocular micrometer. Each amoeba was then transferred to a 25 c. c. Pyrex beaker containing 2 c. c. of the solution to be used in the contemplated experiment. Each amoeba and any cell originating from it was examined every 24 hours, using a binocular dissecting microscope, and at the time of examination was transferred to a fresh beaker containing the freshly made solution as before. When all examinations had been completed at the end of the experiment, the amoebae were fixed in 20 per cent acetic acid and examined with a compound microscope for nuclear changes, etc.

The organisms were kept throughout the experiments in a metal chamber which was provided with a water jacket, through which tap water from the city water supply was constantly flowing. This served to prevent rapid fluctuations in temperature.

The Effect of Glutathione on Division in Amoeba Under Survival Conditions

1. THE EFFECT OF REDUCED (SH) GLUTATHIONE

Preliminary experiments were performed to ascertain what concentration of the reagent was to be used. Small numbers (6 to 12) of amoebae were isolated into solutions containing SH glutathione in concentrations from M/10,000 to M/1,000,000 for periods of four days, and it was found that the greater number of nuclear divisions occurred in the solution containing M/50,000 and M/100,000 SH glutathione. The concentration of M/100,000 SH glutathione made up in standard saline was accordingly chosen for the initial tests; it is referred to hereafter as SH glutathione solution.

It was deemed advisable in view of both a possible nutrient effect of the nitrogen of the glutathione and the emphasis placed by Hammett on the SH group, to select for control a solution that would very closely approximate the glutathione solution as to nitrogen content and general chemical structure, but differ in containing no substance possessing the SH group. We therefore used a solution containing M/100,000 each of alanin, glycine, and glutamic acid, made up in the

standard saline. This solution is referred to hereafter as control solution.

The initial question was whether either control or glutathione solutions so prepared would be of nutritional value to amoebae. To test this 60 amoebae were selected. Twenty were individually isolated into standard saline and 20 into control solution. All solutions were buffered to pH 7.0. Daily observation, change of containers, and renewal of solutions were made, as described in the section on materials and methods, for a period of nine days (Sunday excepted). The results, plotted in terms of percentage of survivors as a function of time, are presented in graph A, Figure 1.

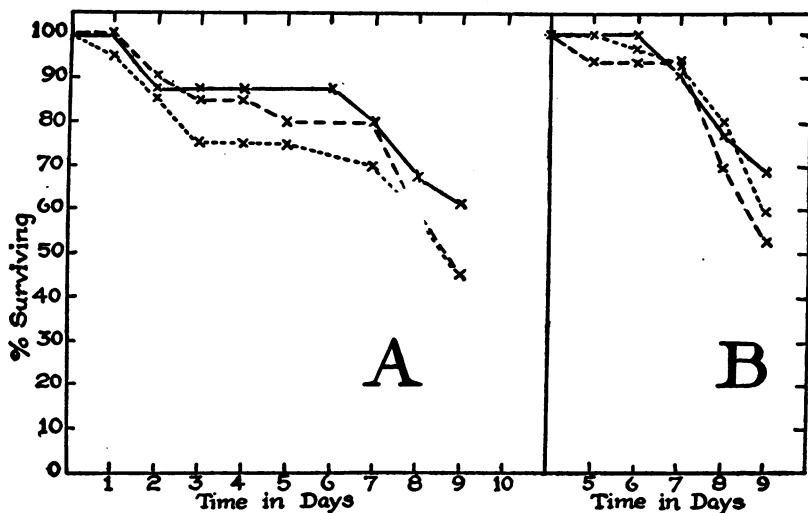


FIGURE 1.—Graph showing the survival curves obtained from amoebae in three different nonnutrient solutions. Solid line, curve obtained in solution of M/100,000 SH glutathione in saline; broken line, curve obtained in solution of M/100,000 alanine, M/100,000 glycine, and M/100,000 glutamic acid in saline; dotted line, curve obtained in saline alone. Graph A shows these curves for a period of nine days from the time of transfer of the amoebae to these solutions. Graph B the curves obtained by taking the survivals in each solution at the close of the fourth day as 100 per cent. Graph A shows the total death rates due to shock and starvation. Graph B those due to starvation. The figures for cell volume are in arbitrary units. Actual volumes in cubic millimeters may be obtained by multiplying the given figure by 0.000098.

From this graph it will be seen that the positions of the respective curves indicate that the total death rate was greatest in saline, less in the control, and least in the SH glutathione. It will be noted, however, that this difference is largely due to the differences in the deaths during the first three days of the experiment. These deaths are evidently *not* due to starvation, since they precede a period of cessation of death, but must be ascribed to shock of some sort incident to the transfer of the amoebae from the culture. It is then fairly evident that the effect of the solutions as to nutrition can best be judged by comparing the segments of the curves following this period

(roughly over the third and fourth day) during which no deaths occurred in any solution. This was done by taking the survivors in each solution on the fourth day as 100 and plotting survivals in each solution for the following days in percentages as before. The results obtained are given in graph B, Figure 1. It will be at once apparent that the curves obtained are, within experimental error, identical. The curve for the saline, which certainly represents the solution of least nutritional value, lies median to the other two. It is concluded, therefore, that the control and SH glutathione solutions must be considered as contributing nothing to the general nutrition of the cell that would not be as well supplied by a simple saline solution.

This ascertained, the effect of SH glutathione on cell division was taken up. Now, it appeared to us likely that cells that had just divided and cells just about to divide would react differently, in regard to division, to substances introduced into the surrounding medium. It further seemed probable that a given number of small cells would include a majority of cells just divided, and a given number of large cells a majority just about to divide; so that, if the cells were selected according to size, these differences in reaction to a given substance would become evident. We accordingly performed the following three experiments:

In the first experiment 40 large amoebae (volumes approximately between 17 and 30 in arbitrary units) were individually isolated, 20 into glutathione solution and 20 into control solution. In the second experiment, 60 amoebae were selected, 40 large and 20 small. Of these, 20 large amoebae were individually isolated into glutathione and 20 into the control solution, and the 20 small amoebae (volumes approximately from 5 to 13 in arbitrary units) were individually isolated into glutathione for comparison. In the third experiment 120 amoebae were used. Of these, 40 were large in volume, 40 medium (13 to 16 arbitrary units), and 40 small. Twenty of each of these lots of 40 were individually isolated into glutathione solution and 20 into control. All solutions in all experiments were buffered to pH 7.0.

In all three experiments daily observations of divisions and deaths were recorded and daily renewals of containers and solutions were made for four days. Then the living amoebae were fixed and their nuclear condition was observed and recorded. The results of the three experiments as to cell division were plotted in terms of per cent division as a function of time, and as to nuclear division as per cent over the total time. (Figs. 2, 3, and 4, respectively.)

In the presentation of the results with respect to cell division, the effect of the death of undivided organisms was allowed for in calculating the percentages, by taking as the basis for each day's calculation the number of living amoebae found at the previous day's count,

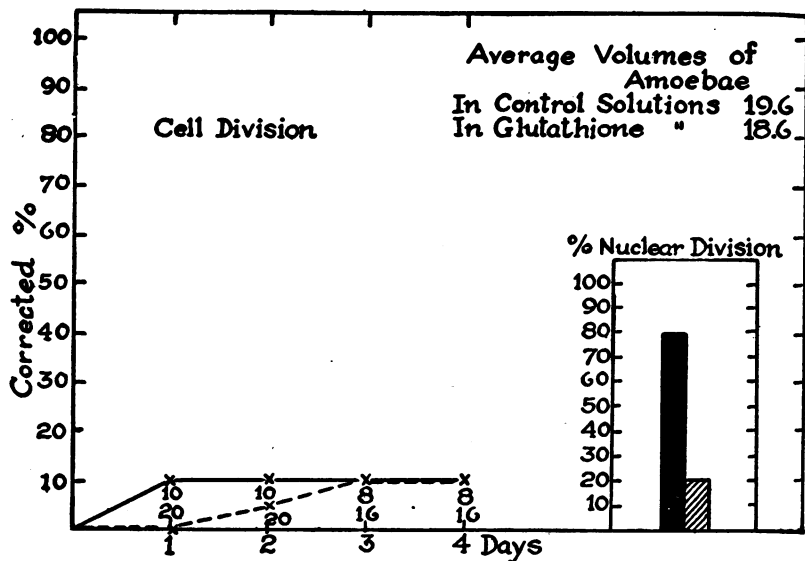


FIGURE 2.—Graph showing the effect of $M/100,000$ SH glutathione upon nuclear and cell division of amoebae of large cell volume under survival conditions. Solid line, curve for cell division obtained in $M/100,000$ glutathione; broken line, curve for cell division obtained in control solution; ordinates corrected total percentage of cell division; solid column, total percentage of nuclear division in glutathione solution; shaded column total percentage of nuclear division in control solution. The figures for cell volumes are in arbitrary units; these may be converted to actual volumes in cubic millimeters by multiplying the given figure by 0.000098

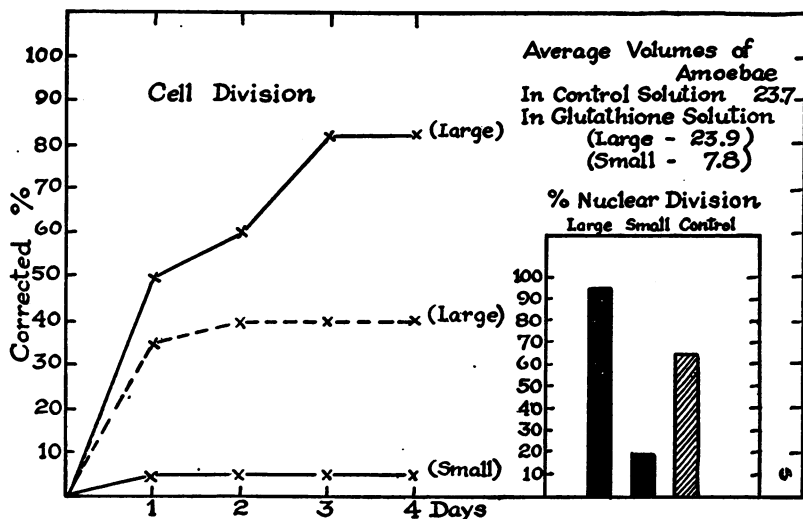


FIGURE 3.—Graph showing the effect of $M/100,000$ SH glutathione upon nuclear and cell division in amoebae of large and of small volumes under survival conditions. Solid line, curves for cell division obtained in glutathione solution; broken line, curve for cell division obtained in control solution; ordinates, corrected total percentage of cell division; solid column total percentage of nuclear division in glutathione solution; shaded column total percentage of nuclear division in control solution. Cell volumes are given in arbitrary units; the actual volumes in cubic millimeters may be obtained by multiplying the given figures by 0.000098

excluding one of the daughter cells in each case of division. The reason for excluding the one daughter cell was that it was considered (and this consideration proved correct) that the chance for a cell to divide twice under the conditions used was almost negligible. On all curves plotted, the number of survivors is given for each day for each point obtained. Thus if it is desired to perform the calculation on some other basis, the data are available.

In respect to nuclear division the basis of calculation is the original number of cells taken. Since the daily observations revealed cell divisions only, nuclear divisions not followed by cytoplasmic division were detected only on fixation on the fourth day. From Figure 2

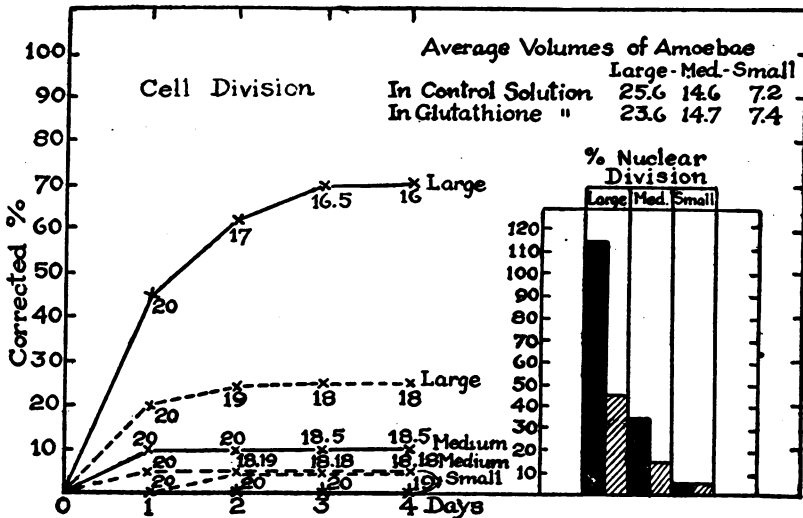


FIGURE 4.—Graph showing the effect of M/100,000 SH glutathione upon nuclear and cell division in amoebae of large, medium, and small cell volume under survival conditions. Solid lines, curves for cell division obtained in M/100,000 glutathione solution; broken lines, curves for cell division obtained in control solution; ordinates, corrected total percentage of cell division; solid column, total percentage of nuclear division in glutathione solution; shaded column, total percentage of nuclear division in control solution. The figures for cell volumes are in arbitrary units and may be converted to actual volumes in cubic millimeters by multiplying by 0.000098

it will be noted that in this experiment, which unfortunately was performed during a period when the laboratory temperature was so high (29° to 30° C.) that the cultures available were not in the best of condition, no difference as to cell division occurred between the amoebae in glutathione and those in the control solution; but a very large difference in nuclear division appeared, 80 per cent against 20 per cent, proving a considerable independence of nuclear division with regard to division of the cytoplasm, and indicating that the effect of the SH glutathione is principally upon the former.

From Figure 3, illustrating an experiment performed under more favorable conditions, it will be seen that the cell volume evidently

plays a rôle of great importance. The large amoebae show a significantly greater proportion of division, both nuclear and cell, in the glutathione than in the control solution, whereas the small amoebae exposed to glutathione show a very low percentage of cell and nuclear division.

The relation between cell size and glutathione effect is still more strikingly brought out in the third experiment illustrated by Figure 4, where it will be seen that this effect varies directly with the average volumes of the three groups of cells used.

We conclude, therefore, that exposure of amoebae under survival conditions to SH glutathione in a concentration of M/100,000 at pH 7.0 results in an increase in both nuclear and cell division, which increase tends to vary directly with the volume of the cells so exposed.

It is at this point suggestive to note that in these three experiments in the results obtained with the *large* cells, the per cent of nuclear division occurring in a given solution tends to vary less than the per cent of cell division. The average deviations from the mean values in the solutions are as follows: In the glutathione solutions, for nuclear divisions 10 per cent of the mean, and for cell divisions 52 per cent of the mean; in the controls, for nuclear division 28 per cent of the mean, and for cell division 40 per cent of the mean.

2. THE EFFECT OF REDUCED (SH) GLUTATHIONE AT DIFFERENT HYDROGEN-ION CONCENTRATIONS

It is well known that the rate of oxidation of sulphydril compounds to the corresponding disulphides is a function of the hydrogen ion concentration. Since it has been asserted by Hammett that the sulphydril group is the active factor in acceleration of cell division, it is of interest to ascertain what result changes in hydrogen ion concentration will have in respect to the effect of SH glutathione upon both nuclear and cell division.

To ascertain this, two experiments were performed. Ninety large amoebae were used in each. In lots of 15 these amoebae were individually isolated, one lot into each of three SH glutathione solutions buffered to pH 6.0, 7.0, and 8.1, respectively, and one lot into each of three control solutions similarly buffered. The experiments were each run for a period of four days, and daily observations, renewals of containers and solutions, and final fixations and observations made as in the previous experiments. One of these experiments was performed under more favorable temperature conditions than the other. The results obtained, plotted in the same way as those for the preceding experiments, are presented in Figures 5 and 6.

From these two figures it is at once seen that throughout the range of hydrogen ion concentration used there is once more a marked difference in per cent of *nuclear division* in favor of the amoebae in

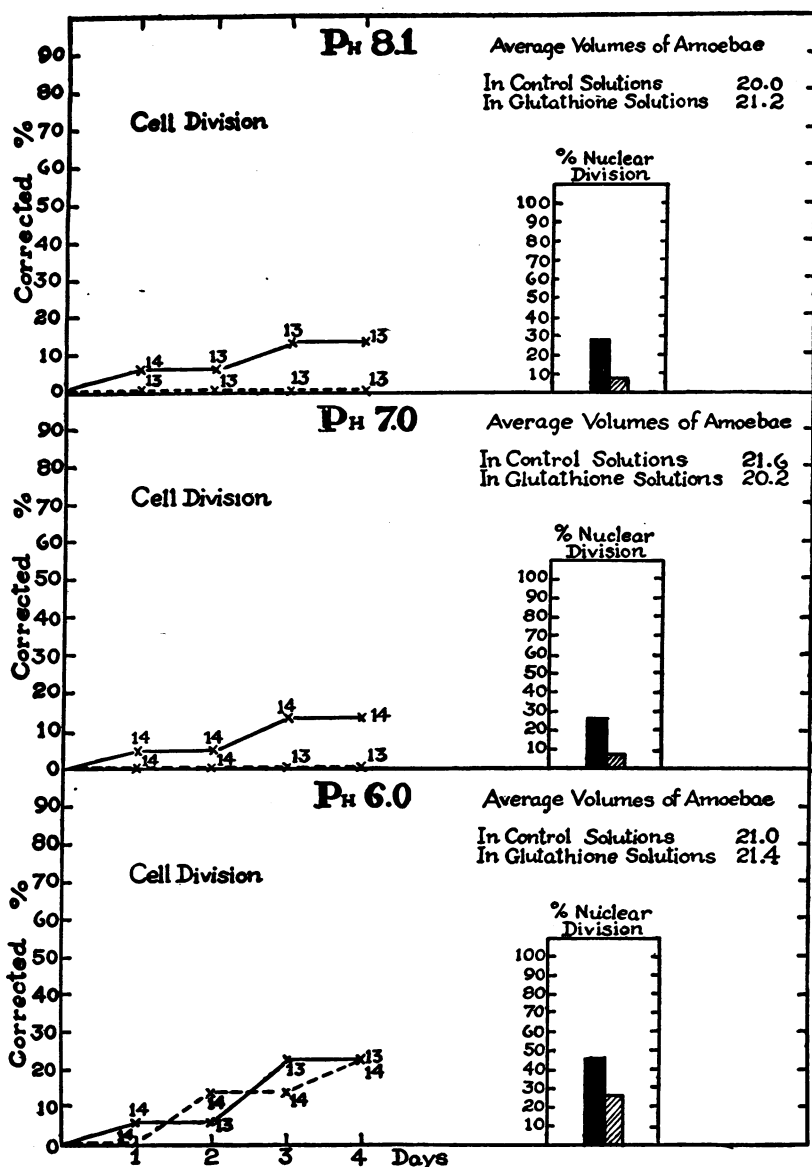


FIGURE 5.—Graph showing the effect of $M/100,000$ SH glutathione upon nuclear and cell division in amoebae under survival conditions at different hydrogen ion concentrations (under unfavorable (27–30° C.) temperature conditions). Solid lines, curves for cell division in glutathione solutions; broken lines, curves obtained in control solutions; ordinates, corrected total percentage of cell divisions; solid columns, total percentages of nuclear division in glutathione solution; shaded columns, total percentages of nuclear division in control solutions. The figures for cell volumes are in arbitrary units and may be converted to actual volumes in cubic millimeters by multiplying by 0.000098

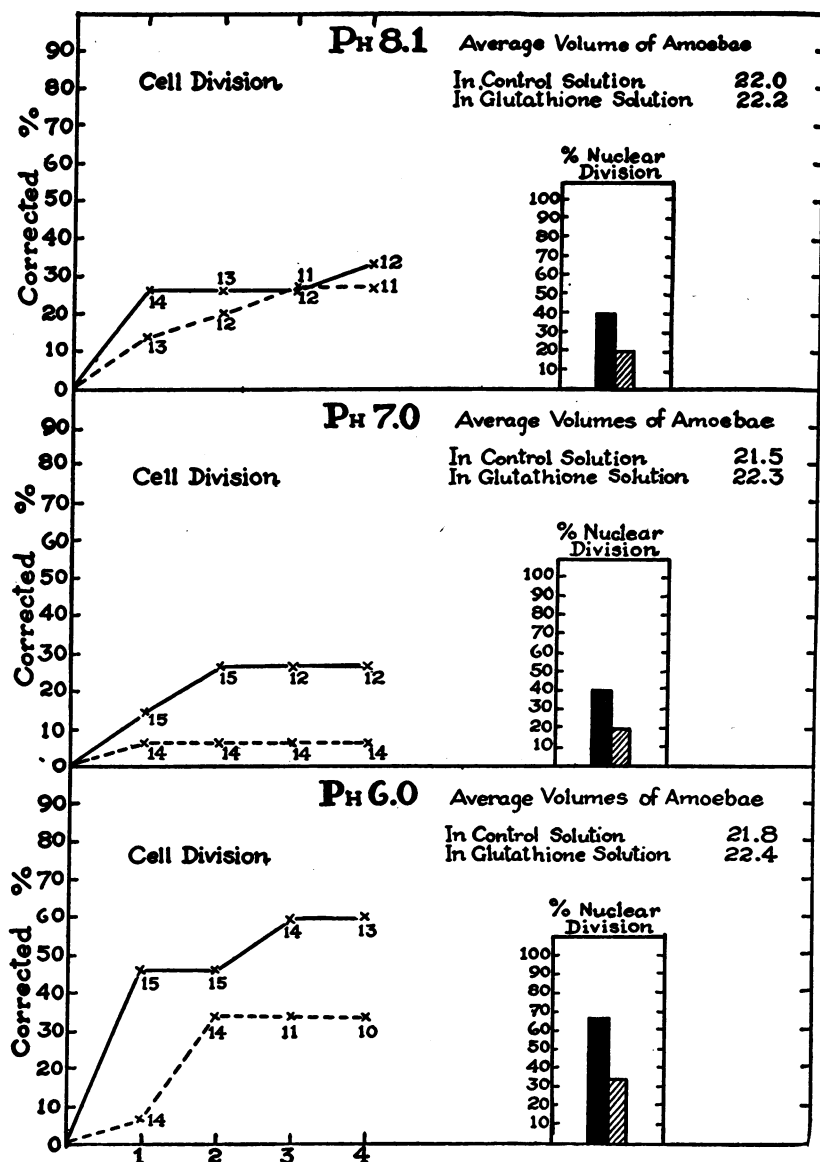


FIGURE 6.—Graph showing the effect of $M/100,000$ SH glutathione upon nuclear and cell division in amoebae under survival conditions at different hydrogen ion concentrations (under favorable (20–24° C.) temperature conditions). Solid lines, curves for cell division obtained in glutathione solutions; broken lines, curves for cell division obtained in control solutions; ordinates, corrected total percentages of cell divisions; solid columns, total percentages of nuclear division in glutathione solution; shaded columns, total percentages of nuclear division in control solutions. The figures for cell volumes are in arbitrary units and may be converted to actual volumes in cubic millimeters by multiplying by 0.000098

the SH glutathione solutions, but that the per cent of division in these solutions is less in both experiments at pH 7.0 and 8.1 than at 6.0. However, the percentage difference in favor of the cells in glutathione as compared with the controls is in one experiment (fig. 6) practically the same throughout the range and in the other (fig. 5) markedly greater at the neutral and alkaline points. This last result probably has little significance in view of the small number of divisions actually found (one in each control solution). With regard to *cell division*, it will be seen that the results given in Figure 5 (which represent those obtained under the unfavorable conditions), indicate only a slight increase of cell division in the glutathione solutions, but that as with nuclear division the per cent is greatest in the solution at pH 6.0. In Figure 6 the same relation appears emphasized, except that there is evident an increase at pH 6.0 and 7.0 in the per cent of cell division in the SH glutathione solution over the control, while at pH 8.1 the per cent of cell division is approximately the same in both solutions. It will be noted that again cell division shows greater variability than nuclear division.

The percentage increase above controls as shown for nuclear division in Figure 6 (which, as it represents the data gathered under the best temperature conditions, is reasonably taken as the more accurate experiment) is practically the same (100 per cent) over the pH range used. Hence it would seem that the results show that no effect due to the hydrogen ion concentration upon the influence of SH glutathione on nuclear division is indicated.

In both figures it will also be noted that there is apparent for all solutions a direct variation of per cent of nuclear and cell division with acidity. This seems to indicate that the hydrogen ion concentration may *per se* exert an effect on nuclear and cell division.

3. THE EFFECT OF OXIDIZED (S-S) GLUTATHIONE

To ascertain more exactly whether an evident difference exists between the effect of the sulphydryl and disulphide forms of glutathione, it was decided to test the effect of the disulphide form directly.

For this test two experiments were performed, 40 amoebae being used in each, and in each 20 amoebae were individually isolated into control and 20 into S-S glutathione solutions, both buffered to pH 7.0. Large amoebae were used. The usual procedure as to observation, renewal of solutions, etc., was observed, and the experiments were each conducted over a 4-day period. The results obtained were plotted, as the similar experiments with the SH form of glutathione, and are presented in Figure 7.

From this figure it is at once evident that the results of both experiments show clearly that in the S-S glutathione solution there is a

significant increase in nuclear division over the controls, and that this is also true for cell division. It must be concluded that under the conditions obtaining there is no evidence that any *qualitative* difference results if S-S glutathione is added to the medium instead of SH glutathione.

4. COMBINATION OF RESULTS

The results of the foregoing experiments clearly indicate that glutathione exerts an influence leading to increase in nuclear and cell division in amoeba. However, in order to bring out this effect with more convincing clarity and to eliminate variables, such as cultural

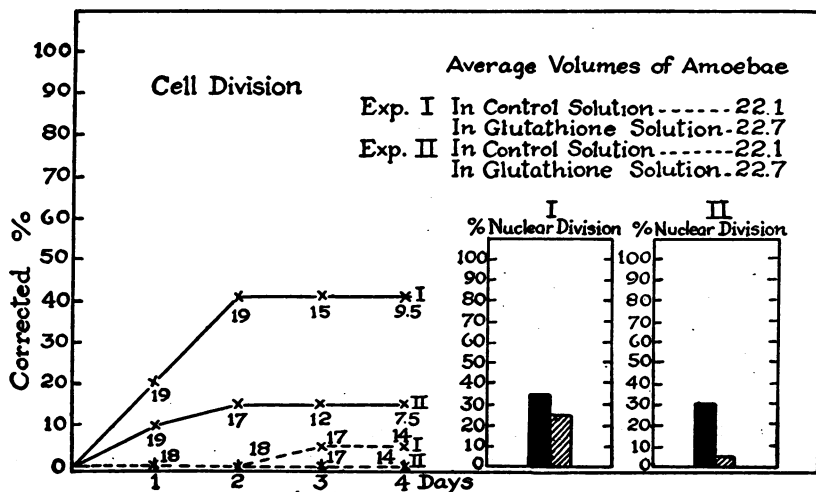


FIGURE 7.—Graph showing the effect of M/100,000 S-S glutathione upon nuclear and cell division in amoebae under survival conditions (two experiments). Solid lines, curves for cell division obtained in glutathione solution; broken lines, curves for cell division obtained in control solution; ordinates, corrected total percentage of cell division; solid columns, total percentage of nuclear division in glutathione solution; shaded columns, total percentage of nuclear division in control solution. The figures for cell volumes are in arbitrary units and may be converted into actual volumes in cubic millimeters by multiplying by 0.000098

conditions and temperature, which may have influenced the results of the individual experiments, we combined all results obtained with SH glutathione. They were plotted so as to bring out the relation of the effect of glutathione with respect to cell volume. In doing this the number of amoebae used, that had volumes between 5 and 10, 10 and 15, and so on, were counted and the average volume for each group was ascertained. Then the number of nuclear divisions, cell divisions, and the number of polynuclears at the end of the experiments in each group were counted and expressed as per cent of the total number of amoebae in the group. The results were then plotted, giving these percentages as a function of cell volume. Curves were also plotted giving the average survival, and average divisions per

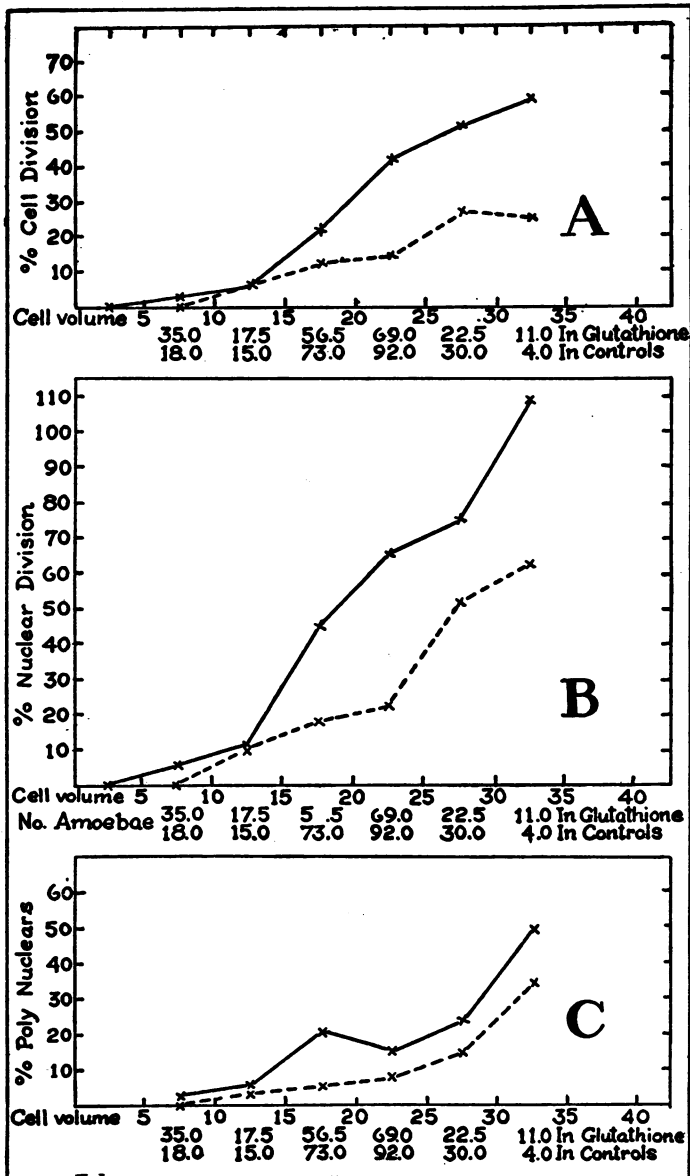


FIGURE 8.—Graph showing the relations between cell division, nuclear division, the number of polynuclear cells formed in and persisting to the end of a 4-day period, and the volume of the cell in amoebae in $M/100,000$ SH glutathione and in control solutions under survival conditions. Solid lines, curves obtained in glutathione solutions; broken lines, curves obtained in control solutions. The figures for cell volume are in arbitrary units and may be converted to actual volumes in cubic millimeters by multiplying by 0.000008

day for the total number of experimental and control organisms. The curves relating, respectively, per cents of cell division, nuclear division, and polynuclear cells found (for both the control and SH glutathione solutions) to cell volume are given in Figure 8, graphs A, B, and C.

From these curves it is at once evident that nuclear and cell division in glutathione and control solution are definitely functions of cell volume, as is also the number of polynuclears that arise and persist during the 3 to 4 day interval covered by our experiments. It will be remembered that all amoebae were mononuclear at the beginning

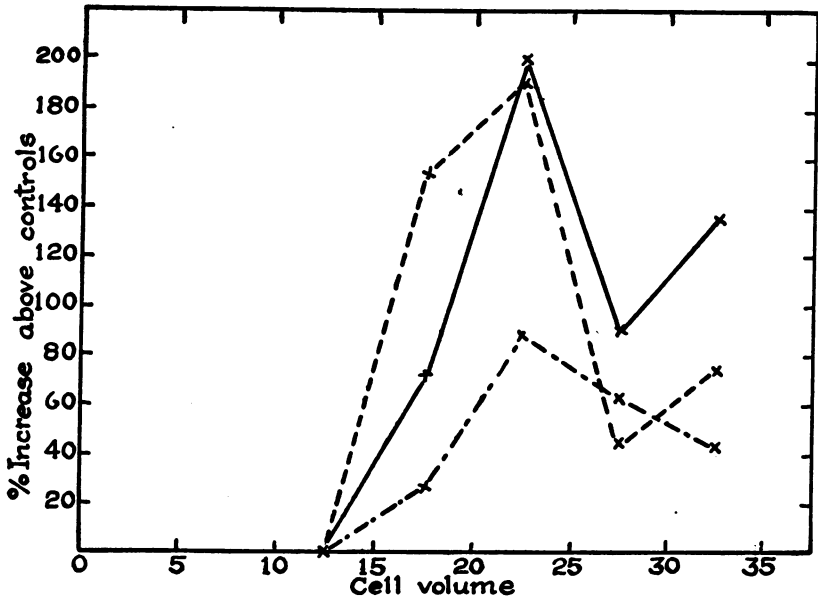


FIGURE 9.—Graph showing the relation between cell volume and the percentage increase for amoebae in M/100,000 SH glutathione solution over amoebae in control solution in regard to cell division, nuclear division, and in the number of polynuclear cells formed in and persisting to the end of a 4 day period, under survival conditions. Solid line, curve for increase in cell division; dotted line, curve for increase in nuclear division; dotted and dashed line, curve for increase in polynuclears. The figures for cell volumes are given in arbitrary units and may be converted to actual volumes in cubic millimeters by multiplying by 0.000008.

of any experiment. It will be seen that the curves obtained for amoebae under control conditions show a distinct tendency for nuclear division to increase rapidly after a volume between 20 to 25 is reached, and that at this point there is also a rapid increase in per cent of polynuclears. There is also a flattening of the cell division curve at 25 to 30. This, if continued, would indicate that amoebae over 20 to 25 in volume tend to become polynucleate. In fact, it was a difficult matter to find mononucleate amoebae of greater volume than about 24 in our cultures; and, in general, the larger the animals examined, the scarcer became the mononuclears. Variation in this

respect occurs between cultures. The curves obtained for the amoebae in glutathione solution show the same general trend as do those for the control animals, but the increase in nuclear and cell division over the latter is most marked at a volume of 20 to 25. *It is also striking that the effect of SH glutathione is itself a function of cell volume, and that no effect is evident on cells below the point 10 to 15.*

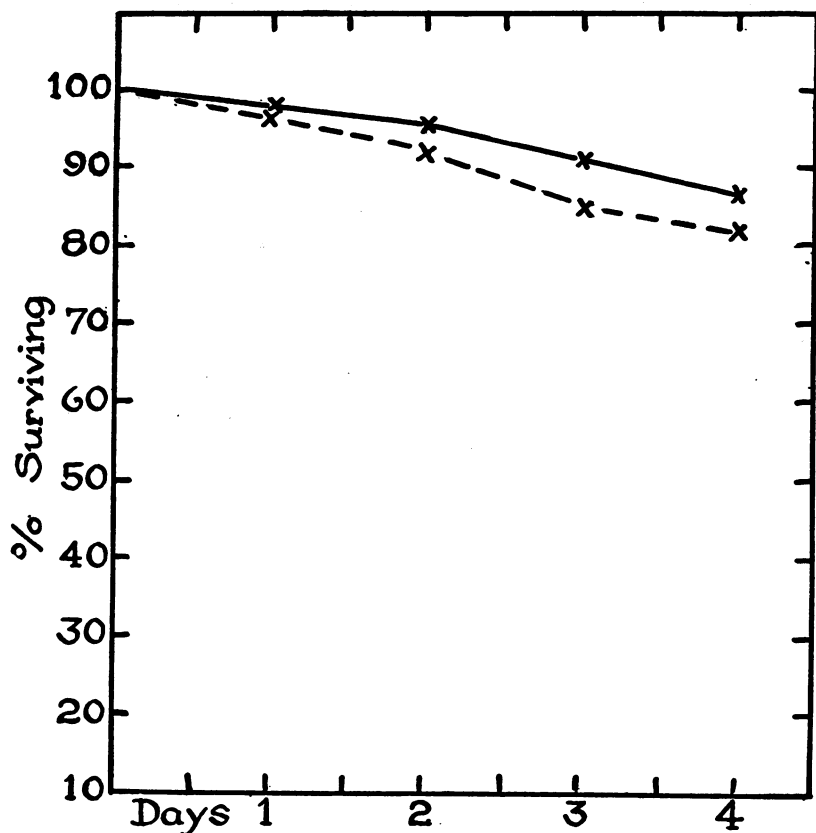


FIGURE 10.—Graph showing curves of daily per cent survival in $M/100,000$ SH glutathione and in control solution for all amoebae used. Solid line, curve obtained in glutathione solutions; broken line, curve obtained in control solutions

Considering that, in general, cell volume must be a function of physiological maturity, we can state that the effects of glutathione are dependent on the physiological maturity of the cell. To define this more accurately, the percentage increase over the controls, due to glutathione, for the three variables, per cent nuclear division, per cent cell division, and per cent of polynuclears, was plotted as a function of cell volume. The results are given in Figure 9. From this it is readily seen that glutathione exerts its greatest effect on cells having a volume of about 20 to 25.

There remains the question as to how far differences in death rates could account for the results obtained. The percentage of the original number of amoebae surviving at the end of each day, in glutathione and control solutions, respectively, is given in Figure 10. It will be seen that, while there is a slight difference in survivals in favor of cells exposed to glutathione, it is probably negligible. This is definitely shown by combining all experiments to give curves like those used for the individual experiments with glutathione on division and allowing for the greater survival in the glutathione solutions, on the basis of the percentage daily survivals given in Figure 10. The compilation of the results on this basis is presented in Figure 11. It will be seen that the average corrected percentage in nuclear division during the four days for all experiments with glutathione solutions is roughly 100 per cent above the average for the controls, after

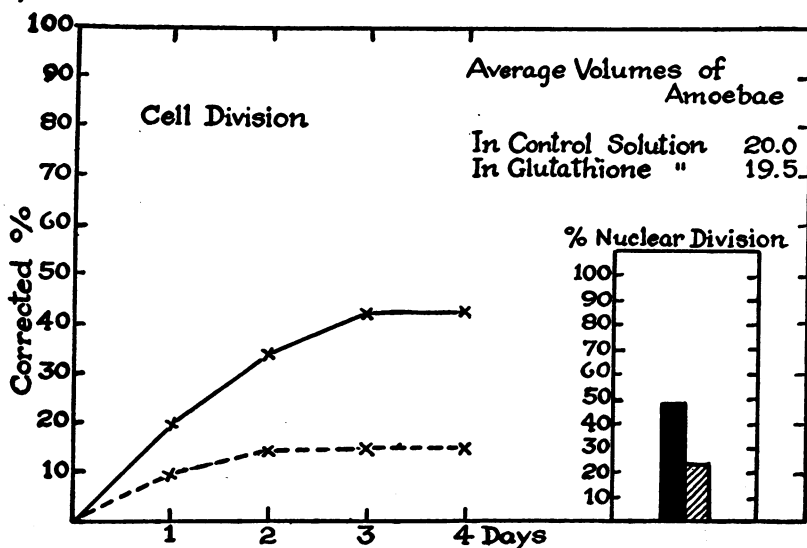


FIGURE 11.—Graph showing the effect of $M/100,000$ SH glutathione upon cell and nuclear division in amoebae under survival conditions obtained from the combined results of all experiments with SH glutathione. Solid line, curve for cell division obtained in glutathione solutions; broken line, curve for cell division obtained in control solutions; ordinates, corrected total percentage of cell division; solid column, total percentage of nuclear division in the glutathione solutions; shaded column, total percentage of nuclear division in control solutions

due allowance is made for deaths; and that cell division shows an increase of 180 per cent above the controls.¹

General Discussion of Results

The following discussion of the interesting results obtained in this investigation of course applies only to *Amoeba proteus*, studied under the conditions chosen by us for reasons which were mentioned in the

¹ The greater percentage of cell divisions over nuclear divisions is, of course, due to the different basis for calculation, as was previously explained.

introduction. Some of the conclusions to be drawn may have a more general biological significance, but this will have to be confirmed by experiments on other types of cells.

The selection of *Amoeba* as the experimental cell and the choice of survival conditions, instead of conditions under which food is present, have been fortunate. Survival conditions eliminate the uncontrollable nutritional factors, but are somewhat complicated by the low death rate resulting from the transfer of the cells from the culture medium to the solutions used in the experiments. However, the exact chemical reproducibility of these solutions more than compensates for this disadvantage. In fact, we have found in preliminary experiments carried out in the presence of food organisms that such conditions are extremely difficult to control.

The first important result is the clear-cut demonstration that *the process of cell division depends on cell volume*, irrespective of whether the cells are immersed in control or glutathione solution. This is particularly well shown in Figure 8, which is based on a large number of cells. We have already referred to this relationship as indicating that cell division is dependent on cell maturation. In using the term maturation we are fully aware that it is impossible at present to explain it on a chemical and physical basis. However, the much greater chance of a larger cell to exhibit signs of cell division as compared with a very small cell, must indicate that the chemical state (to use a word with broad meaning) of the very small cell and particularly its nucleus differs from that of a larger cell.

The second important point is *the relative independence of nuclear and cytoplasmic division* of the experimental and control animals. This point will be more forcibly brought out in the discussion of the glutathione effect.

The third result indicates, but does not prove, that *the hydrogen ion concentration of the solution may exert an effect on the process of cell division*. It is necessary to point out, however, that it is practically impossible to buffer the solutions at different pH levels without introducing slight variations in the concentration of the different inorganic ions used for their buffer action. Further work is therefore required to establish this important relationship of pH of the medium to cell division.

As to the action of the glutathione, it can be stated without reservation that *glutathione favors the process of cell division*, and it is significant that this action is exerted by such low concentrations of the substance that an ordinary nutritional effect can be ruled out. A further significant fact is that the state of oxidation of the sulphur in the glutathione of the solution in which the cells are immersed apparently does not influence the result. Both SH and S-S glutathione favor the division process. We must emphasize again that

the SH glutathione employed was a beautifully crystalline substance yielding correct S and N figures on analysis, whereas the S-S glutathione was contaminated by small amounts of impurities.

A further important fact is *the much greater effect of SH glutathione on the division of the nucleus than on the cytoplasm of cells of lesser maturity.* (Fig. 9.) This may indicate that the seat of the glutathione action is principally on the nucleus as far as the various parts of the division process of the cell as a whole are concerned. It does not necessarily follow, however, that glutathione does not effect the metabolism of the cytoplasm, but only that cytoplasmic division *per se* is not so markedly influenced by glutathione until the cell reaches a greater state of maturity. We believe that this is the first instance in which a substance is shown to favor more or less specifically the division of the nucleus. This is particularly significant in view of the normal occurrence of glutathione in cells of widely different origin, including also tumor cells.

The action of glutathione clearly depends on the stage of maturation of the cell upon which this substance is allowed to act. It is perfectly obvious that glutathione does not appreciably influence cell division, nuclear division, or the occurrence of polynuclear cells, when amoebae of *very small* cell volume are used. (Fig. 8.) As the cells mature, the glutathione effect upon the division process evidences itself and reaches a maximum for cells of an average volume between 20 and 25 arbitrary units. (Fig. 9.) The state of maturation of the nucleus therefore is a determining factor, as to whether or not exposure of a given cell to glutathione will be followed by nuclear division.

We do not intend in this paper to speculate on the chemical mechanism underlying the action of glutathione on the division process.

Conclusions

A method is described for the study of the influence of chemical substances upon the division of *Amoeba* under conditions which almost completely eliminate the uncontrollable nutritional factors. Using this technique, the following results were obtained:

1. The percentage of occurrence of nuclear divisions and cell divisions and the number of polynuclear cells found at the end of the experiments vary directly with the volume of the cells used. The process of cell division, therefore, depends on the cell volume.

2. The percentage of occurrence of nuclear, and probably of cell division apparently varies directly with the hydrogen ion concentration over the range covered.

3. Exposure of amoebae to SH or S-S glutathione results in more nuclear and cell divisions and more polynucleate cells than in the controls. This is true for nuclear division, and to some extent for cell division, between pH 6.0 and 8.1. However, the percentage

increase in nuclear division in SH glutathione over that in the controls is probably not influenced by the hydrogen ion concentration over the range covered.

4. The percentage increase in nuclear division and cell division and the number of polynuclear cells in SH glutathione solution, as compared with the controls, vary with the volume of the cells used, and reach a maximum in all three, when the cells used are about 0.002 to 0.0025 cubic millimeters in volume.

5. The effect of SH glutathione is much greater on nuclear than on cell division on cells having volumes between about 0.00125 and 0.0022 cubic millimeters. This indicates that glutathione exerts a more marked influence on nuclear division than on cell division on cells of this range of volume (maturity).

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THE BLACKTONGUE PREVENTIVE VALUE OF MINOT'S LIVER EXTRACT

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Goldberger, Wheeler, Lillie, and Rogers (1) have shown that dried pig's liver is a good source of the antipellagric vitamin. Minot and his associates (2) have shown that an extract of liver is potent in the treatment of pernicious anemia, and Cohn, Minot, Alles, and Salter (3) present evidence which indicates that the antipellagric vitamin is not responsible for the effectiveness of liver in pernicious anemia. It was, however, considered worth while to investigate the antipellagric activity of Minot's liver extract. Through the courtesy of Dr. George R. Minot we were furnished, by Eli Lilly and Co., with a supply of Minot's liver extract No. 343, which had been tested and found potent in the treatment of pernicious anemia.

The study was carried out on dogs and consisted of both a preventive and a therapeutic test. The animals were taken care of as described in a previous publication from this laboratory (4).

Goldberger and his associates (1, 4) have already demonstrated the relationship between blacktongue of dogs and pellagra of man, and the evidence which they have presented warrants the assumption that both diseases are caused by a lack of the antipellagric vitamin.

EXPERIMENTAL

Goldberger, Wheeler, Lillie, and Rogers (5) have reported, on the basis of six dogs, that our diet No. 268 (Table 1) produced blacktongue in a period which did not exceed 46 days.

TABLE 1.—*Composition of experimental blacktongue-producing diet No. 268*¹

[Total calories, 2,400]

Article of diet	Quantity	Nutrients		
		Protein	Fat	Carbo- hydrate
	<i>Grams</i>	<i>Grams</i>	<i>Grams</i>	<i>Grams</i>
Corn meal ²	400	33.6	18.8	266.0
Cowpeas (<i>Vigna sinensis</i>) ³	50	10.7	.7	36.4
Casein (purified) ⁴	95	82.6	.5	
Cottonseed oil.....	30		30.0	
Cod-liver oil.....	15		15.0	
Salt mixture ⁵	22			
Total nutrients.....		126.9	65.0	328.4
Nutrients per 1,000 calories.....		52.9	27.0	136.0

¹ The corn meal and cowpeas (previously coarsely ground) are stirred into water and cooked about 1½ hours. Then the other ingredients are well stirred in, the total weight being brought to 2,400 grams with water (so that 1 gram represents 1 calorie), and the finished mixture served to the dog ad libitum.

² Whole maize meal (white) sifted as for human consumption.

³ The variety known as the California black-eyed pea.

⁴ Commercial casein leached for 1 week in daily changes of acidulated water, after McCollum (6).

⁵ After Osborne and Mendel (7).

* This study was organized prior to the death of Surgeon Joseph Goldberger, on January 17, 1929, and was, in part, carried out under his direction.

As a control on the present experiments, two dogs (Nos. 59 and 125) were placed on diet No. 268. The significant details in regard to each of these animals are as follows:

Dog 59.—Female. Whelped in the laboratory November 4, 1923. Raised on miscellaneous stock diet. Served in two previous experiments but has not had blacktongue. On stock diet from April 11, 1928, to May 15, 1928.

May 15, 1928: Weighs 6.3 kilograms. In good condition; begins test diet No. 268.

September 1: At the end of a period of 108 days presents first signs of an attack of blacktongue, reddening of mucosa of cheeks, floor of mouth, and upper lip.

September 4: Weighs 4.9 kilograms. Further history not relevant.

Dog 125.—Female. Acquired May 25, 1927, between which date and April 11, 1928, served in one experiment and suffered no attack of blacktongue. On stock diet from April 11 to May 15, 1928.

May 15, 1928: Weighs 7.2 kilograms. In good condition; begins test diet No. 268.

July 3: Weighs 7.9 kilograms.

July 7: At the end of a period of 53 days presents first signs of an attack of blacktongue, a reddening of the mucosa of the cheeks, floor of the mouth and left side of the upper lip. Further history not relevant.

Summary.—The two control animals developed blacktongue in 108 and 53 days, respectively. On the basis of the 6 dogs already reported by Goldberger, Wheeler, Lillie, and Rogers (5), and on the two additional controls here reported, our diet No. 268 produced blacktongue within a period which did not exceed 108 days, and in 7 of the 8 animals did not exceed 53 days. It thus appears that the basic diet No. 268 is a potent blacktongue producer.

PREVENTIVE TEST ²

Five dogs (Nos. 65, 68, 86, 131, and 132) were placed on the basic diet No. 268, plus a daily dose of Minot's liver extract equivalent to 100 grams of fresh liver, given in gelatin capsules. The significant details in regard to each of the experimental animals are as follows:

Dog 65.—Female. Acquired January 28, 1924. Served in several experiments and suffered one attack of blacktongue, which began April 22, 1924. On stock diet from September 7, 1927, to November 16, 1927.

November 15, 1927: Weighs 10 kilograms.

November 16: Discontinues stock diet No. 156; in good condition; begins test diet No. 268 plus Minot's liver extract, in a daily dose equivalent to 100 grams of fresh liver.

May 15, 1928: Weighs 9.1 kilograms.

May 19: Has not shown any evidence of blacktongue. Liver extract discontinued at the end of a period of 185 days. Continues diet No. 268.

July 10: Weighs 9 kilograms.

July 12: 54 days from the date of discontinuing Minot's liver extract showed first signs of an attack of blacktongue, an injection of the floor of the mouth and reddening of the mucosa of the cheeks. Further history not relevant.

² Carried out with the assistance of Surg. L. M. Rogers.

Dog 68.—Female. Whelped in the laboratory November 25, 1923. Served in two experiments and suffered no attack of blacktongue. On stock diet from September 7, 1927, to November 16, 1927.

November 15, 1927: Weighs 9.7 kilograms.

November 16: Begins test diet No. 268, plus a daily supplement of Minot's liver extract equivalent to 100 grams of fresh liver.

May 15, 1928: Weighs 9.5 kilograms.

May 19: At the end of a period of 185 days discontinues liver extract in good condition; no signs of blacktongue at any time; continues diet No. 268.

January 2, 1929: Weighs 9.1 kilograms. At the end of a period of 228 days from discontinuing the Minot's liver extract presents first signs of a beginning attack of blacktongue, an injection of the floor of the mouth. Further history not relevant.

Dog 86.—Female. Whelped in the laboratory October 12, 1924. Served in several experiments and suffered one definite attack of blacktongue, which began January 23, 1927. On stock diet from September 27, 1927, to November 16, 1927.

November 15, 1927: Weighs 9.1 kilograms.

November 16: Begins test diet No. 268 plus a daily dose of Minot's liver extract equivalent to 100 grams of fresh liver.

May 15, 1928: Weighs 10 kilograms.

May 19: At the end of a period of 185 days liver extract discontinued; animal in good condition; no evidence of blacktongue; continues diet No. 268.

July 10: Weighs 9.5 kilograms. At the end of a period of 52 days from discontinuing the liver extract presents first signs of a beginning attack of blacktongue, reddening of the floor of the mouth and a faint reddened band on the mucosa of each side of the upper lip. Further history not relevant.

Dog 131.—Female. Whelped in the laboratory June 28, 1927, and raised on stock diet.

January 3, 1928: Weighs 5.4 kilograms.

January 4: In good condition; begins test diet No. 268 plus daily supplement of Minot's liver extract equivalent to 100 grams of fresh liver.

June 30: Presented slight injection of the floor of the mouth, which lasted one day.

July 10: Weighs 6.9 kilograms.

July 12: At the end of a period of 189 days discontinues experiment; in good condition. Further history not relevant.

Dog 132.—Female. Whelped in the laboratory June 28, 1927, and reared on stock diet.

January 3, 1928: Weighs 7.3 kilograms.

January 4: Begins test diet No. 268 plus a daily supplement of Minot's liver extract equivalent to 100 grams of fresh liver; in good condition.

July 10: Weighs 8.4 kilograms.

July 12: At the end of a period of 189 days discontinues experiment, without having shown any signs of blacktongue; in good condition. Further history not relevant.

Summary.—Five animals were carried on the basic blacktongue producing diet No. 268 plus a daily supplement of Minot's liver extract equivalent to 100 grams of fresh liver, for a period of from 185 to 189 days, without developing blacktongue. One animal (No. 131) presented a fleeting injection of the floor of the mouth 177 days from the beginning of the experiment, which may possibly be an indication

that the quantity of liver extract given was barely enough to maintain the animal. The Minot's liver extract supplement was then discontinued with three of the animals (Nos. 65, 68, and 86) and signs of blacktongue appeared in 54, 228, and 52 days, respectively. The cause of the long delay in onset in the case of dog No. 68 (228 days) is not clear.

CURATIVE TEST

Five dogs (Numbers 150, 182, 189, 192, and 193) were placed on the basic diet No. 268 and allowed to develop blacktongue. After the appearance of the first definite signs of blacktongue a daily dose of Minot's liver extract equivalent to 100 grams of fresh liver was given each animal, in gelatin capsules. The significant details in regard to each of the experimental animals are as follows:

Dog 193.—Female. Acquired June 27, 1929. On stock diet to September 19, 1929.

September 17, 1929: Weighs 6.4 kilograms.

September 19: In good condition; begins test diet No. 268.

February 11, 1930: Weighs 6.5 kilograms.

February 13: 147 days from the beginning of the experiment presents first signs of an attack of blacktongue, a streaky injection of the floor of the mouth.

February 23: Floor diffusely and intensely reddened, cheeks reddened and covered by thin pseudomembrane, faint blush on the mucosa of each side of the upper lip. Begins daily dose of Minot's liver extract equivalent to 100 grams of fresh liver.

February 24: Temperature 40° C. Condition of mouth worse.

February 27: Found dead at 1.30 p. m. Autopsy; advanced blacktongue and bronchopneumonia.

Dog 182.—Female. Acquired May 2, 1929. On stock diet to September 19, 1929.

September 17, 1929: Weighs 6.8 kilograms.

September 19: In good condition; begins test diet No. 268.

November 5: 47 days from the beginning of the experiment presents first signs of an attack of blacktongue, a diffuse injection of the floor of the mouth, faint reddening of the mucosa of the cheeks, elongated reddened patch on each side of the upper lip over the canine teeth.

November 6: Begins daily dose of a quantity of Minot's liver extract equivalent to 100 grams of fresh liver.

November 17: Mouth normal.

March 25, 1930: Weighs 7.4 kilograms.

March 26: Discontinues experiment in good condition, after a period of 140 days on Minot's liver extract. Has not presented any signs of a recurrence of blacktongue. Further history not relevant.

Dog 192.—Female. Acquired June 27, 1929. On stock diet to September 19, 1929.

September 17: Weighs 9 kilograms.

September 19: In good condition; begins test diet No. 268.

October 19: 30 days from the beginning of the experiment presents first signs of beginning attack of blacktongue, a faint streaky injection of the floor of the mouth.

October 21: Floor of the mouth and soft palate injected; cheeks faintly reddened; reddened patch on each side of the upper lip over the canines. Begins daily dose of liver extract equivalent to 100 grams of fresh liver.

October 26: Mouth normal.

February 9, 1930: Reddened patch on each side of the upper lip over the canine teeth, which slowly faded during the next several days.

March 25: Weighs 9.5 kilograms.

March 26: Discontinues the experiment in good condition, after a period of 156 days on Minot's liver extract.

Dog 189.—Female. Acquired June 27, 1929. On stock diet to September 19, 1929.

September 17: Weighs 9.8 kilograms.

September 19: Begins test diet No. 268 in good condition.

October 15: Weighs 9.8 kilograms. Twenty-six days from the beginning of the experiment presents first signs of an attack of blacktongue, an intense injection of the floor of the mouth.

October 21: Floor of mouth streakily injected, soft palate injected, mucosa of cheeks reddened, reddened patch on each side of the upper lip over the canine teeth. Begins daily dose of liver extract equivalent to 100 grams of fresh liver.

October 28: Mouth normal.

March 25, 1930: Weighs 9.6 kilograms.

March 26: Discontinues experiment in good condition, after a period of 156 days on liver extract. Has not presented any signs of a recurrence of black tongue. Further history not relevant.

Dog 150.—Male. Acquired September 20, 1928, between which date and June 25, 1929, served in one experiment and suffered an attack of blacktongue, which began February 23, 1929. On stock diet for reconditioning from June 25, 1929, to September 19, 1929.

September 17, 1929: Weighs 8 kilograms.

September 19: Begins test diet No. 268 in good condition.

October 15: Weighs 8.8 kilograms.

October 17: Presented first premonitory signs of an attack of black tongue, a faint streaky injection of the floor of the mouth.

October 29: Weighs 8.9 kilograms.

October 30: 41 days from the beginning of the experiment presents first signs of a definite attack of blacktongue, an elongated, reddened patch on each side of the upper lip over the canine teeth. Cheeks and soft palate reddened. Floor of mouth injected. Begins daily dose of Minot's liver extract equivalent to 100 grams of fresh liver.

November 5: Weighs 9 kilograms. Mouth normal.

January 28, 1930: Injection of the floor of the mouth, diffuse reddening of the mucosa of each side of the upper lip.

February 1: Mouth normal.

March 25: Weighs 10.2 kilograms.

March 26: Discontinues experiment in good condition after a period of 147 days on liver extract.

Summary.—All of the animals developed blacktongue in from 26 to 147 days. One animal (No. 193) died in 14 days from the onset of the first signs of blacktongue, after having received liver extract for four days. A complicating bronchopneumonia, revealed at autopsy, and the delay in beginning the liver extract, probably account for the death of this animal. The remaining four animals

promptly recovered from the attack of blacktongue. Two of the animals were maintained in good condition for an additional period of 140 to 156 days. The other two animals (dog No. 192 and dog No. 150) presented what may have been fleeting evidence of a recurrence 111 and 90 days, respectively, from the beginning of the treatment with Minot's liver extract. This may indicate that while the dose of liver extract was sufficiently large to cure the acute attack, it was barely enough to maintain the animals. Goldberger, Wheeler, Lillie, and Rogers (1) have already pointed out that care must be taken in interpreting the curative test in blacktongue on account of the relapsing nature of the disease. However, when a constantly curative effect is produced, such as occurred in this experiment, and is taken in conjunction with a preventive test, the results become of significance.

DISCUSSION AND CONCLUSIONS

It has been shown that dogs on the basic blacktongue-producing diet No. 268 develop signs of blacktongue in a period which only occasionally exceeds 53 days. When Minot's liver extract, in a daily dose equivalent to 100 grams of fresh liver, was given to five dogs on this diet, the occurrence of blacktongue was prevented for a period of at least 185 days. Three of the animals were continued on the basic diet after discontinuing the liver extract; these animals then developed blacktongue in 54, 228, and 52 days, respectively, thus further strengthening the presumption that the delaying effect was due to the liver extract. The same quantity of Minot's liver extract, given daily to dogs that had developed signs of blacktongue on the basic diet No. 268, caused a recession of symptoms in 4 out of 5 dogs and prevented a recurrence, except for possible fleeting signs in 2 animals, for at least 140 days. The period of observation was too short to warrant the statement that blacktongue would not have developed at a later date, and the possibility of fleeting signs of recurrence in two of the dogs may indicate that the quantity given was barely sufficient to maintain the animals.

It appears, however, that Minot's liver extract, given to dogs on a basic blacktongue-producing diet, in a daily dose equivalent to 100 grams of fresh liver, has a very definite delaying effect on the occurrence of symptoms, and when fed to dogs in an attack of blacktongue has a very definite curative effect. The most reasonable explanation for this action seems to be that the liver extract carries the anti-pellagric vitamin with it. In view of the evidence herein presented, it seems that Minot's liver extract is a fairly good source of the anti-pellagric vitamin, and given in larger quantity would be of value as a temporary expedient in the treatment of pellagra.

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 - (3) Cohn, Minot, Alles, and Salter: The nature of the material in liver effective in pernicious anemia. J. Biol. Chem., Vol. LXXVII, No. 2 (May, 1928), pp. 325-358.
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 - (6) McCollum, Simmonds, Shipley, and Park: Studies on experimental rickets, etc. Bull. Johns Hopkins Hosp., 1922, vol. 33, p. 298.
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COURT DECISION RELATING TO PUBLIC HEALTH

Prevention of pollution of stream used for domestic purposes.—(Utah Supreme Court; *Bountiful City v. DeLuca et al.*, 292 P. 194; decided Oct. 10, 1930.) An action was brought by Bountiful City to restrain the defendants from keeping or grazing goats or other livestock within 300 feet on either side of a certain creek, its tributaries, or sources of supply, some of the waters of which were used by the city and its inhabitants for culinary and domestic purposes, and from permitting such animals to drink out of such creek, its tributaries, or sources of supply, and from in any manner contaminating such waters.

Under State statutes, cities of the class of Bountiful City were authorized to construct waterworks within or without their corporate limits, and, for the purpose of maintaining and protecting the same from injury or pollution, their jurisdiction was extended over the territory occupied by such works and over all reservoirs, streams, etc., used in and necessary for the maintenance and operation of such works and over streams and sources from which the water was taken, for 15 miles above the point from which it was taken and for a distance of 300 feet on each side of the stream. Authority was given to enact ordinances and regulations necessary to carry the conferred powers into effect and to prevent pollution of streams from which the inhabitants of the cities derived their water supply. Bountiful City passed an ordinance which defined the watershed area of

the city as the entire area in any canyon above the intake of the city within which water drained into any stream or tributary thereof where such stream was taken by the city into its waterworks system for culinary and domestic purposes. The ordinance made it unlawful for any person to permit any loose cattle, horses, sheep, or other animals to run at large, except where such livestock were more than 300 feet from any stream or source of water supply within the watershed area, or to permit animals to water directly from the stream or to remain in or near or to pollute such stream.

In the instant case the creek involved flowed through the lands of the defendants. Such lands were suitable only for grazing purposes and were not capable of being used for any other purpose. The defendants used their lands for grazing from 300 to 500 goats and were engaged in selling goat's milk and manufacturing cheese and other products from goat's milk.

The judgment of the trial court was in favor of the city, and the defendants appealed. The supreme court stated that the proper disposition of the case involved the question of whether the statute, ordinance, and decree amounted to a taking or deprivation of property without compensation or due process of law. The court came to the conclusion that neither the statute nor the ordinance was "an unreasonable regulation when properly and reasonably applied and enforced." But with respect to the decree, the court's finding was as follows:

Thus, in so far as the decree restrains the defendants from corralling or bedding or holding their goats or other livestock within the 300-foot limit above the intake of the city, from suffering or permitting any dead animals to be in or near the creek or any tributary thereof whether within the 300-foot limit or beyond it, from in any manner unnecessarily or unreasonably or negligently so using their premises as to cause dung from animals or other refuse to be cast or washed into the creek and which in the exercise of all reasonable care and caution may be avoided or prevented, from suffering or permitting any of their animals above the city's intake to drink directly from the creek or any of its sources of supply, and which in the exercise of all reasonable care and caution may be avoided and prevented, and from in any manner polluting or contaminating any of the waters of the creek or of any of its sources of supply, which, in the making of a proper, reasonable, and necessary use of the lands, and in the exercise of all reasonable care and caution may be avoided and prevented, the judgment is affirmed. In so far as the decree, without compensation, restrains the defendants from grazing their lands within the 300-foot limit under any and all circumstances, though in so doing the defendants do not make any unreasonable, unnecessary, or negligent use of their lands and use all reasonable care and caution to avoid or prevent any pollution or contamination of the waters of the creek or of any of its sources of supply, the judgment is reversed. * * *

DEATHS DURING WEEK ENDED NOVEMBER 22, 1930

Summary of information received by telegraph from industrial insurance companies for the week ended November 22, 1930, and corresponding week of 1929. (From the Weekly Health Index issued by the Bureau of the Census, Department of Commerce)

	Week ended Nov. 22, 1930	Corresponding week, 1929
Policies in force.....	75, 226, 750	75, 155, 310
Number of death claims.....	14, 232	13, 602
Death claims per 1,000 policies in force, annual rate.....	9.9	9.4

Deaths ¹ from all causes in certain large cities of the United States during the week ended November 22, 1930, infant mortality, annual death rate, and comparison with corresponding week of 1929. (From the Weekly Health Index issued by the Bureau of the Census, Department of Commerce)

[The rates published in this summary are based upon mid-year population estimates derived from the 1930 census. The rates are not exactly comparable with similar rates published in the Public Health Reports earlier than the issue of August 22, 1930, which were based upon estimates made before the 1930 census was taken]

City	Week ended Nov. 22, 1930				Corresponding week 1929		Death rate ² for first 47 weeks	
	Total deaths	Death rate ¹	Deaths under 1 year	Infant mortality rate ¹	Death rate ¹	Deaths under 1 year	1930	1929
Total (77 cities).....	7, 739	11.8	696	56	11.7	678	11.9	12.6
Akron.....	36	7.4	4	37	8.5	4	7.9	9.4
Albany ¹	38	15.5	5	103	12.8	4	14.8	16.3
Atlanta.....	83	16.2	5	51	15.9	10	15.7	16.0
White.....	45		2	32		5		
Colored.....	38	(9)	3	86	(9)	5	(9)	(9)
Baltimore ¹	200	13.0	14	49	13.4	25	14.1	14.6
White.....	152		10	44		17		
Colored.....	48	(9)	4	64	(9)	8	(9)	(9)
Birmingham.....	57	11.5	7	67	12.2	8	13.7	15.9
White.....	21		1	16		4		
Colored.....	36	(9)	6	147	(9)	4	(9)	(9)
Boston.....	208	13.8	23	67	12.9	17	14.1	14.9
Bridgeport.....	35	12.4	4	68	11.7	2	10.9	12.0
Buffalo.....	151	13.7	16	71	10.1	9	13.0	14.0
Cambridge.....	28	12.8	1	20	11.0	5	11.8	12.5
Camden.....	30	13.3	5	88	7.1	2	13.7	14.4
Canton.....	23	11.3	2	53	9.0	2	9.9	11.2
Chicago ¹	704	10.8	54	48	11.5	63	10.4	11.3
Cincinnati.....	138	16.0	9	53	15.8	14	15.7	17.0
Cleveland.....	229	13.2	20	60	11.2	17	11.1	12.4
Columbus.....	68	12.2	4	39	12.7	4	15.5	14.8
Dallas.....	59	11.7	5		12.5	7	11.5	11.5
White.....	45		3			7		
Colored.....	14	(9)	2		(9)	0	(9)	(9)
Dayton.....	34	8.8	6	90	12.2	1	10.7	11.5
Denver.....	100	18.1	12	131	16.1	6	14.9	14.8
Des Moines.....	33	12.0	2	37	10.0	2	11.7	11.5
Detroit.....	273	9.0	24	52	10.3	40	9.3	11.1
Duluth.....	25	12.9	2	54	11.4	0	11.5	11.5
El Paso.....	38	19.3	4		13.5	4	17.2	19.5
Erie.....	31	13.9	1	22	10.9	1	11.2	12.1
Fall River ¹	18	8.2	3	69	11.8	0	11.7	13.6
Flint.....	22	7.3	1	12	9.9	8	9.2	10.7
Fort Worth.....	36	11.6	6		11.1	4	11.0	12.3
White.....	27		6			2		
Colored.....	9	(9)	0		(9)	2	(9)	(9)
Grand Rapids.....	20	6.2	6	90	7.2	1	10.1	10.2
Houston.....	71	12.7	6		10.2	4	12.2	12.6
White.....	44		3			4		
Colored.....	27	(9)	3		(9)	0	(9)	(9)
Indianapolis.....	99	14.1	7	53	17.6	6	14.5	14.8
White.....	86		7	60		6		
Colored.....	13	(9)	0	0	(9)	0	(9)	(9)
Jersey City.....	72	11.9	14	121	10.4	15	11.4	12.4
Kansas City, Kans.....	26	11.1	1	22	9.4	1	11.7	12.8
White.....	21		1	28		1		
Colored.....	5	(9)	0	0	(9)	0	(9)	(9)
Kansas City, Mo.....	109	14.4	11	92	13.9	6	13.5	13.9
White.....	24	11.8	3	70	13.1	6	13.6	13.9
Colored.....	18		3	78		4		
Colored.....	6	(9)	0	0	(9)	1	(9)	(9)

Footnotes at end of table.

Deaths¹ from all causes in certain large cities of the United States during the week ended November 22, 1930, infant mortality, annual death rate, and comparison, with corresponding week of 1929. (From the Weekly Health Index issued by the Bureau of the Census, Department of Commerce)—Continued

[The rates published in this summary are based upon mid-year population estimates derived from the 1930 census. The rates are not exactly comparable with similar rates published in the Public Health Reports earlier than the issue of August 22, 1930, which were based upon estimates made before the 1930 census was taken]

City	Week ended Nov. 22, 1930				Corresponding week 1929		Death rate ² for first 47 weeks	
	Total deaths	Death rate ²	Deaths under 1 year	Infant mortality rate ³	Death rate ²	Deaths under 1 year	1930	1929
Los Angeles	243	10.2	7	21	10.9	18	11.0	11.3
Lowell ⁴	23	12.0	4	106	17.5	3	13.4	14.1
Lynn	25	12.7	4	112	7.7	1	10.4	11.1
Memphis	60	12.4	6	71	14.0	3	17.0	18.8
White	33		3	54		3		
Colored	27	(⁵)	3	101	(⁵)	0	(⁵)	(⁵)
Milwaukee	107	9.8	8	35	9.4	9	9.8	11.0
Minneapolis	93	10.4	10	66	10.2	6	10.7	10.8
Nashville	59	20.9	13	204	17.8	5	17.4	18.7
White	38		13	273		4		
Colored	21	(⁵)	0	0	(⁵)	1	(⁵)	(⁵)
New Bedford ⁷	23	10.6	0	0	12.0	1	10.9	12.1
New Haven	37	11.9	6	92	13.5	1	12.7	13.5
New Orleans	160	18.2	13	72	16.0	10	17.5	17.6
White	96		6	51		2		
Colored	64	(⁵)	7	113	(⁵)	8	(⁵)	(⁵)
New York	1,297	9.7	107	45	10.2	121	10.7	11.3
Bronx Borough	193	7.9	19	55	7.6	10	7.9	8.2
Brooklyn Borough	409	8.2	33	35	9.3	38	9.7	10.2
Manhattan Borough	543	15.3	43	55	14.6	57	16.0	16.4
Queens Borough	121	5.8	11	44	6.6	12	7.0	7.6
Richmond Borough	31	10.2	1	19	15.5	4	14.0	15.9
Newark, N. J.	95	11.1	8	42	11.2	8	12.0	12.6
Oakland	75	13.7	13	161	9.7	1	11.0	11.2
Oklahoma City	38	10.7	2	36	12.1	5	10.8	10.9
Omaha	63	15.3	4	49	15.5	7	13.6	13.6
Paterson	34	12.8	1	17	15.5	4	12.1	13.3
Philadelphia	470	12.5	46	68	12.3	42	12.5	13.1
Pittsburgh	171	13.3	26	92	14.6	34	13.8	14.8
Portland, Oreg.	66	11.5	2	25	11.4	1	12.2	12.7
Providence	53	11.0	1	9	11.1	2	12.9	14.5
Richmond	53	15.1	5	73	10.9	7	14.9	16.2
White	31		3	66		4		
Colored	22	(⁵)	2	85	(⁵)	3	(⁵)	(⁵)
Rochester	71	11.4	4	36	10.8	7	11.8	12.3
St. Louis	227	14.4	13	45	14.5	15	14.1	14.6
St. Paul	53	10.2	4	40	10.1	4	10.1	10.4
Salt Lake City ⁵	42	15.6	4	63	13.9	5	12.5	13.0
San Antonio	60	12.2	10		17.9	13	14.4	14.5
San Diego	47	16.4	3	63	12.4	0	14.3	15.0
San Francisco	222	18.4	8	54	14.4	7	13.2	13.0
Schenectady	18	9.8	3	93	9.8	2	11.2	12.1
Seattle	74	10.6	1	10	10.9	6	10.9	11.2
Somerville	12	6.0	2	63	9.1	2	9.7	9.2
Spokane	26	11.7	1	26	12.7	0	12.5	12.7
Springfield, Mass.	25	8.7	4	69	13.4	0	12.1	12.7
Syracuse	46	11.5	5	62	7.9	0	11.7	12.8
Tacoma	18	8.8	1	27	7.4	0	12.5	11.7
Toledo	50	8.9	6	55	13.4	9	12.7	13.7
Trenton	39	16.6	6	115	14.9	0	16.6	17.1
Utica	30	15.2	1	28	12.8	1	14.7	15.4
Washington, D. C.	149	16.0	23	135	13.0	5	15.2	15.3
White	100		9	79		2		
Colored	49	(⁵)	14	250	(⁵)	3	(⁵)	(⁵)
Waterbury	17	8.7	2	49	7.3	3	9.3	9.4
Wilmington, Del. ⁷	23	11.4	2	48	9.4	5	14.6	13.8
Worcester	57	15.1	7	97	9.9	1	12.7	12.6
Yonkers	25	9.6	1	24	8.7	5	8.1	9.3
Youngstown	45	13.8	2	29	13.3	3	10.4	12.2

¹ Deaths of nonresidents are included. Stillbirths are excluded.

² These rates represent annual rates per 1,000 population, as estimated for 1930 and 1929 by the arithmetical method.

³ Deaths under 1 year of age per 1,000 live births. Cities left blank are not in the registration area for births.

⁴ Data for 72 cities.

⁵ Deaths for week ended Friday.

⁶ For the cities for which deaths are shown by color the colored population in 1920 constituted the following percentages of the total population: Atlanta, 31; Baltimore, 15; Birmingham, 39; Dallas, 15; Fort Worth, 14; Houston, 25; Indianapolis, 11; Kansas City, Kans., 14; Knoxville, 15; Memphis, 38; Nashville, 30; New Orleans, 26; Richmond, 32; and Washington, D. C., 25.

⁷ Population Apr. 1, 1930; decreased 1920 to 1930; no estimate made.

PREVALENCE OF DISEASE

No health department, State or local, can effectively prevent or control disease without knowledge of when, where, and under what condition cases are occurring

UNITED STATES

CURRENT WEEKLY STATE REPORTS

These reports are preliminary, and the figures are subject to change when later returns are received by the State health officers

Reports for Weeks Ended November 29, 1930, and November 30, 1929

Cases of certain communicable diseases reported by telegraph by State health officers for weeks ended November 29, 1930, and November 30, 1929

Division and State	Diphtheria		Influenza		Measles		Meningococcus meningitis	
	Week ended Nov. 29, 1930	Week ended Nov. 30, 1929	Week ended Nov. 29, 1930	Week ended Nov. 30, 1929	Week ended Nov. 29, 1930	Week ended Nov. 30, 1929	Week ended Nov. 29, 1930	Week ended Nov. 30, 1929
New England States:								
Maine.....	5	6	1	7	15	6	0	1
New Hampshire.....	3	4		5		71	0	0
Vermont.....	3	3				5	0	0
Massachusetts.....	68	131	3	3	162	91	1	2
Rhode Island.....	4	17	3		3	2	0	0
Connecticut.....	9	25	3	1	85	2	1	0
Middle Atlantic States:								
New York.....	93	173	15	11	112	164	11	21
New Jersey.....	65	182	8	4	120	31	4	4
Pennsylvania.....	108	171			359	302	12	2
East North Central States:								
Ohio.....	84	89	18	15	29	361	8	10
Indiana.....	46	39	6		84	12	5	0
Illinois.....	179	231	7	16	113	325	6	9
Michigan.....	77	194	9	6	68	179	6	7
Wisconsin.....	18	36	25	13	205	508	1	3
West North Central States:								
Minnesota.....	13	22	2		8	57	2	5
Iowa.....	9	8			5	78	0	1
Missouri.....	52	45	2	16	331	12	4	7
North Dakota.....	6	4			3	10	0	0
South Dakota.....	6	2			2	6	1	0
Nebraska.....	19	19	5	5	3	49	0	1
Kansas.....	15	46	1	3	10	50	0	3
South Atlantic States:								
Delaware.....	5	7			3		0	0
Maryland.....	40	32	9	32	8	30	0	2
District of Columbia.....	3	21			1		0	1
West Virginia.....	19	39	32	35	27	23	1	0
North Carolina.....	98	112	4	6	25		2	1
South Carolina.....	34	35	58	57			1	0
Georgia.....	11	22	53	53	3	16	1	0
Florida.....	9	19	2	1	2	5	0	0
East South Central States:								
Kentucky.....	15	27				135	0	1
Tennessee.....	23	34	75	82	17	1	1	5
Alabama.....	70	51	64	67	28	2	0	1
Mississippi.....	35	41					1	0

¹ New York City only.

² Week ended Friday.

Cases of certain communicable diseases reported by telegraph by State health officers for weeks ended November 29, 1930, and November 30, 1929—Continued

Division and State	Diphtheria		Influenza		Measles		Meningococcus meningitis	
	Week ended Nov. 29, 1930	Week ended Nov. 30, 1929	Week ended Nov. 29, 1930	Week ended Nov. 30, 1929	Week ended Nov. 29, 1930	Week ended Nov. 30, 1929	Week ended Nov. 29, 1930	Week ended Nov. 30, 1929
West South Central States:								
Arkansas.....	33	20	31	65	1	1	1	2
Louisiana.....	34	41	8	28	8	10	2	2
Oklahoma ¹	56	87	27	125	34	14	3	2
Texas.....	60	115	44	10	1	2	1	1
Mountain States:								
Montana.....	2	4			5	56	0	2
Idaho.....		1			1	20	4	1
Wyoming.....	1	7					0	1
Colorado.....	17	6			101	7	1	0
New Mexico.....	10	8		3	24	15	1	1
Arizona.....	4	20	2	5	100		1	10
Utah ¹	6	2	5	1	2	18	1	3
Pacific States:								
Washington.....	3	8			6	18	0	5
Oregon.....	6	10	13	22	29	13	1	4
California.....	66	73	43	65	188	132	4	7
Division and State	Poliomyelitis		Scarlet fever		Smallpox		Typhoid fever	
	Week ended Nov. 29, 1930	Week ended Nov. 30, 1929	Week ended Nov. 29, 1930	Week ended Nov. 30, 1929	Week ended Nov. 29, 1930	Week ended Nov. 30, 1929	Week ended Nov. 29, 1930	Week ended Nov. 30, 1929
New England States:								
Maine.....	2	0	12	42	0	0	9	3
New Hampshire.....	0	0	8	21	0	0	1	0
Vermont.....	0	0	1	11	1	1	0	0
Massachusetts.....	14	2	175	193	0	0	10	2
Rhode Island.....	0	0	14	17	0	0	0	0
Connecticut.....	0	0	36	52	0	0	3	3
Middle Atlantic States:								
New York.....	4	0	380	266	3	16	22	13
New Jersey.....	1	1	149	121	0	0	5	5
Pennsylvania.....	1	9	399	347	0	4	30	22
East North Central States:								
Ohio.....	17	4	470	346	53	176	20	22
Indiana.....	2	1	145	111	62	113	1	2
Illinois.....	11	1	245	478	25	82	4	10
Michigan.....	6	2	25	256	50	36	6	5
Wisconsin.....	3	0	90	87	7	21	7	52
West North Central States:								
Minnesota.....	2	0	36	94	2	2	0	5
Iowa.....	0	1	69	50	10	48	6	7
Missouri.....	3	0	68	95	6	11	14	2
North Dakota.....	0	0	16	20	13	11	4	9
South Dakota.....	1	0	13	50	16	22	3	1
Nebraska.....	5	0	18	50	33	33	1	0
Kansas.....	4	0	52	111	12	35	6	3
South Atlantic States:								
Delaware.....	0	0	9	4	0	0	4	0
Maryland ¹	0	1	68	41	0	0	12	8
District of Columbia.....	0	0	28	8	0	0	2	0
West Virginia.....	0	0	87	84	59	9	22	25
North Carolina.....	1	5	103	94	5	6	8	7
South Carolina.....	0	0	32	27	1	0	19	8
Georgia.....	0	3	16	39	0	0	5	1
Florida.....	0	0	6	10	0	1	2	0
East South Central States:								
Kentucky.....	2	1	41	73	0	12	10	5
Tennessee.....	1	2	44	53	1	0	18	19
Alabama.....	3	0	79	39	1	0	8	4
Mississippi.....	0	0	31	19	0	0	11	5

¹ Week ended Friday.

¹ Figures for 1930 are exclusive of Oklahoma City and Tulsa.

Cases of certain communicable diseases reported by telegraph by State health officers for weeks ended November 29, 1930, and November 30, 1929—Continued

Division and State	Poliomyelitis		Scarlet fever		Smallpox		Typhoid fever	
	Week ended Nov. 29, 1930	Week ended Nov. 30, 1929	Week ended Nov. 29, 1930	Week ended Nov. 30, 1929	Week ended Nov. 29, 1930	Week ended Nov. 30, 1929	Week ended Nov. 29, 1930	Week ended Nov. 30, 1929
West South Central States:								
Arkansas.....	2	0	14	42	1	3	29	13
Louisiana.....	3	3	26	16	2	2	20	11
Oklahoma ¹	0	0	48	54	4	35	24	25
Texas.....	4	0	27	34	4	16	23	3
Mountain States:								
Montana.....	1	0	33	43	6	17	1	3
Idaho.....	0	0	2	10	1	1	1	0
Wyoming.....	0	0	3	1	0	15	0	0
Colorado.....	2	0	40	30	6	31	5	0
New Mexico.....	0	0	1	6	0	1	3	5
Arizona.....	1	0	1	15	0	0	1	2
Utah ¹	0	0	11	15	3	1	0	1
Pacific States:								
Washington.....	0	0	37	40	11	62	3	1
Oregon.....	0	1	26	42	10	10	4	2
California.....	27	2	96	281	18	27	8	5

¹ Week ended Friday.

² Figures for 1930 are exclusive of Oklahoma City and Tulsa.

SUMMARY OF MONTHLY REPORTS FROM STATES

The following summary of cases reported monthly by States is published weekly and covers only those States from which reports are received during the current week.

State	Cerebro-spinal meningitis	Diphtheria	Influenza	Malaria	Measles	Pellagra	Poliomyelitis	Scarlet fever	Smallpox	Typhoid fever
<i>September, 1930</i>										
New Hampshire.....		11	5				6	8		6
<i>October, 1930</i>										
Colorado.....	5	50	2		328		23	99	8	33
Montana.....	3	8	10		5		6	74	6	13
Nevada.....									3	
Oklahoma ¹	6	245	65	283	30	35	14	145	38	153
Oregon.....		11	55	4	201		7	54	15	15
South Dakota.....	2	45	7		15		58	27	77	9
Tennessee.....	23	257	53	142	40	14	17	248	14	206
Virginia.....	2	360	827	69	256	32	11	366	18	168
Washington.....	11	140	14		29		10	208	99	52
Wisconsin.....	11	95	90		531		65	375	27	35

¹ Exclusive of Oklahoma City and Tulsa

October, 1930

	Cases	Ophthalmia neonatorum:	Cases
Anthrax:		Montana.....	1
South Dakota.....	1	Oklahoma ¹	1
Chicken pox:		Tennessee.....	3
Colorado.....	222	Paratyphoid fever:	
Montana.....	187	Washington.....	1
Nevada.....	17	Scabies:	
Oklahoma ¹	17	Oklahoma.....	1
Oregon.....	102	Oregon.....	12
South Dakota.....	50	Washington.....	17
Tennessee.....	43	Septic sore throat:	
Virginia.....	181	Oklahoma ¹	25
Washington.....	217	Oregon.....	1
Wisconsin.....	981	Tennessee.....	1
Conjunctivitis:		Washington.....	2
Oklahoma ¹	1	Tetanus:	
Diarrhea and dysentery:		Oklahoma ¹	1
Virginia.....	478	Tennessee.....	2
Dysentery:		Trachoma:	
Montana.....	1	Oklahoma ¹	6
Oklahoma ¹	29	South Dakota.....	4
Tennessee.....	8	Tularaemia:	
Washington.....	1	Montana.....	34
German measles:		Nevada.....	2
Colorado.....	1	Virginia.....	4
Washington.....	9	Undulant fever:	
Impetigo contagiosa:		Oklahoma ¹	2
Colorado.....	7	South Dakota.....	1
Oregon.....	13	Virginia.....	1
Tennessee.....	2	Washington.....	1
Washington.....	3	Wisconsin.....	8
Leprosy:		Vincent's angina:	
Colorado.....	1	Oregon.....	3
Lethargic encephalitis:²		Tennessee.....	1
Oregon.....	1	Washington.....	1
Washington.....	3	Whooping cough:	
Wisconsin.....	2	Colorado.....	117
Mumps:		Montana.....	88
Colorado.....	98	Nevada.....	16
Montana.....	23	Oklahoma ¹	36
Nevada.....	99	Oregon.....	49
Oregon.....	53	South Dakota.....	9
South Dakota.....	3	Tennessee.....	66
Tennessee.....	13	Virginia.....	182
Washington.....	135	Washington.....	93
Wisconsin.....	171	Wisconsin.....	580

¹ Exclusive of Oklahoma City and Tulsa.² The 15 cases of lethargic encephalitis published in Public Health Reports dated November 28, 1930, as reported in North Dakota should have been published as reported in New York. No case of this disease was reported in North Dakota during October.³ 1 case of tularaemia for June, 1930, included.

GENERAL CURRENT SUMMARY AND WEEKLY REPORTS FROM CITIES

The 94 cities reporting cases used in the following table are situated in all parts of the country and have an estimated aggregate population of more than 30,420,000. The estimated population of the 88 cities reporting deaths is more than 29,680,000. The estimated expectancy is based on the experience of the last nine years, excluding epidemics.

Weeks ended November 22, 1930, and November 23, 1929

	1930	1929	Estimated expectancy
<i>Cases reported</i>			
Diphtheria:			
45 States.....	1,917	2,312	-----
94 cities.....	595	1,071	1,091
Measles:			
45 States.....	2,331	2,681	-----
94 cities.....	402	322	-----
Meningococcus meningitis:			
46 States.....	84	138	-----
94 cities.....	41	68	-----
Poliomyelitis:			
46 States.....	184	55	-----
Scarlet fever:			
46 States.....	3,943	3,835	-----
94 cities.....	1,168	1,254	979
Smallpox:			
46 States.....	457	1,095	-----
94 cities.....	20	137	19
Typhoid fever:			
46 States.....	569	378	-----
94 cities.....	90	74	47
<i>Deaths reported</i>			
Influenza and pneumonia:			
88 cities.....	744	619	-----
Smallpox:			
88 cities.....	0	0	-----

City reports for week ended November 22, 1930

The "estimated expectancy" given for diphtheria, poliomyelitis, scarlet fever, smallpox, and typhoid fever is the result of an attempt to ascertain from previous occurrence the number of cases of the disease under consideration that may be expected to occur during a certain week in the absence of epidemics. It is based on reports to the Public Health Service during the past nine years. It is in most instances the median number of cases reported in the corresponding weeks of the preceding years. When the reports include several epidemics, or when for other reasons the median is unsatisfactory, the epidemic periods are excluded, and the estimated expectancy is the mean number of cases reported for the week during nonepidemic years.

If the reports have not been received for the full nine years, data are used for as many years as possible but no year earlier than 1921 is included. In obtaining the estimated expectancy, the figures are smoothed when necessary to avoid abrupt deviation from the usual trend. For some of the diseases given in the table the available data were not sufficient to make it practicable to compute the estimated expectancy.

Division, State, and city	Chicken pox, cases reported	Diphtheria		Influenza		Measles, cases re- ported	Mumps, cases re- ported	Pneu- monia, deaths reported
		Cases, estimated expect- ancy	Cases reported	Cases reported	Deaths reported			
NEW ENGLAND								
Maine:								
Portland	11	1	0		0	1	2	2
New Hampshire:								
Concord	0	0	0		0	0	0	0
Manchester	0	2	2		0	4	0	0
Nashua	0	0	3		0	0	0	0
Vermont:								
Barre	0	1	0		0	0	0	1
Burlington	1	1	0		0	0	0	0
Massachusetts:								
Boston	73	34	28	3	1	32	7	25
Fall River	15	4	1	1	0	1	0	2
Springfield	20	5	4		0	1	5	2
Worcester	32	6	4		0	1	0	5
Rhode Island:								
Pawtucket	1	2	8		0	0	0	3
Providence	6	10	4	1	0	0	0	7
Connecticut:								
Bridgeport	0	6	0	2	2	0	1	2
Hartford	6	6	1		0	31	0	1
New Haven	3	2	1		0	7	4	2
MIDDLE ATLANTIC								
New York:								
Buffalo	62	18	11		0	5	9	22
New York	159	176	49	14	9	76	22	153
Rochester	11	6	1		0	3	0	6
Syracuse	39	3	1		0	0	0	0
New Jersey:								
Camden	11	8	0		0	34	3	5
Newark	26	18	15	3	0	4	7	5
Trenton	6	3	0		1	0	0	5
Pennsylvania:								
Philadelphia	148	71	17	11	3	34	29	58
Pittsburgh	62	28	19		3	10	12	36
Reading	32	3	1		0	1	28	3
EAST NORTH CENTRAL								
Ohio:								
Cincinnati	29	13	3		3	4	15	9
Cleveland	103	57	11	2	0	3	53	21
Columbus	30	11	8	2	0	1	0	5
Toledo	126	10	7	2	1	4	6	5
Indiana:								
Fort Wayne	9	6	0		0	2	0	4
Indianapolis	39	13	18		0	3	5	8
South Bend	4	2	2		1	1	0	1
Terre Haute	2	2	0		0	1	0	0
Illinois:								
Chicago	151	147	102	7	1	21	55	49
Springfield	0	2	1		0	0	0	3
Michigan:								
Detroit	127	69	45	8	1	4	7	22
Flint	28	5	1		0	4	0	3
Grand Rapids	5	2	0		0	3	0	1

City reports for week ended November 22, 1930—Continued

Division, State, and city	Chicken pox, cases reported	Diphtheria		Influenza		Measles, cases re- ported	Mumps, cases re- ported	Pneu- monia, deaths reported
		Cases, estimated expect- ancy	Cases reported	Cases reported	Deaths reported			
EAST NORTH CEN- TRAL—contd.								
Wisconsin:								
Kenosha.....	67	2	0	2	0	0	2	1
Madison.....	42	2	0	—	—	0	5	—
Milwaukee.....	133	22	9	3	2	3	42	5
Racine.....	52	2	0	—	0	0	1	0
Superior.....	6	1	0	—	0	0	0	1
WEST NORTH CENTRAL								
Minnesota:								
Duluth.....	9	0	1	—	0	1	3	2
Minneapolis.....	79	34	5	—	1	1	8	13
St. Paul.....	39	15	0	—	0	0	0	7
Iowa:								
Davenport.....	8	1	2	—	—	0	0	—
Des Moines.....	4	3	0	—	—	0	0	—
Sioux City.....	12	2	5	—	—	0	2	—
Waterloo.....	19	0	0	—	—	3	1	—
Missouri:								
Kansas City.....	44	11	9	—	1	0	1	13
St. Joseph.....	2	1	1	—	0	0	0	4
St. Louis.....	—	46	—	—	—	—	—	—
North Dakota:								
Fargo.....	13	0	0	—	0	0	5	0
Grand Forks.....	0	0	0	—	—	0	5	—
South Dakota:								
Aberdeen.....	0	0	0	—	—	1	0	—
Sioux Falls.....	0	1	1	—	—	0	0	—
Nebraska:								
Omaha.....	10	11	8	—	0	1	4	6
Kansas:								
Topeka.....	1	2	2	—	0	0	0	0
Wichita.....	2	3	1	—	0	0	0	1
SOUTH ATLANTIC								
Delaware:								
Wilmington.....	2	2	0	—	0	0	0	0
Maryland:								
Baltimore.....	40	29	13	10	2	9	6	27
Cumberland.....	0	0	0	—	0	0	0	1
Frederick.....	1	0	2	—	0	0	1	0
District of Columbia:								
Washington.....	10	21	14	3	2	6	0	13
Virginia:								
Lynchburg.....	2	3	2	—	1	0	2	2
Norfolk.....	12	3	2	—	0	0	1	3
Richmond.....	0	18	15	—	1	6	0	4
Roanoke.....	12	4	2	—	0	1	0	2
West Virginia:								
Charleston.....	17	2	1	1	1	1	8	2
Wheeling.....	11	2	1	—	0	1	0	1
North Carolina:								
Raleigh.....	1	3	5	—	0	0	0	1
Wilmington.....	2	1	0	—	0	1	0	0
Winston-Salem.....	4	4	2	—	0	0	0	1
South Carolina:								
Charleston.....	0	0	2	26	1	1	0	3
Columbia.....	3	1	3	—	0	1	2	7
Greenville.....	1	2	0	—	0	0	0	0
Georgia:								
Atlanta.....	—	8	—	—	—	—	—	—
Brunswick.....	0	0	0	—	0	0	0	0
Savannah.....	0	3	1	2	0	1	0	4
Florida:								
Miami.....	2	3	4	—	0	0	0	0
St. Petersburg.....	—	1	—	—	0	—	—	—
Tampa.....	0	3	7	—	0	1	1	0

1 One case nonresident.

City reports for week ended November 22, 1930—Continued

Division, State, and city	Chicken pox, cases reported	Diphtheria		Influenza		Measles, cases re- ported	Mumps, cases re- ported	Pneu- monia, deaths reported
		Cases, estimated expect- ancy	Cases reported	Cases reported	Deaths reported			
EAST SOUTH CENTRAL								
Kentucky:								
Covington.....	0	2	0	-----	0	0	0	2
Tennessee:								
Memphis.....	53	8	19	-----	0	1	0	5
Nashville.....	0	4	0	-----	2	6	0	5
Alabama:								
Birmingham.....	7	7	18	2	0	18	0	12
Mobile.....	1	2	8	1	0	0	0	3
Montgomery.....	2	2	1	1	-----	0	1	-----
WEST SOUTH CENTRAL								
Arkansas:								
Fort Smith.....	0	2	0	-----	-----	0	0	-----
Little Rock.....	5	2	1	-----	0	0	3	1
Louisiana:								
New Orleans.....	0	15	16	3	4	1	0	10
Shreveport.....	0	1	0	-----	0	0	0	3
Oklahoma:								
Oklahoma City..	0	5	9	-----	0	0	0	6
Texas:								
Dallas.....	3	18	13	3	1	0	2	6
Fort Worth.....	14	8	6	-----	1	0	0	4
Galveston.....	0	1	1	-----	0	0	0	2
Houston.....	3	9	15	-----	2	0	0	5
San Antonio.....	0	6	3	-----	3	0	0	5
MOUNTAIN								
Montana:								
Billings.....	2	0	0	-----	0	0	0	2
Great Falls.....	10	0	0	-----	0	0	0	0
Helena.....	6	0	0	-----	0	1	0	0
Missoula.....	0	0	0	-----	0	0	0	0
Idaho:								
Boise.....	4	0	1	-----	0	0	0	0
Colorado:								
Denver.....	58	12	2	-----	3	0	6	14
Pueblo.....	1	2	0	-----	1	36	0	0
New Mexico:								
Albuquerque.....	3	1	0	-----	0	2	0	0
Arizona:								
Phoenix.....	0	1	0	-----	0	0	0	2
Utah:								
Salt Lake City..	26	5	0	-----	3	0	0	3
Nevada:								
Reno.....	0	0	0	-----	0	0	0	0
PACIFIC								
Washington:								
Seattle.....	11	5	4	-----	-----	0	8	-----
Spokane.....	20	3	0	-----	-----	2	0	-----
Tacoma.....	7	4	12	-----	0	1	0	2
Oregon:								
Portland.....	46	11	2	-----	0	5	5	3
Salem.....	0	0	1	-----	0	0	0	0
California:								
Los Angeles.....	29	43	12	23	2	10	17	9
Sacramento.....	5	3	1	-----	0	-----	19	5
San Francisco.....	-----	16	-----	-----	-----	-----	-----	-----

City reports for week ended November 22, 1930—Continued

Division, State, and city	Scarlet fever		Smallpox			Tuber- culosis, deaths re- ported	Typhoid fever			Whoop- ing cough, cases re- ported	Deaths, all causes
	Cases, esti- mated expect- ancy	Cases re- ported	Cases, esti- mated expect- ancy	Cases re- ported	Deaths re- ported		Cases, esti- mated expect- ancy	Cases re- ported	Deaths re- ported		
NEW ENGLAND											
Maine:											
Portland	3	4	0	0	0	0	1	1	0	8	21
New Hampshire:											
Concord	1	0	0	0	0	0	0	0	0	0	7
Manchester	2	3	0	0	0	0	0	0	0	0	10
Nashua	0	0	0	0	0	0	0	0	0	0	-----
Vermont:											
Barre	0	0	0	0	0	0	0	0	0	0	2
Burlington	0	0	0	0	0	0	0	0	0	0	6
Massachusetts:											
Boston	57	50	0	0	0	6	2	5	0	18	208
Fall River	2	2	0	0	0	2	0	1	0	5	18
Springfield	6	5	0	0	0	1	0	0	0	1	23
Worcester	10	23	0	0	0	3	0	0	0	2	57
Rhode Island:											
Pawtucket	1	3	0	0	0	1	0	0	0	1	20
Providence	10	3	0	0	0	3	0	0	0	10	53
Connecticut:											
Bridgeport	7	2	0	0	0	3	0	0	0	0	35
Hartford	5	5	0	0	0	2	0	0	0	0	20
New Haven	4	1	0	0	0	0	0	0	0	2	37
MIDDLE ATLANTIC											
New York:											
Buffalo	22	18	0	0	0	7	1	0	0	17	146
New York	111	102	0	0	0	70	16	8	0	125	1,297
Rochester	5	30	0	0	0	6	1	1	0	13	66
Syracuse	8	6	0	0	0	1	0	0	0	3	46
New Jersey:											
Camden	3	2	0	0	0	2	0	0	0	1	30
Newark	13	10	0	0	0	10	1	0	0	21	99
Trenton	4	12	0	0	0	2	0	0	0	1	39
Pennsylvania:											
Philadelphia	68	115	0	0	0	22	5	2	0	31	470
Pittsburgh	34	54	0	0	0	10	0	0	1	2	171
Reading	2	2	0	0	0	2	0	0	0	0	27
EAST NORTH CENTRAL											
Ohio:											
Cincinnati	15	26	0	0	0	6	1	2	1	6	138
Cleveland	29	43	0	0	0	14	1	4	1	15	229
Columbus	10	10	1	0	0	4	0	0	0	0	68
Toledo	12	8	0	1	0	2	1	0	0	1	50
Indiana:											
Fort Wayne	3	0	0	0	0	0	0	1	0	0	21
Indianapolis	14	36	2	0	0	9	0	0	0	13	-----
South Bend	2	6	0	0	0	0	0	0	0	0	24
Terre Haute	4	2	0	0	0	0	0	1	0	0	11
Illinois:											
Chicago	102	170	1	0	0	33	3	1	0	60	704
Springfield	2	7	0	0	0	0	0	0	0	2	17
Michigan:											
Detroit	79	73	0	0	0	14	2	2	2	39	273
Flint	13	11	0	0	0	1	0	0	0	2	22
Grand Rapids	9	14	0	0	0	0	0	0	0	3	20
Wisconsin:											
Kenosha	2	4	0	0	0	0	0	1	0	3	5
Madison	1	0	0	0	-----	-----	0	0	-----	-----	-----
Milwaukee	19	12	0	0	0	4	0	0	0	34	107
Racine	4	0	0	0	0	0	0	1	0	6	13
Superior	3	1	0	0	0	1	0	2	1	13	14

City reports for week ended November 22, 1930—Continued

Division, State, and city	Scarlet fever		Smallpox			Tuber- culo- sis, deaths re- ported	Typhoid fever			Whoop- ing cough, cases re- ported	Deaths, all causes
	Cases, esti- mated expect- ancy	Cases re- ported	Cases, esti- mated expect- ancy	Cases re- ported	Deaths re- ported		Cases, esti- mated expect- ancy	Cases re- ported	Deaths re- ported		
WEST NORTH CENTRAL											
Minnesota:											
Duluth.....	9	0	0	0	0	1	0	0	0	1	25
Minneapolis.....	44	20	0	0	0	1	0	2	0	5	93
St. Paul.....	21	11	2	0	0	1	0	0	0	11	58
Iowa:											
Davenport.....	1	1	0	3			0	0		0	
Des Moines.....	11	9	1	3			0	0			33
Sioux City.....	2	2	0	0			0	4	1	1	1
Waterloo.....	3	2	0	0			0	1		3	
Missouri:											
Kansas City.....	15	9	0	0	0	10	1	0	0	0	109
St. Joseph.....	3	5	0	0	0	1	0	0	0	0	20
St. Louis.....	32		1				2				
North Dakota:											
Fargo.....	3	0	0	0	0	1	0	0	0	1	9
Grand Forks.....	0	0	1	0			0	0			
South Dakota:											
Aberdeen.....	1	0	0	0			0	0		0	
Sioux Falls.....	2	0	0	1			0	0		0	8
Nebraska:											
Omaha.....	5	19	1	10	0	2	0	1	0	4	63
Kansas:											
Topeka.....	4	0	0	0	0	0	0	0	0	0	6
Wichita.....	5	4	0	2	0	1	0	0	0	0	22
SOUTH ATLANTIC											
Delaware:											
Wilmington.....	2	5	0	0	0	0	0	0	0	0	23
Maryland:											
Baltimore.....	20	26	0	0	0	7	2	7	1	10	200
Cumberland.....	0	3	0	0	0	1	0	0	0	0	13
Frederick.....	0	1	0	0	0	0	0	0	0	0	1
District of Colum- bia:											
Washington.....	19	37	0	0	0	4	1	1	1	3	149
Virginia:											
Lynchburg.....	1	1	0	0	0	0	0	0	0	0	9
Norfolk.....	3	4	0	0	0	1	0	0	0	2	
Richmond.....	8	7	0	0	0	3	1	1	0	0	42
Roanoke.....	3	5	0	0	0	0	0	0	0	1	10
West Virginia:											
Charleston.....	2	1	0	0	0	0	0	2	0	0	36
Wheeling.....	2	0	0	0	0	1	0	0	0	0	9
North Carolina:											
Raleigh.....	2	1	0	0	0	2	0	0	0	1	15
Wilmington.....	1	2	0	0	0	0	0	0	0	1	7
Winston-Salem.....	2	2	0	0	0	1	0	0	0	0	14
South Carolina:											
Charleston.....	1	2	0	0	0	3	0	1	0	0	39
Columbia.....	0	1	0	0	0	1	0	0	0	0	47
Greenville.....	2	0	0	0	0	0	0	0	0	0	
Georgia:											
Atlanta.....	6		1				1				
Brunswick.....	0	0	0	0	0	0	0	0	0	0	4
Savannah.....	1	3		0	0	0	0	1	0	0	33
Florida:											
Miami.....	2	1	0	0	0	3	0	0	0	0	21
St. Petersburg.....	0		0		0	0	0		0		6
Tampa.....	1	1	0	0	0	3	0	0		1	16
EAST SOUTH CENTRAL											
Kentucky:											
Covington.....	2	4	0	0	0	1	0	0	0	0	17
Tennessee:											
Memphis.....	6	10	0	0	0	3	1	2	0	2	60
Nashville.....	3	2	0	0	0	1	1	0	0	2	59
Alabama:											
Birmingham.....	6	15	0	0	0	3	1	0	0	0	57
Mobile.....	0	3	0	0	0	1	0	0	0	0	34
Montgomery.....	1	1	0	0			0	0		1	

1 Nonresident.

City reports for week ended November 22, 1930—Continued

Division, State, and city	Scarlet fever		Smallpox			Tuber- cul- sis, deaths re- ported	Typhoid fever			Whoop- ing cough, cases re- ported	Deaths, all causes
	Cases, esti- mated expect- ancy	Cases re- ported	Cases, esti- mated expect- ancy	Cases re- ported	Deaths re- ported		Cases, esti- mated expect- ancy	Cases re- ported	Deaths re- ported		
WEST SOUTH CENTRAL											
Arkansas:											
Fort Smith.....	1	0	0	0			0	0		0	
Little Rock.....	2	3	1	0	0	1	0	0	0	0	
Louisiana:											
New Orleans....	9	10	0	1	0	16	1	5	1	4	160
Shreveport.....	2	0	0	0	0	2	1	0	2	1	29
Oklahoma:											
Oklahoma City..	3	0	0	8	0	0	0	4	2	0	36
Texas:											
Dallas.....	7	10	0	0	0	3	1	3	0	5	59
Fort Worth.....	2	4	0	1	0	2	0	0	0	0	36
Galveston.....	1	1	0	0	0	1	0	16	1	0	15
Houston.....	3	2	1	0	0	1	6	0	1	0	71
San Antonio....	2	1	0	0	0	9	0	0	0	0	60
MOUNTAIN											
Montana:											
Billings.....	1	1	0	3	0	0	0	1	0	3	10
Great Falls.....	1	6	1	1	0	1	0	0	0	0	7
Helena.....	0	0	0	0	0	0	0	0	0	0	6
Missoula.....	0	0	0	0	0	0	0	0	0	0	7
Idaho:											
Boise.....	0	2	0	0	0	0	0	0	0	0	3
Colorado:											
Denver.....	11	21	0	0	0	11	0	2	0	23	101
Pueblo.....	1	1	0	1	0	0	0	3	0	0	12
New Mexico:											
Albuquerque....	0	1	0	0	0	5	0	0	0	0	9
Arizona:											
Phoenix.....	2	0	0	0	0	4	0	0	0	0	16
Utah:											
Salt Lake City..	4	1	1	0	0	2	1	0	0	8	42
Nevada:											
Reno.....	0	0	0	0	0	0	0	0	0	0	1
PACIFIC											
Washington:											
Seattle.....	9	10	2	0			1	3		16	
Spokane.....	10	2	3	1			0	0		4	
Tacoma.....	2	3	1	1	0	0	0	0	0	0	18
Oregon:											
Portland.....	8	7	4	0	0	2	0	1	0	1	66
Salem.....	0	0	0	0	0	0	0	0	0	0	
California:											
Los Angeles....	30	12	2	0	0	12	1	1	1	11	243
Sacramento....	3	4	0	0	0	2	0	0	0	1	28
San Francisco..	13		0				1				

City reports for week ended November 22, 1930—Continued

Division, State, and city	Meningococcus meningitis		Lethargic encephalitis		Pellagra		Polio myelitis (infantile paralysis)		
	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases, estimated expectancy	Cases	Deaths
NEW ENGLAND									
Massachusetts:									
Boston.....	2	2	1	1	0	0	2	7	0
Fall River.....	1	0	0	0	0	0	0	0	0
Worcester.....	0	0	0	0	0	0	0	1	0
Connecticut:									
Bridgeport.....	1	0	0	0	0	0	0	0	0
Hartford.....	0	0	0	0	0	0	0	1	0
MIDDLE ATLANTIC									
New York:									
New York.....	2	3	1	0	0	0	3	2	0
Rochester.....	0	0	0	0	0	0	0	2	0
Syracuse.....	0	0	0	0	0	0	0	1	1
New Jersey:									
Newark.....	1	0	0	0	0	0	0	0	0
Pennsylvania:									
Philadelphia.....	4	2	1	0	0	0	0	1	1
Pittsburgh.....	1	2	0	0	0	0	0	1	0
EAST NORTH CENTRAL									
Ohio:									
Cincinnati.....	0	0	1	0	0	0	0	0	0
Cleveland.....	3	1	0	0	0	0	0	4	0
Columbus.....	0	0	0	0	0	0	0	0	1
Indiana:									
Indianapolis.....	0	1	0	0	0	0	0	0	0
Illinois:									
Chicago.....	2	1	0	0	0	0	1	3	0
Michigan:									
Detroit.....	3	2	0	0	0	0	1	3	2
Wisconsin:									
Milwaukee.....	0	0	0	0	0	0	0	2	0
WEST NORTH CENTRAL									
Minnesota:									
Duluth.....	2	1	0	0	0	0	0	0	0
Minneapolis.....	0	0	0	0	0	0	0	2	2
Iowa:									
Des Moines.....	0	0	0	0	0	0	0	1	0
Sioux City.....	1	0	0	0	0	0	0	0	0
Missouri:									
Kansas City.....	2	2	1	0	1	0	0	5	0
North Dakota:									
Fargo.....	0	0	0	0	0	0	0	0	1
Nebraska:									
Omaha.....	3	1	0	0	0	0	0	0	0
Kansas:									
Wichita.....	0	0	0	0	0	0	0	1	0
SOUTH ATLANTIC ³									
Maryland:									
Baltimore.....	0	1	0	0	0	0	1	1	0
District of Columbia:									
Washington.....	1	0	0	0	0	0	0	0	0
Virginia:									
Norfolk.....	2	0	0	0	0	0	0	0	0
North Carolina:									
Raleigh.....	0	0	0	0	1	0	0	0	0
South Carolina:									
Charleston ²	0	0	0	0	1	0	0	0	0
Columbia.....	0	1	0	0	0	0	0	0	0

¹ Nonresident.² Dengue, 2 cases at Charleston, S. C.³ Typhus fever, 2 cases at Savannah, Ga.

City reports for week ended November 22, 1930—Continued.

Division, State, and city	Meningococcus meningitis		Lethargic encephalitis		Pellagra		Poliomyelitis (infantile paralysis)		
	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases, estimated expectancy	Cases	Deaths
EAST SOUTH CENTRAL									
Tennessee:									
Memphis.....	1	0	0	0	0	0	0	0	0
Nashville.....	1	0	0	0	0	0	0	0	0
Alabama:									
Birmingham.....	2	0	0	0	0	0	0	1	1
WEST SOUTH CENTRAL									
Louisiana:									
New Orleans.....	2	0	0	0	0	0	0	0	0
Shreveport.....	0	0	0	0	0	1	0	1	0
Oklahoma:									
Oklahoma City.....	0	0	0	0	0	1	0	0	0
Texas:									
Dallas.....	0	0	0	0	1	1	0	1	0
Fort Worth.....	1	0	0	0	0	0	0	0	0
Houston.....	1	1	0	0	0	2	0	0	0
San Antonio.....	0	0	0	0	0	0	0	1	0
MOUNTAIN									
Colorado:									
Denver.....	2	1	0	0	0	0	0	0	1
Arizona:									
Phoenix.....	0	0	0	0	0	0	0	0	1
Utah:									
Salt Lake.....	1	0	0	0	0	0	0	0	0
PACIFIC									
Washington:									
Seattle.....	0	0	0	0	0	0	0	1	0
California:									
Los Angeles.....	0	1	0	0	0	0	1	0	0

The following table gives the rates per 100,000 population for 98 cities for the 5-week period ended November 22, 1930, compared with those for a like period ended November 23, 1929. The population figures used in computing the rates are approximate estimates, authoritative figures for many of the cities not being available. The 98 cities reporting cases have an estimated aggregate population of more than 32,000,000. The 91 cities reporting deaths have more than 30,500,000 estimated population.

Summary of weekly reports from cities October 19 to November 22, 1930—Annual rates per 100,000 population, compared with rates for the corresponding period of 1929¹

DIPHTHERIA CASE RATES

	Week ended—									
	Oct. 25, 1930	Oct. 26, 1929	Nov. 1, 1930	Nov. 2, 1929	Nov. 8, 1930	Nov. 9, 1929	Nov. 15, 1930	Nov. 16, 1929	Nov. 22, 1930	Nov. 23, 1929
98 cities.....	79	134	91	143	* 84	156	91	159	* 102	* 186
New England.....	97	110	84	114	* 79	119	75	168	113	117
Middle Atlantic.....	36	86	47	99	35	104	46	112	54	123
East North Central.....	106	163	131	168	110	195	130	205	125	302
West North Central.....	65	137	91	160	* 75	200	104	165	* 789	169
South Atlantic.....	97	139	106	144	79	125	110	122	* 143	135
East South Central.....	202	185	331	205	243	219	209	232	310	239
West South Central.....	86	396	108	434	213	480	172	427	183	446
Mountain.....	60	26	34	17	120	61	26	44	26	* 69
Pacific.....	118	121	78	111	109	97	73	84	* 94	60

MEASLES CASE RATES

98 cities.....	37	30	61	38	* 58	44	93	56	* 69	* 72
New England.....	69	29	126	27	* 94	20	157	45	164	56
Middle Atlantic.....	30	21	29	33	35	20	71	26	80	34
East North Central.....	16	47	18	40	16	68	17	91	31	94
West North Central.....	140	21	288	52	* 275	94	491	50	* 17	81
South Atlantic.....	13	9	18	15	44	9	24	7	* 59	24
East South Central.....	27	21	47	0	94	7	20	14	169	14
West South Central.....	4	15	0	0	0	4	0	19	4	27
Mountain.....	137	26	403	244	223	61	300	252	318	* 107
Pacific.....	21	63	28	58	28	113	38	142	* 42	290

SCARLET FEVER CASE RATES

98 cities.....	123	138	165	155	* 172	191	191	205	* 200	218
New England.....	144	162	195	177	* 204	276	253	265	217	249
Middle Atlantic.....	82	75	139	89	140	102	133	135	168	127
East North Central.....	172	192	220	226	234	295	290	311	266	347
West North Central.....	114	173	159	160	* 137	187	140	139	* 199	223
South Atlantic.....	148	174	152	139	145	167	141	238	* 198	163
East South Central.....	169	109	277	205	331	178	310	157	236	157
West South Central.....	75	149	71	149	97	162	127	152	101	156
Mountain.....	163	235	335	226	275	357	378	226	275	* 267
Pacific.....	104	104	54	181	111	176	116	179	* 101	261

¹ The figures given in this table are rates per 100,000 population, annual basis, and not the number of cases reported. Populations used are estimates as of July 1, 1930, and 1929, respectively.

² Hartford, Conn., and Waterloo, Iowa, not included.

³ St. Louis, Mo., Atlanta, Ga., and San Francisco, Calif., not included.

⁴ Reno, Nev., not included.

⁵ Hartford, Conn., not included.

⁶ Waterloo, Iowa, not included.

⁷ St. Louis, Mo., not included.

⁸ Atlanta, Ga., not included.

⁹ San Francisco, Calif., not included.

Summary of weekly reports from cities October 19 to November 22, 1930—Annual rates per 100,000 population, compared with rates for the corresponding period of 1929—Continued

SMALLPOX CASE RATES

	Week ended—									
	Oct. 25, 1930	Oct. 26, 1929	Nov. 1, 1930	Nov. 2, 1929	Nov. 8, 1930	Nov. 9, 1929	Nov. 15, 1930	Nov. 16, 1929	Nov. 22, 1930	Nov. 23, 1929
98 cities.....	2	10	3	13	2	9	4	13	3	21
New England.....	0	0	0	0	0	2	0	25	0	0
Middle Atlantic.....	0	0	0	0	0	0	0	0	0	0
East North Central.....	2	12	1	20	4	15	2	22	0	33
West North Central.....	0	31	19	42	6	29	21	42	33	50
South Atlantic.....	0	0	0	0	0	0	0	0	0	2
East South Central.....	0	0	0	14	0	0	0	0	0	0
West South Central.....	7	0	4	27	7	8	4	4	4	38
Mountain.....	0	52	9	61	9	17	0	9	43	71
Pacific.....	21	51	17	29	7	19	21	31	7	111

TYPHOID FEVER CASE RATES

98 cities.....	18	15	14	11	11	9	15	8	15	13
New England.....	27	16	4	7	5	11	22	22	15	11
Middle Atlantic.....	13	8	10	8	5	8	4	3	5	10
East North Central.....	5	7	8	6	9	6	5	6	9	9
West North Central.....	8	6	13	17	4	12	19	4	22	12
South Atlantic.....	37	21	29	13	20	13	31	9	26	19
East South Central.....	94	48	115	34	27	21	54	14	13	34
West South Central.....	26	42	15	19	30	11	93	8	90	34
Mountain.....	77	200	0	78	17	17	26	44	51	36
Pacific.....	19	5	21	2	19	7	12	10	13	5

INFLUENZA DEATH RATES

91 cities.....	5	9	9	11	9	8	10	9	10	8
New England.....	2	0	2	2	2	4	4	9	7	4
Middle Atlantic.....	7	12	9	9	13	8	9	4	8	9
East North Central.....	3	10	6	9	6	8	9	9	5	6
West North Central.....	9	3	9	6	3	3	6	3	6	9
South Atlantic.....	4	4	16	19	9	4	5	11	16	4
East South Central.....	7	22	15	30	29	37	44	22	15	30
West South Central.....	8	20	23	27	15	12	31	31	38	16
Mountain.....	9	17	17	26	9	0	9	26	60	9
Pacific.....	9	3	3	3	9	16	6	9	10	6

PNEUMONIA DEATH RATES

91 cities.....	89	108	101	105	104	105	118	98	120	101
New England.....	91	63	95	74	82	119	104	88	115	88
Middle Atlantic.....	108	144	115	113	122	115	136	103	140	106
East North Central.....	63	91	88	101	75	78	86	71	83	96
West North Central.....	59	72	95	135	86	108	77	120	136	102
South Atlantic.....	125	112	123	116	139	137	157	107	137	94
East South Central.....	96	134	74	157	155	90	214	231	199	254
West South Central.....	134	86	111	105	119	125	111	121	123	120
Mountain.....	77	122	163	131	189	131	215	157	163	107
Pacific.....	74	44	40	31	52	72	83	85	76	23

¹ Hartford, Conn., and Waterloo, Iowa, not included.

² St. Louis, Mo., Atlanta, Ga., and San Francisco, Calif., not included.

³ Reno, Nev., not included.

⁴ Hartford, Conn., not included.

⁵ Waterloo, Iowa, not included.

⁶ St. Louis, Mo., not included.

⁷ Atlanta, Ga., not included.

⁸ San Francisco, Calif., not included.

⁹ Atlanta, Ga., and San Francisco, Calif., not included.

FOREIGN AND INSULAR

CANADA

Provinces—Communicable diseases—Week ended November 22, 1930.—The Department of Pensions and National Health of Canada reports cases of certain communicable diseases for the week ended November 22, 1930, as follows:

Province	Cerebro-spinal fever	Influenza	Lethargic encephalitis	Polio-myelitis	Small-pox	Typhoid fever
Prince Edward Island ¹						
Nova Scotia		1				1
New Brunswick			1	1		1
Quebec				3		17
Ontario		2		6	7	24
Manitoba	1					9
Saskatchewan				1	2	9
Alberta					1	
British Columbia				1		5
Total	1	3	1	12	10	66

¹ No case of any disease included in the table was reported during the week.

Quebec Province—Communicable diseases—Week ended November 22, 1930.—The Bureau of Health of the Province of Quebec, Canada, reports cases of certain communicable diseases for the week ended November 22, 1930, as follows:

Disease	Cases	Disease	Cases
Chicken pox	138	Poliomyelitis	3
Diphtheria and croup	62	Scarlet fever	182
Erysipelas	3	Smallpox	1
German measles	1	Tuberculosis	62
Measles	54	Typhoid fever	17
Mumps	42	Whooping cough	71
Paratyphoid fever	2		

CZECHOSLOVAKIA

Communicable diseases—September, 1930.—During the month of September, 1930, cases of certain communicable diseases were reported in the Republic of Czechoslovakia, as follows:

Disease	Cases	Deaths	Disease	Cases	Deaths
Anthrax	15	1	Paratyphoid fever	17	2
Cerebrospinal meningitis	3	1	Puerperal fever	45	22
Diphtheria	2,097	101	Scarlet fever	2,130	45
Dysentery	149	17	Trachoma	145	
Malaria	32		Typhoid fever	843	49

LATVIA

Communicable diseases—September, 1930.—During the month of September, 1930, cases of certain communicable diseases were reported in Latvia as follows:

Disease	Cases	Disease	Cases
Anthrax.....	1	Poliomyelitis.....	13
Cerebrospinal meningitis.....	7	Puerperal fever.....	7
Diphtheria.....	62	Scarlet fever.....	112
Dysentery.....	1	Tetanus.....	3
Erysipelas.....	48	Trachoma.....	66
Influenza.....	368	Typhoid fever.....	136
Lethargic encephalitis.....	1	Typhus fever.....	2
Measles.....	67	Whooping cough.....	70
Mumps.....	22		

MEXICO

Vera Cruz—Deaths from certain diseases—Six weeks ended November 15, 1930.—During the six weeks ended November 15, 1930, deaths from certain diseases were reported in Vera Cruz, Mexico, as follows:

Disease	Week ended—					
	Oct. 11, 1930	Oct. 18, 1930	Oct. 25, 1930	Nov. 1, 1930	Nov. 8, 1930	Nov. 15, 1930
Anthrax.....		1				
Bronchitis.....		2	3		2	2
Cancer.....		1		1	1	
Cerebrospinal meningitis.....			1			
Diphtheria.....		1				
Gastrointestinal disorders.....	3	2	3	6	6	4
Hookworm disease.....		1	3		1	
Locomotor ataxia.....						1
Malaria.....	1	1			1	2
Measles.....	1					
Pneumonia.....	2	1	4	1		2
Sprue.....					1	
Syphilis.....	1				1	
Tetanus.....		1	2			
Tuberculosis.....	5	3	4	2	4	2
Whooping cough.....						1

VIRGIN ISLANDS

Communicable diseases—October, 1930.—During the month of October, 1930, cases of certain communicable diseases were reported in the Virgin Islands as follows:

St. Thomas and St. John:	Cases	St. Croix:	Cases
Chicken pox.....	1	Gonorrhea.....	4
Gonorrhea.....	3	Mumps.....	2
Syphilis.....	13	Pellagra.....	2
		Syphilis.....	1
		Uncinariasis.....	1

YUGOSLAVIA

Communicable diseases—October, 1930.—During the month of October, 1930, certain communicable diseases were reported in Yugoslavia, as follows:

Disease	Cases	Deaths	Disease	Cases	Deaths
Anthrax.....	92	13	Poliomyelitis.....	6	1
Cerebrospinal meningitis.....	9	4	Puerperal fever.....	11	2
Diphtheria and croup.....	1,402	166	Scarlet fever.....	1,518	160
Dysentery.....	171	23	Tetanus.....	35	15
Leprosy.....	3	2	Typhoid fever.....	784	54
Lethargic encephalitis.....	1		Typhus fever.....	2	1
Measles.....	620	2			

Country or Territory	Population	Area (sq. miles)	Capital	Government	Religion	Language	Notes
India (Portuguese)	40	32	11	1	1	1	
Indo-China (see also table below):	18	22	6	1	1	1	
Prompenh.....	48	10	5	1	1	1	
Saigon and Cholon.....	23	3	1				
Philippine Islands: *							
Ports—							
Cebu.....	1	65	9	1	1	1	
Iloilo.....		20	8	1	1	1	
Manila.....		64	3	1	2	1	
Provinces—		22	56	4	3	2	
Antique.....			1	16	10	4	
Bohol.....			1	5	6	1	
Bulacan.....	3	4	1	25	12	8	
Capiz.....	1	3	2	1	7	10	
Cebu.....	355	713	85	1	14	12	
Iloilo.....	2	303	50	1	14	7	
La Union.....	1	309	571	71	4	8	
Leyte.....	47	193	376	45	1	1	
Masbate.....	19	11					
Misamis, Occidental.....	3	92	34				
Negros, Occidental.....	140	568	343	40	15	8	
Negros, Oriental.....	88	237	237	32	9	6	
Nueva Acija.....		23	8				
Pampanga.....	2	1	1				
Pangasinan.....		3	1				
Rizal.....	1	1					
Samar.....		18	16	3	1	4	
Sorsogon.....	1	1					

¹ An outbreak of cholera was reported in June, 1930, in Afghanistan.

PLAGUE

[C indicates cases; D, deaths; P, present]

Place	June 1-28, 1930	June 29- July 26, 1930	July 27- Aug. 30, 1930	Week ended—											
				September, 1930				October, 1930				November, 1930			
				6	13	20	27	4	11	18	25	1	8	15	22
				Aug. 30, 1930											
Algeria:															
Algiers.....		3	7	1	2	6	2	1	1	2	2	5	1		
Constantine.....	1	1										3			
Oran.....		3	4	1	2	3	4		4	4	2	1	1		
Plague-infected rats.....					10										
Philippeville.....		2			1			2		1	1	1			
Belgian Congo.....		2													
British East Africa (see also table below):		2	2	2	3										
Uganda.....	400	228	236	44	40	67	61	65	18	32					
Canary Islands: Las Palmas.....	328	213	229	37	39	55	60	65	18	32					
Ceylon:			1												
Colombo.....	1	3	2	2				1	1					1	
Plague-infected rats.....	1	3	2	3				1	1					1	
China:															
Manchuria—Tungliang and Nungan.....			30			29	P	2							
Shensi.....						P	P				P				
Dutch East Indies:															
Batavia and West Java.....	98	84	83	13	14	26	26	22	14	26					
Plague-infected rats.....	98	84	83	12	14	26	24	22	14	26					
Java and Madura.....	4		1		1	1	1								
Ecuador (see table below).	202	217	188	55	54	67	84	75	68	95	97	124			
Egypt:															
Alexandria.....	19	23	11	3	3	2	2	2	1	3	3	2	1	3	
Assiout.....	9	10	6	5	1	2		3	1	1	1	3	2	2	
Bent Suet.....	9	2													
Dakar.....	3														
Dakar.....	1		1												
Ghardaia.....															
Girga.....															
Nimneh.....		1	1												
Port Said.....	10	3													
	1	1													
	2	1	1									1			

Place	May, 1939	June, 1939	July, 1939	Aug., 1939	Sept., 1939	Oct., 1939
Nigeria: Lagos.....	5	1	1	1	1	2
Plague-infected rats.....	5	1	1	1	1	2
Senegal (see table below).	11	18	8	3	3	3
Siam.....						
Bangkok.....			7	3	3	1
Nagara Rajstima.....			3	2	2	1
Syria: Beirut.....			3			
Tripolitania.....			2			
Tunisia.....			2			
Tunis.....			2			
Sfax district.....	0	6	1			
Tunis.....	1	5				
Union of Socialist Soviet Republics:						
Saksk Region.....	2	5	7			
Staropol Region.....	1	4	5			
Union of South Africa:						
Cape Province.....	1	1	1			
Orange Free State.....						
British East Africa (see also table above):						
Kenya.....	171	107	97	87	53	50
Ecuador: Guayaquil.....	0	0	0	0	0	0
Plague-infected rats.....	0	0	0	0	0	0
Greece (see also table above).....	0	1	1	2	4	
Indo-China (see also table above).....						
Madagascar (see also table above):						
Amboitra Province.....	1					
Antistrabe Province.....	10	3	24	11		
Marinarivo Province.....	18	3	24	11		
Moramanga Province.....	5	1	1	2		
.....	1	3	1	27		
Madagascar (see also table above)—Con:						
Tanarivo Province.....	15	16	28	39		
Senegal:						
Baol.....	18	2	62	70	48	53
Dakar.....	11	2	48	20	22	35
Louga.....	52	52	140	108	3	
Thies.....	42	117	122	90	8	
Tivouane.....	54	60	138	75	61	37
.....	27	21	103	30	25	25
.....	21	52	54	34	12	24
.....	8	32	30	50	4	13
.....	135	43	119	110	20	13
.....	69	28	70	54	14	31

¹ Incomplete reports.

[illegible]

¹ From Jan. 1 to May 31, 1930, 44 deaths from smallpox were reported in La Paz, Bolivia.

CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER—Continued

TYPHUS FEVER—Continued

[C Indicates cases; D, deaths; P, present]

Place	May, 1930	June, 1930	July, 1930	Aug., 1930	Sept., 1930	Oct., 1930	Place	May, 1930	June, 1930	July, 1930	Aug., 1930	Sept., 1930	Oct., 1930
China: Harbin (see also table above).....	240	2	14	5	1	1	Lithuania.....	27	16	18	7	24	1
China: Seoul.....	43	1	3	2	1	1					1	2	
Czechoslovakia.....	12	1	1	1	1	1	Turkey.....	16	2	7	2		
Greece: Athens.....	3	3	6	6	4	4	Yugoslavia.....	16	6				
Latvia.....	3	3	3	1	2	2		1					
.....													

YELLOW FEVER

Place	May, 1930	June, 1930	July, 1930	Aug., 1930	Sept., 1930	Oct., 1930	Place	May, 1930	June, 1930	July, 1930	Aug., 1930	Sept., 1930	Oct., 1930
Brasil:							Gold coast:						
Campos, Rio de Janeiro Province, May 23, 1930.....							July 10, 1930.....						
Para, June 23, 1930.....							Albosso, Aug. 5, 1930 (deaths).....						
.....							Liberia, Monrovia, June 3, 1930.....						
.....							Nigeria, Lagos, July 12, 1930 (probably laboratory infection).....						

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