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Author(s): Ronald Ross
Reviewed work(s):
Source: *Proceedings of the Royal Society of London. Series A, Containing Papers of a Mathematical and Physical Character*, Vol. 92, No. 638 (Feb. 1, 1916), pp. 204-230
Published by: The Royal Society
Stable URL: http://www.jstor.org/stable/93760
Accessed: 19/01/2012 04:40

An Application of the Theory of Probabilities to the Study of a priori *Pathometry*.—Part I.

By Lieut.-Colonel Sir Ronald Ross, K.C.B., F.R.S., R.A.M.C.T.F.

(Received July 14, 1915.)

CONTENTS.

I.

Prefatory.—It is somewhat surprising that so little mathematical work should have been done on the subject of epidemics, and, indeed, on the distribution of diseases in general. Not only is the theme of immediate importance to humanity, but it is one which is fundamentally connected with numbers, while vast masses of statistics have long been awaiting proper examination. But, more than this, many and indeed the principal problems of epidemiology on which preventive measures largely depend, such as the rate of infection, the frequency of outbreaks, and the loss of immunity, can scarcely ever be resolved by any other methods than those of analysis. For example, infectious diseases may perhaps be classified in three groups: (1) diseases such as leprosy, tuberculosis, and (?) cancer, which fluctuate comparatively little from month to month, though they may slowly increase or decrease in the course of years; (2) diseases such as measles, scarlatina, malaria, and dysentery, which, though constantly present in many countries, flare up in epidemics at frequent intervals; and (3) diseases such as plague or cholera, which disappear entirely after periods of acute epidemicity.

To what are these differences due? Why, indeed, should epidemics occur at all, and why should not all infectious diseases belong to the first group and always remain at an almost flat rate? Behind these phenomena there must be causes which are of profound importance to mankind and which probably can be ascertained only by those principles of careful computation which have yielded such brilliant results in astronomy, physics, and mechanics. Are the epidemics in the second class of diseases due (1) to a sudden and simultaneous increase of infectivity in the causative agents living in affected persons; or (2) to changes of environment which favour their dissemination from person to person; or (3) merely to the increase of susceptible material in a locality due to the gradual loss of acquired immunity in the population there; or to similar or other causes? And why should diseases of the third class disappear, as they undoubtedly do, and diseases of the first class remain so persistently?—all questions which immediately and obviously present themselves for examination.

The whole subject is capable of study by two distinct methods which are used in other branches of science, which are complementary of each other, and which should converge towards the same results—the *a posteriori* and the *a priori* methods. In the former we commence with observed statistics, endeavour to fit analytical laws to them, and so work backwards to the underlying cause (as done in much statistical work of the day); and in the latter we assume a knowledge of the causes, construct our differential equations on that supposition, follow up the logical consequences, and finally test the calculated results by comparing them with the observed statistics.

Apparently the first *a posteriori* work of importance on epidemics was a communication by Dr. William Farr in 1866 (1), in which he maintained, in connection with an epidemic of cattle plague, that the course of the epidemic would follow a curve of which the third difference of the logarithm was a negative constant. In 1873–74, Dr. G. H. Evans (2) endeavoured to extend this law to other epidemics, but ended by expressing disappointment with his results. Quite recently, however, Dr. J. Brownlee has continued the work in a series of excellent papers (3–8). In the first of these he said that Dr. Farr's curve is the normal curve of probability, but, after studying a number of epidemics, found that Pearson's Type IV fitted better, and he concluded (p. 567) that "an epidemic is an organic phenomenon, the course of which seems to depend on the acquisition by an organism of a high grade of infectivity at the point where the epidemic starts, this infectivity being lost from that period till the end of the epidemic at a rate approaching to the terms of a geometrical progression." He admitted, however (p. 517), that "other factors, which are not clear, seem to come into play"; but added, "that the epidemic ends because of the lack of susceptible persons has no evidence in its favour, either from the form of the curve or from the facts" (see also pp. 500 and 501). It is obvious from the mere examination of many curves of epidemics that they are often remarkably symmetrical bell-shaped curves, which, however, frequently tend to fall somewhat more slowly than they rose; and in a later paper (4) Brownlee emphasises this feature of symmetry, and says (p. 2) that "the deduction from this phenomenon is direct and complete, namely, that the want of persons liable to infection is not the cause of the decay of the epidemic. On no law of infection which I have been able to devise would such a cause permit of epidemic symmetry. The fall must in all such cases be much more rapid than the rise, though, on the contrary, when asymmetry is markedly present the opposite holds." In still later papers (6, 7) he gives much evidence to show that measles and smallpox have distinct periods of recrudescence.

So far as I can ascertain, *a priori* researches on epidemiology were first commenced by myself since 1899 in connection with malaria. In 1904 I read a paper (9) concerned with the random migration of mosquitoes, a subject of vital importance in the theory of malaria, which was subsequently dealt with, at my suggestion, by Prof. K. Pearson, whose researches were then employed by Brownlee (5). Subsequently I endeavoured to find the malaria equations by *a priori* reasoning (10), and in the second edition of my book (11) extended this method to a preliminary general "Theory of Happenings," employing chiefly the Finite Calculus (which is useful for malaria). Quite recently I published a very brief note (13) recording further advances; and Brownlee added another (7), showing how he arrived at some of his results.

The present paper is a much more advanced and general development of the work commenced in Section 66 (14) of the second edition of my book (11, p. 676). It deals merely with the curves which are theoretically obtained when we suppose that the infectivity-ratio remains constant or proportional to the number of individuals already affected, while, simultaneously, some of these are constantly "reverting," or losing immunity, and while both the affected and the unaffected groups are subject to special rates of birth, death, immigration, and emigration—as defined in the following section. This thesis does not consider progressive decline of the infectivity; yet we shall see in Section VII, that, contrary to what Dr. Brownlee supposed, it does often yield curves which are bell-shaped, nearly symmetrical, or, when otherwise, decline more slowly than they rose—that is, yields curves of the type frequently found in epidemics and does so without demanding any other cause for the decline than the exhaustion of susceptible material.

The thesis is stated in terms which are certainly academical, but into which it has been resolved only after very careful thought. It has not only been dealt with in considerable detail, but some of the more immediate consequences have been followed out—because I think that it must first be examined and used as a standard before we can proceed to discuss variations due to changes in the infectivity. As will be seen, the mathematics presents few difficulties; but, owing to the nature of the subject, I have thought it wise to labour the proofs somewhat more than some readers will require.

Beyond this point I have not endeavoured to go, because the application of the equations to numbers of known epidemics (which will ultimately be required) can be made only at great length. The paper is therefore purely theoretical; but it is one which I think will be needed for future studies. In stating the results I do not at all wish to contest the conclusions of Drs. Farr and Brownlee, which may quite possibly be ultimately found capable of being superimposed upon mine.

Dr. Farr's communication (1) is not republished in his collected works ('Vital Statistics,' edited by N. A. Humphreys, London, 1885), but has recently been recovered with some difficulty by Dr. Brownlee. It is interesting to note that he seems to have attributed the decline of epidemics partly to the attenuation of infectivity, but also partly to "the fact that the individuals left are less susceptible of attack, either by the constitution or hygienic conditions, than those destroyed." The descriptions of his methods furnished by himself and by Evans are, however, almost unintelligible; but it is evident from "the calculated series by law" which he gives, that the third difference (not the second, as Brownlee said) of the logarithms of the series is a negative constant.

Some of Brownlee's equations are also difficult to interpret in terms of the numbers of individuals affected. I have therefore thought it best to proceed in this paper entirely on the basis of my own previous work.

Part II (which is not yet finished) will contain Sections VIII (Hypothetical Epidemics), IX (Hypometric Happening), X (Parameter Analysis), XI (Variable Happening), and XII (Discussion).

II.

The problem before us is as follows. Suppose that we have a population of living things numbering P individuals, of whom a number Z are affected by *something* (such as a disease), and the remainder A are not so affected; suppose that a proportion $h.dt$ of the non-affected become affected in every element of time dt, and that, conversely, a proportion $r.dt$ of the affected become unaffected, that is, revert in every element of time to the non-affected group; and, lastly, suppose that both the groups, the affected and the non-affected, are subject also to possibly different birth-rates, death-rates, and immigration and emigration rates in an element of time; then what will be the number of affected individuals, of new cases, and of the total population living at any time t?

For the solution of this and the subsidiary problems I have ventured to suggest the name "Theory of Happenings." It covers many cases which occur not only in pathometry but in the analysis of questions connected with statistics, demography, public health, the theory of evolution, and even commerce, politics, and statesmanship. The name *pathometry* (*pathos*, a happening) was previously suggested by myself in antithesis to *nosometry* (*nosos*, a disease) for the quantitative study of parasitic invasions in the individual.

III.

(i) Let ndt, mdt, idt, edt denote respectively the nativity, mortality, immigration, and emigration rates of the non-affected part of the population in the element of time dt; and $\mathrm{N}dt$, $\mathrm{M}dt$, $\mathrm{I}dt$, $\mathrm{E}dt$ denote the similar rates among the affected part. Then, as argued in my previous writings and as will be easily seen, the problem before us may be put in the form of the following system of differential equations:—

$$d\mathrm{P} = (n-m+i-e)dt \,.\, \mathrm{A}+(\mathrm{N}-\mathrm{M}+\mathrm{I}-\mathrm{E})dt \,.\, \mathrm{Z}, \tag{1}$$

$$d\mathrm{A} = (n-m+i-e-h)dt \,.\, \mathrm{A}+(\mathrm{N}+r)dt \,.\, \mathrm{Z}, \tag{2}$$

$$d\mathrm{Z} = hdt \,.\, \mathrm{A}+(-\mathrm{M}+\mathrm{I}-\mathrm{E}-r)dt \,.\, \mathrm{Z}. \tag{3}$$

Here $d\mathrm{P}$ consists only of the *variation-elements* n, m, i, e, N, M, I, E, with their proper signs, while $d\mathrm{A}$ and $d\mathrm{Z}$ contain also the *happening-element* h

and the *reversion-element* r. Obviously $dP = dA + dZ$, as it should do, the elements h and r disappearing in the summation because they denote only change of condition and not of being. The number of the non-affected who become affected in the element of time is $hdt.A$, and, of course, this number pass over from group A to group Z—as shown in equations 2 and 3. Similarly $rdt.Z$ is the number of the affected who revert in the element of time and therefore pass over from group Z to group A. The equations are not quite symmetrical, since N, which should appear in equation 3, appears in equation 2—because the progeny of the affected group, namely $Ndt.Z$, will generally be born not affected—an important fact which modifies almost all the results.

(ii) The variation-elements n, m, i, e, and N, M, I, E, may sometimes be functions of time, especially if the considered events extend over long periods; but it will quite suffice at present to take them as being constants. If we have sufficient data regarding them, we can generally calculate them by the methods of Section VIII for whatever small unit of time we adopt; otherwise they must be conjectured or assumed to begin with, and be then ascertained by a comparison of the integrated equations with known facts. It is convenient to write

$$v \equiv n - m + i - e,$$
$$V \equiv N - M + I - E. \tag{4}$$

In some kinds of happening which have no marked effect on the birth-rates, death-rates, and immigrations—such for instance as mild maladies, enlistments in civil professions, conversions to religious or political parties, entries into unlimited societies or trades-unions, etc.—we may have $n = N$, $m = M$, $i = I$, $e = E$, and, consequently, $v = V$. In other cases, quite possibly we may still have $v = V$, though the individual items may be different. Generally in marriages $N > n$; in accidents $M > m$; in vaccinations $M < m$; in total-abstainers $N > n$ and $M < m$; in military enlistments and in many diseases $N < n$ and $M > m$; while in certain alarming epidemics, especially cholera, plague, and malaria, we find in addition that $I < i$ and $E > e$—so that in these cases, which are particularly our present subject of study, we generally have $v > V$. In fatal accidents $M = 1$ and N, I, and E all $= 0$. When considering happenings among the *same* individuals, we also put N, I and E at zero, though M may be anything; and in other special cases we omit various elements. If the surrounding population is not affected, $I = 0$; and if the affected individuals cannot move, $E = 0$: so that it will be seen that the equations can be made to cover a wide field. The theory will sometimes also apply to inanimate objects—as for instance in commerce, where the variation-elements may be taken to mean manufacture, waste, exportation and importation, though the original equations may have to be somewhat modified.

(iii) The *reversion-element* may also at present be taken as a constant and be calculated for the same unit of time as is used for the other elements. In the case of independent happenings (to be defined presently) rdt means merely the proportion of affected individuals which become, in element of time, capable of being re-affected—as by divorce in marriage, and by discharge in certain employments. In dependent happenings, however, it implies also the loss of capacity for affecting others. Thus in infectious diseases (which are dependent happenings) it implies loss both of immunity and of infectivity—not recovery from sickness, which is merely an episode of affectedness from disease. In some diseases, such probably as leprosy and organic diseases, r is zero or nearly zero; in others with long-continued immunity, such as many zymotic diseases, it is low; and in others again, with comparatively quick loss of immunity and infectivity, such possibly as nasal catarrh or dengue, it must be larger. In many diseases, however, it is quite unknown at present and must in fact be calculated from the integrated equations (which, it is hoped, will prove of use for this very purpose). In the case of slight accidents it is unity; in fatal accidents it is zero; and in snake-bite or heat-stroke, where recovery is quick if it occurs, it is high, though at the same time the death-rate M is also high. In controversial parties due to rational divergence of opinion it should be high; in ordinary party-politics it is, in fact, very low.

(iv) The most important element is the *happening-element, h.* We should clearly understand that in most cases the happening, whatever it is, does not select only the non-affected, but tends to fall on both groups alike. If, however, it chances to fall upon individuals who are already affected, it merely re-affects them and does not cause them to pass from one group to another. Really the total number of individuals to whom the happening occurs in element of time is $hdt\,.\,\mathrm{P}$, that is, $hdt\,.\,(\mathrm{A}+\mathrm{Z})$. But the individuals numbering $hdt\,.\,\mathrm{Z}$ do not count because they are already affected, and therefore do not appear in the equations. On the other hand, the actual number of *new cases* (which we may denote by $\mathrm{F}dt$) is $hdt\,.\,\mathrm{A}$; and this quantity does appear in the equations 2 and 3. Or we may obtain F independently from the proportion

$$\frac{\mathrm{F}dt}{hdt\,.\,\mathrm{P}} = \frac{\mathrm{A}}{\mathrm{P}}, \tag{5}$$

so that, again, $\mathrm{F} = h\mathrm{A} = h\,(\mathrm{P}-\mathrm{Z})$. This is an important subfunction in all cases.

(v) Different kinds of happenings may be separated into two classes, namely (a) those in which the frequency of the happening is *independent* of the number of individuals already affected; and (b) those in which the frequency of the happening *depends* upon this quantity. To class (a) belong such happenings as many kinds of accidents and non-infectious diseases due to causes which operate, so to speak, from outside; and to class (b) belong infectious diseases, membership of societies and sects with propagandas, trade-unions, political parties, etc., due to propagation from within, that is, from individual to individual. In the former case, h or F will be constants; in the latter case they will be functions of Z.

To proceed now to the integration of equations 1, 2, and 3—we may observe that the solutions, though they belong to the same class of functions, differ specifically in different cases. The integrals are easy to obtain by ordinary methods*; but the most elegant and useful method is to put all the cases into similar forms which can be brought by substitutions into the same immediately-integrable differential equation of the simplest type. We will first take a rapid survey of each solution as it is obtained.

IV.

(i) *Independent Happenings.*—Here h or F is supposed to be constant. If h is constant, the happening falls on the same proportion, hdt, of the population in every element of time.

Putting $\mathrm{P}-\mathrm{Z}$ for A, using v and V for the variation-elements as in 4, and setting $x \equiv \mathrm{ZP}$, equations 1 and 3 become

$$d\mathrm{P}/dt = v\mathrm{P}-(v-\mathrm{V})x\mathrm{P}, \tag{6}$$

$$dx\mathrm{P}/dt = h\mathrm{P}(1-x)+(\mathrm{V}-\mathrm{N}-r)x\mathrm{P}, \tag{7}$$

$$dx\mathrm{P}/dt = xd\mathrm{P}/dt+\mathrm{P}dx/dt.$$

Eliminating $dx\mathrm{P}/dt$ and $d\mathrm{P}/dt$ from these, we find that P cancels out also, so that we have

$$dx/dt = h-(h+v-\mathrm{V}+\mathrm{N}+r)x+(v-\mathrm{V})x^2. \tag{8}$$

This has one integral form if $v = \mathrm{V}$, and another if $v \neq \mathrm{V}$.

(ii) *The Equivariant Case.*—Here the happening is such that it does not affect the *sum* of the variation-elements of the affected group—though, as already mentioned, the separate variation-elements may be different; that is, the total population is not altered. An example is conversion to some philosophical creed without propagandism. Another example is the

* The equations are familiar in connection with many statistical, chemical, and physical problems.

happening of slight accidents—in which, however, r is generally unity; and a third example is the happening of a certain standard of wealth, which, we assume, tends to diminish the birth-rate, death-rate, and immigration and emigration of the affected, each by an equal decrement, simultaneously. In this last case, however, as the children of the affected will tend to be born affected, we should remove N from equation 2 to equation 3, and omit it from equations 7 and 8. In all these cases $v = V$.

(iii) To integrate equation 8, however, write it in the form

$$dx/dt = K(L-x), \tag{9}$$

where $K \equiv h+N+r$ and $L \equiv h/K$. Observe that the tangential, dx/dt, vanishes when $x = L$ and becomes negative when $x > L$. Put $y \equiv L-x$; so that $x = L-y$. Then

$$dx/dt = -dy/dt = Ky,$$

$$1/y \,.\, dy = -K dt. \tag{10}$$

Integrating both sides of this,

$$\log y = -Kt + \text{constant}.$$

If y_0 is the value of y at the beginning of the happening,

$$\log y_0 = \text{constant},$$

and
$$y = y_0 \epsilon^{-Kt}. \tag{11}$$

Therefore
$$(L-x) = (L-x_0)\epsilon^{-Kt},$$

and
$$x = L-(L-x_0)\epsilon^{-Kt}. \tag{12}$$

This gives the proportion, x, of the total population who are affected at the time t, this proportion being x_0 when $t=0$.

To find P, put $v-V = 0$ in equation 6, and we obtain at once a differential equation of the same form as equation 9: so that

$$P = P_0 \epsilon^{vt}, \tag{13}$$

where P_0 is the total population at the beginning of the happening, when $t = 0$. This is an important function which expresses the *natural* increase of the whole population due only to the natural variation-elements, v. Of course v is small when the increase of population is not very rapid. When $v = 0$, the population remains constant, the births, deaths, immigrations and emigrations annulling each other.

To find Z we have $Z = xP$.

In III (iv), we defined F to be the number of new cases and showed that $F = h(P-Z)$. If $f \equiv F/P$, we have, when $x_0 = 0$,

$$f = h(1-x) = h(1-L+L\epsilon^{-Kt}). \tag{14}$$

The functions for Z and x give what may be called respectively the *actual* and *proportional curves of affected individuals;* and those for F and f give respectively the *actual* and *proportional curves of new cases.*

To find t for any assigned value of x, we have

$$\mathrm{K}t = \log_\epsilon(\mathrm{L}-x_0)-\log_\epsilon(\mathrm{L}-x) = 2{\cdot}3025851 \log_{10}[(\mathrm{L}-x_0)/(\mathrm{L}-x)]. \quad (15)$$

The following equations are required for analysing the curves x and f:—

$$d^2x/dt^2 = -\mathrm{K}^2(\mathrm{L}-x), \quad (16)$$

$$df/dt = -h\mathrm{K}(\mathrm{L}-x)(1-x), \quad (17)$$

$$d^2f/dt^2 = h\mathrm{K}^2(\mathrm{L}-x)(\mathrm{L}+1-2x), \quad (18)$$

(iv) In order to analyse the curve x (of affected individuals) we first observe that as h, N, r are always positive, K and L are also always positive and L is always less than unity, while $\epsilon^{-\mathrm{K}t}$ diminishes and finally vanishes as t increases. Hence when t is very large, x reaches the limit L (equation 12) and never exceeds it. Its tangential (equation 9) begins at the value $\mathrm{KL}\,(=h)$ when $x_0 = 0$, always remains positive, and gradually diminishes to zero when $x = \mathrm{L}$ and $t = \infty$. Its second tangential (equation 16) is always negative. Hence as t increases from zero to infinity, x also increases, but with a diminishing increment, until it approximates to the asymptote L; and it is always convex to the axis of t.

On the other hand the curve f (equation 14, of new cases) begins at its greatest value h (when $x_0 = 0$) and constantly diminishes, its tangential (equation 17) being always negative. Its second tangential is always positive, since $\frac{1}{2}(\mathrm{L}+1)$ is greater than L; and the curve is, therefore, convex to the axis of t, and, when t is large, approaches its final value $h(1-\mathrm{L})$, that is $(\mathrm{N}+r)\mathrm{L}$, which is always less than h. Let this constant be denoted by l.

It may have been thought that, at least in the case of constant happenings, the whole population would become affected; but it has been shown that this is not the case, because x cannot exceed L, which is a proper fraction. What is it then that limits the value of x? Equation 8 may be written (when $v = \mathrm{V}$)

$$dx/dt = h(1-x)-(\mathrm{N}+r)x = f-(\mathrm{N}+r)x, \quad (19)$$

and dx/dt vanishes when $f = (\mathrm{N}+r)\,x$. When it vanishes, $x = \mathrm{L}$ and $f = l$; that is, the proportion of affected individuals comes to a limit when the proportion of new cases exactly balances the proportion of recoveries and births (it being assumed by supposition that the progeny of the affected are born not affected). If, however, N and r are zero (and only then), $\mathrm{L} = 1$, and the whole population does become affected in time. It should also be observed that $l = h(1-\mathrm{L}) = h\mathrm{A_L}/\mathrm{P}$, where $\mathrm{A_L}$ is the final number of non-affected individuals when $x = \mathrm{L}$ and t is very large; that is to say, even after the limit of x has been nearly approached, the happening continues and constantly affects the same proportion of the non-affected population as before—but now A also comes to a limit, namely $\mathrm{P}(1-\mathrm{L})$.

The easiest way to assess the increase of x as a function of t is to give to $\epsilon^{\mathrm{K}t}$ the successive values 1, 2, 3, 4 ... 10, 100, 1000 .... Then it is clear from equation 12 that, if $x_0 = 0$, x will have the corresponding values 0, $\frac{1}{2}\mathrm{L}$, $\frac{2}{3}\mathrm{L}$, $\frac{3}{4}\mathrm{L}$, ... 0·9L, 0·99L, 0·999L, and t will have the values

$$\frac{2{\cdot}302...}{\mathrm{K}} \log_{10}(1, 2, 3, \ldots 10, 100, 1000 \ldots).$$

An important point is reached when $\epsilon^{\mathrm{K}t} = 10$, for then

$$t = \frac{1}{\mathrm{K}} 2{\cdot}302... \equiv \tau\,(\text{say}). \tag{20}$$

At this point x has increased to 9/10ths of its ultimate value L—that is, most of the change of which it is capable has been effected, and it increases only slightly afterwards, namely only by 0·09 and 0·009 when $t = 2\tau$, and $= 3\tau$, and so on. On the other hand, x reaches half its ultimate value very quickly when $t = \frac{1}{3}\tau$ nearly.

However large t may be, $\epsilon^{-\mathrm{K}t}$ never quite vanishes, and therefore x never quite reaches L. It is convenient, then, to find the value of t when the number of affected individuals reaches the limit *less one individual*—that is, when $\mathrm{Z} = \mathrm{LP}-1$. This is obtained at once from equation 15, since $\mathrm{L}/(\mathrm{L}-x) = \mathrm{LP}/(\mathrm{LP}-\mathrm{Z})$; and the required value is

$$t = \tau \log_{10}\mathrm{LP} \equiv \tau'\,(\text{say}). \tag{21}$$

For example, if $\mathrm{L} = \frac{1}{2}$ and $\mathrm{P} = 2{,}000{,}000$ and remains nearly constant, the number of affected individuals is 900,000 when $t = \tau$, and is 999,999 when $t = 6\tau$.

The ratio x/t is the tangent of the radius-vector from the origin to the point (x, t). If $x_0 = 0$ the value of this tangent is h, that is, dx_0/dt, when $t = 0$; and is $9\mathrm{L}/10\tau$, that is, $0{\cdot}39086h$, when $t = \tau$; so that, as the curve of x increases from zero to nine-tenths of its ultimate value, it lies wholly within the angle formed by these vectors. And the magnitude of this angle depends only upon h, and not upon the other elements, N and r.

The constants L, l, and τ may be written in detail,

$$\mathrm{L} = \frac{1}{1+(\mathrm{N}+r)h^{-1}}, \quad l = \frac{1}{h^{-1}+(\mathrm{N}+\bar{r})^{-1}}, \quad \tau = \frac{2{\cdot}302...}{h+\mathrm{N}+r}. \tag{22}$$

From these equations it will be easily seen that if h increases while N and r remain constant, L and l will increase and τ will diminish; but if h remains constant while N or r or both increase, L and τ will diminish and l will increase—just as may be expected. If $r = 1$ and $N \neq 0$, $l > L$, since $l = (N+r)L$; that is, as all the cases recover as soon as they occur, the total number of cases will not exceed the new cases during unit of time—as happens with slight accidents such as mosquito bites, where there is nothing in one happening to prevent a second or third occurrence of it. If $N+r = 0$, $L = 1$, $l = 0$, and $\tau = h$, and if $h = N+r$, $L = \frac{1}{2}$, $l = \frac{1}{2}h$, and $\tau = 1{\cdot}151\ldots$.

(v) It remains to examine some questions which require for their solution the integrals of P, Z, A, and F—all easily obtained.

From equation 13 we have at once

$$\int P dt = \int P_0 \epsilon^{vt} dt = P/v + \text{constant},$$

$$\int_0^t P dt = (P - P_0)/v. \tag{23}$$

To find the integrals of Z, A, and F, we integrate both sides of equation 7 as there written, or as written in the form $dz/dt = hP - (K-V)Z$, and obtain

$$Z = \int F dt + (V - N - r)\int Z dt, \tag{24}$$

or

$$= h\int P dt - (K-V)\int Z dt; \tag{25}$$

whence

$$\int_0^t Z dt = J\frac{P-P_0}{v} - J\frac{Z-Z_0}{h}, \tag{26}$$

$$\int_0^t A dt = (1-J)\frac{P-P_0}{v} + J\frac{Z-Z_0}{h}, \tag{27}$$

where $J = h/(K-V)$ and $1-J = -(V-N+r)$. And, of course,

$$\int_0^t F dt = h\int_0^t A dt.$$

The same equations can be readily obtained by direct integration from equations 12, 13, etc.

The concrete interpretation of these definite integrals of P, Z, and A, is that they express the total number of *time-units lived* during the period t by the whole population, by the affected population, and by the non-affected population respectively.

For example, suppose that a population P_0 has doubled itself in 1000 time-units, then, since $1000v = \log_\epsilon 2$, $v = 0{\cdot}00069315$, and the total number of time-units lived by all the individuals together is $P_0(2-1)/v$—that is, $1442{\cdot}7\,P_0$ time-units.

It should be observed that if v is very small, equation 23 takes an indeterminate form, the value of which is the value of $P_0(\epsilon^{vt}-1)/v$ when

$v = 0$—namely, tP_0. That is, when the population remains nearly constant, the total number of time-units lived during t is tP_0, as we should expect.

The same integrals divided by t will give the *mean numbers* of the total, the affected, and the non-affected populations respectively during the period t. Thus, if the happening is such that it does not affect the normal rate of increase or decrease of population, then the mean population will be $(P-P_0)/\log_\epsilon P/P_0$—as we should expect.

When multiplied by the appropriate constants, these integrals will also give the total number of the *variation-events*, births, deaths, immigrations and emigrations. Thus the total *progeny* of the non-affected will number $n\int_0^t Adt$, and the total *deaths* among the affected will number $M\int_0^t Zdt$. The sum of the natural variation-events in the whole population is $(n-m+i-e)\int_0^t Pdt$, that is, $P-P_0$. Similarly $r\int_0^t Zdt$ gives the total *reversions*: and the integrals multiplied by h give the total number of time-units lived in which the *happenings* have occurred—which is the same as the number of individuals to which the happenings have occurred. Thus $h\int_0^t Adt$ is the total number of happenings (not necessarily for the first time) among the non-affected—that is the total number of *new cases*, $\int_0^t Fdt$.

It is now easy to interpret equations 24, 25, 26, 27. Since $V-N-r = I-E-M-r$, equation 24 means that Z, the total number of affected individuals remaining alive at the time t, is equal to the sum of all the new cases plus the affected immigrations and less the affected emigrations, deaths, and recoveries. Also as $K-V = h+r+M+E-I$, equation 25 means that the same quantity Z is equal to the total happenings plus the affected immigrations, less the affected emigrations, deaths, and recoveries, and also less the happenings among the affected—which, as stated in III (iv), do not count.

V.

(i) *Independent Happenings: the General Case:* $v \neq V$.—The method of working employed for the equivariant case has been given at some length because it will serve also for the other cases. We now proceed to integrate the general equation 8, namely

$$dx/dt = h-(h+v-V+N+r)x+(v-V)x^2.$$

Write this in the form

$$dx/dt = \mathrm{K}(\mathrm{L}-x)(\mathrm{L}'-x), \tag{28}$$

where $\mathrm{K} = v-\mathrm{V}$ and L and L′ are the two roots of the quadratic in x. Let $\mathrm{L} = \alpha-\beta$ and $\mathrm{L}' = \alpha+\beta$, where $\alpha = (h+\mathrm{N}+r+\mathrm{K})/2\mathrm{K}$ and $\beta^2 = \alpha^2-h/\mathrm{K}$. These roots are always real because

$$(h+\mathrm{N}+r+\mathrm{K})^2-4h\mathrm{K} = (h-\mathrm{K})^2+2(h+\mathrm{K})(\mathrm{N}+r)+(\mathrm{N}+r)^2,$$

of which the left side is positive when K is negative, and the right side is positive when K is positive. And the roots are both positive when $v > \mathrm{V}$. Observe that dx/dt vanishes when $x = \mathrm{L}$ or L′, if this ever occurs.

(ii) Put

$$y \equiv (\mathrm{L}'-x)/(\mathrm{L}-x), \quad x = \mathrm{L}+(\mathrm{L}'-\mathrm{L})/(y-1). \tag{29}$$

Then $$\frac{dx}{dt} = \frac{\mathrm{L}'-\mathrm{L}}{(y-1)^2}\frac{dy}{dt} = \mathrm{K}y(\mathrm{L}-x)^2 = \mathrm{K}y\left(\frac{\mathrm{L}-\mathrm{L}'}{y-1}\right)^2;$$

$$dy/dt = \mathrm{K}(\mathrm{L}'-\mathrm{L})y, \qquad y = y_0\epsilon^{\mathrm{K}(\mathrm{L}'-\mathrm{L})t}, \tag{30}$$

as in equation 11. Therefore, as $\mathrm{L}'-\mathrm{L} = 2\beta$,

$$\frac{\mathrm{L}'-x}{\mathrm{L}-x} = \frac{\mathrm{L}'-x_0}{\mathrm{L}-x_0}\epsilon^{2\mathrm{K}\beta t}; \tag{31}$$

or $$x = \mathrm{L} - \frac{2\beta(\mathrm{L}-x_0)}{(\mathrm{L}'-x_0)\epsilon^{2\mathrm{K}\beta t}-(\mathrm{L}-x_0)};$$

$$= \mathrm{L}\left\{1-\frac{\mathrm{L}'-\mathrm{L}}{\mathrm{L}'\epsilon^{2\mathrm{K}\beta t}-\mathrm{L}}\right\} \text{when } x_0 = 0. \tag{32}$$

The first tangential of this is given in equation 28; the second tangential is

$$d^2x/dt^2 = -2\mathrm{K}^2(\alpha-x)(\mathrm{L}-x)(\mathrm{L}'-x). \tag{33}$$

(iii) The analysis of x, *the proportional curve of affected individuals*, depends upon whether K, that is $v-\mathrm{V}$, is positive or negative. If it is positive, we are generally concerned with cases of Injurious Happenings; because, as explained in Section III (ii), the nativity, mortality, immigration and emigration are likely to be respectively less, greater, less, and greater among the affected in such cases than among the non-affected. Non-infective diseases should be examples in point. On the other hand, if $v-\mathrm{V}$ is negative, we shall be generally concerned with cases of Beneficial Happenings, which improve the natural variation elements of the affected—such for example as conversions to total abstinence are said to be (if they do not diminish i and increase e in places where they prevail, such as the Prohibition States in America.)

If K is positive, $\epsilon^{2\mathrm{K}\beta t}$ in equations 31 and 32 increases indefinitely with t

(since β is the positive value of the radicle in the roots L and L′); so that x approaches the limit L, that is, $\alpha-\beta$; and never exceeds it, and therefore never reaches the greater root L′, that is, $\alpha+\beta$. Therefore dx/dt is always positive for values of x between zero and L; and d^2x/dt^2 is always negative for the same values, since $\alpha>\alpha-\beta$. Hence in this case x has a form similar to what it has in the equivariant case. That is, it begins (when $x_0=0$) at zero at an angle of which the tangent is h; constantly increases with a decreasing increment, so that it always remains concave to the axis of t; and finally approaches the limit L when t is very large.

When K is negative, the quadratic expression in equations 8 and 28 has only one change of sign, and therefore only one positive root, L′, or $\alpha+\beta$. The other root, L, does not concern us because we consider only positive values of x. In this case, $\epsilon^{2K\beta t}$ diminishes indefinitely as t increases, and x finally reaches the limit L′. Here, too, dx/dt always remains positive for possible values of x, that is, while t varies from zero to positive infinity; so that x again always increases from zero to L′. If $h+v-V+N+r$, that is, $2K\alpha$, is positive, d^2x/dt^2 is always negative in this case also, and x is therefore concave to the axis of x as before. But if this expression is negative, d^2x/dt^2 will be positive at first, but will change sign when $x=\alpha$, and finally vanish when $x=L'$; so that, in this case, x will be first convex and then concave to the axis of t. This is the only difference in general form. It is seldom that $v-V$ can be greater than $h+N+r$, which is always positive; hence x has the same form in most cases where h is a constant.

(iv) For the proportional curve of new cases, f, we have

$$f=h(1-x); \tag{34}$$

$$df/dt=-h\,dx/dt \qquad\qquad d^2f/dt^2=-h\,d^2x/dt^2 \tag{35}$$

Hence, when $x_0=0$, f begins at the value h and, as t increases, gradually falls to the limit $h(1-L)$ when K is positive, and to the limit $h(1-L')$ when K is negative. The curvature is the opposite of that of x—as in the equivariant case.

To find the value of P, the total population, write equation 6 in the form,

$$1/P\,.\,dP/dt=v-Kx,$$

Therefore

$$\begin{aligned}\log P &= vt-\int Kx\,dt\\ &= vt-KLt+\int\frac{2K\beta\epsilon^{-2K\beta t}}{y_0-\epsilon^{-2K\beta t}}\\ &= (v-KL)t+\log(y_0-\epsilon^{-2K\beta t})+\text{constant.}\end{aligned}$$

On evaluating the constant we find that we can arrange P in either of two ways, namely,

$$P = P_0\epsilon^{vt}\frac{y_0-\epsilon^{-2K\beta t}}{y_0-1}\epsilon^{-2KLt} \text{ or } P = P_0\epsilon^{vt}\frac{y_0\epsilon^{2K\beta t}-1}{y_0-1}\epsilon^{-KL't}. \qquad (36)$$

If $x_0 = 0$ and t is large, these become, when $K>0$ and $K<0$, respectively,

$$P = P_0\epsilon^{vt}\frac{L'}{L'-L}\epsilon^{-KLt} \text{ or } P = P_0\epsilon^{vt}\frac{-L}{L'-L}\epsilon^{-KL't} \qquad (37)$$

The former expressions are suitable when K is positive, and the latter when it is negative. Thus in the case of injurious happenings when K is positive, the population will diminish indefinitely unless the natural increase denoted by v is large enough to compensate for the decrease, KL, due to the happening (L being positive in this case). In the case of beneficial happenings when K is negative, L is also negative while L′ remains positive, so that the happening enhances the natural increase of the population due to the happening.

As with equivariant happenings, x never quite reaches either L or L′; and it will therefore be useful to find the value of t when the affected population equals the limit less one individual, that is, when $Z = LP-1$ or $L'P-1$, or when $x = L-1/P$, or $L'-1/P$. This can easily be ascertained from equations 29 and 30, and we have to find t from the equation $1/P = (L'-L)/(y-1)$ when K is positive, and from the equation $1/P = y(L'-L)/(y-1)$ when K is negative. From these we have when $x_0 = 0$

$$\begin{aligned}(KL'-v)t &= \log_\epsilon LP \qquad &(K>0)\\ (KL-v)t &= \log_\epsilon L'P \qquad &(K<0)\end{aligned} \qquad (38)$$

To find the integral of P, we write P in the form (when $x_0 = 0$)

$$P = \frac{L'P_0}{L'-L}\epsilon^{(v-KL)t} - \frac{LP_0}{L'-L}\epsilon^{(v-KL')t}.$$

Therefore

$$\int_0^t Pdt = P_0\epsilon^{vt}\frac{L'}{L'-L}\,\frac{\epsilon^{-KLt}-\epsilon^{-KL}}{v-KL} - P_0\epsilon^{vt}\frac{L}{L'-L}\,\frac{\epsilon^{-KL't}-\epsilon^{-KL'}}{v-KL'}. \qquad (39)$$

The integrals of Z and F are found from this by the same methods as were used in equations 24 and 25, or by integrating both sides of equation 6. From the latter we have

$$(v-V)\int_0^t Zdt = v\int_0^t Pdt-(P-P_0). \qquad (40)$$

The remarks made in Section IV (v) apply here also.

VI.

Independent Happenings: Constant New Cases.—A third example of independent happenings remains to be considered, namely, the one referred to at the beginning of Section IV, in which F, the number of new cases, is always a constant. The only instances of this which I can recall are the cases of certain societies (such as the Royal Society) which elect a fixed number of new members every year. Indeed, this process of increment seems to be too artificial to be seen in nature, unless, perhaps, in certain cases of seeding or spore formation, and we need only note the form of the principal function for future reference if required.

Here, since F is a constant, let $F = c$. Then equations 6 and 7 become

$$dP/dt = vP-(v-V)Z, \tag{41}$$

$$\begin{aligned} dZ/dt &= c+(V-N-r)Z, \\ &= K(L-Z). \end{aligned} \tag{42}$$

where $K \equiv M-I+E+r$ and $L \equiv c/K$. The solution of this is given in equation 12, except that Z is here substituted for x. If $Z_0 = 0$, we have

$$Z = c\frac{1-\epsilon^{-(M-I+E-r)t}}{M-I+E+r}.$$

It is to be hoped that the case of the Royal Society is at least an equivariant one.

VII.

(i) *Dependent Happenings: Proportional Happening.*—Referring to the definition of dependent happenings in Section III (v), we see that in such h must be a function of Z, and consequently of t. First consider the case in which each affected individual affects or infects c other individuals in unit of time, c being a constant. This may be taken as being a first approximation to the study of those very important happenings, the infectious diseases.

The total number of the happenings which occur in element of time will be $cZ\,dt$; but, as in the preceding cases, some of these may chance upon individuals who are already affected, and the number of new cases in element of time, namely, $F\,dt$, will therefore most probably be given by the proportion

$$Fdt/cZdt = A/P, \tag{43}$$

that is $F = cZ(1-x)$, and $h = cx$.

(ii) Equations 1 and 3 now become

$$dP/dt = vP-(v-V)xP, \tag{44}$$

$$dxP/dt = cxP(1-x)+(V-N-r)xP. \tag{45}$$

Treating these as in Section IV (i), we find that, as before, on eliminating $dx\mathrm{P}/dt$ and $d\mathrm{P}/dt$, P also cancels out, and we have

$$dx/dt = (c-v+\mathrm{V}-\mathrm{N}-r)x-(c-v+\mathrm{V})x^2, \tag{46}$$

$$= \mathrm{K}x(\mathrm{L}-x), \tag{47}$$

where $\mathrm{K} \equiv c-v+\mathrm{V}$ and $\mathrm{L} \equiv 1-(\mathrm{N}+r)/\mathrm{K}$. Here again dx/dt vanishes when $x = \mathrm{L}$. Integrating by substitution as before, put

$$y = (\mathrm{L}-x)/x, \quad x = \mathrm{L}/(1+y). \tag{48}$$

Hence $$-\frac{\mathrm{L}}{(1+y)^2}\frac{dy}{dt} = \mathrm{K}\frac{\mathrm{L}}{1+y}\left(\mathrm{L}-\frac{\mathrm{L}}{1+y}\right) = \mathrm{KL}\frac{y}{(1+y)^2}$$

$$dy/y = -\mathrm{KL}\,dt \qquad y = y_0\epsilon^{-\mathrm{KL}t} \tag{49}$$

$$x = \frac{\mathrm{L}}{1+(\mathrm{L}/x_0-1)\,\epsilon^{-\mathrm{KL}t}}$$

$$= \frac{\mathrm{L}x_0\epsilon^{\mathrm{KL}t}}{x_0\epsilon^{\mathrm{KL}t}+(\mathrm{L}-x_0)}. \tag{50}$$

Before analysing this it is advisable to obtain the integrated expressions for P and Z. Dividing equation (44) by P and integrating both sides, we have

$$\log \mathrm{P} = vt-(v-\mathrm{V})\int xdt$$

$$= vt-(v-\mathrm{V})/\mathrm{K}\,.\log(x_0\epsilon^{\mathrm{KL}t}+\mathrm{L}-x_0)+\text{constant},$$

whence $$\mathrm{P} = \mathrm{P}_0\epsilon^{vt}\left(\frac{\mathrm{L}}{x_0\epsilon^{\mathrm{KL}t}+\mathrm{L}-x_0}\right)^{(v-\mathrm{V})/\mathrm{K}} \tag{51}$$

and $$\mathrm{Z} = \mathrm{Z}_0\epsilon^{vt}\epsilon^{\mathrm{KL}t}\left(\frac{\mathrm{L}}{x_0\epsilon^{\mathrm{KL}t}+\mathrm{L}-x_0}\right)^{c/\mathrm{K}}, \tag{52}$$

where the fraction within the brackets obviously $= (x/x_0)\,\epsilon^{-\mathrm{KL}t}$.

The explicit value of t is given by

$$\mathrm{KL}t = \log_\epsilon\frac{\mathrm{L}-x_0}{x_0}-\log_\epsilon\frac{\mathrm{L}-x}{x}. \tag{53}$$

(iii) For analysing the *proportional curve of affected individuals, x,* the first tangential is given in equation 47. The second and third tangentials are

$$d^2x/dt^2 = \mathrm{K}^2x(\mathrm{L}-x)(\mathrm{L}-2x), \tag{54}$$

$$d^3x/dt^3 = \mathrm{K}^3x(\mathrm{L}-x)(\mathrm{L}^2-6\mathrm{L}x+6x^2). \tag{55}$$

From these and from equations 50, it will be seen that x and all its tangentials are zero when $x = 0$ and $= \mathrm{L}$. If x_0 is very small, the curve begins at nearly zero when $t = 0$; and then increases very slowly at first and more rapidly afterwards, remaining convex to the axis of t to begin with.

When, however, $x = \frac{1}{2}L$, there is a change of curvature and x becomes concave to the axis of t, and then finally approaches the ultimate limit L when t is very large, and never exceeds that limit. Its maximum rate of increase, namely $\frac{1}{4}KL^2$, is reached when $x = \frac{1}{2}L$; and then

$$KLt = \log[(L-x_0)/x_0].$$

The curve is now seen to be a symmetrical one with this point as the centre of symmetry. Moving the origin to the point by putting $x = \frac{1}{2}L + x'$ and $t = 1/KL \,.\, \log[(L-x_0)/x_0] + t'$, we obtain

$$x' = \tfrac{1}{2}L(1-\epsilon^{-KLt'})/(1+\epsilon^{-KLt'}). \qquad (56)$$

Substituting $-t'$ for t' in this, we find that x' also merely changes its sign without changing its numerical value. In fact, x has the general shape of a long-drawn-out letter S.

(iv) The curve dx/dt is also a symmetrical one with its centre of symmetry at the same distance from the primary origin, namely $\log[(L-x_0)/x_0]$. When x_0 is small, the curve increases slowly at first, then rapidly; reaches a maximum value, $\frac{1}{4}KL^2$, at the centre of symmetry, and then falls just as it rose. It has two changes of curvature which are the two roots of the quadratic expression in d^3x/dt^3, namely when $x = (\frac{1}{2} \mp \sqrt{\frac{1}{12}})L$; that is when

$$x' = \mp 0{\cdot}28867L,$$

and $$KLt' = \mp \log[(\sqrt{3}-1)/(\sqrt{3}+1)] = \mp 1{\cdot}31697. \qquad (57)$$

At these points the ordinate of dx/dt, that is, of $Kx(L-x)$, is

$$KL^2(\tfrac{1}{2}+\sqrt{\tfrac{1}{12}})(1-\tfrac{1}{2}-\sqrt{\tfrac{1}{12}}),$$

that is $\frac{2}{3}\frac{1}{4}KL^2$, or two-thirds of the maximum ordinate at the centre of symmetry; and the ordinate is, of course, the same at both points of change of its curvature, as also at other points equidistant from the centre of symmetry.

The curve of dx/dt is therefore a *regular bell-shaped curve*, very similar to those often found in epidemics.

By the conditions of this kind of happening, x_0 and Z_0 can never be zero, for if they were there would be no new cases. It is convenient therefore to take Z_0 as being one individual—that is, $Z_0 = 1$, $x_0 = 1/P_0$, and $dx/dt = K(P_0-1)/P_0^2$, or nearly K/P_0.

As with the kinds of happening previously considered (see equation 21), x and Z never quite reach the limits L and LP respectively; it is useful then to find when the number of affected individuals reaches the limit less one individual, that is when $Z = LP-1$ and $x = L-1/P$. If $Z_0 = 1$ and

$x_0 = 1/P_0$ as just suggested, then, owing to the symmetry of the curves, this figure will be reached when $x = L - x_0$; that is (equation 53) when

$$\begin{aligned} KLt &= \log [(L-x_0)/x_0] - \log [x_0/(L-x_0)], \\ &= 2 \log (LP_0 - 1) = 2KL\tau \text{ (say).} \end{aligned} \tag{58}$$

Thus if the total population is large and L is not very small, τ, the abscissa of the centre of symmetry when $x_0 = 1/P_0$, is very nearly equal to $1/KL \,.\, \log LP_0$; and at twice this period from the beginning the limit of affected individuals less one will be reached. We observe also that when $t = 2\tau$ the ordinate of dx/dt will be the same as it was at the beginning, namely nearly K/P_0.

If $x_0 = 1/P_0$, the tangent of the radius-vector from the origin to the summit of dx/dt is $\frac{1}{4}KL^2/\tau$, that is

$$K^2L^3/4 \log (LP_0 - 1). \tag{59}$$

From equations 48 and 49 we have

$$\epsilon^{KLt} = \frac{x}{x_0} \frac{L-x_0}{L-x} = \frac{xP}{x_0P_0} \frac{LP_0 - x_0P_0}{LP - xP} = \frac{Z}{Z_0} \frac{LP_0 - Z_0}{LP - Z}. \tag{60}$$

This provides a useful formula for a cursory estimation of the increase of Z with respect to t when the latter is small. For if P_0 and P, Z_0 and Z are not very different, and LP_0 is large and Z_0 small—as at the commencement of the happening—then this equation is nearly

$$Z = Z_0 \epsilon^{KLt}.$$

Suppose that Z_0 is one individual ($t = 0$), then $Z = 2, 3, 4, \ldots$ individuals as ϵ^{KLt} increases through the values $2, 3, 4, \ldots$; that is, as t increases through the values $1/KL \,.\, \log_{10} (2, 3, 4, \ldots)$. This same thing does not hold true, however, when Z is larger.

Similarly, we may have at first $F = cZ_0\epsilon^{KLt} - \dfrac{1}{P_0} c(Z_0\epsilon^{KLt})^2$.

(v) The *actual* and *proportional curves of new cases* are respectively:—

$$\begin{aligned} F &= cZ(1-x), \\ f &= cx(1-x). \end{aligned} \tag{61}$$

To analyse f we have

$$df/dt = cKx(L-x)(1-2x), \tag{62}$$

$$d^2f/dt^2 = cK^2x(L-x)\{L - 2(2L+1)x + 6x^2\}. \tag{63}$$

And, since $L = 1 - (N+r)/K$, we may also write f in the form

$$Kf/c = dx/dt + (N+r)x. \tag{64}$$

The form of the curve f depends upon the value of L. If $L = 1$, that is, if $(N+r)/K$ is zero or very small, the curve f equals or approximates to the curve dx/dt multiplied by the constant c/K—which is generally greater than unity. That is, in this case f is a symmetrical bell-shaped curve with the properties just described. In any case, however, f is such a curve plus the constantly-increasing function $c(N+r)x/K$, or $c(1-L)x$. We may, therefore, expect that, at first, when x is small f will follow the graph of dx/dt, but that as x increases, the ordinates of f will become increasingly greater than those of dx/dt. At last, when t is very large and x approximates to L, dx/dt becomes nearly zero and f approaches the constant value $cL(1-L)$, at which it remains indefinitely. Thus f is quite symmetrical only if $L = 1$; but is nearly symmetrical if L is only a little less than unity.

It is evident from equation 62 that df/dt vanishes when x equals either L or $\frac{1}{2}$. That is, if $L > \frac{1}{2}$, f reaches a maximum when $x = \frac{1}{2}$, the ordinate of this maximum being exactly $c\frac{1}{2}(1-\frac{1}{2})$, or $\frac{1}{4}c$; and as x increases above this value, f then decreases, and *falls* towards its ultimate constant value $cL(1-L)$ as x approaches L. If $L = \frac{1}{2}$ exactly, df/dt vanishes only once (and that not quite), namely, when $x = L = \frac{1}{2}$, so that f now *always increases* until it reaches its maximum, $\frac{1}{4}c$—which is also its ultimate value. If $L < \frac{1}{2}$, however, x never attains the value $\frac{1}{2}$, and consequently df/dt has no vanishing point for any values of x between x_0 and L, and therefore again *always increases* for all considered values of x and therefore of t. Hence the curve of f has two forms: (Type I) if $L > \frac{1}{2}$, an irregular bell-shaped form (becoming regular if $L = 1$); and (Type II) if $L \ngtr \frac{1}{2}$, a drawn-out S-shaped form somewhat similar to that of x itself, but not usually symmetrical.

From equation 63 it will be seen that f *may* have two changes of curvature as x varies from x_0 to L, namely, at the two roots of the quadratic expression in the value of d^2x/dt^2. The roots are

$$6x = (2L+1) \pm \sqrt{[(2L+1)^2 - 6L]}; \tag{65}$$

and are real and positive. The lesser root is always less than L, and is therefore always attained by x as it varies from x_0 to L—so that f always has at least one change of curvature. The greater root is also less than L when $L > \frac{1}{2}$; is equal to L when $L = \frac{1}{2}$; but is greater than L when $L < \frac{1}{2}$—so that the second change of curvature occurs only when $L > \frac{1}{2}$. (As x never quite reaches L, there is no second change of curvature when $L = \frac{1}{2}$.) These results are therefore as were to be expected from the two forms of the curve of f already discussed.

As already seen, when $L > \frac{1}{2}$, the summit of the f-curve is $\frac{1}{4}c$ and is reached when $x = \frac{1}{2}$. The corresponding value of t is

$$t = \tau - 1/KL \,.\, \log(2L-1), \tag{66}$$

the logarithm being negative since $2L-1$, that is, $1-2(N+r)/K$, is less than unity.

It has also been seen that when $L > \frac{1}{2}$, f falls after reaching its maximum, $\frac{1}{4}c$, to a constant value, $cL(1-L)$. The difference between the maximum and the ultimate values of f is therefore

$$\tfrac{1}{4}c(2L-1)^2,$$

and their ratio is $$1/4L(-L) = \lambda \text{ (say)}. \qquad (67)$$

As with independent happenings (*e.g.* equation 22), we shall use the symbol l to denote the limit which f approaches when t is very large, and this will be examined further in Section VIII (iii) (Part II).

(vi) The curves of new cases in proportional happenings are especially important because, if the original assumptions upon which they are based are sufficient in themselves to explain time-to-time variations in the frequency of infectious diseases, these curves should agree, at least for a first approximation to the truth, with the curves of new cases actually observed in such diseases. Now, according to Brownlee (Section I), the curves of many epidemics, especially of the short and sharp zymotic diseases, tend to be *remarkably symmetrical bell-shaped curves*, roughly similar, in fact, to the f-curve developed from certain values of the constants.

We now proceed, therefore, to examine these constants with greater care. They are in detail,

$$K = c-v+V, \quad KL = c-v+V-N-r, \quad L = 1-(N+r)/(c-v+V) \qquad (68)$$

The particular elements have been already discussed in Sections III and V. The natural-variation element v governs the natural increase of the population apart from exceptional happenings; but V, N, r are connected with the special happening under consideration. If the period covered by such happening is short compared with the average life of the individuals concerned, v may be so small as to be negligible, and N also may be very small. In injurious happenings such as infectious diseases, $v-V$ should be positive (Section V (iii)), and V will be negative if $M > N$ and $E > I$, so that $v-V$ still remains positive even when $v = 0$; but, as a rule, except in very fatal diseases, $v-V$ is very small. The element r may be unity when reversion is immediate, as in slight accidents, but may be nearly zero when the immunity conferred by one attack of a disease lasts for a long time on the average, as in many zymotic diseases. Both N and r are only positive quantities, so that $v-V+N+r$ is usually a small or very small positive fraction in the case of infectious diseases (its actual magnitude depending, of course, on the magnitude of the time-unit taken as well as on the elements themselves). The element of special importance is c, that is the average number of individuals infected or reinfected in unit of time by each already infected individual. But while v, V, N, r may be taken as fixed for the kind of happening considered, c is generally unknown, and, indeed, one of the ultimate objects of such studies as these will be to ascertain its value. At present, however, we take it to be a constant.

We observe first from equation 53 that if KL is negative x must constantly diminish as t increases, which means that a change must have occurred in at least one of the original constants. Hence we assume at present that KL is is positive, and reserve the study of the case when it is negative for Section IX (Hypometric Happenings; Part II).

Secondly, as KL is taken to be positive, c, whatever it is, must be greater than $v-\mathrm{V}+\mathrm{N}+r$—generally a small positive fraction; and therefore greater than each item individually.

Thirdly, as $c > v-\mathrm{V}+\mathrm{N}+r$ and N and r are positive, $c > v-\mathrm{V}$; that is, K is always positive.

Fourthly, as $\mathrm{KL} > 0$, $\mathrm{K} > \mathrm{N}+r$, and therefore L is always less than unity (as it must otherwise obviously be), and always positive. Clearly also, L increases with the increase of c and V, but diminishes with the increase of v, r, and N (the last of which exists in K but cancels out from KL).

We must now examine the conditions which hold respectively if f is to be of Type II or Type I, or is to be nearly or quite symmetrical.

It will be of Type II, that is, always increasing in a drawn-out S-shape [(v) above] if L is not greater than $\frac{1}{2}$; that is, if $c \ngtr v-\mathrm{V}+2(\mathrm{N}+r)$. But as just shown, in the cases which we are now considering, c must always be greater than $v-\mathrm{V}+\mathrm{N}+r$. Hence in order that f shall be of Type II, c must lie between the limits $v-\mathrm{V}+2(\mathrm{N}+r)$ and $v-\mathrm{V}+(\mathrm{N}+r)$. Now if $\mathrm{N}+r$ is small, as is usually the case in short and sharp epidemics of zymotic diseases with long immunity, these limits will be narrow; in other words, out of the whole range of possible values of c, that is of infectivity, only a small sector, and that the lowest one, will make f of Type II.

On the other hand, f will be of Type I, that is, of a bell-shape, regular or irregular, if $\mathrm{L} > \frac{1}{2}$—that is, if c is any number greater than $v-\mathrm{V}+2(\mathrm{N}+r)$. In this case f rises to a maximum ordinate $\frac{1}{4}c$ and then falls to a constant level $c\mathrm{L}(1-\mathrm{L})$. Lastly, f becomes nearly symmetrical (see (v) above) when $\mathrm{L} = 1$ nearly, that is, when $c = v-\mathrm{V}+(1+\gamma)(\mathrm{N}+r)$, where γ is considerable; and also of course when N and r are very small. These are probably just the conditions which hold in many of the short and sharp epidemics of zymotic diseases, such as measles, scarlatina, and dengue; and they produce curves which differ from the perfectly symmetrical curve of $c/\mathrm{K} \,.\, dx/dt$ only by a small increasing term which, however, never exceeds $c/\mathrm{K} \,.\, (\mathrm{N}+r)\mathrm{L}$.

For an example, suppose the case of a human infectious disease in which $v-\mathrm{V} = 0{\cdot}002$, $\mathrm{N} = 0{\cdot}0004$, $r = 0{\cdot}02$, all assumed for a time-unit of one week. Then KL will not be positive unless $c > 0{\cdot}0224$; that is, the happening will have no effect unless, say 1000 affected individuals infect or re-infect 22·4 individuals per week on the average. If 1000 such persons can infect or reinfect 42·8 persons per week or less, the f-curve will be of Type II and will always ascend to the limit $\frac{1}{4}c$ (that is, 0·0107 if $c = 0{\cdot}0428$), at which figure it will remain indefinitely. If, however, c is greater than this—if the 1000 affected persons can infect or re-infect say 100 persons per week—then the f-curve will rise to a maximum value of 0·025 of the total population, and afterwards decline to the constant value of 0·01647 of the total population, or 16·47 per thousand, at which it will remain (L being 0·792 in this case). If c is still greater, if each affected person can affect one other person per week, so that $c = 1$, then $\mathrm{L} = 0{\cdot}9795$, that is, nearly the whole population ultimately becomes affected. Here f, the proportion of new cases, reaches a maximum of one quarter the whole population and thereafter declines to the constant value of 0·01997, or nearly 2 per cent. of the population, at which it remains indefinitely. (For further examples see Section IX, Part II.)

(vii) Integral expressions for P and Z were obtained in equations 51 and 52 by integrating both sides of equation 44. These may be written

$$\mathrm{P} = \mathrm{P}_0\epsilon^{vt}(x/x_0 \,.\, \epsilon^{-\mathrm{KL}t})^{(v-\mathrm{V})/\mathrm{K}} = \mathrm{P}_0(x/x_0)^{(v-\mathrm{V})/\mathrm{K}}\epsilon^{vt}\epsilon^{-(v-\mathrm{V})\mathrm{L}t}, \tag{69}$$

$$\mathrm{Z} = \mathrm{Z}_0\epsilon^{vt}\epsilon^{\mathrm{KL}t}(x/x_0 \,.\, \epsilon^{-\mathrm{KL}t})^{c/\mathrm{K}} = \mathrm{Z}_0(x/x_0)^{c/\mathrm{K}}\epsilon^{vt}\epsilon^{-(v-\mathrm{V})\mathrm{L}t}. \tag{70}$$

Two important special cases present themselves here. If $v-\mathrm{V} = 0$, the happening has no effect on the total number of the population, as in mild infectious diseases such as chicken pox or (?) dengue or party politics. This should be called the Equivariant Case of Proportional Happening. In it, $\mathrm{P} = \mathrm{P}_0\epsilon^{vt}$ as in Section IV (ii), and of course $\mathrm{Z} = \mathrm{Z}_0\epsilon^{vt}$. But if $v-\mathrm{V}$ is small without being zero, care must be taken with the functions if c, N, and r are small.

The other special case occurs when $v = 0$, and may be called the Case of Constant Natural Population. It is particularly important, since happenings which are considered during only a short period compared with the average length of life of the individuals concerned approximate to this type, because then v, the element of natural increase, is generally so small compared with the other constants that it may be neglected; in fact, the *a priori* curves of most epidemic diseases may be considered on this basis.

If $v = 0$ and V is negative (as in all injurious happenings) we see that, since

$$\mathrm{P} = \mathrm{P}_0(x/x_0)^{-\mathrm{V}/(c+\mathrm{V})}\epsilon^{\mathrm{VL}t}, \tag{71}$$

the population diminishes indefinitely as time progresses ; which is, of course, what was to be expected since by supposition there is no natural increase to compensate for the loss due to the happening.

If neither $v = 0$ nor $v - \mathrm{V} = 0$ then, since $x = \mathrm{L}$ ultimately, that is, a constant, the question whether the population will finally increase or diminish depends upon the sign of the expression

$$v-(v-\mathrm{V})\mathrm{L} = \mathrm{V}+[(v-\mathrm{V})(\mathrm{N}+r)]/(c-v+\mathrm{V}). \tag{72}$$

An important value of P is reached when the x-curve attains its centre of symmetry, that is when $x = \frac{1}{2}\mathrm{L}$ and $t = \tau = 1/\mathrm{KL}\ .\ \log\,[(\mathrm{L}-x_0)/x_0]$ (see (iii) above). Then

$$\begin{aligned} \mathrm{P} &= \mathrm{P}_0\,(\mathrm{L}/2x_0)^{(v-\mathrm{V})/\mathrm{K}}\,[(\mathrm{L}-x_0)/x_0]^{[v-(v-\mathrm{V})\,\mathrm{L}]/\mathrm{KL}}, \\ &= \mathrm{P}_0\,(\tfrac{1}{2})^{(v-\mathrm{V})/\mathrm{K}}\,(\mathrm{LP}_0)^{v/\mathrm{KL}}, \end{aligned} \tag{73}$$

if x_0 is very small, as when it equals $1/\mathrm{P}_0$.

Another important value of P is reached when $\mathrm{Z} = \mathrm{LP}-1$, that is when $t = 2\tau$ (equation 58). Then

$$\mathrm{P} = \mathrm{P}_0\,[(\mathrm{L}-x_0)/x_0]^{[2v-(v-\mathrm{V})\,\mathrm{L}]/\mathrm{KL}}. \tag{74}$$

A third important value of P is reached (if $\mathrm{L} > \frac{1}{2}$) when the f-curve attains its maximum ; that is, when $x = \frac{1}{2}$ and $t = \tau'$ (equation 66). Then

$$\mathrm{P} = \mathrm{P}_0\,(1/2x_0)^{(v-\mathrm{V})/\mathrm{K}}\,[1/x_0\,.\,(\mathrm{L}-x_0)/(2\mathrm{L}-1)]^{[v-(v-\mathrm{V})\,\mathrm{L}]/\mathrm{KL}}. \tag{75}$$

These expressions are required to estimate the actual values of Z and F at these points; but, if L is not very small, τ will not be very large (see Section VIII (vii)), and therefore P can vary but little in that period from its original value P_0, and, at least for rough calculations, can be taken as remaining constant.

(viii) It remains to consider the integrals of P, Z and F, which will be required for the analysis of several questions. We proceed as in the case of constant happenings (Section IV (v)) by integrating both sides of the fundamental differential equations (44 and 45). Hence

$$\mathrm{P}-\mathrm{P}_0 = v\int_0^t \mathrm{P}dt-(v-\mathrm{V})\int_0^t \mathrm{Z}dt, \tag{76}$$

$$\mathrm{Z}-\mathrm{Z}_0 = \int_0^t \mathrm{F}dt+(\mathrm{V}-\mathrm{N}-r)\int_0^t \mathrm{Z}dt. \tag{77}$$

To interpret the first of these equations, we note that the actual change in the total population effected during the period t, namely $\mathrm{P}-\mathrm{P}_0$, equals what the change would have been by natural-variation only, namely $\int_0^t v\mathrm{P}dt$, less the difference between the natural-variation and the happening-variation in the affected part of the population, namely $\int_0^t (v-\mathrm{V})\,\mathrm{Z}dt$. The second equation, which is the same as equation 24, has been already interpreted in Section IV (v). It means that the total change in the number of the affected during the period t, namely, $\mathrm{Z}-\mathrm{Z}_0$, is equal to the sum of new cases, namely $\int_0^t \mathrm{F}dt$, plus the affected immigrations, and less the affected emigrations, deaths, and recoveries, namely, $\int_0^t (\mathrm{I}-\mathrm{E}-\mathrm{M}-r)\,\mathrm{Z}dt$. Both these interpretations agree with what was to be expected.

The integrals of F and Z can be obtained at once in the important case when $v = 0$; and are

$$\int_0^t \mathrm{Z}dt = (\mathrm{P}-\mathrm{P}_0)/\mathrm{V}, \tag{78}$$

$$\int_0^t \mathrm{F}dt = \mathrm{Z}-\mathrm{Z}_0-(\mathrm{V}-\mathrm{N}-r)(\mathrm{P}-\mathrm{P}_0)/\mathrm{V}. \tag{79}$$

If in these we have also $\mathrm{V} = 0$, then $(\mathrm{P}-\mathrm{P}_0)/\mathrm{V}$ becomes indeterminate since P remains constant; but the value of the fraction then is, from equation 71,

$$(\mathrm{P}-\mathrm{P}_0)/\mathrm{V} = \mathrm{L}t-\frac{1}{c}\log_\epsilon(\mathrm{L}/x_0). \tag{80}$$

The integrals of Z and F can also be easily obtained by direct integration of their values when $v = 0$.

We should note that the total births, deaths, immigrations, emigrations, and recoveries among the affected during the period t are given, as with constant happenings, by multiplying $\int_0^t \mathrm{Z}dt$ by N, M, I, E, and r respectively.

The main result has already been summarised in the prefatory section. We can see from (vi) above that, for many values of the constants, the solution of the fundamental proposition stated in Section II yields curves generally similar to the curves frequently found in epidemics—that is, curves which are bell-shaped and nearly symmetrical, and tend to decline more slowly than they rose. This decline is in the case of the *a priori* curves due merely to the exhaustion of susceptible material; but the further studies contained in the second part must be considered before attempts are made to apply the results to actual observations.

For the projected contents of Part II see end of Section I above (p. 208).

REFERENCES.

1. William Farr, "On the Cattle Plague," 'Daily News,' February 17, 1866, and 'Journ. of Social Science,' London, March 20, 1866.
2. G. H. Evans, "Some Arithmetical Considerations on the Progress of Epidemics," 'Trans. Epidemiolog. Soc. of London,' vol. 3, Part III, p. 551 (1873–75).
3. J. Brownlee, "Studies in Immunity: Theory of an Epidemic," 'Proc. Roy. Soc. Edin.,' vol. 26, Part IV, p. 484 (1906).
4. J. Brownlee, "Certain Considerations on the Causation and Course of Epidemics," 'Proc. Roy. Soc. Med. London,' June, 1909.
5. J. Brownlee, "The Mathematical Theory of Random Migration and Epidemic Distribution," 'Proc. Roy. Soc. Edin.,' vol. 31, Part II, p. 261 (1910).
6. J. Brownlee, "Periodicity in Infectious Disease," 'Proc. Roy. Phil. Soc. Glasgow,' 1914.
7. J. Brownlee, "Investigations into the Periodicity of Infectious Diseases by the Application of a Method hitherto only used in Physics," 'Public Health,' London, vol. 28, No. 6 (1915).
8. J. Brownlee, "On the Curve of the Epidemic," 'Brit. Med. Journ.,' May 8, 1915, p. 599.
9. Ronald Ross, 'The Logical Basis of the Sanitary Policy of Mosquito Reduction,' Congress of Arts and Sciences, St. Louis, U.S.A., vol. 6, p. 89 (1904); also 'Brit. Med. Journ.,' May 13, 1905.
10. Ronald Ross, 'The Prevention of Malaria in Mauritius,' Waterlow and Sons, London, 1908, pp. 29–40.
11. Ronald Ross, 'The Prevention of Malaria,' John Murray, London, 1910; also 2nd Edition, 1911, 'A Special Addendum on the Theory of Happenings,' pp. 651–686.
12. Ronald Ross, "Some Quantitative Studies in Epidemiology," 'Nature,' London, October 5, 1911. Italian translation, 'Malaria,' Rome, November, 1911.
13. Ronald Ross, "Some *a priori* Pathometric Equations," 'Brit. Med. Journ.,' March 27, 1915.
14. H. Waite, "Mosquitoes and Malaria," 'Biometrika,' London, October, 1910, vol. 7, No. 4, p. 421.