STUDIES IN THE MEANING AND RELATIONSHIPS OF BIRTH AND DEATH RATES.

V.

On the difficulty that in applying the laws of physical chemistry to life processes, indices occur which suggest the actions of fractions of a molecule.

By JOHN BROWNLEE, M.D., D.Sc.

In a large number of cases the curves which describe the rate at which ferments, antibodies, etc., disappear in the body accord in form with the equations of physical chemistry, but not so as to be readily interpretable. If one molecule, two molecules, etc., take part in a reaction then it is clear that the indices in the equations must bear certain relations to whole numbers. Failure to conform to these relations seems at first sight to imply that a fraction of a molecule takes part in a reaction, but this is not necessarily the case. Such a failure has been found to appear when the curves of many vital phenomena, *e.g.* the disappearance of agglutins in an organism, are fitted to physico-chemical equations. A possible meaning, however, can easily be seen.

Firstly, as the monomolecular reaction is so frequent in life phenomena, it is quite reasonable to assume that it is the rule. Secondly, it is highly improbable that such a substance as an agglutin is a simple substance. It is much more probably a group of substances each of which has its own rate of decay. If each member of this group be taken to obey the monomolecular reaction, the amount of agglutin present at a definite time x, instead of being represented by the form ae^{-kx} as is required by the monomolecular theory, will be represented by a sum of such forms, each substance disappearing at a different rate, and each present originally in a different amount.

Now certain curves of frequency exist which may be tried. If the frequency of each value of k be denoted $a\kappa^n e^{-\gamma\kappa}$ (Pearson's Type III, a curve having a very wide range of forms) the amount of the substance after a period x will be represented by

$$a\int_{\kappa}^{\infty} e^{-\kappa x}\,\kappa^n e^{-\gamma\kappa}\,dk,$$

https://doi.org/10.1017/S0022172400006112 Published online by Cambridge University Press

or (M being a constant)

$$\frac{M}{(x+\gamma)^{n+1}} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots \text{(A)},$$

which is the form required by a multimolecular reaction where $k+1$ is equal to $\frac{1}{p-1}$, p being an integer. But on the theory here developed the values of n are not circumscribed in this way, and p may be any number, fractional, or integral. Thus a possible explanation of a common phenomenon is obtained.

It is to be noted that the rates of the disappearance of the agglutins or the precipitins formed when the same organism is inoculated into different animals vary greatly, implying that the amount of each separate agglutinin with its special rate of decay may be very different even in nearly allied forms. The experimental working of this subject opens a wide field.

It is not necessary to quote examples that are familiar to all workers in this subject. To illustrate the range, however, an example from the statistics of children's diseases, namely the death rate from whooping cough, has been chosen, as death from whooping cough is due to a considerable variety of causes—convulsions, broncho-pneumonia, etc.

In the accompanying table the numbers of admissions and of deaths, and the case mortality of persons suffering from whooping cough, treated in the City of Glasgow Hospital, Belvidere, between the years 1885 and 1902 are given. The theoretical mortality is calculated on the hypothesis above stated. The theoretical numbers of deaths, calculated from the number of cases, which being the larger number

Table showing that the case mortality of cases of whooping cough from one year to ten is completely described by the curve $y = \frac{4090}{(4 \cdot 7 + x)^{2 \cdot 688}}$, *where* y *is the case mortality and* x *the age in years.*

		No. of deaths		Case mortality	
Age	No. of cases	Actual	Theoretical	Actual	Theoretical
1– 2	619	233	233	38·0	38·0
2– 3	742	190	183	25·6	24·6
3– 4	779	119	130	15·3	16·7
4– 5	695	81	85	11·7	12·2
5– 6	585	53	53	9·1	9·1
6– 7	420	28	29	6·6	7·0
7– 8	228	13	13	5·7	5·5
8– 9	112	6	5	5·3	4·4
9–10	55	2	2	3·6	3·6

https://doi.org/10.1017/S0022172400006112 Published online by Cambridge University Press

has the smaller probable error, are added to admit of statistical comparison. The correspondence is exceedingly close since $\chi^2 = 1{\cdot}9$ and $P = {\cdot}99$. This is not a solitary example, and others will be discussed later when some of the problems of special diseases are considered.

In what has gone before, the distribution of the value of k has been assumed to be that of Type III. It may, however, be at least equally probably assumed to be normal. In this case, the resulting equation giving the amount of the original substances present at the time, x is of the form:

$$y = a\int_{-\infty}^{\infty} e^{-\kappa x}\, e^{-\frac{(\kappa-k)^2}{2\sigma^2}}\, d\kappa,$$

k being the mean value of κ, or when integration is effected:

$$y = Me^{-kx-2\sigma^2x^2},$$

M being a constant. If the range of κ is large, *i.e.* if $\frac{k}{\sigma}$ is small, the deviation from the simple exponential curve is considerable. If, however, the range of κ is small, *i.e.* if $\sigma \fallingdotseq 0$, the resulting formula is approximately the simple exponential. A certain variation in the value of κ may, therefore, take place, without the result of the experiments being found to diverge much from the monomolecular law.

A simple case which may be of interest is that of a mixture of two substances, both decaying according to the monomolecular law, of which the values of κ are somewhat different. To illustrate the point, imagine the sum of two geometrical progressions, one which has a ratio of $\frac{3}{4}$ and the other of $\frac{1}{2}$. The figures are given below:

1·0000	·7500	·5625	·4218	·3146	·2373	·1780	·1335
1·0000	·5000	·2500	·1250	·0625	·0313	·0156	·0078
2·0000	1·2500	·8125	·5469	·3789	·2686	·1936	·1413
2·0000	1·2514	·8138	·5470	·3779	·2677	·1936	·1424

Beneath the sums of the two progressions, a series of theoretical figures are added, which have been obtained by fitting the descending series to an equation of the form:

$$y = \frac{4225600}{(10{\cdot}659 + x)^{5{\cdot}2285}}.$$

The correspondence is as absolute as could be expected in any series of observations made on experiments. It is obvious here that the power to which the denominator is raised is the equivalent of a reaction in which the fractions of a molecule take part.