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Summary.

(1) The measurements of Shaw and Butler of the partial pressures of water and ethyl alcohol in solutions containing lithium chloride have been extended to solutions containing 2 and 4 mols. per cent. of ethyl alcohol.

(2) A discussion is given of the thermodynamics of salting out. It is pointed out that the salting out is properly measured, not by the change of the activity of the non-electrolyte produced by the salt, but by the difference between this quantity and the normal effect, which is defined.

(3) The partial free energies of transfer of lithium chloride from water to alcoholic solutions have been calculated from the partial pressures of water and alcohol. The variation is approximately linear with the molar fraction of alcohol.

Contributions to the Mathematical Theory of Epidemics. III.—*Further Studies of the Problem of Endemicity.*

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Introduction.

In a previous paper† (Part II of this series) an attempt was made to treat from a general point of view the problem of a single disease in a population which consisted of three categories of people—namely, never infected, sick and recovered—and in which the infectivity of the disease was a function of the period of illness, whilst the susceptibility of a recovered person was a function of the period which had elapsed since the time of his recovery. New individuals entering the population either by birth or by immigration naturally entered the category of the never infected which for convenience we called " virgins." It was pointed out that the results obtained were subject to two important limitations: (1) that the disease under consideration was the only cause of

† ' Proc. Roy. Soc.,' A, vol. 138, p. 55, (1932).

death, and (2) that the age of the individuals did not affect their infectivity, susceptibility or reproductiveness.

It is the purpose of the present paper to remove the first of these limitations by the introduction of constant non-specific death rates, which for the sake of generality are assumed to be different for virgins, sick, and recovered. It may be stated at once that the introduction of this additional factor produces surprisingly little change in the general nature of the results previously obtained, and that the conclusions of the previous paper hold with very little modification.

In the previous paper the results were first of all worked out for constant infectivity, recovery and death rates, and the more general problem, in which these rates were variable, was thereafter considered. The algebra for constant coefficients was relatively very simple. It is now found, however, that with the introduction of non-specific death rates, the simple case increases in complexity relatively much more than does the general case, so that the advantage of treating it separately largely disappears. In particular, whereas the various expressions for steady state levels previously came out explicitly as fairly simple functions of the constant coefficients, they are now dependent on a somewhat complicated quadratic equation. On the other hand the equations which refer to the case with variable rates, although they now contain a few extra terms, remain qualitatively similar in type to those previously obtained, and the same method of treatment leads at once to identical or closely similar results. We shall not therefore, in the present communication, treat in detail the case of constant rates but only give some of the main results. It may be mentioned, however, that the general equations have been checked at the various points by the introduction of constant rates, and comparison has been made between the formulæ so obtained and those found when constant rates were used throughout.

As in the previous paper the equations which describe the progress of small variations about the steady state are formulated, but their fuller discussion has at present been reserved.

It will be recalled that in Part II a number of special cases were discussed either because they had some special practical importance, or because they exhibited peculiarities from the mathematical point of view. With the introduction of non-specific death rates, a number of new special cases requiring detailed consideration came to light. To appreciate the relationship between all these cases it became necessary to adopt a scheme of classification, which although multiplying the total number of special cases considerably, made

their treatment much simpler, and except in two instances only very brief discussion was required. The five special cases of Part II are readily accommodated in the new scheme.

A question of some practical importance is the effect upon the size of the population, the number of sick, and the relative incidence of the disease, of changes in the various parameters which characterize either the population or the disease. These points were investigated to some extent in the previous paper, but are more fully considered in the present communication both in connection with the general case, and with a number of the special cases referred to above. The results obtained are not always in accordance with expectation.

General Case.

General Equations.—A detailed description of the population under discussion will be found on pages 59 and 63 of the previous paper (Part II). The nomenclature and notation previously adopted remains unaltered, and to economize space will not be explained again here. The new death rates, which are now introduced, are denoted by $\bar{\pi}$, π and ρ for virgins, recovered persons, and sick, respectively, so that certain equations in Part II have to be modified. For convenience of reference the same numbers are used to denote the equations, an asterisk being added where alteration has been necessary. In the case of equations which do not correspond to numbers in Part II, index numbers consecutive to those in that paper have been employed. It is to be noted that the variables employed refer throughout to population densities, but if the area be considered as fixed, the population size may be employed in place of the less usual conception of population density.

Equations (15), (16), and (17) become

$$\frac{d\bar{x}}{dt} + \overline{\pi x} = \bar{u}_t - \bar{v}_t, \tag{15*}$$

$$\frac{dx}{dt} + \pi x = u_t - \bar{v}_t, \tag{16*}$$

$$\frac{dy}{dt} + \rho y = v_t - w_t - u_t, \tag{17*}$$

equations (19) to (27) remain unaltered.

To express $\bar{u}_{t\lambda}$ in terms of $\bar{u}_t$ we have the equation

$$\frac{\partial \bar{u}_{t\lambda}}{\partial t} + \frac{\partial \bar{u}_{t\lambda}}{\partial \lambda} = -\bar{u}_{t\lambda} \bar{f}(t) - \overline{\pi u}_{t\lambda}, \tag{28*}$$

whence

$$\bar{u}_{t\lambda} = \bar{u}_{t-\lambda}\, e^{-\int_0^\lambda [\bar{f}(t-\lambda')+\bar{\pi}]\, d\lambda'}. \tag{32*}$$

In a similar manner it can be shown that

$$v_{t\theta} = v_{t-\theta}\, e^{-\int_0^\theta (l_{\theta'}+d_{\theta'}+\rho)\, d\theta'}, \tag{29*}$$

whence

$$\bar{f}(t) = \int_0^\infty \bar{k}_\theta v_{t-\theta} \mathrm{N}_\theta\, d\theta, \qquad \text{where} \qquad \mathrm{N}_\theta = e^{-\int_0^\theta (l_{\theta'}+d_{\theta'}+\rho)\, d\theta'} \tag{30*}$$

$$= \int_0^\infty \bar{\mathrm{K}}_\theta v_{t-\theta}\, d\theta, \qquad \text{where} \qquad \bar{\mathrm{K}}_\theta = \bar{k}_\theta \mathrm{N}_\theta. \tag{31}$$

By equation (19),

$$\bar{x} = \int_0^\infty \bar{u}_{t-\lambda}\, e^{-\int_0^\lambda [\bar{f}(t-\lambda')+\bar{\pi}]\, d\lambda'}\, d\lambda. \tag{33*}$$

Also

$$u_{t\tau} = u_{t-\tau}\, e^{-\int_0^\tau [f(t-\tau+\xi)\,\omega_\xi+\pi]\, d\xi}, \tag{37*}$$

$$= u_{t-\tau} \mathrm{F}(t-\tau, \tau), \quad \text{where} \quad \mathrm{F}(t-\tau, \tau) = e^{-\int_0^\tau [f(t-\tau+\xi)\,\omega_\xi+\pi]\, d\xi}, \tag{38*}$$

hence by equation (20)

$$x = \int_0^\infty \mathrm{F}(t-\tau, \tau)\, u_{t-\tau}\, d\tau. \tag{39}$$

Equations (40) to (45) remain formally unaltered.

Equations for Steady State.—In finding the conditions for a steady state certain modifications are necessary.

Clearly

$$\mathrm{L} + \mathrm{D} + \rho\mathrm{N} = \int_0^\infty (l_{\theta'} + d_{\theta'} + \rho)\, e^{-\int_0^\theta (l_{\theta'}+d_{\theta'}+\rho)\, d\theta'}\, d\theta = 1, \tag{46*}$$

while as before

$$\bar{\mathrm{U}} = \bar{\mu}\bar{\mathrm{X}} + \mu\mathrm{X} + \nu\mathrm{Y} + m. \tag{47}$$

The other relations in equations (47), (48) and (49) no longer hold.

By (33*)

$$\bar{\mathrm{X}} = \bar{\mathrm{U}} \int_0^\infty e^{-\int_0^\lambda [\bar{f}(t-\lambda')+\bar{\pi}]\, d\lambda'}\, d\lambda,$$

but

$$\bar{f}(t) = \bar{\mathrm{K}}\mathrm{V}, \tag{50}$$

whence

$$\bar{\mathrm{X}} = \bar{\mathrm{U}} \int_0^\infty e^{-(\bar{\mathrm{K}}\mathrm{V}+\bar{\pi})\lambda}\, d\lambda$$

$$= \frac{\bar{\mathrm{U}}}{\bar{\mathrm{K}}\mathrm{V} + \bar{\pi}}. \tag{51*}$$

By (39)

$$X = U \int_0^\infty F(t - \tau, \tau)\, d\tau.$$

But

$$F(t - \tau, \tau) = e^{-\int_0^\tau [f(t-\tau+\xi)\,\omega_\xi + \pi]\, d\xi},$$

and

$$f(t) = \Phi V, \tag{52}$$

hence

$$\int_0^\infty F(t - \tau, \tau)\, d\tau = \int_0^\infty e^{-\int_0^\tau (\Phi V \omega_\xi + \pi)\, d\xi}\, d\tau,$$

$$= F(V), \tag{53*}$$

thus

$$X = UF(V). \tag{54}$$

As previously

$$Y = NV, \qquad U = LV \qquad \text{and} \qquad X = LVF(V). \tag{55)-(57)}$$

Also

$$\tilde{V} = \Phi V G(V)\, U, \tag{58) (in part)}$$

where

$$G_1'(V) = \int_0^\infty G(t - \tau, \tau)\, d\tau,$$

$$= \int_0^\infty \omega_\tau F(t - \tau, \tau)\, d\tau,$$

$$= \int_0^\infty \omega_\tau e^{-\int_0^\tau (\Phi V \omega_\xi + \pi)\, d\xi}\, d\tau,$$

$$= \frac{1 - \pi F}{\Phi V}. \tag{59*}$$

Thus

$$\tilde{V} = U(1 - \pi F). \tag{58*}$$

As before

$$\bar{V} = \overline{XKV} \qquad \text{and} \qquad W = DV. \tag{60) and (61)}$$

From these relations it follows that

$$\left.\begin{aligned} U &= LV, \\ \tilde{V} &= LV(1 - \pi F), \\ \bar{V} &= \frac{\bar{K} V \bar{U}}{\bar{K} V + \bar{\pi}}, \\ W &= DV, \\ \bar{X} &= \frac{\bar{U}}{\bar{K} V + \bar{\pi}}, \\ X &= LFV, \\ Y &= NV. \end{aligned}\right\} \tag{62*}$$

The condition for a steady state of the total population is by equations (15*), (16*) and (17*)

$$\bar{U} = W + \pi\bar{X} + \pi X + \rho Y,$$

whence after substituting the above values of $\bar{X}$, X, Y and W,

$$\bar{U} = \frac{(D + \pi LF + \rho N)(\bar{K}V + \bar{\pi})}{\bar{K}}.$$

But by equation (47),

$$\bar{U} = m + \bar{\mu}\bar{X} + \mu X + \nu Y,$$

whence, on substitution,

$$\bar{U} = \frac{(m + \mu LFV + \nu NV)(\bar{K}V + \bar{\pi})}{\bar{K}V + \bar{\pi} - \bar{\mu}}.$$

Continuing these two expressions for U, we have, for the steady state, V given by

$$\Theta(V) = LF\left\{\mu - \pi + \frac{\pi(\bar{\mu} - \bar{\pi})}{\bar{K}V}\right\} + \nu N - D - \rho N + \frac{m}{V} + \frac{(\bar{\mu} - \bar{\pi})(D + \rho N)}{\bar{K}V} = 0. \tag{65*}$$

Also the total number of individuals is

$$\begin{aligned} n &= \bar{X} + X + Y, \\ &= \frac{D + \pi LF + \rho N}{\bar{K}} + LFV + NV, \\ &= \frac{1 - L(1 - \pi F)}{\bar{K}} + (LF + N)V. \end{aligned} \tag{64*}\dagger$$

We shall now consider the nature of the real positive roots of equation (65*), and we shall assume that $\bar{\mu} > \bar{\pi}$, and $\mu > \pi$.

Clearly as $V \to 0$, $\Theta(V) \to +\infty$. It is also obvious by inspection that $\Theta(V)$ decreases, as V increases. Thus the equation $\Theta(V) = 0$ will have one real positive root or no real positive roots, according as $\Theta(V)_{V \to \infty}$ is negative or positive.

Clearly

$$\Theta(V)_{V \to \infty} = \{LF(\mu - \pi) + \nu N - D - \rho N\}_{V \to \infty}.$$

† [Erratum: Equation (64) of Part II should read $n = \frac{D}{\bar{K}} + (LF + N)V$].

As in Part II, p. 70, we shall assume that ω_ξ has the following properties. It is equal to zero between $\tau = 0$ and $\tau = \varepsilon$, it increases monotonically, and it has a constant value ω when $\tau > \eta$. Then

$$F = \int_0^\epsilon e^{-\pi\tau}\, d\tau + \int_\epsilon^\eta e^{-(\Phi V\bar{\Omega}_\tau + \pi\tau)}\, d\tau + \int_\eta^\infty e^{-\Phi V[\bar{\Omega}_\eta + \omega(\tau-\eta)] - \pi\tau}\, d\tau, \qquad (67^*)$$

$\left(\text{where as before } \bar{\Omega}_\tau = \int_0^\tau \omega_\xi\, d\xi\right)$,

$$= \frac{1 - e^{-\pi\epsilon}}{\pi} + (\eta - \varepsilon)\, e^{-(\Phi V\bar{\Omega}_\sigma + \pi\sigma)} + \frac{e^{-(\Phi V\bar{\Omega}_\eta + \pi\eta)}}{\Phi V\omega + \pi},$$

(where σ is some value of τ between ε and η).

Thus

$$F(V)_{V\to\infty} = \frac{1 - e^{-\pi\epsilon}}{\pi},$$

and

$$\Theta(V)_{V\to\infty} = (\mu - \pi)\, L\, \frac{(1 - e^{-\pi\epsilon})}{\pi} + \nu N - D - \rho N. \qquad (68^*)$$

Therefore $\Theta(V) = 0$ has no real root if $D + \rho N - \nu N - (\mu - \pi)\, L\, \dfrac{(1 - e^{-\pi\epsilon})}{\pi}$ is negative, and has one real root if this expression is positive. If it is zero then there is a root $V = \infty$.

Thus the sufficient conditions that there should be one and only one real positive root are

$$\left.\begin{aligned} &\bar{\mu} > \bar{\pi}, \qquad \mu > \pi \\ \text{and} \quad &D + \rho N - \nu N - (\mu - \pi)\, L\, \frac{(1 - e^{-\pi\epsilon})}{\pi} > 0. \end{aligned}\right\} \qquad (103)$$

The third condition may also be written in the form

$$1 - L - \nu N - (\mu - \pi)\, L\, \frac{(1 - e^{-\pi\epsilon})}{\pi} > 0.$$

It may be remarked that these conditions although sufficient are not necessary. When ε is zero the third condition becomes $\dfrac{D}{N} + \rho > \nu$, and in the case of constant coefficients this gives $d + \rho > \nu$. This means that the total deaths amongst the sick are greater than the births among the sick, and this is clearly necessary to balance the excess of births over deaths in the healthy, if a steady state is to be maintained.

As has been remarked in the introduction, we do not propose to give the detailed working for the case with constant coefficients. It may, however, be shown either by working from first principles, or by using equation (65*), calculating all the terms in it for constant coefficients, and substituting $V = Y(d + l + \rho)$, that Y is given by the quadratic

$$k\bar{k}(d+\rho-\nu)\,Y^2 - k\bar{k}\left\{m + \frac{(\bar{\mu}-\bar{\pi})(d+\rho)}{\bar{k}} - \frac{\pi(d+\rho-\nu)}{k} + (\mu-\pi)\frac{l}{k}\right\} Y$$
$$- \pi\{\bar{k}m + (\bar{\mu}-\bar{\pi})(d+l+\rho)\} = 0. \quad (104)$$

The quadratic has one real positive and one real negative root if $\bar{\mu} > \bar{\pi}$, and $d + \rho > \nu$. On account of the complicated nature of the quadratic, it happens that it is in some respects easier to deal with the general case than with this very special case of constant coefficients.

Effect of Variations of Parameters on Steady State.—Having assumed that the three conditions found above are satisfied, we shall now investigate the variation of the absolute rate of incidence of the disease V, and of the proportional rate of incidence $T = \frac{V}{n}$, with changes in the immigration, birth and death rates.

From equation (65*) we have

$$\frac{\partial V}{\partial m} = -\frac{\dfrac{\partial\Theta}{\partial m}}{\dfrac{\partial\Theta}{\partial V}}, \qquad \frac{\partial V}{\partial \bar{\pi}} = -\frac{\dfrac{\partial\Theta}{\partial \bar{\pi}}}{\dfrac{\partial\Theta}{\partial V}}, \qquad \text{etc.} \quad (105)$$

also

$$\left.\begin{aligned} &\frac{\partial\Theta}{\partial m} = \frac{1}{V}, \qquad \frac{\partial\Theta}{\partial\bar{\mu}} = \frac{D + \rho N + L\pi F}{\bar{K}V} = \frac{1 - L(1-\pi F)}{\bar{K}V}, \\ &\frac{\partial\Theta}{\partial\mu} = LF, \qquad \frac{\partial\Theta}{\partial\nu} = N, \qquad \frac{\partial\Theta}{\partial\bar{\pi}} = -\frac{1 - L(1-\pi F)}{\bar{K}V}, \end{aligned}\right\} \quad (106)$$

and

$$\frac{\partial\Theta}{\partial\pi} = -LF\frac{(\bar{K}V - \bar{\mu} + \bar{\pi})}{\bar{K}V} + L\left\{(\mu-\pi) + \pi\frac{(\bar{\mu}-\bar{\pi})}{\bar{K}V}\right\}\frac{\partial F}{\partial\pi}. \quad (107)$$

But

$$\frac{\partial F}{\partial\pi} = -\int_0^\infty \pi e^{-\int_0^\tau (\Phi V\omega_\xi + \pi)\,d\xi}\,d\tau,$$

and is therefore negative; and, by (15*)

$$\bar{\pi}\bar{X} = \bar{U} - \bar{V}$$
$$= m + \bar{\mu}\bar{X} + \mu X + \nu Y - \bar{K}VX \qquad \text{(by (47) and (60)),}$$

hence

$$\bar{X}(\bar{K}V - \bar{\mu} + \bar{\pi}) = m + \mu X + \nu Y,$$

which is a positive quantity, so that

$$\bar{K}V - \bar{\mu} + \bar{\pi} \tag{108}$$

is necessarily positive.

Thus $\partial\Theta/\partial m$, $\partial\Theta/\partial\bar{\mu}$, $\partial\Theta/\partial\mu$ and $\partial\Theta/\partial\nu$ are each positive, whilse $\partial\Theta/\partial\bar{\pi}$ and $\partial\Theta/\partial\pi$ are negative. As ρ is contained in the expressions N, L, D, F, etc., the value of $\partial\Theta/\partial\rho$ does not seem to be unambiguously either positive or negative.

Further

$$\frac{\partial\Theta}{\partial V} = LF'\left\{\mu - \pi + \frac{\pi(\bar{\mu} - \bar{\pi})}{\bar{K}V}\right\} - \frac{m}{V^2} - \frac{\{1 - L(1 - \pi F)\}(\bar{\mu} - \bar{\pi})}{\bar{K}V^2}, \tag{109}$$

and must be negative since F is positive, and F′ is negative.

Hence $\partial V/\partial m$, $\partial V/\partial\bar{\mu}$, $\partial V/\partial\mu$, and $\partial V/\partial\nu$ are each positive, whilst $\partial V/\partial\bar{\pi}$ and $\partial V/\partial\pi$ are negative.

[The sign of $\partial V/\partial\rho$ may be either positive or negative. It may readily be shown that if $\bar{\mu} = \bar{\pi}$ and $\mu = \pi$, $\partial\Theta/\partial\rho$ is negative, whilst if $\bar{\mu} > \bar{\pi}$, $\mu > \pi$, $\nu = 0$ and $l_\theta = 0$, $\partial\Theta/\partial\rho$ is positive.]

Let $T = V/n$, so that, as before, 100T is the percentage rate of incidence of fresh cases of the disease, then

$$\frac{1}{T} = \frac{\bar{X}}{V} + \frac{X}{V} + \frac{Y}{V}$$

$$= \frac{1 - L(1 - \pi F)}{\bar{K}V} + LF + N, \tag{110}$$

and

$$-\frac{1}{T^2}\frac{\partial T}{\partial V} = \frac{-\{1 - L(1 - \pi F)\}}{\bar{K}V^2} + LF' + \frac{\pi LF'}{\bar{K}V}. \tag{111}$$

Since F′ is negative, $\partial T/\partial V$ is positive.

Consequently as T does not contain m, $\bar{\mu}$, μ, ν or $\bar{\pi}$ except implicitly in V, $\partial T/\partial m$, $\partial T/\partial\bar{\mu}$, $\partial T/\partial\mu$ and $\partial T/\partial\nu$ are positive, whilst $\partial T/\partial\bar{\pi}$ is negative.

The variation of T with π requires further consideration.

$$\frac{\partial T}{\partial\pi} = \frac{\partial' T}{\partial'\pi} + \frac{\partial T}{\partial V}\frac{\partial V}{\partial\pi},$$

where $\partial' T/\partial'\pi$ refers to partial differentiation with respect to π directly, and apart from V.

Thus

$$\frac{\partial T}{\partial \pi} = -\frac{T^2}{\dfrac{\partial \Theta}{\partial V}} \begin{vmatrix} \dfrac{\partial' \frac{1}{T}}{\partial' \pi}, & \dfrac{\partial \frac{1}{T}}{\partial V} \\ \dfrac{\partial \Theta}{\partial \pi}, & \dfrac{\partial \Theta}{\partial V} \end{vmatrix}.$$

After substituting in the Jacobean and reducing, we find

$$\frac{\partial T}{\partial \pi} = -\frac{T^2}{\dfrac{\partial \Theta}{\partial V}} \Big[\Big\{ \frac{L^2 F}{\bar{K}V} \frac{\partial F}{\partial V} \Big(\mu - \pi + \pi \frac{\bar{\mu} - \bar{\pi}}{\bar{K}V} \Big) - \frac{1 - L(1 - \pi F)}{\bar{K}V^2} LF + \frac{L^2 (\bar{K}V + \pi)}{\bar{K}V} F \frac{\partial F}{\partial V} \frac{\bar{K}V - \bar{\mu} + \bar{\pi}}{\bar{K}V} \Big\} - \Big(\frac{LF}{\bar{K}V} + L \frac{\bar{K}V + \pi}{\bar{K}V} \frac{\partial F}{\partial \pi} \Big) \frac{m}{\bar{V}^2} - \frac{1 - L(1 - \pi F)}{\bar{K}V^2} L\sigma \frac{\partial F}{\partial \pi} \Big]. \quad (112)$$

The terms within the curly brackets are readily seen to be negative, whilst the last term is positive or negative according as

$$\sigma = (\bar{\mu} - \bar{\pi}) - (\mu - \pi), \quad (113)$$

is greater or less than zero. Hence if $m = 0$, and $\sigma \leqslant 0$, $\partial T/\partial \pi$ is negative. If $\sigma > 0$, or if m is not zero, the sign of $\partial T/\partial \pi$ is not certain. By considering the extreme case $\omega = 0$, it may easily be shown that the coefficient of m is not necessarily negative.

So far we have been investigating the effect on the steady state of the disease of changes in the parameters which characterize the population. It is of interest to find the effects of alterations in the parameters which characterize the disease. These are $\bar{k}$, ϕ, ω, l, and d. Owing to the fact that l and d (like ρ) appear in N it does not seem possible to obtain any simple general result as to the effect of alteration of these parameters.

As the factor $\bar{k}$ enters into the equations for Θ and T only in the form of $\bar{K}$, it is sufficient to investigate $\partial V/\partial \bar{K}$ and $\partial T/\partial \bar{K}$.

$$\frac{\partial \Theta}{\partial \bar{K}} = -\frac{\{1 - L(1 - \pi F)\}}{\bar{K}^2 V} (\bar{\mu} - \bar{\pi}), \quad (114)$$

and is necessarily negative [or zero if $\bar{\mu} = \bar{\pi}$], hence $\partial V/\partial \bar{K}$ is negative (or zero if $\bar{\mu} = \bar{\pi}$).

Now

$$\frac{\partial T}{\partial \overline{\overline{K}}} = \frac{\partial' T}{\partial' \overline{\overline{K}}} + \frac{\partial T}{\partial \overline{V}} \frac{\partial V}{\partial \overline{\overline{K}}},$$

$$= -\frac{T^2}{\partial \overline{\Theta}} \begin{vmatrix} \partial' \frac{1}{\overline{T}}, & \partial \frac{I}{\overline{T}} \\ \overline{\partial \overline{\overline{K}}}, & \overline{\partial V} \\ \frac{\partial \Theta}{\partial \overline{\overline{K}}}, & \frac{\partial \Theta}{\partial \overline{V}} \end{vmatrix}$$

$$= -\frac{T^2}{\partial \overline{\Theta}} \frac{1 - L(1 - \pi F)}{\overline{K}^2 V} \left(\frac{m}{V^2} + L\sigma \frac{\partial F}{\partial \overline{V}} \right), \qquad (115)$$

which is positive if $\sigma = (\overline{\mu} - \overline{\pi}) - (\mu - \pi)$ is negative or equal to zero. If σ is positive, the sign is ambiguous unless $m = 0$, in which case $\partial T/\partial K$ is negative. If $m = 0$ and $\sigma = 0$, $\partial T/\partial \overline{K} = 0$, that is, T is independent of $\overline{K}$.

Similarly as ϕ occurs in Θ and T only in the form of Φ it is sufficient to investigate $\partial V/\partial \Phi$ and $\partial T/\partial \Phi$.

$$\frac{\partial \Theta}{\partial \Phi} = \frac{\partial \Theta}{\partial F} \frac{\partial F}{\partial \Phi}$$

$$= L\{\mu - \pi + \pi(\overline{\mu} - \overline{\pi})\} \frac{\partial F}{\partial \Phi}. \qquad (116)$$

Thus as $\partial F/\partial \Phi$ is negative, $\partial \Theta/\partial \Phi$ is negative, so that $\partial V/\partial \Phi$ is negative. Also

$$\frac{\partial T}{\partial \Phi} = -\frac{T^2}{\partial \overline{\Theta}} \begin{vmatrix} \partial' \frac{1}{\overline{T}}, & \partial \frac{1}{\overline{T}} \\ \overline{\partial' \Phi}, & \overline{\partial V} \\ \frac{\partial \Theta}{\partial \overline{V}}, & \frac{\partial \Theta}{\partial \overline{V}} \end{vmatrix},$$

$$= -\frac{T^2}{\partial \overline{\Theta}} \frac{\delta F}{\partial \Phi} \begin{vmatrix} \partial' \frac{1}{\overline{T}}, & \partial \frac{1}{\overline{T}} \\ \overline{\partial' F}, & \overline{\partial V} \\ \frac{\partial \Theta}{\partial \overline{F}}, & \frac{\partial \Theta}{\partial \overline{V}} \end{vmatrix},$$

$$= -\frac{T^2}{\partial \overline{\Theta}} \frac{\partial F}{\partial \Phi} \left(-\frac{1}{V^2} \right) \left[m \frac{\overline{K}V + \pi}{\overline{K}V} + \sigma\{1 - L(1 - \pi F)\} \right]. \qquad (117)$$

Similarly it may readily be shown that $\partial V/\partial \omega$ is negative, and that $\partial T/\partial \omega$ is equal to the same expression as the above for $\partial T/\partial \Phi$, except that $\partial F/\partial \omega$

takes the place of $\partial F/\partial \Phi$, where $\partial F/\partial \omega$ like $\partial F/\partial \Phi$ is necessarily negative. It follows that $\partial T/\partial \Phi$ and $\partial T/\partial \omega$ are positive if σ is positive or equal to zero. If σ is negative $\partial T/\partial \Phi$ and $\partial T/\partial \omega$ are ambiguous in sign unless m is zero, in which case they are of negative sign. If m is zero and σ is zero, $\partial T/\partial \Phi$ and $\partial T/\partial \omega$ are both zero. It may be noted that if there is a general increase in infectivity or susceptibility, T will increase provided that σ is zero, unless m is also zero, when T will remain constant. If σ is not zero the net result would appear to be ambiguous.

From equations (65*), (110) and (46*) we may obtain T in the form

$$\left.\begin{aligned} T &= \frac{\bar{\mu} - \bar{\pi}}{1 - L + N(\bar{\mu} - \bar{\pi} - \nu) + \sigma LF - \dfrac{m}{\bar{V}}}, \\ \text{or} \quad T &= \frac{\bar{\mu} - \bar{\pi}}{D + N(\bar{\mu} - \bar{\pi} - \nu + \rho) + \sigma LF - \dfrac{m}{\bar{V}}}. \end{aligned}\right\} \tag{118}$$

It is at once evident that if $m = 0$, and σ or $L = 0$, T is independent of $\bar{K}$, Φ and ω, thus verifying the above somewhat unexpected result. If in addition $\bar{\mu} - \bar{\pi} = \nu - \rho$, that is if the differences between birth and death rates are the same for all three categories—virgin, recovered and sick—then

$$T = \frac{\bar{\mu} - \bar{\pi}}{D}. \tag{119}$$

The conclusion that, if $\bar{\mu} - \bar{\pi} = \mu - \pi$ (a condition which, it might be expected will probably be satisfied in many cases), T is independent of the infectivity of the disease and of susceptibility to it, is one which would scarcely have been anticipated.

It is to be noticed that when V is zero, the equation

$$n = \frac{1 - L(1 - \pi F)}{\bar{K}} + (LF + N)V$$

becomes

$$n = \frac{1}{\bar{K}}. \tag{120}$$

In this case $\bar{X} = 1/\bar{K}$, $X = 0$, and $Y = 0$. It follows that no endemic disease can exist in a population which has a density of less than $1/\bar{K}$. This conclusion may be compared with the result found in the first paper of this series,† viz.,

† 'Proc. Roy. Soc.,' A, vol. 105, p. 700 (1927).

that no epidemic can take place in a non-multiplying population provided that the density is less than 1/A. If it be noted that $\bar{K}$ is essentially equivalent to A, it is clear that the two results in a general way agree with one another. Actually the *threshold* value $n_0 = \bar{X} = 1/\bar{K}$ can only exist as a steady state when $\bar{\mu} = \bar{\pi}$. If $\bar{\mu} = \bar{\pi} + \varepsilon$, where ε is a small quantity, and if $m = 0$, the following approximate results are readily found :—

$$V = \frac{\varepsilon}{\bar{K}\left(1 - \nu N - L\frac{\mu}{\pi}\right)}, \tag{121}$$

$$Y = \frac{N\varepsilon}{\bar{K}\left(1 - \nu N - L\frac{\mu}{\pi}\right)}, \tag{122}$$

$$X = \frac{L\varepsilon}{\pi\bar{K}\left(1 - \nu N - L\frac{\mu}{\pi}\right)}, \tag{123}$$

$$\bar{X} = \frac{1}{\bar{K}} + \frac{L\Phi\tilde{\Omega}\pi\varepsilon,}{\bar{K}^2\left(1 - \nu N - L\frac{\mu}{\pi}\right)}, \tag{124}$$

where

$$\tilde{\Omega} = \frac{1}{\pi}\int_0^\infty \omega_\tau e^{-\pi\tau}\, d\tau.$$

There are two possibilities :—

(1) $1 - \nu N - L\frac{\mu}{\pi} > 0$. In this case, when ε is small, V represents the unique positive solution known to exist, when the three conditions mentioned above are satisfied. When ε tends to 0, V tends to 0, and n tends to $1/\bar{K}$, so that $1/\bar{K}$ does in fact constitute a *threshold* value for n.

(2) $1 - \nu N - L\frac{\mu}{\pi} < 0$. In this case, when ε is small and positive, the real positive root which necessarily exists does not become zero with ε, so than $\varepsilon \to 0$ does not imply that $V \to 0$. It is, however, true that n is never less than $1/\bar{K}$, so that in this case $1/\bar{K}$ may be regarded as a lower limit to the density of a population in which there is an endemic disease in a steady state.

It is readily found that

$$X + \bar{X} = \frac{1}{\bar{K}} + \frac{L\varepsilon}{\bar{K}^2\left(1 - \nu N - L\frac{\mu}{\pi}\right)}\int_0^\infty (\bar{K} - \Phi\omega_\tau)\, e^{-\pi\tau}\, d\tau, \tag{125}$$

and therefore must exceed $1/\overline{K}$, provided that $\Phi\omega_\tau$ never exceeds $\overline{K}$, that is, as long as those recovered from the disease are not at any stage more liable to infection than the virgins.

Equations for Variations about Steady State.

The equations relating to the stability of the steady state are as follows :—

$$\frac{d\overline{x}'}{dt} = \overline{u}'_t - \overline{v}'_t - \overline{\pi x}', \tag{74*}$$

$$\frac{dx'}{dt} = u'_t - \tilde{v}'_t - \pi x', \tag{75*}$$

$$\frac{dy'}{dt} = v'_t - w'_t - u'_t - \rho y', \tag{76*}$$

$$\overline{u}'_t = \overline{\mu x}' + \mu x' + \nu y', \tag{77}$$

$$u'_t = \int_0^\beta L_\theta v'_{t-\theta}\, d\theta, \qquad (\beta = \infty) \tag{78}$$

$$v'_t = \tilde{v}'_t + \overline{v}'_t, \tag{79}$$

$$\overline{v}'_t = \overline{x}'\overline{K}V + \overline{X}\int_0^\beta \overline{K}_\theta v'_{t-\theta}\, d\theta, \qquad (\beta = \infty) \tag{80}$$

$$w'_t = \int_0^\beta D_\theta v'_{t-\theta}\, d\theta, \qquad (\beta = \infty) \tag{81}$$

$$y' = \int_0^\beta N_\theta v'_{t-\theta}\, d\theta + \int_0^\beta v_{t\theta_1}\, d\theta_1, \qquad (\beta = \infty) \tag{82}$$

$$\overline{x}' = \int_0^\beta \overline{u}'_{t-\lambda} e^{-(\overline{K}V+\overline{\pi})\lambda}\, d\lambda - \overline{U}\int_0^\beta e^{-(\overline{K}V+\overline{\pi})\lambda}\int_0^\lambda\int_0^{\beta-\lambda'} \overline{K}_\theta v'_{t-\lambda'-\theta}\, d\theta\, d\lambda'\, d\lambda + \int_0^\infty \overline{u}_{t\lambda_1}\, d\lambda_1, \tag{84*}$$

$$\tilde{v}'_t = \Phi VU\int_0^\beta \omega_\tau F'(t-\tau, \tau)\, d\tau + \Phi V\int_0^\beta \omega_\tau F_\tau u'_{t-\tau}\, d\tau + UG\int_0^\beta \Phi_\theta v'_{t-\theta}\, d\theta, \tag{85}\dagger$$

† In the previous paper a slight omission occurs in equation 85, which should read as above.

$(\beta = \infty)$. [where $F_\tau = e^{-\int_0^\tau (\Phi V \omega_\xi + \pi)\, d\tau}$

and $F'(t-\tau, \tau) = -F_\tau \int_0^\tau \int_0^\infty \Phi_\theta v'_{t-\tau+\xi-\theta}\, d\theta \omega_\xi\, d\xi$,

so that $F = \int_0^\infty F_\tau\, d\tau$,

and $G = \int_0^\infty \omega_\tau\, e^{-\int_0^\tau (\Phi V \omega_\xi + \pi)\, d\xi}\, d\tau$.]

and

$$x' = U \int_0^\beta F'(t-\tau, \tau)\, d\tau + \int_0^\beta F_\tau\, u'_{t-\tau}\, d\tau + \int_0^\beta u_{t\tau_1}\, d\tau_1 \,. \quad (\beta = \infty). \qquad (86)$$

Also we have

$$v_{t\theta_1} = {}_0v_{\theta_1}\, e^{-\int_{\theta_1}^{t+T+\theta_1} (l_{\theta'} + d_{\theta'} + \rho)\, d\theta'}, \qquad (87^*)$$

$$\bar{u}_{t\lambda_1} = {}_0\bar{u}_{\lambda_1}\, e^{-\int_{\lambda_1}^{t+T+\lambda_1} [\bar{f}(t-\lambda') + \bar{\pi}]\, d\lambda'}, \qquad (88^*)$$

$$= {}_0\bar{u}_{\lambda_1}\, e^{-(\bar{K}V + \bar{\pi})(t+T)}, \qquad (89^*)$$

$$u_{t\tau_1} = {}_0u_{\tau_1} \frac{F(-T-\tau_1, t+T+\tau_1)}{F(-T-\tau_1, \tau_1)}, \qquad (90)$$

$$= {}_0u_{\tau_1}\, e^{-\int_{\tau_1}^{t+T+\tau_1} (\Phi V \omega_\xi + \pi)\, d\xi}. \qquad (91^*)$$

Equations (84*), (86), (82), (78), and (79) (using (85) and (80)) with upper limit $\beta = t + T$, correspond to the five equations (92) to (96) of the previous paper.

Special Cases.

So far the problem has been considered in its most general form. In the previous paper certain particular cases were discussed which appeared to be of special interest from the practical point of view. With the increased generality of the results now obtained, the number of special cases to be studied has naturally increased, and it becomes desirable to classify them according to some general scheme. It will be noted that in the theory as elaborated above, the conclusions arrived at depend upon certain relationships between $\bar{\mu}$, μ, ν, $\bar{\pi}$, π and ρ. It is therefore convenient in the first instance to classify the special cases according to the values of these six rates. We thus have the following five cases :—

Case 0 : general case, with conditions $\bar{\mu} \geqslant \bar{\pi}$, $\mu \geqslant \pi$, and

$$D + \rho N - \nu N - \frac{(1 - e^{-\pi\epsilon})}{\pi} L(\mu - \pi) > 0.$$

Case 1 : $\overline{\mu} = \mu, \overline{\pi} = \pi, \nu = 0.$

Case 2 : $\overline{\mu} = \overline{\pi}, \mu = \pi$ and $\nu = \rho.$

Case 3 : $\overline{\mu} = \mu = \nu = \overline{\pi} = \pi = \rho = 0.$

Case 4 : $\overline{\mu} = \mu = \nu = 0.$

It will be seen that the general conditions are satisfied in cases 0, 1, 2 and 3, and all the above theory holds. Case 4, however, is different in that the conditions $\overline{\mu} \geqslant \overline{\pi}$ and $\mu \geqslant \pi$ are definitely not satisfied, so that the question of the number of steady states in this instance requires special investigation.

If in the above classes we put $m = 0$, *i.e.*, exclude immigration, we have another set of special cases which we shall denote by 0′, 1′, 2′, etc. Cases 0′ and 1′ involve no new features and no special comment is necessary, but case 2′ is characterized by the fact that the births balance the deaths from causes other than the disease under consideration, so that a steady state cannot exist unless $d_\theta = 0$. The same applies to case 3′. Further, case 4′ does not in any condition give a population in which a disease may exist in a steady state.

It is thus seen that, by considering the values of $\overline{\mu}$, μ, ν, $\overline{\pi}$, π, ρ and m, nine types are obtained of which only one requires special investigation from the point of view of the number of steady states which are possible.

It is, however, of special interest to subdivide each type according to the nature of the disease, which may be either fatal or non-fatal, and may or may not allow of recovery. Each type therefore gives rise to four varieties, namely:

(*a*) $l \neq, d \neq 0,$

(*b*) $l = 0, d \neq 0,$

(*c*) $l \neq 0, d = 0,$

(*d*) $l = 0, d = 0.$

These will be denoted by 0, 0_l, 0_d and 0_{ld}, etc. We have thus 36 different cases, but, as will be seen, certain of them do not give steady states corresponding to a finite population with endemic disease. For example, 3_d is obviously of this nature, as, by hypothesis, there are no deaths so that the population necessarily increases continually as the result of immigration. A steady state is therefore impossible. These cases will be indicated in the mathematical working by the emergence of values $V = 0$ or ∞.

The various cases are indicated in the following table, in which, for convenience of reference, the case numbers used in Part II are given in brackets. Where a blank occurs no steady state is possible.

	$l \neq 0, d \neq 0.$	$l = 0, d \neq 0.$	$l \neq 0, d = 0.$	$l = 0, d = 0.$
General case, $m \neq 0$	0	0_l	0_d	0_{ld}
General case, $m = 0$	$0'$	$0'_l$	$0'_d$	$0'_{ld}$
$\bar{\mu} = \mu, \bar{\pi} = \pi, \nu = 0, m \neq 0$	1	1_l	1_d	1_{ld}
$\bar{\mu} = \mu, \bar{\pi} = \pi, \nu = 0, m = 0$	$1'$	$1'_l$	$1'_d$	$1'_{ld}$
$\bar{\mu} = \bar{\pi}, \mu = \pi, \nu = \rho, m \neq 0$	2	2_l	—	—
$\bar{\mu} = \bar{\pi}, \mu = \pi, \nu = \rho, m = 0$	—	—	$2'_d$	$2'_{ld}$
$\bar{\mu} = \mu = \nu = \bar{\pi} = \pi = \rho = 0, m \neq 0$	3 (3)	3_l (4)	—	—
$\bar{\mu} = \mu = \nu = \bar{\pi} = \pi = \rho = 0, m = 0$	—	—	$3'_d$ (5)	$3'_{ld}$
$\bar{\mu} = \mu = \nu = 0$, $\pi \neq 0, \pi \neq 0, \rho \neq 0$, $m \neq 0$	4	4_l	4_d	4_{ld}

Another contingency may arise, as in cases $2'_d$, $2'_{ld}$, $3'_d$ and $3'_{ld}$, in which the equation for V becomes indeterminate. In these cases the size of the population cannot alter, so that the total population is fixed by the initial conditions. A new equation for V has to be obtained by equating the sum of $\bar{X}$, X and Y to this fixed number n. The conditions under which this equation yields a definite and unique steady state require special investigation. It is sufficient to examine case $2'_d$ as the other three are particular cases of it. It may be remarked that case $3'_d$ corresponds to case 5 in the previous paper. In the next two sections we shall therefore investigate the equations for V relating to cases 4 and $2'_d$. In addition a few remarks will be added in certain cases in which $l = 0$, a condition which makes the equation for V relatively simple, so that more definite results can be obtained than in the general case.

Case 4.—In case 4, $\bar{\mu} = \mu = \nu = 0$, and $m \neq 0$, that is to say there is immigration but no reproduction. It is obvious that the conditions $\bar{\mu} \geqslant \bar{\pi}$ and $\mu \geqslant \pi$ are not satisfied (except when $\bar{\pi}$ and π are both zero), so that the conclusions drawn above for the general case do not necessarily hold. It was pointed out above that the conditions for a definite and unique steady state were sufficient but not necessary, so that it is possible for definite and unique steady states to exist when these conditions are not satisfied. It happens, as will be shown below, that with certain assumptions the present special case is an example of such an exception.

The equation for V is in this case

$$V\Theta(V) = -LF\pi\frac{(\bar{K}V + \bar{\pi})}{\bar{K}} - (D + \rho N)V + m - \frac{\bar{\pi}}{\bar{K}}(D + \rho N) = 0, \quad (126)$$

hence when V is zero,

$$V\Theta(V) = -\frac{LF\pi\bar{\pi}}{\bar{K}} + m - \frac{\bar{\pi}}{\bar{K}}(D + \rho N). \tag{127}$$

But when V is zero

$$F = \int_0^\infty e^{-\pi\tau}\, d\tau = \frac{1}{\pi}, \tag{128}$$

hence in the limit $(V \to 0)$

$$V\Theta(V) = -\frac{L\bar{\pi}}{\bar{K}} + m - \frac{\bar{\pi}}{\bar{K}}(D + \rho N),$$

$$= m - \frac{\bar{\pi}}{\bar{K}}. \tag{129}$$

Also

$$\begin{aligned}\{V\Theta(V)\}_{V\to\infty} &= -LF\pi V - (D + \rho N)\, V,\\ &= -LV(1 - e^{-\pi\epsilon}) - (1 - L)\, V \text{ (above (68*)) },\\ &= -V(1 - Le^{-\pi\epsilon}),\end{aligned} \tag{130}$$

but L cannot be greater than unity so that $Le^{-\pi\epsilon} < 1$, hence

$$\{V\Theta(V)\}_{V\to\infty} \to -\infty. \tag{131}$$

Thus there will certainly be one real root, and there may be an odd number of real roots if $m > \bar{\pi}/\bar{K}$, whilst there may be no real roots or an even number if $m < \bar{\pi}/\bar{K}$.

We shall now find the conditions which will ensure that $V\Theta(V)$ decreases monotonically with V.

$$-V\Theta(V) = (1 - L)\, V + LF\pi\,\frac{\bar{K}V + \bar{\pi}}{\bar{K}} - m + \frac{\bar{\pi}}{\bar{K}}(1 - L).$$

Now

$$(\bar{K}V + \bar{\pi})\, F = (\bar{K}V + \pi)\, F - (\pi - \bar{\pi})\, F,$$

but

$$\begin{aligned}(\bar{K}V + \pi)\, F &= \int_0^\infty (\bar{K}V + \pi)\, e^{-\int_0^\tau (\Phi V\omega_\xi + \pi)\, d\xi}\, d\tau\\ &= \int_0^\infty (\Phi V\omega_\tau + \pi)\, e^{-\int_0^\tau (\Phi V\omega_\xi + \pi)\, d\xi}\, d\tau\\ &\qquad + \int_0^\infty V(\bar{K} - \Phi\omega_\tau)\, e^{-\int_0^\tau (\Phi V\omega_\xi + \pi)\, d\xi}\, d\tau\\ &= 1 - \int_0^\infty \frac{\bar{K} - \Phi\omega_\tau}{\Phi\omega_\tau} e^{-\pi\tau}\, de^{-\int_0^\tau \Phi V\omega_\xi d\xi}\\ &= 1 + \left(\frac{\bar{K}}{\Phi\omega_0} - 1\right) - \int_0^\infty \left\{\pi\left(\frac{\bar{K}}{\Phi\omega_\tau} - 1\right) + \frac{\bar{K}}{\Phi\omega^2_\tau}\frac{d\omega_\tau}{d\tau}\right\} e^{-\int_0^\tau (\Phi V\omega_\xi + \pi)\, d\xi}\, d\tau,\end{aligned} \tag{132}$$

where ω_0 is the value of ω_τ when τ is zero. We shall temporarily assume that ω_0 is not zero. We shall also assume as in the previous paper that $d\omega_\tau/d\tau$ is never negative, and further that $\Phi\omega_\tau$ is never greater than $\bar{K}$; that is to say, that the infectivity of the recovered never decreases, and that it never exceeds the infectivity of the virgins. If these conditions are satisfied the expression

$$\pi\left(\frac{\bar{K}}{\Phi\omega_\tau} - 1\right) + \frac{\bar{K}}{\Phi\omega^2_\tau}\frac{d\omega}{d\tau}$$

is never negative.

We have in the above assumed that ω_0 is not zero. It may, however, easily be shown by a method similar to that employed in the previous paper (p. 79) that this assumption is not essential.

If, further, π is not less than $\bar{\pi}$, the term $-(\pi - \bar{\pi})F$ will increase with V (or remain constantly zero) so that $F(\bar{K}V + \bar{\pi})$ will increase with V. Also the term $(1 - L)V$ cannot decrease with V, since $L \leqslant 1$, so that $-V\Theta(V)$ increases with V, or $V\Theta(V)$ decreases with V provided that

$$\pi \geqslant \bar{\pi}, \tag{133}$$

$$\omega_\tau \leqslant \frac{\bar{K}}{\Phi} \text{ for all values of } \tau, \tag{134}$$

and

$$d\omega/d\tau \tag{135}$$

is never negative.

If these three conditions are satisfied a unique steady state will exist provided that $m > \bar{\pi}/\bar{K}$, whilst no steady state in which the disease is endemic will exist if $m < \bar{\pi}/\bar{K}$. Conditions (133) to (135) imply that the chances of death of the members of the population from general causes are not decreased by an attack of the disease; that the susceptibility after an attack remains steady or increases monotonically but never exceeds that which exists in the virgin individual.

We shall now investigate the dependence of V upon m, $\bar{\pi}$, π and ρ. As $V\Theta(V)$ constantly decreases with V, provided that the above conditions are satisfied,

$$\frac{\partial V\Theta(V)}{\partial V}$$

is always negative. Also

$$\left.\begin{aligned} &\frac{\partial}{\partial m} V\Theta(V) = 1\,; \frac{\partial}{\partial \bar{\pi}} V\Theta(V) = -\frac{LF\pi}{\bar{K}} - \frac{(1-L)}{\bar{K}} \\ &\text{and is therefore negative;} \\ &\frac{\partial}{\partial \pi} V\Theta(V) = -L\frac{(\bar{K}V + \bar{\pi})}{\bar{K}}\left(F + \pi\frac{\partial F}{\partial \pi}\right). \end{aligned}\right\} \tag{136}$$

But

$$\pi \frac{\partial F}{\partial \pi} = -\int_0^\infty \pi\tau e^{-\int_0^\tau \Phi V \omega_\xi d\xi} e^{-\pi\tau} d\tau$$

$$= \left| \tau e^{-\int_0^\tau \Phi V \omega_\xi d\xi} e^{-\pi\tau} \right|_0^\infty - \int_0^\infty e^{-\pi\tau} e^{-\int_0^\tau \Phi V \omega_\xi d\xi} d\tau$$

$$+ \int_0^\infty \tau \Phi V \omega_\tau e^{-\int_0^\tau \Phi V \omega_\xi d\xi} e^{-\pi\tau} d\tau \qquad (137)$$

$$= -F + \text{a positive quantity.}$$

Hence $F + \pi \frac{\partial F}{\partial \pi}$ is positive, and consequently $\frac{\partial}{\partial \pi} V\Theta(V)$ is negative.

Further

$$\frac{\partial V\Theta(V)}{\partial \rho} = \frac{\partial V\Theta(V)}{\partial \bar{K}} \frac{\partial \bar{K}}{\partial \rho} + \frac{\partial V\Theta(V)}{\partial L} \frac{\partial L}{\partial \rho} + \frac{\partial V\Theta(V)}{\partial F} \frac{\partial F}{\partial \rho}.$$

Now

$$\frac{\partial V\Theta(V)}{\partial \bar{K}} = \frac{LF\pi\bar{\pi}}{\bar{K}^2} + \frac{(1-L)\bar{\pi}}{\bar{K}^2}, \qquad (138)$$

which is positive.

Also

$$\frac{\partial V\Theta(V)}{\partial L} = \left(V + \frac{\bar{\pi}}{\bar{K}}\right)(1 - \pi F); \qquad (139)$$

but

$$F = \int_0^\infty e^{(\pi\tau + \int_0^\tau \Phi V \omega_\xi d\xi)} d\tau,$$

$$\leqslant \int_0^\infty e^{-\pi\tau} d\tau,$$

$$\leqslant \frac{1}{\pi};$$

hence $1 - \pi F \geqslant 0$, and $\frac{\partial V\Theta(V)}{\partial L}$ is positive (or zero in the particular case where ω_τ is always zero).

Again

$$\frac{\partial V\Theta(V)}{\partial F} = -L\pi \frac{\bar{K}V + \bar{\pi}}{\bar{K}}, \qquad (140)$$

which is negative.

As $\partial\bar{K}/\partial\rho$ and $\partial L/\partial\rho$ are negative, whilst $\partial F/\partial\rho$ is zero, $\partial V\Theta(V)/\partial\rho$ is always negative.

It follows from the above that $\partial V/\partial m$ is always positive, whilst $\partial V/\partial \bar{\pi}$, $\partial V/\partial \pi$ and $\partial V/\partial \rho$ are negative provided that the conditions (133) to (135) are satisfied. Also since $\partial T/\partial V$ is positive (111), it follows that $\partial T/\partial m$ is positive, and $\partial T/\partial \bar{\pi}$ is negative. The signs of $\partial T/\partial \pi$ nas $\partial T/\partial \rho$ appear to be ambiguous.

In this case then, when the conditions (133) to (135) are satisfied and $m > \bar{\pi}/\bar{K}$, the absolute rate of infection V, and the proportional rate T both increase with the rate of immigration m, but decrease with increase in the general death rate ($\bar{\pi}$) of the virgin group. If $m < \bar{\pi}/\bar{K}$ no disease will exist in the community, so that $m = \bar{\pi}/\bar{K}$ is the threshold immigration rate.

As regards the dependence of V upon $\bar{K}$, Φ and ω, we find

$$\frac{\partial V\Theta(V)}{\partial \bar{K}} = \frac{\bar{\pi}}{\bar{K}^2}\{1 - L(1 - \pi F)\}, \tag{141}$$

$$\frac{\partial V\Theta(V)}{\partial \Phi} = -L\frac{\pi}{\bar{K}}(\bar{K}V + \bar{\pi})\frac{\partial F}{\partial \Phi}, \tag{142}$$

and

$$\frac{\partial V\Theta(V)}{\partial \omega} = -L\frac{\pi}{\bar{K}}(\bar{K}V + \bar{\pi})\frac{\partial F}{\partial \omega}, \tag{143}$$

which are each positive, hence

$$\frac{\partial V}{\partial \bar{K}}, \qquad \frac{\partial V}{\partial \Phi} \qquad \text{and} \qquad \frac{\partial V}{\partial \omega}$$

are positive.

Also

$$\frac{\partial T}{\partial \bar{K}} = \frac{-T^2}{\dfrac{\partial V\Theta(V)}{\partial V}}\frac{\{1 - L(1 - \pi F)\}}{\bar{K}^2 V}\left\{\frac{1 - L(1 - \pi F)}{\bar{K}V}(\bar{K}V + \pi) - L\pi\frac{\partial F}{\partial V}\frac{\sigma}{\bar{K}}\right\} \tag{144}$$

where σ reduces in this case to $\pi - \bar{\pi}$, and

$$\frac{\partial T}{\partial \Phi} = \frac{-T^2}{\dfrac{\partial V\Theta(V)}{\partial V}}\left(-\frac{L}{\bar{K}V}\frac{\partial F}{\partial \Phi}\right)\left[\{1 - L(1 - \pi F)\}(\bar{K}V + \pi) + \pi\frac{(\bar{K}V + \bar{\pi})\{1 - L(1 - \pi F)\}}{\bar{K}V}\right]. \tag{145}$$

$\partial T/\partial \omega$ is equal to the same expression as the above for $\partial T/\partial \Phi$ except that $\partial F/\partial \omega$ takes the place of $\partial F/\partial \Phi$, where $\partial F/\partial \omega$ like $\partial F/\partial \Phi$ is necessarily negative.

It follows that $\partial T/\partial \Phi$ and $\partial T/\partial \omega$ are positive, whilst $\partial T/\partial \bar{K}$ is positive if σ is positive or zero, and ambiguous when σ is negative ($m \neq 0$).

In the special case 4_l where $l_\theta = 0$, that is to say where there is no recovery from the disease, we have $V = m - \bar{\pi}/\bar{K}$, and all the quantities $\bar{X}$, X, etc., are given explicitly in terms of the various constants. The results are in general the same as in case 4, except that the conditions (133) to (135) are now meaningless, as the constants concerned do not enter into the problem.

Case $2'_d$.—This case which calls for special consideration refers to a community in which there is a non-fatal disease, but which does not form a completely closed system. Births and deaths from other causes are taking place, but at such a rate as to balance each other, so that the total number of the population remains constant. Immigration is excluded. The conditions are $\lambda = 0$, $\bar{\mu} = \bar{\pi}$, $\mu = \pi$, $\nu = \rho$ and $d = 0$ (whence $L + \rho N = 1$). The equation for V vanishes completely, and we find that if $n = \bar{X} + X + Y$, $dn/dt = 0$. n is thus defined by the equation $n = \bar{X} + X + Y$ where n is the total number of individuals in the system. Thus

$$n = \frac{1 - L(1 - \pi F)}{\bar{K}} + LVF + NV. \tag{147}$$

We have to examine the nature of the roots of this equation. Let

$$\chi(V) = \frac{L}{\bar{K}}(\bar{K}V + \pi)F + \frac{1 - L}{\bar{K}} + NV - n. \tag{148}$$

It is readily seen that

$$\chi(V)_{V \to \infty} \to + \infty,$$

also

$$\chi(V)_{V \to 0} \to \frac{L\pi}{\bar{K}} F_{V \to 0} + \frac{1 - L}{\bar{K}} - n.$$

but

$$F_{V \to 0} \to \int_0^\infty e^{-\pi\tau} d\tau = 1/\pi,$$

as by assumption ω_τ is always finite.

Hence

$$\chi(V)_{V \to 0} \to \frac{L}{\bar{K}} + \frac{1 - L}{\bar{K}} - n = \frac{1}{\bar{K}} - n. \tag{149}$$

There may thus be an even number of roots if $n < 1/\bar{K}$, and there will be an odd number if $n > 1/\bar{K}$. Clearly $n_0 = 1/\bar{K}$ represents a *threshold* density in the same sense as $n_0 = 1/\Phi\omega$ represented a *threshold* density in case 5

of the previous paper (p. 79), *i.e.*, $3'_d$ according to the present system of classification.

We shall now find the conditions under which $\chi(V)$ increases monotonically with V, so that there will be one root or none at all according as n is greater or less than $1/\bar{K}$

We have shown above (132) that $(\bar{K}V + \pi)F$ is never negative provided that $d\omega_\tau/d\tau$ is never negative, and $\Phi\omega_\tau$ is never greater than $\bar{K}$, that is to say that the infectivity of the recovered never decreases, and that it never exceeds the infectivity of the virgins. We have in fact

$$\chi(V)=1+\left(\frac{\bar{K}}{\Phi\omega_0}-1\right)-\int_0^\infty\left\{\pi\left(\frac{\bar{K}}{\Phi\omega_\tau}-1\right)+\frac{\bar{K}}{\Phi\omega^2}\frac{d\omega}{d\tau}\right\}e^{-\int_0^\tau(\Phi V\omega_\xi)\,d\xi}\,e^{-\pi\tau}\,d\tau$$
$$+\frac{(1-L)}{\bar{K}}+NV-n, \qquad (150)$$

and, as the expression within curly brackets within the integral is never negative on the above assumptions, it is readily seen that $\chi(V)$ always increases with V. Thus the equation $\chi(V)=0$ has one and only one real positive root provided that $n > 1/\bar{K}$, whilst if $n < 1/\bar{K}$ there is no real positive root. When $n = 1/\bar{K}$ there is only one root namely $V = 0$.

In case $2'_{ld}$, *i.e.*, an incurable but non-fatal disease,

$$V=\rho\left(n-\frac{1}{K}\right). \qquad (151)$$

The more general conclusions arrived at above hold, except that the condition $\bar{K} \geqslant \Phi\omega_\tau$ is now meaningless, and therefore unnecessary. The *threshold* density $n_0 = 1/\bar{K}$ exists as before.

Other Special Cases.—As when $l_\vartheta = 0$, V can always be expressed explicitly in terms of the various constants, it is desirable to consider the most general case of this type, namely 0_l. We have

$$V=\frac{m+\dfrac{\bar{\mu}-\bar{\pi}}{\bar{K}}}{1-\nu N}. \qquad (152)$$

This is certainly positive provided that $\bar{\mu} > \bar{\pi}$, and $\nu N < 1$. The latter condition is the third condition for the existence of a unique steady state (103), when L is zero. The second condition, namely $\mu > \pi$, becomes meaningless, and is therefore unnecessary.

It is still impossible to determine unambiguously the sign of $\partial V/\partial \rho$, but if $\nu = 0$, it may readily be shown that $\partial V/\partial \rho$ is positive, and $\partial S/\partial \rho$ is negative, where $S = \frac{Y}{X+Y}$, *i.e.*, the proportion of sick. These results may be verified for constant coefficients, and it may also be shown that in this case the equilibrium is a stable one.

A few remarks may be added regarding a special group of cases, which are important in practice but do not require special treatment as no fundamentally new consideration arises. When permanent and complete immunity is conferred by an attack of the disease, $\omega = 0$, and $F = 1/\pi$. The equation for V becomes

$$V = \frac{m + \frac{\bar{\mu} - \bar{\pi}}{\bar{K}}}{1 - \nu N - L\frac{\mu}{\pi}}. \tag{153}$$

These cases are closely related to the group in which $l_\theta = 0$ and are probably of considerable importance as describing the group of virus diseases in which immunity appears often to be permanent and complete.

Discussion.

The main results detailed in the above investigation may be summarized by saying that the existence of a death rate from causes other than the particular disease which is operating, does not materially alter any of the results obtained in Part II of this investigation. We have not yet taken into account the effect of variation in age-constitution, nor have variations in natural immunity been allowed for.

The chief feature of the systems treated here, and in the previous paper, is the existence of a steady state, which is unique provided that certain conditions, which are likely to exist in nature, are satisfied (equation (103), also (133) to (135)). This steady state is naturally a function both of the parameters characteristic of the disease—the infectivity, death and recovery rates—and of the other parameters which refer more particularly to the population—the birth rate, the immigration rate, and the non-specific death rates.

The incidence of disease is raised when the immigration or birth rates are increased (p. 102). This statement holds whether the incidence of disease is measured by (1) the number of sick Y; (2) the relative number of sick $S = Y/n$; (3) the incidence rate V; or (4) the relative incidence rate

$T = V/n$. Further, the incidence constantly decreases with increase in the death rate of the virgins, but whereas Y and V decrease with increase in the death rate of the recovered, the behaviour of S and T is more complex and depends upon the value of σ (112). The effect of the non-specific death rate of the sick (ρ) is complicated, and obscure.

When we turn to the effect on the incidence of the characteristic features of the disease (p. 103), the most interesting results are those relating to the effect of variations in infectivity. It is found that by such an alteration both the total population and the number of diseased persons in it are changed. For example, increase in the susceptibility of the virgins, leading to an increase in $\bar{K}$, causes a decrease in the size of the population n, and also a decrease both of Y and of V. The effect on T and S is more complicated and depends upon the value of σ (113). If there is no immigration and $\sigma = 0$, then change in susceptibility does not alter T or S (p. 105). Likewise Y and V both decrease with increase in ω_r, the susceptibility of the recovered, as well as with Φ which measures the infectivity of the disease; whilst the changes undergone by T and S again depend upon the value of σ. As before, when $m = 0$, and $\sigma = 0$, T and S do not alter with changes in susceptibility or infectivity. It follows that an increase in infectivity resulting in greater chances of infection of both virgins and recovered will decrease both V and Y, but will not alter T and S provided that $m = 0$ and $\sigma = 0$. If, however, these latter conditions are not satisfied, it does not appear possible to predict in a general way what alteration in T and S will ensue. It is to be noted that the condition $\sigma = 0$ means that the difference between the birth rate and the non-specific death rate is the same for virgins as for recovered, a condition which is usually approximately fulfilled. It is at first sight surprising that in these circumstances ($m = 0$ and $\sigma = 0$), alterations in infectivity or susceptibility should be without effect on the relative prevalence of the disease in the community, but the fact is that the relative prevalence can then be expressed by a formula which does not involve either $\bar{K}$ Φ, or ω_r (equation (118)) so that changes in these parameters do not affect the result.

It will be seen from the above that, other things being equal, decrease in infectivity or susceptibility is always an advantage since it enables a larger total population density to exist. If, however, the goal desired is to reduce the relative disease rate in the community to a minimum, then it is far from certain that decrease in infectivity or susceptibility of the disease will bring about the desired result, whilst it would appear certain that the absolute number of the diseased, as well as the absolute rate of incidence, will actually

increase as the infectivity or susceptibility falls. There seems, of course, little doubt that the immediate effect of a reduction in infectivity or susceptibility is to bring about a fall in all these numbers, but the population density then begins to increase and when a steady state is again reached the increase is of such a magnitude as to more than compensate for the immediate effects. It must be emphasized that, when the effect of the variation of a parameter is considered in the present section, the comparison is between the steady state which is possible after the parameter has been varied, and that which existed before the variation took place. We are not concerned with the immediate effect of the parameter variation on the system, which will temporarily have been disturbed from a steady state.

It has been shown (p. 105) in the general case that when disease exists in a community the population density is necessarily greater than $1/\bar{K}$. The existence of a *threshold* value in relation to an observed quantity implies that the process under consideration (*e.g.*, the existence of disease in a steady state) may exist whenever the quantity in question exceeds that value, whilst it cannot exist when the quantity is equal to or less than that value. Let us consider a system in which the quantity in question is initially below the threshold. The system may be such that the quantity cannot change its value, and therefore the process or event to which the threshold refers, can never under any circumstances occur. A threshold of this nature may be called a *threshold of the first type*. On the other hand the system may be such that, when the magnitude in question is below the threshold, the system gradually alters until the threshold is exceeded. The process to which the threshold has reference may then appear, but it could not possibly have appeared until this adjustment had taken place. That the magnitude should initially exceed the threshold value is not then necessary in order that the process should ultimately exhibit itself, nevertheless the process will not exhibit itself until the magnitude has exceeded its threshold value. Such a threshold may be called a *threshold of the second type*. It is clear that the population density $1/\bar{K}$ referred to above is a threshold of the second type, whilst the threshold in case 4 (p. 114) referring to immigration, and that in case $2'_d$ (p. 115) referring to the total population, are of the first type.

In case $2'_d$ the population though not really a closed one is virtually of this nature, because the births just balance the non-specific deaths, and here a threshold value ($1/\bar{K}$) of the total population exists which is such that no disease can occur if the population density is less than this quantity. This result may be compared with that obtained in case 5 of the second paper of this

series, that is to say in case $3'_a$ in the present classification, where a threshold value of $1/\Phi\omega$ was found. This latter case is obtained from case $2'_a$ by putting $\overline{\mu}$, μ, ν, $\overline{\pi}$, π and ρ equal to zero, so that one would at first sight expect that the threshold would continue to be $1/\overline{K}$. However, as there are no births, $\overline{K}$, which refers to the virgins, comes ultimately to have no significance, and the result shows that under these conditions the threshold alters to $1/\Phi\omega$, which by hypothesis, is either greater than or equal to $1/\overline{K}$.

In case 4 it is the rate of immigration m which has a threshold value. If the immigration rate fails to reach the value $\overline{\pi}/\overline{K}$ then the disease cannot exist in the community in an endemic form. If $\overline{\pi}$ is very small, the threshold value will also tend to be very low, that is to say, very slow immigration would keep the disease going, but it would appear that if, as in most cases, non-specific deaths cannot be absolutely excluded, and if the population density is sufficiently great, then the threshold immigration rate, though small, will be finite.

In a series of interesting papers Greenwood and Topley and their collaborators* have investigated the progress of disease in communities of mice under various experimental conditions. Amongst their conclusions they emphasize the influence on the progress of the infection of immigration of healthy animals into the community. For example† "The sole condition required for the indefinite propagation of an endemic disease is a continuous immigration of susceptible individuals." The conditions of the experiments of these authors would seem to be approximately represented by case 4 above, as the mice were not increasing in number by reproduction, and at the same time were subject to a certain number of non-specific deaths. Further they come to the conclusion that the increase in resistance of exposed animals as compared with that of fresh individuals, is caused by active immunization as the result of an attack of the disease, rather than to selection working upon individual differences originally present. This is accommodated by the condition that $\Phi\omega$ is less than $\overline{K}$, which we found it necessary to assume, p. 112. It would therefore be expected that a threshold rate of immigration would exist under these conditions, but their figures do not actually reveal its existence. However, as shown above, the threshold immigration rate is equal to $\overline{\pi}/\overline{K}$, and it is clear that in their experiments $\overline{\pi}$ was relatively small (probably about 1 per cent. per day) so that the threshold immigration rate is probably also quite small. The lowest rate employed was one mouse in three days, and it is to be noted

* Topley and Wilson "Principles of Bacteriology and Immunity," vol. II, p. 767 (1929), and related papers, especially 'J. Hyg.,' vol. 24, p. 45 (1925).

† *loc. cit.*, p. 782.

that in this experiment, the disease remained practically quiescent for a period of 70 to 80 days, apart from a small increase in deaths at one point. During the whole period the size of the population was rising slightly, so that it seems clear that the rate of immigration was just slightly too high to allow the non-specific death rate to keep the population at a constant level, and thus to render a steady state possible. An experiment on a larger scale with a proportionally smaller immigration rate would probably reveal the existence of a threshold.

We realize that the discussion of epidemics developed in this and in the previous papers is at best only a schematic representation of the invasion of a community by an infective disease, and is far from giving a representation at all adequate or complete. The mathematical analysis so far presented may, however, be regarded as first step in the elucidation of the problem from the theoretical point of view. The experimental work of Greenwood and Topley and others gives another complementary method of approach. So far the two lines of attack can be brought into relation with each other only very incompletely, but it is to be hoped that as the experimental material becomes more extensive, and the mathematical investigation becomes more comprehensive, a relatively complete understanding of the processes involved in endemic and epidemic invasion may emerge.

Summary.

(1) The mathematical investigation of the progress of an infectious disease in a community of susceptible individuals has been extended to include the case where members of the community are removed as the result of some general cause of death acting according to constant non-specific death rates, as well as by death from the disease itself. Under the more general conditions here dealt with the main conclusions arrived at in the previous paper remain qualitatively unaltered. The limitations which remain are that the susceptibility and the infective power of the individual are supposed to be independent of his age, and further that specific individual immunity does not exist in the sense that the part of the population which escapes infection is assumed to be just as susceptible as the whole population would have been if it had not been infected.

(2) In the general case a unique steady state is found to exist provided that certain relatively simple conditions are satisfied. In the special cases considered a unique steady state in general exists when these conditions continue to be satisfied; but in particular instances, when these conditions are not

satisfied, unique steady states will exist provided that certain other requirements are fulfilled.

(3) Increase of birth rates, in general, increases both the absolute and the relative prevalence of the disease in its steady state. The effect of increase in the non-specific death rates is less simple, but has been worked out at some length.

Decrease in the infectivity of the disease or in the susceptibility of the uninfected results in an increase in the whole population density as well as in an increase in the number of infected. The effect upon the relative incidence of the disease cannot be simply expressed, but it has been worked out in detail in the text. In the absence of immigration, and with the birth rates and also the non-specific death rates equal for virgins and recovered, variation in infectivity or susceptibility will not alter the relative incidence of the disease. The total population, however, will increase with decrease of either of these two factors, whilst the number of diseased will also increase proportionately.

(4) Two types of threshold values have been encountered. In the first type the quantity in question must initially exceed the threshold value if the event or process is to occur in the population. Two examples of this type have been found, namely, in cases 4 and $2'_a$. In the second type the quantity in question need not initially exceed the threshold value, but may gradually change as the system developes. The event or process to which the threshold refers can only take place when the threshold value has been exceeded. The total population density has a threshold value of this second kind with reference to the existence of steady states.