stichting mathematisch centrum



AFDELING TOEGEPASTE WISKUNDE (DEPARTMENT OF APPLIED MATHEMATICS)

TW 162/76

DECEMBER

J. GRASMAN & B.J. MATKOWSKY

EVOLUTION OF AN EPIDEMIC WITH A SMALL NUMBER INITIAL INFECTIVES

Preprint

2e boerhaavestraat 49 amsterdam

Printed at the Mathematical Centre, 49, 2e Boerhaavestraat, Amsterdam.

The Mathematical Centre, founded the 11-th of February 1946, is a non-profit institution aiming at the promotion of pure mathematics and its applications. It is sponsored by the Netherlands Government through the Netherlands Organization for the Advancement of Pure Research (Z.W.0).

Evolution of an epidemic with a small number of initial infectives*)

by

J. Grasman & B.J. Matkowsky **)

ABSTRACT

This paper deals with the mathematical model of an epidemic with a small number of initial infectives \mathbf{I}_0 . The time development of the epidemic is approximated with singular perturbation techniques. The asymptotic result for $\mathbf{I}_0 \to 0$ shows that when the number of infectives exceeds a fixed small value (independent of \mathbf{I}_0) the time course of the epidemic is fixated; its shape is independent of the age distribution of the initial infectives. The time needed to pass this value is of the order $0(-\log \mathbf{I}_0)$.

KEY WORDS & PHRASES: epidemic, integro-differential equation, asymptotic approximation

^{*)} This report will be submitted for publication elsewhere.

^{**)}B.J. Matkowsky, Dept. of Mathematical Sciences, Rensselaer Polytechnic
Institute, Troy N.Y., U.S.A.

1. INTRODUCTION

In this paper an epidemic model first formulated by KERMACK and McKENDRICK [6] ia analyzed.

The population is divided into a fraction of susceptibles S and a fraction of infectives I, and we follow the evolution of S starting from an initially small number \mathbf{I}_0 of infectives. We employ singular perturbation techniques to obtain the asymptotic behavior of the solution as \mathbf{I}_0 tends to zero. The behaviour depends crucially on the parameter γ defined by

(1.1)
$$\gamma = \int_{0}^{\infty} A(\tau) d\tau,$$

where $A(\tau)$ is the age dependent infectiousness function. An epidemic will develop according as $Y \gtrless 1$. This property is commonly referred to as the threshold theorem of KERMACK and McKENDRICK [6]. For $\gamma > 1$ we find that two time intervals can be distinguished: (a) the pre-epidemic phase, in which S decays slowly; at the end of the interval S is still close to the initial fraction of susceptibles S_0 , and (b) the epidemic phase, where S decreases from a value near S_0 to a value near $S_\infty(S(t) \rightarrow S_\infty$ as $t \rightarrow \infty$). We employ a variant of the method of matched asymptotic expansions to determine the behavior of the solution. It is interesting to note that the pre-epidemic phase increases with $O(-\log I_0)$ so that it may take quite a long time for the epidemic to develop. In addition for, $I_0 \rightarrow 0$ the solution in the epidemic phase tends to a fixed shape independent of the initial distribution of infectives. The solutions to different (small) values of I_0 are approximately translations in time of one another.

In section 2 we formulate the mathematical model and consider two special cases for which an exact solution is available. In section 3 the limit value S_{∞} is derived and the dependence upon the parameter γ is discussed. A formal asymptotic solution is presented in section 4. In section 5 we deal with an infectiousness function that depends on the age of the infectives as well as on time. Finally, in section 6 this asymptotic solution is compared with numerical results.

2. THE MATHEMATICAL MODEL

KERMACK and McKENDRICK [6] were the first to prove the threshold theorem for the model we will investigate. The biological interpretations of it were reconsidered by REDDINGIUS [9]. A more general class of models, including Kermack and McKendrick's was considered by HOPPENSTEADT [4,5] and also by WILSON [11]. METZ [7] recently published an extensive paper on the same type of epidemic we deal with; he gives new results for the deterministic as well as for the stochastic problem.

We consider a population divided into two classes: the susceptibles S and the infectives I. The infectives have an age-dependent infectiousness given by the function $A(\tau)$, where τ denotes the time an individual is in class I. There is no removal of recovery, so that the total number of susceptibles and infectives is constant. In the sequel S and I denote the fractions of the populations in the two classes; at any time t we have

(2.1)
$$S(t) + \int_{0}^{\infty} I(\tau,t)dt = 1.$$

The decrease of susceptibles is assumed to be proportional to S and to the total infectiousness, so

(2.2)
$$\frac{dS}{dt} = -S(t) \int_{0}^{\infty} A(\tau)I(\tau,t)dt.$$

The dynamic equation of the infectives reads

(2.3)
$$\frac{\partial I}{\partial t} + \frac{\partial I}{\partial \tau} = 0, \ t, \tau > 0.$$

It is supposed that initially the population consists of S_0 susceptibles and ϵ infectives distributed over all ages according to the given function $f(\tau)$,

(2.4ab)
$$S(0) = S_0$$
, $I(\tau, 0) = \varepsilon f(\tau)$, with

(2.5)
$$S_0 + \varepsilon = 1, \qquad \int_0^\infty f(\tau) d\tau = 1.$$

Since all new infectives enter from the class of susceptibles, we have the boundary condition

(2.6)
$$I(0,t) = -\frac{dS}{dt}, \quad t > 0.$$

From (2.3), (2.4b) and (2.6) we deduce

$$I(\tau,t) = \varepsilon f(\tau-t)$$
 for $t < \tau$,

(2.7)

$$I(\tau,t) = -S'(t-\tau)$$
 for $t > \tau$,

Substitution of (2.7) into (2.2) yields the integro-differential equation

(2.8)
$$\frac{dS}{dt} = S(t) \left\{ \int_{0}^{t} A(\tau) \dot{S}'(t-\tau) d\tau - \varepsilon B(t) \right\},$$

where

(2.9)
$$B(t) = \int_{t}^{\infty} A(\tau)f(\tau-t)d\tau.$$

The problem (2.8)-(2.9) with initial condition (2.4a) forms the starting-point of our mathematical analysis. REDDINGIUS [9] and HOPPENSTEADT [4] have proved that this problem has a unique solution. Before analyzing the general problem, we give two examples of epidemics for which the mathematical model can be solved exactly.

EXAMPLE 2.1

Let us assume that the infectives have an exponentially decreasing infectiousness and that the initial infectives are fresh ill.

 $I(\tau,0) = 2\epsilon\delta(\tau)$ with $\delta(\tau)$ the delta function of Dirac.

Then S satisfies (2.8) with

$$A(t) = B(t) = \beta e^{-\lambda t}$$
.

It is easily verified that this model is equivalent with an epidemic where the infectives have a constant infectiousness and are removed at a constant rate λ . The corresponding differential equations for such epidemic read

$$\frac{dS}{dt} = - \beta SI$$

(2.10b)
$$\frac{dI}{dt} = \beta SI - \lambda I$$

(2.11)
$$S(0) = 1 - \epsilon$$
, $I(0) = \epsilon$, $0 < \epsilon < < 1$.

In the S, I-plane the trajectories of (2.10) satisfy

$$\frac{dI}{dS} = -1 + \frac{\lambda}{\beta S} .$$

Integration yields

(2.12)
$$I = 1 - S + \frac{\lambda}{\beta} \log \frac{S}{1-\epsilon},$$

and substitution of (2.12) into (2.10a) gives

$$\frac{dS}{dt} = \beta S(t) \left\{ 1 - S(t) + \frac{\lambda}{\beta} \log \frac{S(t)}{1 - \epsilon} \right\},\,$$

which can be solved by separation of variables

(2.13)
$$t = -\int_{1-\varepsilon}^{S} \frac{dU}{U\{\beta(1-U) + \lambda \log \frac{U}{1-\varepsilon}\}}.$$

The solution is determined by (2.12) and (2.13). Equation (2.12) gives information about the behavior of the epidemic for increasing t. There are two qualitatively different cases: for $\gamma = \beta/\lambda < 1$ the fraction of infectives decrease monotonic, while for $\gamma = \beta/\lambda > 1$ the fraction of infectives first increases. In the last case the limit fraction of susceptibles S_{∞} is substantially less than S(0), see figure 1.

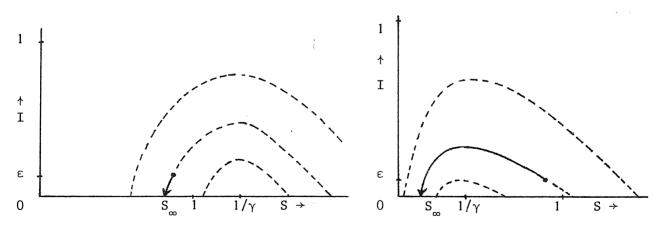


Fig.1. Phase plane of Eq. (2.10) for $\gamma < 1$ and $\gamma > 1$.

EXAMPLE 2.2

In this model there is the following age dependence: the infectives are removed after staying a fixed time σ in class I. Initially, there is a fraction $I_0(0)$ of infectives of different ages. Their removal is described by a given, decreasing function

$$I_0(t) = \varepsilon F(t)$$

with

$$\int_{0}^{\sigma} F(t)dt = 1 \text{ and } F(t) = 0 \text{ for } t > \sigma.$$

Assuming constant infectiousness we obtain the following dynamic equations

(2.14a)
$$S'(t) = -rSI, S(0) = S_0,$$

(2.14b)
$$I'(t) = -S'(t) + I_0'(t), \quad 0 < t < \sigma,$$

(2.14c)
$$I'(t) = -S'(t) + S'(t-\sigma), \sigma < t.$$

Substitution of the integrated equations (2.14bc) into (2.14a) gives

(2.15a)
$$S'(t) = -rS(t) \left\{ \dot{S}_0 - S(t) + I_0(t) \right\}, \quad 0 < t < \sigma$$

(2.15b)
$$S'(t) = -rS(t) \{S(t-\sigma) - S(t)\}, \quad 0 < t.$$

Ιf

$$A(\tau) = r$$
 for $0 \le \tau \le \sigma$
 $A(\tau) = 0$ for $\sigma < \tau$

and

$$f(\tau) = - F^{\dagger}(\sigma - \tau),$$

equation (2.8) is equivalent to (2.15). By transforming it into a linear system, WILSON [11] derives the exact solution of this system of equations.

3. THE THRESHOLD THEOREM

Integration of (2.8) yields

(3.1)
$$\ln \frac{S}{S_0} = \int_0^t A(\tau)S(t-\tau)d\tau - S_0 \int_0^t A(\tau)d\tau - \varepsilon \int_0^t B(\tau)d\tau.$$

Letting $t \rightarrow \infty$ we obtain an equation for the limit value S

(3.2)
$$\ln \frac{S_{\infty}}{S_0} = (S_{\infty} - S_0) \gamma - \epsilon Q,$$

where

$$Q = \int_{0}^{\infty} B(t)dt.$$

For each positive value of γ equation (3.2) has two roots as sketched in figure 2. Since the fraction of susceptibles is bounded by S = 1, the limit S_{∞} can only have a value corresponding to the lower root. For ε small the limit value S_{∞} changes considerably from S_{0} when γ exceeds the value 1. below this critical value there is no substantial decrease of the fraction of susceptibles, while above this value of γ the effectiviness of the infectives is sufficiently large to trigger an epidemic. The threshold theorem establishes this dependence upon γ . In the next section, we will follow the time development of the epidemic with $\gamma > 1$ and $0 < \varepsilon < 1$. Furthermore, it is assumed that B(t) > 0 for some $t \ge 0$. This last condition quarantees that a certain fraction of the initial infectives I_{0} indeed infects the susceptible population.

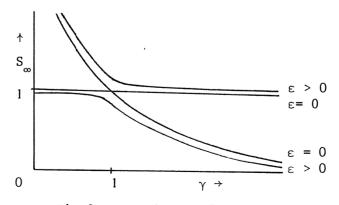


Fig.2. Dependence of S_{∞} upon γ .

4. THE ASYMPTOTIC SOLUTION

Before constructing the asymptotic solution of (2.8), we make an assumption about the infectiousness function. We suppose that for a given $\delta > 0$ a parameter β exists satisfying

$$\int_{0}^{\infty} e^{\beta \tau} A(\tau) d\tau = \delta$$

For $\delta > \gamma$ this is not necessarily the case as seen from examples with $A(\tau) \approx \tau^{-2}$ for $\tau \to \infty$.

In section 2 we derived the equation

(4.1)
$$\frac{dS}{dt} = S(t) \left\{ \int_{0}^{t} A(\tau)S'(t-\tau)d\tau - \varepsilon B(t) \right\},$$

which together with the initial condition

(4.2)
$$S(0) = 1 - \epsilon, \quad 0 < \epsilon < 1$$

describes the problem completely. Although it is in this particular problem more advantageous to take integral equation (3.1) as starting-point, we will investigate the local behavior of S from (4.1). In this way we hope ot make the reader familiar with singular perturbation techniques for this type of problems. It is noted that in section 5 we will deal with problems for which the step from (4.1) to (3.1) cannot be made. It is remarked that problems of type (3.1) and its linearizations are investigated in MILLER [8].

Let us assume that within a certain time interval starting at t=0 the solution can be expanded in powers of ϵ .

(4.3)
$$S(t;\varepsilon) = S_0(t) + \varepsilon S_1(t) + \varepsilon^2 S_2(t) + \dots$$

Employing (4.3) in (4.1) and (4.2) and equating the coefficient of each power of ε separately to zero yields the following set of problems to be solved iteratively for the coefficients $S_n(t)$:

(4.4)
$$\frac{dS_0}{dt} = S_0(t) \int_0^t A(\tau)S_0'(t-\tau)d\tau, \quad S_0(0) = 1$$

(4.5)
$$\frac{dS_1}{dt} = S_0(t) \int_0^t A(\tau)S_1'(t-\tau)d\tau + S_1(t) \int_0^t A(\tau)S_0'(t-\tau)d\tau - S_0(t)B(t),$$

$$S_1(0) = -1$$

(4.6)
$$\frac{dS_n}{dt} = \sum_{j=0}^{n} S_j(t) \int_{0}^{t} A(\tau)S_{n-j}^{\dagger}(t-\tau)d\tau - S_{n-1}(t)B(t), \quad S_j(0) = 0.$$

The solution of (4.4) is given by $S_0(t) = 1$. Employing this result in (4.5) and integrating we find

(4.7)
$$S_{1}(t) = \int_{0}^{t} A(\tau)S_{1}(t-\tau)d\tau + \int_{0}^{t} A(\tau)d\tau - \int_{0}^{t} B(\tau)d\tau - 1.$$

Equation (4.6) with n = 2 can also be integrated giving

$$S_2(t) = \int_0^t A(\tau)S_2(t-\tau)d\tau + \frac{1}{2}S_1^2(t).$$

In appendix A it is shown that for $t \rightarrow \infty$

(4.8)
$$S_{1}(t) = -Ce^{\beta t} + L + \sum_{k=1}^{m} \sum_{\ell=1}^{\nu} \left\{ C_{k\ell}^{+} e^{i\alpha_{k}t} + C_{k\ell}^{-} e^{-i\alpha_{k}t} \right\} t^{\ell-1} e^{\beta_{k}t} + V(t),$$

$$0 \le \beta_{k} < \beta, \qquad L = (Q + 1 - \gamma)/(\gamma - 1),$$

with $V(t) \rightarrow 0$ as $t \rightarrow \infty$ and with β satisfying

(4.9)
$$\int_{0}^{\infty} e^{-\beta t} A(\tau) d\tau = 1.$$

In the sequel we deal with the simplest case (m = 0), while in appendix B we work out the case $m \ge 1$.

Thus, for t large, the solution leaves the ε -neighborhood of the line S=1 at exponential rate. Clearly, the expansion (4.3) is not valid uniformly for all time t. According to (4.8) it is expected that at $t=\beta^{-1}\ln\varepsilon^{-1}$ the distance is O(1). Therefore, to determine the asymptotic behavior for large t we reconsider the problem (4.1) by introducing the

local variable ξ defined by

$$(4.10) \xi = t - \frac{1}{\beta} \ln \frac{1}{\varepsilon}.$$

This transformation denotes a time-shift which makes the problem different from a usual singular perturbation problem where a local variable is introduced by a stretching transformation. For the dependence upon ξ we employ the notation

(4.11)
$$S(t) \equiv S(\frac{1}{6} \ln \frac{1}{\epsilon} + \xi) \equiv S[\xi].$$

The system (4.1) then transforms into

$$(4.12) \qquad \frac{\mathrm{dS}}{\mathrm{d}\xi} = \mathrm{S}[\xi] \left\{ \int_{0}^{\xi + \frac{1}{\beta}} \ln \frac{1}{\varepsilon} \mathrm{A}(\overline{\xi}) \mathrm{S}'[\xi - \overline{\xi}] \mathrm{d}\overline{\xi} - \varepsilon \mathrm{B}(\frac{1}{\beta} \ln \frac{1}{\varepsilon} + \xi) \right\}.$$

We now assume that we may write

(4.13)
$$S[\xi] = U_0[\xi] + \varepsilon U_1[\xi] + R[\xi;\varepsilon],$$

where $R[\xi;\epsilon] = o(\epsilon)$. The leading term of (4.13) satisfies (4.12) with $\epsilon = 0$ or

$$(4.14) \qquad \frac{dU_0}{d\xi} = U_0[\xi] \left\{ \int_0^\infty A(\overline{\xi}) U_0'[\xi - \overline{\xi}] d\overline{\xi} \right\}.$$

Integrating this equation once we have

(4.15)
$$\ln U_0 = \int_0^\infty A(\overline{\xi}) U_0[\xi - \overline{\xi}] d\overline{\xi} + K,$$

where K is determined by matching (4.13) to (4.3). For matching it is necessary that $U_0 \to 1$ as $\xi \to -\infty$. Since the left-hand side of (4.15) vanishes for $U_0 \to 1$, the right-hand side must vanish too which occurs for $K = -\gamma$. Equation (4.15) with $K = -\gamma$ does not have a unique solution. In particular there exists a family of positive and monotone nonincreasing solutions bounded from above by the line $U_0 = 1$ and from below by the line $U = S_\infty^{(0)}$ satisfying (3.2) with $\varepsilon = 0$. This class of solutions, which are identical except for an arbitrary translation constant, has been investigated by 0. DIEKMANN [2]. Linearization about $U_0 = 1$ yields

$$(4.16) U_0[\xi] \approx 1 - Ee^{\beta \xi} for \xi \rightarrow -\infty,$$

where the arbitrary constant E also indicates the invariance of the solution under translation. According to (4.8) $U_0[\xi]$ matches the solution (4.3) for E=C. We note that equation (4.15) does not depend on the initial state (2.4). Thus, to a first order approximation the curve describing the epidemic has a fixed shape independent of f(t). From (4.10) we see that this curve still may shift in time: the smaller the fraction of initial infectives ϵ is, the longer the epidemic is postponed, see figure 3. Substitution of (4.13) into (4.12) and equation of the terms of $O(\epsilon)$, gives

$$(4.17) \qquad \frac{\mathrm{d} U_1}{\mathrm{d} \xi} = U_1[\xi] \int_0^\infty A(\overline{\xi}) U_0'[\xi - \overline{\xi}] \mathrm{d} \overline{\xi} + U_0[\xi] \int_0^\infty A(\overline{\xi}) U_1'[\xi - \overline{\xi}] \mathrm{d} \overline{\xi}.$$

Using (4.14) we rewrite equation (4.17) as

(4.18)
$$\int_{0}^{\infty} A(\overline{\xi}) U_{1}^{\dagger} [\xi - \overline{\xi}] d\overline{\xi} - \frac{U_{1}^{\dagger}}{U_{0}} + \frac{U_{1}}{U_{0}^{2}} \frac{dU_{0}}{d\xi} = 0.$$

Integration gives

(4.19)
$$\int_{0}^{\infty} A(\overline{\xi}) U_{1}[\xi - \overline{\xi}] d\overline{\xi} - \frac{U_{1}}{U_{0}} = P,$$

where the constant P follows from matching $U_1^{[\xi]}$ for $\xi \to -\infty$ to (4.3) for $t \to \infty$ giving

$$(4.20) P = Q + 1 - \gamma.$$

For $\xi \to \infty$ $\mathbb{U}_0^{[\xi]}$ tends to the limiting value $S_{\infty}^{(0)}$ satisfying (3.2) with $\varepsilon = 0$. From (4.19) we see that

(4.21)
$$\lim_{\xi \to \infty} U_1[\xi] = \frac{(Q+1-\gamma)S_{\infty}^{(0)}}{S_{\infty}^{(0)}\gamma-1}.$$

This result has to agree with (3.2). Writing

(4.22)
$$S_{\infty} = S_{\infty}^{(0)} + \varepsilon S_{\infty}^{(1)} + o(\varepsilon),$$

we find from (3.2) that indeed

(4.23)
$$S_{\infty}^{(1)} = \frac{(Q+1-\gamma)S_{\infty}^{(0)}}{S_{\infty}^{(0)}\gamma-1}.$$

5. TIME-DEPENDENT INFECTIOUSNESS

We consider now an epidemic under a less restricting condition. It will be assumed that the infectiousness function A depends not only on the age τ of the susceptibles but also on time t. This dependence is such that A varies slowly with t or

(5.1)
$$A = A(\tau, \delta t), \quad 0 < \delta < 1.$$

The asymptotic solution for ϵ and δ small depends strongly on the path in the ϵ, δ -plane along which the origin is approached. With singular perturbation techniques we are able to deal with problems for which $\delta/\ln\epsilon$ remains bounded. Let us investigate in more detail the limit case

$$(5.2) \qquad \delta = -1/\ln \epsilon$$

According to (5.1) we will have now

(5.3)
$$\gamma(\eta) = \int_{0}^{\infty} A(\tau, \eta) d\tau, \qquad \eta = -t/\ln \epsilon$$

We take $\gamma(\eta) > 1$ for all positive η then a positive function $\beta(\eta)$ exists satisfying

(5.4)
$$\int_{0}^{\infty} A(\tau, \eta) e^{-\beta(\eta)\tau} d\tau = 1.$$

The asymptotic solution of the problem with time-dependent infectiousness will consist of about the same elements as in the case of time-independent infectiousness. For S(t) near 1 we assume the following expansion to hold

(5.5)
$$S(t;\varepsilon) = 1 + \varepsilon S_1(t;1/\ln\varepsilon) + \varepsilon^2 S_2(t;1/\ln\varepsilon) + \dots$$

From point of view of formal asymptotic expansions, it would be better to write (5.5) as a double series with respect to ε and $ln\varepsilon$. Since we are only interested in the term of order $O(\varepsilon)$, we will not do so. Moreover, we skip

the terms of $O(\delta^k)$; they vanish because of the initial condition (4.2). Substitution into the integro-differential equation

(5.6)
$$\frac{dS}{dt} = S \left\{ \int_{0}^{t} A(\tau, -t/\ln \epsilon) S'(t-\tau) d\tau - \epsilon B(t; 1/\ln \epsilon) \right\}$$

with

$$B(t;1/\ln \varepsilon) = \int_{t}^{\infty} A(\tau,-t/\ln \varepsilon) f(\tau-t) d\tau$$

yields an equation for $S_1^{(0)} = S_1(t;0)$:

(5.7)
$$S_{1}^{(0)}(t) = \int_{0}^{t} A(\tau,0)S_{1}^{(0)}(t-\tau)d\tau + \int_{0}^{t} A(\tau,0)d\tau - \int_{0}^{t} B(\tau;0)d\tau.$$

Thus, $S_1^{(0)}$ is identical to S_1 satisfying (4.7) with $A(\tau)$ replaced by $A(\tau;0)$. For increasing t the solution leaves an ϵ -neighborhood of the line S=1. After a sufficient long period the distance from this line will be of order O(1); the solution then enters the epidemic phase. In section 4 the transition to the epidemic phase was characterized by the exponential growth of S_1 , see (4.8). In the present problem the transient situation is more complicated as β now varies with $t/\ln\epsilon$. The behavior is analyzed by introduction of a slow time variable η and a translated time variable ξ :

(5.8)
$$t = \eta \ln \frac{1}{\varepsilon} + \xi.$$

We assume that for t large S can be expanded as

(5.9)
$$S(\xi,\eta;\epsilon) = 1 + v_1(\epsilon,\eta)S_1(\xi,\eta;1/\ln\epsilon) + v_2(\epsilon,\eta)S_2(\xi,\eta;1/\ln\epsilon) + \dots$$

Equation (5.6) will have the form

$$(5.10) \qquad \frac{\partial S}{\partial \zeta} - \frac{1}{\ln \varepsilon} \frac{\partial S}{\partial \eta} = S \left[\int_{0}^{\xi - \eta \ln \varepsilon} A(\overline{\xi}, \eta) \left\{ \frac{\partial S}{\partial \xi} (\xi - \overline{\xi}, \eta; \varepsilon) - \frac{1}{\ln \varepsilon} \frac{\partial S}{\partial \eta} (\xi - \overline{\xi}, \eta; \varepsilon) \right\} d\overline{\xi} \right] \\ - \varepsilon B(\xi - \eta \ln \varepsilon; \frac{1}{\ln \varepsilon}) .$$
Substitution of (5.9) into (5.10) gives a function S_1 satisfying

$$\begin{split} \frac{\partial S_1}{\partial \xi} - \frac{1}{\ln \varepsilon} \, \frac{\partial S_1}{\partial \eta} &= \int\limits_0^{\xi - \eta \ln \varepsilon} A(\overline{\xi}, \eta) \bigg\{ \frac{\partial S_1}{\partial \xi} (\xi - \overline{\xi}, \eta; \, \frac{1}{\ln \varepsilon}) - \frac{1}{\ln \varepsilon} \, \frac{\partial S_1}{\partial \eta} (\xi - \overline{\xi}, \eta; \, \frac{1}{\ln \varepsilon}) \bigg\} d\overline{\xi} \\ &\qquad \qquad - \frac{\varepsilon}{v_1(\varepsilon, \eta)} \, B(\xi - \eta \ln \varepsilon; \, \frac{1}{\ln \varepsilon}). \end{split}$$

Letting $\varepsilon \to 0$ we obtain for $S_1^{(0)} = S_1(\xi,\eta;0)$ the equation

(5.11)
$$\frac{\partial S_1^{(0)}}{\partial \xi} = \int_0^\infty A(\overline{\xi}, \eta) \frac{\partial S_1^{(0)}}{\partial \xi} (\xi - \overline{\xi}, \eta) d\overline{\xi}$$

or

$$S_{1}^{(0)}(\xi,\eta) = \int_{0}^{\infty} A(\overline{\xi},\eta) S_{1}^{(0)}(\xi-\overline{\xi},\eta) d\overline{\xi} + K(\eta).$$

In this limit procedure, it is supposed that

$$\varepsilon B(\xi-\eta \ln \varepsilon; 1/\ln \varepsilon)/v_1(\varepsilon,\eta) \to 0$$
 as $\varepsilon \to 0$,

which turns out to be correct for our choice of $\nu_1(\epsilon,\eta)$ to be made later on. The positive function $S_1^{(0)}$ vanishes for $\xi \to -\infty$ and will be unbounded for $\xi \to \infty$ ($\eta > 0$). These conditions are satisfied for $K(\eta) \equiv 0$ and

(5.12)
$$S_1^{(0)}(\xi,\eta) = e^{\beta(\eta)\xi}$$

As η increases the function $\nu_1(\epsilon,\eta)$ will increase in order of magnitude. Let ξ tend to infinity comparable with $(d\eta)\ln 1/\epsilon$, then the order of magnitude of (5.12) increases with exp $\left\{\beta(\eta)d\eta, \ln 1/\epsilon\right\}$. This increase is transmitted to the order function $\nu_1(\epsilon,\eta)$ which, therefore, will have the form

$$\int_{0}^{\eta} \beta(\overline{\eta}) d\overline{\eta} \ln 1/\epsilon$$

$$v_{1}(\epsilon, \eta) = f(\epsilon)e^{0}$$

and, since $v_1(\epsilon, 0) = \epsilon$, we will have

(5.13)
$$v_{1}(\varepsilon, \eta) = \varepsilon$$

$$1 - \int_{0}^{\eta} \beta(\overline{\eta}) d\overline{\eta}$$

The asymptotic expansion (5.9) will not be valid for $\eta = \eta^*$ with

(5.14)
$$F(\eta^*) = \int_{0}^{\eta^*} \beta(\eta) d\eta = 1,$$

as
$$v_1(\epsilon, \eta^*) = 0(1)$$
.

The solution then enters the epidemic phase where in analogy with (4.31) S is approximated by $U_{\Omega}(\xi,\eta^*)$ satisfying

(5.15)
$$\ln U_0 = \int_0^\infty A(\overline{\xi}, \eta^*) U_0(\xi - \overline{\xi}, \eta^*) d\overline{\xi} - \gamma(\eta^*).$$

In the post-epidemic phase ($\eta > \eta^*$) S will follow the slowly varying solution $V_0(\eta)$ of the equation

(5.16)
$$\ln V_0(\eta) = (V_0(\eta) - 1)\gamma(\eta).$$

It is not clear in which way γ functions as a threshold parameter. When γ oscillates around the value 1, it is not easily understood under what conditions an epidemic may be expected. This case needs a separate analysis. Returning to the above problem with $\gamma(\eta)>1$, we observe that the integral (5.14) plays an important role in the evolution of an epidemic: the epidemic is triggered, when $F(\eta)$ exceeds the value 1.

Finally, we remark that when in the post-epidemic phase γ decreases, the solution S is not able to $\text{follow}^{^{\dagger}}V_0^{}(\eta)$ upwards and, therefore, will remain constant until $V_0^{}(\eta)$ again passes this value downwards.

6. NUMERICAL RESULTS

In this section we will consider two examples for which we compare the numerical solutions with the preceding asymptotic results,

EXAMPLE 6.1

For the numerical integration scheme of our first example we used equation (3.1). In figure 3 we give the numerical solution of this equation with

(6.1)
$$A(t) = B(t) = 4t^{2}e^{-t^{2}}$$

for different value of ϵ . It is observed that the curves are almost identical except for the translation.

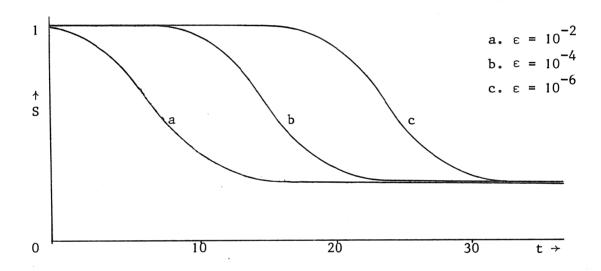


Fig. 3. Time course of the epidemic for different values of ϵ .

For the parameters of the system we find

$$\gamma = \sqrt{\pi}, \quad \beta = .534882.$$

Furhter we define

$$M = (1+S_{\infty}^{(0)})/2.$$

For the case (6.1) it has the value

$$M = .63912.$$

In table 1 we give the value $t=t_M(\epsilon)$ for which S equals M, we also compute $\beta^{-1}\ln\epsilon^{-1}$ for different values of ϵ . It is seen that the difference tends to a fixed value for $\epsilon \to 0$. This result shows that in agreement with (4.10) the epidemic is postponed to a time $0(\beta^{-1}\ln\epsilon^{-1})$.

	(A)	(B)	(B)-(A)
ε	t _M (ε)	$\frac{1}{\beta} \ln \frac{1}{\varepsilon}$	
10 ⁻¹	2.247	4.305	2.058
10 ⁻²	6.606	8.611	2.005
10 ⁻³	11.007	12.916	1.909
10-4	15.331	17.221	1.890
10 ⁻⁵	19.639	21.527	1.888
10 ⁻⁶	23.945	25.832	1.887

Table I

EXAMPLE 6.2

In this example we cannot make use of (3.1) anymore. A numerical solution of the following integro-differential equation is constructed with the trapezium rule,

$$S'(t) = S(t) \left\{ \int_{0}^{t} A(\tau,t)S'(t-\tau)d\tau - \varepsilon A(t,t) \right\},\,$$

$$S(0) = 1-\varepsilon$$

with

$$A(\tau,t) = \tau e^{-\tau} \left\{ 1.5 + e^{t/1n\epsilon} \right\}^2$$

For this equation we find

$$\gamma(\eta) = \left\{1.5 + e^{-\eta}\right\}^2, \quad \eta = - t/\ln\varepsilon,$$

and, since

$$\int_{0}^{\infty} \tau e^{-\tau} e^{-\tau p} d\tau = (1+p)^{-2},$$

we also obtain easily

$$\beta(n) = .5 + e^{-\eta}$$
.

Thus, according to (5.14) the solution is in the epidemic phase for $t = -\eta^* ln\epsilon + \xi^*$, where ξ^* is independent of ϵ and η^* satisfies

$$\int_{0}^{\eta^{*}} (.5 + e^{-\eta}) d\eta = 1$$

or η^* = .85261. In table II we give the value t = $t_M(\epsilon)$, for which S equals M,

$$M = \left\{1 + V_0(\eta^*)\right\}/2 = .51353$$

where V_0 satisfies (5.16). In the same table we also compute $-\eta^* ln\epsilon$ for different values of ϵ . The difference between these two values tends to a fixed value (incidently close to zero).

In the last column the limit value of S for t $\rightarrow \infty$ is printed. It is observed that for $\varepsilon \rightarrow 0$ S_{∞} approaches the value V₀(η^*) = .0270. It should be noted that γ tends to 2.25 as $\eta \rightarrow \infty$. According to (5.16) this would correspond with a value V₀ = .1466. The actual limit S_{∞} lies considerably below this value, because the epidemic started at a time when the total infectiousness $\gamma(\eta^*)$ was lying above the limit value $\gamma(\infty)$.

	(A)	(B)	(A)-(B)	
ε,	-η*1nε	t _M (ε)		S_{∞}
10 ⁻¹	1.963	1.857	.107	.049
10 ⁻²	3.963	3.892	.035	.043
10 ⁻³	5.890	5.870	.020	.039
10 ⁻⁴	7.853	7.837	.015	.036
10 ⁻⁵	9.816	9.803	.013	.035
10 ⁻⁶	11.780	11.768	.011	.033
10 ⁻⁹	17.669	17.661	.007	.031
10-12	23.558	23.553	.005	.030

Table II

APPENDIX A

We consider the integral equation

(A1)
$$S(t) = \int_{0}^{t} A(\tau)S(t-\tau)d\tau - G(t)$$

with

$$G(t) = 1 + \int_{0}^{t} \left\{ B(\tau) - A(\tau) \right\} d\tau.$$

It is noted that

$$G(0) = 1$$
, $\lim_{t\to\infty} G(t) = R$,

where R = 1 + Q - γ is some positive value smaller than 1. Let us write

(A2)
$$S(t) = R(\gamma-1) + V(t)$$
,

so that V(t) must satisfy

(A3)
$$V(t) = \int_{0}^{t} A(\tau)V(t-\tau)d\tau - H(t),$$

$$H(t) = \int_{t}^{\infty} \left\{ A(\tau) - B(\tau) \right\} d\tau.$$

Since

$$\int_{0}^{\infty} H(\tau) d\tau < \infty,$$

equation (A3) and therefore also equation (A1) will have a unique solution, see DOETSCH [3], p. 145. We consider first the special case G(t)=1,

(A4)
$$S_1(t) = \int_0^t A(\tau)S_1(t-\tau)d\tau - 1.$$

We will solve this equation by Laplace transform. If

$$\hat{S}_1(p) = \int_0^\infty e^{-tp} S_1(t) dt, \qquad \hat{A}(p) = \int_0^\infty e^{-tp} A(t) dt,$$

the transformed equation will be

$$\hat{S}_{1}(p) = \hat{A}(p)\hat{S}_{1}(p) - \frac{1}{p}$$
,

so

(A5)
$$\hat{S}_{1}(p) = \frac{-1}{P\{1-\hat{A}(p)\}}$$
.

It has been established ([2]) that the equation

$$1 - \widehat{A}(p) = 0$$

has roots $p = \beta$, $\beta_1 \pm i\alpha_1$, $\beta_2 \pm i\alpha_2$,... of multiplicity $1, \nu_1, \nu_2$,... such that for any real number α only a finite number of them have $\beta_k \ge \alpha$, while $\alpha_k \ne 0$, $\beta > \beta_1$ and $\beta_k \ge \beta_{k-1}$. The original function $S_1(t)$ is found

from (A5) by computing the residues giving

(A6)
$$S_{1}(t) = -\hat{C}e^{\beta t} + \hat{L} + \sum_{k=1}^{\infty} \sum_{\ell=1}^{\nu_{k}} \left\{ \hat{C}_{k\ell}^{+} e^{i\alpha_{k}t} + \hat{C}_{k\ell}^{-} e^{-i\alpha_{k}t} \right\} t^{\ell-1} e^{\beta_{k}t},$$

where

$$\hat{C} = -1/\{\beta \hat{A}^{\dagger}(\beta)\}, \qquad \hat{L} = 1/(\gamma-1).$$

Using the relation

$$S(t) = \frac{d}{dt} \left\{ \int_{0}^{t} S_{1}(t-\tau)G(\tau)d\tau \right\},\,$$

we are able to give an expression for S(t) satisfying (A1) for a general function G(t):

$$(A7) \qquad S(t) = \frac{d}{dt} \left\{ \hat{C} e^{\beta t} \int_{0}^{t} e^{-\beta \tau} G(\tau) d\tau \right\} + \hat{L}G(t) +$$

$$\sum_{k=1}^{\infty} \sum_{\ell=1}^{\nu_k} \frac{d}{dt} \left\{ \hat{C}_{k\ell}^{\dagger} e^{(\beta_k + i\alpha_k)t} \int_{0}^{t} e^{-(\beta_k + i\alpha_k)\tau} (t-\tau)^{\ell-1} G(\tau) d\tau +$$

$$\hat{C}_{k\ell}^{\dagger} e^{(\beta_k - i\alpha_k)t} \int_{0}^{t} e^{-(\beta_k - i\alpha_k)\tau} (t-\tau)^{\ell-1} G(\tau) d\tau \right\}.$$

Examining the first term for t large, we observe that

$$\frac{\mathrm{d}}{\mathrm{d}t} \left\{ \hat{\mathsf{C}} e^{\beta t} \int_{0}^{t} e^{-\beta \tau} \mathsf{G}(\tau) \mathrm{d}\tau \right\} = - \mathsf{C} e^{\beta t} + \mathsf{Z}(t)$$

with

$$C = \widehat{C}\beta \int_{0}^{\infty} e^{-\beta \tau} G(\tau) d\tau,$$

and

$$Z(t) = -\widehat{C}\beta e^{\beta t} \int_{t}^{\infty} e^{-\beta \tau} \left\{ G(\tau) - G(t) \right\} d\tau.$$

It is easily verified that $Z(t)\to 0$ as $t\to \infty$. A similar calculation can be carried out for the other terms of (A7). Thus, we may conclude that for $t\to \infty$

$$S(t) = -Ce^{\beta t} + L + \sum_{k=1}^{m} \sum_{\ell=1}^{\nu} \left\{ c_{k\ell}^{+} e^{i\alpha_k t} + c_{k\ell}^{-} e^{-i\alpha_k t} \right\} t^{\ell-1} e^{\beta_k t} + V(t),$$

$$C = -\hat{G}(\beta)/\hat{A}^{\dagger}(\beta)$$
, $L = R/(\gamma-1) = (1+Q-\gamma)/(\gamma-1)$.

with $V(t) \rightarrow 0$ as $t \rightarrow \infty$ and m such that $\beta_m \ge 0$ and $B_{m+1} < 0$ (if existing).

APPENDIX B

Let (4.8) have the form

(B1)
$$S_1(t) = -Ce^{\beta t} + (C_1^+ e^{-i\alpha_1 t} + C_1^- e^{-i\alpha_1 t})e^{\beta_1 t} + L + V(t),$$

with $0 < \beta_1 < \beta$. For $t = 0(-\beta^{-1} \ln \epsilon)$ the first term of (B1) is of the order $0(\epsilon^{-1})$, while the second term is of $0(\epsilon^{-1})$, We assume that in the epidemic phase the solution can be expanded as

$$(B2) \qquad S[\xi,\varepsilon] = U_0[\xi] + \varepsilon^{\sigma} U^{(1)}[\xi] + \varepsilon^{2\sigma} U^{(2)}[\xi] + \dots + \varepsilon^{k\sigma} U^{(k)}[\xi] + \varepsilon U_1[\xi] + R[\xi;\varepsilon],$$

where $\sigma = (\beta - \beta_1)/\beta$, $k\sigma < 1 \le (k+1)\sigma$ and $R[\xi; \epsilon] = 0(\epsilon)$. Substitution in (4.12) and equation of coefficients of equal powers of ϵ lead to equations for $U_0, U_1, U^{(1)}, U^{(2)}, \dots, U^{(k)}$. U_0 and U_1 satisfy the equation (4.14) and, (4,19) for $(k+1)\sigma \ne 1$. The terms $U^{(j)}$ form a recurrent system

(B3)
$$\frac{d\mathbf{U}^{(1)}}{d\xi} = \mathbf{U}^{(1)} \int_{0}^{\infty} \mathbf{A}(\overline{\xi}) \frac{d\mathbf{U}_{0}}{d\xi} \left[\xi - \overline{\xi} \right] d\overline{\xi} + \mathbf{U}_{0} \left[\xi \right] \int_{0}^{\infty} \mathbf{A}(\overline{\xi}) \frac{d\mathbf{U}^{(1)}}{d\xi} \left[\xi - \overline{\xi} \right] d\xi,$$

(B4)
$$\frac{dU^{(j)}}{d\xi} = \sum_{i=0}^{j} U^{(i)}[\xi] \int_{0}^{\infty} A(\overline{\xi}) \frac{d}{d\xi} U^{(j-i)}[\xi - \overline{\xi}] d\overline{\xi}, \quad j = 2, 3, ..., k,$$

where $U^{(0)} = U_0$. Equation (B3) is identical to equation (4.17) giving

(B5)
$$\int_{0}^{\infty} A(\overline{\xi}) U^{(1)}[\xi - \overline{\xi}] d\overline{\xi} - \frac{U^{(1)}}{U^{(0)}} = P_{1}.$$

The solution of this equation matches (B1) if

$$\mathbf{U}^{(1)} \approx \left\{ \mathbf{C}_{1}^{+} \mathbf{e}^{\mathbf{i}\alpha_{1}\xi} + \mathbf{C}_{1}^{-} \mathbf{e}^{-\mathbf{i}\alpha_{1}\xi} \right\} \mathbf{e}^{\beta_{1}\xi} \quad \text{as} \quad \xi \rightarrow -\infty,$$

which is possible for P = 0. On the other hand for $\xi \to \infty$ $U^{(1)}$ will satisfy equation (B5) with $U^{(0)} \approx S_{\infty}^{(0)}$, so

(B6)
$$U^{(1)}[\xi] \approx S_{\infty}^{(0)} \int_{0}^{\infty} A(\overline{\xi}) U^{(1)}[\xi - \overline{\xi}] d\overline{\xi}.$$

The solution of this type of integral equation is related to the roots of the equation

(B7)
$$S_{\infty}^{(0)} \int_{0}^{\infty} A(t)e^{-pt}dt = 1.$$

According to (3.2)

$$lnS_{\infty}^{(0)} = (S_{\infty}^{(0)} - 1)\gamma,$$

or

$$\gamma S_{\infty}^{(0)} - 1n\gamma S_{\infty}^{(0)} = \gamma - 1n\gamma$$

The equation

$$x - 1nx = q$$

with

$$q = \gamma - 1n\gamma > 1$$

has two roots x_1 and x_2 with $x_1 < 1 < x_2$. Obviously, $x_2 = \gamma > 1$ and since $S_{\infty}^{(0)} \neq 1$ we have $x_1 = \gamma S_{\infty}^{(0)} < 1$. Using theorem 146 of THITCHMARCH [10] equation (B6) will only have solutions that tend to zero as $\xi \rightarrow \infty$ as the

roots of (B7) will have negative real parts. From the above asymptotic analysis we conclude that at the end of the epidemic phase the growing oscillatery term of (B1) is suppressed because of (B6). If $2 \sigma < 1$, we have to carry on these calculations. Equation (B4) with k = 2 turns out to have the form

(B8)
$$\int_{0}^{\infty} A(\overline{\xi}) u^{(2)} \left[\xi - \overline{\xi}\right] d\overline{\xi} - \frac{u^{(2)} \left[\xi\right]}{u_{0} \left[\xi\right]} = P_{2} + \frac{1}{2} \left\{ \frac{u^{(1)} \left[\xi\right]}{u_{0} \left[\xi\right]} \right\}^{2}.$$

Matching with $S_2(t)$ of (4.8) gives $P_2 = 0$. For $\xi \to \infty$ the right-hand side of (B8) will vanish so that $U^{(2)}$ behaves in the same way as $U^{(1)}$ given by (B6). This procedure can be continued until $U^{(k)}$. If (B1) contains more oscillatory growing terms, one has to deal with them likewise.

ACKNOWLEDGEMENTS

The authors are grateful to J.A.J. Metz (Inst. Theor. Biol. Leyden, The Netherlands) for suggesting the problem and to O. Diekmann, F.C. Hoppensteadt and H.A. Lauwerier for valuable remarks during the preparation of this paper. The numerical computations have been carried out on a CD CYBER 73 computer at the Mathematical Center Amsterdam by G.J.M. Laan and J. Schilder. One of the authors (BJM) would like to express his gratitude to Professor L.A. Segel and to the Department of Applied Mathematics at the Weizmann Institute of Science, Rehovoth, Israel, for their warmth hospitality during the concluding phase of this work.

REFERENCES

- COOKE, K.L., Functional-differential equations: Some models and perturbation problems, in Differential Equations and Dynamical Systems,
 J.K. Hale and J.P. LaSalle, eds.. Acad. Press, New York (1967),
 p. 167-1830.
- 2. DIEKMANN, O., Limiting behavior in an epidemic model, Math. Centre Report TW 159 (1976).
- 3. DOETSCH, G., Handbuch der Laplace-Transformation III, Birkhäuser Verlag Basel (1956).
- 4. HOPPENSTEADT, F.C., An age dependent epidemic model, J. Franklin Inst. 297 (1974), p. 325-332.
- 5. HOPPENSTEADT, F.C., Mathematical theories of populations: demographics genetics and epidemics, SIAM Regional Conference Series in Appl. Math. 20 (1975).
- 6. KERMACK, W.O. & A.G. McKENDRICK, A contribution to the mathematical theory of epidemics, Proc. Roy. Soc. <u>A115</u> (1927), p. 700-721.
- 7. METZ, J.A.J., The epidemic in a closed population with all susceptibles equally valuable; some results for some susceptible populations and small initial infections. To appear in Acta Biotheoretica
- 8. MILLER, R.K., Nonlinear Volterra Integral equations, Benjamin Inc. Menlo Park, California (1971).
- 9. REDDINGIUS, J., Notes on the mathematical theory of epidemics, Acta Biotheoretica 20 (1971), p. 125-157.
- 10. TITCHMARSH, E.C., Introduction to the theory of Fourier integrals, Clarendon Press, Oxford (1937).
- 11. WILSON, L.O., An epidemic model involving a threshold, Math. Biosci. 15 (1972) p. 109-121.