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Backward bifurcations in simple vaccination models ☆

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Abstract

We describe and analyze by elementary means some simple models for disease transmission with vaccination. In particular, we give conditions for the existence of multiple endemic equilibria and backward bifurcations. We extend the results to include models in which the parameters may depend on the level of infection.

1. Introduction

In compartmental models for the transmission of communicable diseases there is usually a basic reproductive number R_0, representing the mean number of secondary infections caused by a single infective introduced into a susceptible population. If $R_0 < 1$, there is a disease-free equilibrium which is asymptotically stable, and the infection dies out. If $R_0 > 1$, the usual situation is that there is an endemic equilibrium which is asymptotically stable, and the infection persists. Even if the endemic equilibrium is unstable, the instability commonly arises from a Hopf bifurcation and the infection still persists but in an oscillatory manner. More precisely, as R_0 increases through 1 there is an exchange of stability between the disease-free equilibrium and the endemic equilibrium (which is negative

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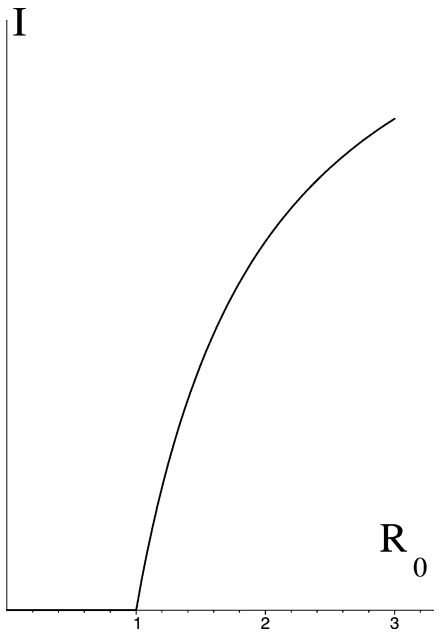

Fig. 1. Forward bifurcation.

as well as unstable and thus biologically meaningless if $R_0 < 1$). There is a bifurcation, or change in equilibrium behavior, at $R_0 = 1$ but the equilibrium infective population size depends continuously on R_0. Such a transition is called a forward, or transcritical, bifurcation.

The behavior at a bifurcation may be described graphically by the bifurcation curve, which is the graph of equilibrium infective population size I as a function of the basic reproductive number R_0. For a forward bifurcation, the bifurcation curve is as shown in Fig. 1.

It has been noted [4–6,11] that in epidemic models with multiple groups and asymmetry between groups or multiple interaction mechanisms it is possible to have a very different bifurcation behavior at $R_0 = 1$. There may be multiple positive endemic equilibria for values of $R_0 < 1$ and a backward bifurcation at $R_0 = 1$. This means that the bifurcation curve has the form shown in Fig. 2 with a broken curve denoting an unstable endemic equilibrium that separates the domains of attraction of asymptotically stable equilibria.

The qualitative behavior of an epidemic system with a backward bifurcation differs from that of a system with a forward bifurcation in at least three important ways. If there is a forward bifurcation at $R_0 = 1$ it is not possible for a disease to invade a population if $R_0 < 1$ because the system will return to the disease-free equilibrium $I = 0$ if some infectives are introduced into the population. On the other hand, if there is a backward bifurcation at $R_0 = 1$ and enough infectives are introduced into the population to put the initial state of the system above the unstable endemic equilibrium with $R_0 < 1$, the system will approach the asymptotically stable endemic equilibrium.

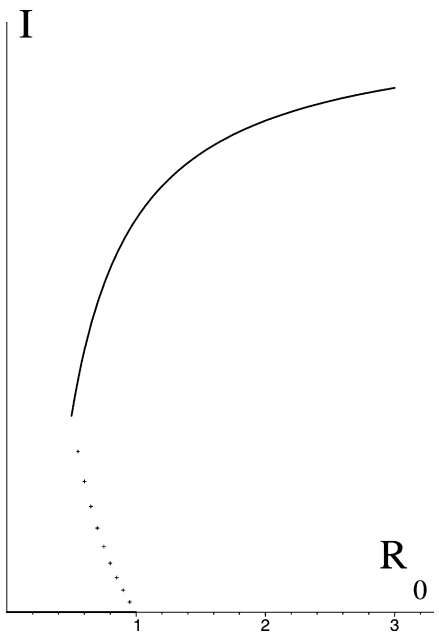

Fig. 2. Backward bifurcation.

Other differences are observed if the parameters of the system change to produce a change in R_0. With a forward bifurcation at $R_0 = 1$ the equilibrium infective population remains zero so long as $R_0 < 1$ and then increases continuously as R_0 increases. With a backward bifurcation at $R_0 = 1$, the equilibrium infective population size also remains zero so long as $R_0 < 1$ but then jumps to the positive endemic equilibrium as R_0 increases through 1. In the other direction, if a disease is being controlled by means which decrease R_0 it is sufficient to decrease R_0 to 1 if there is a forward bifurcation at $R_0 = 1$ but it is necessary to bring R_0 well below 1 if there is a backward bifurcation.

These behavior differences are important in planning how to control a disease; a backward bifurcation at $R_0 = 1$ makes control more difficult. One control measure often used is the reduction of susceptibility to infection produced by vaccination. By vaccination we mean either an inoculation which reduces susceptibility to infection or an education program such as encouragement of better hygiene or avoidance of risky behavior for sexually transmitted diseases. Whether vaccination is inoculation or education, typically it reaches only a fraction of the susceptible population and is not perfectly effective. In an apparent paradox, models with vaccination may exhibit backward bifurcations, making the behavior of the model more complicated than the corresponding model without vaccination. It has been argued [1] that a partially effective vaccination program applied to only part of the population at risk may increase the severity of outbreaks of such diseases as HIV/AIDS.

We will give a complete qualitative analysis of the two-dimensional model examined in [11] where there is a possibility of a backward bifurcation. In [11] the local stability analysis was carried out using the center manifold theorem and examination of normal forms [10]. We are able to obtain the results by an elementary approach and avoid the

center manifold theorem. Also, we extend them to models in which the parameters may depend on the level of infection. However, the center manifold approach remains essential for more complicated models because of the technical complications of an elementary approach.

2. The vaccination model

The model we will study adds vaccination to the simple SIS model

$$\begin{aligned} S' &= \Lambda - \beta SI - \mu S + \gamma I, \\ I' &= \beta SI - (\mu + \gamma)I. \end{aligned} \tag{1}$$

This model is just the basic model of Kermack and McKendrick [9] with the incorporation of a constant birth rate Λ in the susceptible class and a proportional natural death rate μ in each class and no disease deaths.

In (1) the total population size $N = S + I$ and $N' = S' + I' = \Lambda - \mu N$. Then $\lim_{t\to\infty} N(t) = K = \Lambda/\mu$ for every choice of initial values and the system (1) is asymptotically autonomous. The theory of asymptotically autonomous systems [12–14] implies that we may replace N by K and reduce the dimension of the system by using $S = N - I = K - I$ to give the single differential equation

$$I' = \beta I(K - I) - (\mu + \gamma)I. \tag{2}$$

This is easily analyzed completely. There is a disease-free equilibrium $I = 0$ which is globally asymptotically stable if

$$R_0 = \frac{\beta K}{\mu + \gamma} < 1.$$

If $R_0 > 1$ the disease-free equilibrium is unstable but there is an endemic equilibrium $I = K(1 - 1/R_0) > 0$ which is globally asymptotically stable.

According to the theory of asymptotically autonomous systems, this result extends to the system

$$\begin{aligned} S' &= \Lambda(N) - \beta(N)SI - \mu S + \gamma I, \\ I' &= \beta SI - (\mu + \gamma)I, \end{aligned} \tag{3}$$

where the population carrying capacity K is now defined by $\Lambda(K) = \mu K$, $\Lambda'(K) < \mu$ and the contact rate $\beta(N)$ is now a function of total population size with $N\beta(N)$ non-decreasing and $\beta(N)$ non-increasing.

To the model (3) we add the assumption that in unit time a fraction ϕ of the susceptible class is vaccinated. The vaccination may reduce but not completely eliminate susceptibility to infection. We model this by including a factor σ, $0 \leqslant \sigma \leqslant 1$, in the infection rate of vaccinated members with $\sigma = 0$ meaning that the vaccine is perfectly effective and $\sigma = 1$ meaning that the vaccine has no effect. We assume also that the vaccination loses effect at a proportional rate θ. We describe the new model by including a vaccinated class V, with

$$S' = \Lambda(N) - \beta(N)SI - (\mu+\phi)S + \gamma I + \theta V,$$
$$I' = \beta(N)SI + \sigma\beta(N)VI - (\mu+\gamma)I,$$
$$V' = \phi S - \sigma\beta(N)VI - (\mu+\theta)V, \tag{4}$$

and $N = S + I + V$. Again, $N' = \Lambda(N) - \mu N$ and $\lim_{t\to\infty} N(t) = K$ for every choice of initial values and by the theory of asymptotically autonomous systems we may replace N by K and S by $K - I - V$ to give the qualitatively equivalent system

$$I' = \beta\big[K - I - (1-\sigma)V\big]I - (\mu+\gamma)I,$$
$$V' = \phi[K - I] - \sigma\beta VI - (\mu+\theta+\phi)V, \tag{5}$$

with $\beta = \beta(K)$. The system (5) is the basic vaccination model which we will analyze. We remark that if the vaccine is completely ineffective, $\sigma = 1$, then (5) is equivalent to the SIS model (2). If there is no loss of effectiveness of vaccine, $\theta = 0$, and if all susceptibles are vaccinated immediately (formally, $\phi \to \infty$), the model (5) is equivalent to

$$I' = \sigma\beta I(K - I) - (\mu+\gamma)I$$

which is the same as (2) with β replaced by $\sigma\beta$ and has basic reproductive number

$$R_0^* = \frac{\sigma\beta K}{\mu+\gamma} = \sigma R_0 \leqslant R_0.$$

We will think of the parameters μ, γ, θ, ϕ and σ as fixed and will view β as variable. In practice, the parameter ϕ is the one most easily controlled, and later we will express our results in terms of an uncontrolled model with parameters β, μ, γ, θ, and σ fixed and examine the effect of varying ϕ. With this interpretation in mind, we will use $R(\phi)$ to denote the basic reproductive number of the model (5), and we will see that

$$R_0^* \leqslant R(\phi) \leqslant R_0.$$

Equilibria of the model (5) are solutions of

$$\beta I\big[K - I - (1-\sigma)V\big] = (\mu+\gamma)I, \tag{6}$$
$$\phi[K - I] = \sigma\beta VI + (\mu+\theta+\phi)V. \tag{7}$$

If $I = 0$ then (6) is satisfied and (7) leads to

$$V = \frac{\phi}{\mu+\theta+\phi}K.$$

This is the disease-free equilibrium.

The matrix of the linearization of (5) at an equilibrium (I, V) is

$$\begin{bmatrix} -2\beta I - (1-\sigma)\beta V - (\mu+\gamma) + \beta K & -(1-\sigma)\beta I \\ -(\phi + \sigma\beta V) & -(\mu+\theta+\phi+\sigma\beta I) \end{bmatrix}.$$

At the disease-free equilibrium this matrix is

$$\begin{bmatrix} -(1-\sigma)\beta V - (\mu+\gamma) + \beta K & 0 \\ -(\phi+\sigma\beta V) & -(\mu+\theta+\phi) \end{bmatrix}$$

which has negative eigenvalues, implying the asymptotic stability of the disease-free equilibrium, if and only if

$$-(1-\sigma)\beta V-(\mu+\gamma)+\beta K<0.$$

Using the value of V at the disease-free equilibrium this condition is equivalent to

$$R(\phi)=\frac{\beta K}{\mu+\gamma}\cdot\frac{\mu+\theta+\sigma\phi}{\mu+\theta+\phi}=R_0\frac{\mu+\theta+\sigma\phi}{\mu+\theta+\phi}<1.$$

The case $\phi=0$ is that of no vaccination with $R(0)=R_0$, and $R(\phi)<R_0$ if $\phi>0$. In fact, it is not difficult to show, using a standard a priori bound argument, that if $R_0<1$ the disease-free equilibrium is globally asymptotically stable [11]. We note that $R_0^*=\sigma R_0=\lim_{\phi\to\infty}R(\phi)<R_0$.

3. Endemic equilibria

If $\sigma=1$, meaning that the vaccine has no effect, we have seen that (5) is equivalent to the SIS model (2) and if $R_0>1$ there is a unique endemic equilibrium which is globally asymptotically stable. If $0\leqslant\sigma<1$ endemic equilibria are solutions of the pair of equations

$$\begin{aligned}&\beta\big[K-I-(1-\sigma)V\big]=\mu+\gamma,\\&\phi[K-I]=\sigma\beta VI+(\mu+\theta+\phi)V.\end{aligned}\tag{8}$$

We eliminate V using the first equation of (8) and substitute into the second equation to give an equation of the form

$$AI^2+BI+C=0\tag{9}$$

with

$$\begin{aligned}&A=\sigma\beta,\\&B=(\mu+\theta+\sigma\phi)+\sigma(\mu+\gamma)-\sigma\beta K,\\&C=\frac{(\mu+\gamma)(\mu+\theta+\phi)}{\beta}-(\mu+\theta+\sigma\phi)K.\end{aligned}\tag{10}$$

If $\sigma=0$, (9) is a linear equation with unique solution

$$I=K-\frac{(\mu+\gamma)(\mu+\theta+\phi)}{\beta(\mu+\theta)}=K\left[1-\frac{1}{R(\phi)}\right],$$

which is positive if and only if $R(\phi)>1$. Thus if $\sigma=0$ there is a unique endemic equilibrium if $R(\phi)>1$ which approaches zero as $R(\phi)\to1+$ and there cannot be an endemic equilibrium if $R(\phi)<1$. In this case it is not possible to have a backward bifurcation at $R(\phi)=1$.

We note that $C<0$ if $R(\phi)>1$, $C=0$ if $R(\phi)=1$, and $C>0$ if $R(\phi)<1$. If $\sigma>0$, so that (9) is quadratic and if $R(\phi)>1$, then there is a unique positive root of (9) and thus there is a unique endemic equilibrium. If $R(\phi)=1$, then $C=0$ and there is a unique nonzero solution of (9) $I=-B/A$ which is positive if and only if $B<0$. If $B<0$ when $C=0$

there is a positive endemic equilibrium for $R(\phi) = 1$. Since equilibria depend continuously on ϕ there must then be an interval to the left of $R(\phi) = 1$ on which there are two positive equilibria

$$I = \frac{-B \pm \sqrt{B^2 - 4AC}}{2A}.$$

This establishes our first main result.

Theorem 1. *The system* (5) *has a backward bifurcation at* $R(\phi) = 1$ *if and only if* $B < 0$ *when* β *is chosen to make* $C = 0$.

We can give an explicit criterion in terms of the parameters μ, γ, θ, ϕ, σ for the existence of a backward bifurcation at $R(\phi) = 1$. When $R(\phi) = 1$, $C = 0$ so that

$$(\mu + \theta + \sigma\phi)\beta K = (\mu + \gamma)(\mu + \theta + \phi). \tag{11}$$

The condition $B < 0$ is

$$(\mu + \theta + \sigma\phi) + \sigma(\mu + \gamma) < \sigma\beta K$$

with βK determined by (11), or

$$\sigma(\mu + \gamma)(\mu + \theta + \phi) > (\mu + \theta + \sigma\phi)\big[(\mu + \theta + \sigma\phi) + \sigma(\mu + \gamma)\big]$$

which reduces to

$$\sigma(1 - \sigma)(\mu + \gamma)\phi > (\mu + \theta + \sigma\phi)^2. \tag{12}$$

A backward bifurcation occurs at $R(\phi) = 1$, with βK given by (11) if and only if (12) is satisfied. We point out that for an SI model, where $\gamma = 0$, the condition (12) becomes

$$\sigma(1 - \sigma)\mu\phi > (\mu + \theta + \sigma\phi)^2.$$

But

$$\begin{aligned}(\mu + \theta + \sigma\phi)^2 &= \mu^2 + \theta^2 + \sigma^2\phi^2 + 2\mu\theta + 2\sigma\theta\phi + 2\mu\sigma\phi \\ &> 2\mu\sigma\phi > \sigma(1 - \sigma)\mu\phi\end{aligned}$$

because $\sigma < 1$. Thus a backward bifurcation is not possible if $\gamma = 0$, that is, for an SI model. Likewise, (12) cannot be satisfied if $\sigma = 0$.

If $C > 0$ and either $B \geqslant 0$ or $B^2 < 4AC$, there are no positive solutions of (9) and thus there are no endemic equilibria. Equation (9) has two positive solutions, corresponding to two endemic equilibria, if and only if $C > 0$, or $R(\phi) < 1$, and $B < 0$, $B^2 > 4AC$, or $B < -2\sqrt{AC} < 0$. If $B = -2\sqrt{AC}$ there is one positive solution $I = -B/2A$ of (9).

If (12) is satisfied, so that there is a backward bifurcation at $R(\phi) = 1$, there are two endemic equilibria for an interval of values of β from

$$\beta K = \frac{(\mu + \gamma)(\mu + \theta + \phi)}{\mu + \theta + \sigma\phi}$$

corresponding to $R(\phi) = 1$ to a value β_c defined by $B = -2\sqrt{AC}$. To calculate β_c, we let $x = \mu+\gamma-\beta K$, $U = \mu+\theta+\sigma\phi$ to give $B = \sigma x+U$, $\beta C = \beta K U + (\mu+\gamma)(\mu+\theta+\phi)$. Then $B^2 = 4AC$ becomes

$$(\sigma x + U)^2 + 4\beta\sigma K U - 4\sigma(\mu+\gamma)(\mu+\theta+\phi) = 0$$

which reduces to

$$(\sigma x)^2 - 2U(\sigma x) + \left[U^2 + 4\sigma(1-\sigma)(\mu+\gamma)\phi\right] = 0$$

with roots

$$\sigma x = U \pm 2\sqrt{\sigma(1-\sigma)(\mu+\gamma)\phi}.$$

For the positive root $B = \sigma x + U > 0$, and since we require $B < 0$ as well as $B^2 - 4AC = 0$, we obtain β_c from $\sigma x = U - 2\sqrt{\sigma(1-\sigma)(\mu+\gamma)\phi}$ so that

$$\sigma\beta_c K = \sigma(\mu+\gamma) + 2\sqrt{\sigma(1-\sigma)(\mu+\gamma)\phi} - (\mu+\theta+\sigma\phi). \tag{13}$$

Then the critical basic reproductive number R_c is given by

$$R_c = \frac{\mu+\theta+\sigma\phi}{\mu+\theta+\phi} \cdot \frac{\sigma(\mu+\gamma) + 2\sqrt{\sigma(1-\sigma)(\mu+\gamma)\phi} - (\mu+\theta+\sigma\phi)}{\sigma(\mu+\gamma)\phi}$$

and it is easy to verify with the aid of (13) that $R_c < 1$.

4. The bifurcation curve

In drawing the bifurcation curve (the graph of I as a function of $R(\phi)$), we think of β as variable with the other parameters μ, γ, σ, Q, ϕ as constant. Then $R(\phi)$ is a constant multiple of β and we can think of β as the independent variable in the bifurcation curve.

Implicit differentiation of the equilibrium condition (9) with respect to β gives

$$(2AI + B)\frac{dI}{d\beta} = \sigma I(K - I) + \frac{(\mu+\gamma)(\mu+\theta+\phi)}{\beta^2}.$$

It is clear from the first equilibrium condition in (8) that $I \leqslant K$ and this implies that the bifurcation curve has positive slope at equilibrium values with $2AI + B > 0$ and negative slope at equilibrium values with $2AI + B < 0$. If there is not a backward bifurcation at $R(\phi) = 1$, then the unique endemic equilibrium for $R(\phi) > 1$ satisfies

$$2AI + B = \sqrt{B^2 - 4AC} > 0$$

and the bifurcation curve has positive slope at all points where $I > 0$. Thus the bifurcation curve is as shown in Fig. 1.

If there is a backward bifurcation at $R(\phi) = 1$, then there is an interval on which there are two endemic equilibria given by

$$2AI + B = \pm\sqrt{B^2 - 4AC}.$$

The bifurcation curve has negative slope at the smaller of these and positive slope at the larger of these. Thus the bifurcation curve is as shown in Fig. 2.

The condition $2AI + B > 0$ is also significant in the local stability analysis of endemic equilibria.

Theorem 2. *An endemic equilibrium of* (5) *is* (*locally*) *asymptotically stable if and only if it corresponds to a point on the bifurcation curve at which the curve is increasing.*

Proof. The matrix of the linearization of (5) at an equilibrium (I, V) is

$$\begin{bmatrix} -2\beta I - (1-\sigma)\beta V - (\mu+\gamma) + \beta K & -(1-\sigma)\beta I \\ -(\phi + \sigma\beta V) & -(\mu+\theta+\phi+\sigma\beta I) \end{bmatrix}.$$

Because of the equilibrium conditions (8), the matrix at an endemic equilibrium (I, V) is

$$\begin{bmatrix} -\beta I & -(1-\sigma)\beta I \\ -(\phi+\sigma\beta V) & -(\mu+\theta+\phi+\sigma\beta I) \end{bmatrix}.$$

This has negative trace, and its determinant is

$$\begin{aligned} &\sigma(\beta I)^2 + \beta I(\mu+\theta+\phi) - (1-\sigma)\phi\beta I - (1-\sigma)\beta V \cdot \sigma\beta I \\ &\quad = \beta I\big[2\sigma\beta I + (\mu+\theta+\sigma\phi) + \sigma(\mu+\gamma) - \sigma\beta K\big] = \beta I[2AI + B]. \end{aligned}$$

If $2AI + B > 0$, that is, if the bifurcation curve has positive slope, then the determinant is positive and the equilibrium is asymptotically stable. If $2AI + B < 0$ the determinant is negative and the equilibrium is unstable. In fact, it is a saddle point and its stable separatrices in the (I, V) plane separate the domains of attraction of the other (asymptotically stable) endemic equilibrium and the disease-free equilibrium. □

5. Global behavior

In order to examine the global behavior of solutions of the system (5), we begin by showing that every solution with $I(0) \geqslant 0$, $V(0) \geqslant 0$ remains bounded for all $t \geqslant 0$. To show this we first show that the triangular region $I \geqslant 0$, $V = 0$, $I + V \leqslant K$ is an invariant set. If $I = 0$ then $I' = 0$ and a solution which reaches $I = 0$ must remain on $I = 0$. If $V = 0$ and $I < K$ then $V' > 0$ and a solution which reaches $V = 0$ cannot cross into the region $V < 0$. If $I + V = K$ then $(I+V)' = K' + V' = -(\mu+\gamma)I - (\mu+\theta)V < 0$ and a solution for which $I + V$ reaches K cannot cross into the region $I + V > K$. This shows that once a solution enters the region $I \geqslant 0$, $V \geqslant 0$, $I + V \leqslant K$ it remains in this region. If $I(0) + V(0) > K$, since $(I+V)' < 0$ so long as $I + V > K$ the solution must cross the line $I + V = K$ and enter the region $I = 0$, $V = 0$, $I + V \leqslant K$. Thus every solution with $I(0) \geqslant 0$, $V(0) \geqslant 0$ is bounded for $0 \leqslant t < \infty$.

The next step is to show that there are no periodic solutions of the system (5), which we do by means of the Dulac criterion [3] using the Dulac function $h(I, V) = 1/IV$. Because

$$\begin{aligned} &\left[\frac{\beta[K - I - (1-\sigma)V]I - (\mu+\gamma)I}{IV}\right]_I + \left[\frac{\phi(K-I) - \sigma\beta VI - (\mu+\theta+\phi)V}{IV}\right]_V \\ &\quad = -\frac{\beta}{V} - \frac{\phi K}{IV^2} + \frac{\phi}{V^2} = -\frac{\beta}{V} - \frac{\phi(K-I)}{IV^2} < 0, \end{aligned}$$

provided $0 < I < K$, $V > 0$, there is no periodic solution of (5) in this region.

To complete the analysis we now use the Poincaré–Bendixson theorem to conclude that every solution of (5) approaches an equilibrium. Since we know the possible equilibria and their domains of attraction if there is more than one equilibrium we now have a complete understanding of the behavior of solutions of the vaccination model (5).

6. Dependence on vaccination rate

In applications of the model (5) it may be useful to think of the parameters β, γ, μ, σ, K, and θ as fixed and ϕ as a control parameter. The parameters μ and K are properties of the population being studied but the parameter β may change as this population's behavior evolves. While it may be possible to change σ and θ by improving the vaccine and γ by improving treatment, the choice of vaccination rate ϕ is at the discretion of those attempting to use a vaccination program to control the infection.

If $R_0 < 1$ a vaccination program may control the infection more rapidly but the infection will die out even without vaccination. If $R_0^* = \sigma R_0 > 1$, a vaccination program will decrease the number of infectives but will not by itself be able to wipe out the infection. Thus from a public health point of view the interesting case is $R_0^* < 1 < R_0$ for which there is a value ϕ_0 which will decrease the basic reproductive number to 1, namely

$$\phi_0 = (\mu+\theta)\frac{\beta K - (\mu+\gamma)}{\mu+\gamma-\sigma\beta K} = (\mu+\theta)\frac{R_0-1}{1-R_0^*}. \tag{14}$$

Vaccination at a rate ϕ_0 is necessary to control the infection. This is also the interesting case from a mathematical point of view because if there is a backward bifurcation at $R(\phi)=1$ then control of the infection would require a further reduction of the basic reproductive number meaning a greater vaccination rate. To explore this question we re-examine the analysis of Section 3 viewing β as fixed and ϕ as variable.

From this perspective, Theorem 1 tells us that there is a backward bifurcation at $R(\phi)=1$ if and only if B, given by (10) is negative for $\phi=\phi_0$. Thus there is a backward bifurcation at $R(\phi)=1$ if and only if

$$\mu+\theta+\sigma\phi_0+\sigma(\mu+\gamma)-\sigma\beta K < 0.$$

Using (14), we may reduce this condition to

$$(1-\sigma)(\mu+\gamma)(\mu+\theta) < \sigma\big[\beta K-(\mu+\gamma)\big]\big[(\mu+\gamma)-\sigma\beta K\big],$$

or

$$(1-\sigma)(\mu+\theta) < \sigma(R_0-1)\big(1-R_0^*\big)(\mu+\gamma). \tag{15}$$

Since this cannot be satisfied when $\sigma=0$ there cannot be a backward bifurcation if σ is sufficiently small.

The maximum value ϕ_c of ϕ such that there are two endemic equilibria if (15) is satisfied is given by $B=-2\sqrt{AC}$, or $B^2=4AC$, $B<0$. The condition (13), now viewed as an equation for ϕ instead of as an equation for β is a quadratic equation in $\phi^{1/2}$. Then $\sqrt{\phi_c}$ is the smaller root of

$$\sigma\big(\sqrt{\phi}\big)^2 - 2\sqrt{\sigma(1-\sigma)(\mu+\gamma)}\sqrt{\phi} + \big[\mu+\theta+\sigma\big\{\beta K-(\mu+\gamma)\big\}\big] = 0. \tag{16}$$

After solving for ϕ_c we may then calculate the corresponding critical basic reproductive number $R_c = R(\phi_c)$. If there is a backward bifurcation at $R(\phi) = 1$ then R_c is the basic reproductive number which must be achieved by vaccination in order to control the infection. The calculation of ϕ_c and R_c in terms of the model parameters is technically messy but is easily done numerically for any given set of parameter values.

For example, with the parameter values $\beta K = 50$, $\mu = 0.1$, $\gamma = 12$, $\theta = 0.5$, $\sigma = 0.2$ we have $R_0 = 4.13$, $R_0^* = 0.83$ and $\phi_0 = 10.83$. Since $B < 0$ when $\phi = 3.0$ there is a backward bifurcation at $R(\phi) = 1$. We find from (16) that $\phi_c = 17.8$ and thence that $R_c = 0.93$. Thus while it is possible to bring the basic reproductive number down to 1 with a vaccination rate of 3.0, a much higher vaccination rate of 17.8 is needed to bring the infective population size down to zero. We could also find the value of ϕ_c by simulations of the system (5) with a range of values of the parameter ϕ. In doing this, if we are not careful to take the initial conditions in the domain of attraction of the endemic equilibrium we may be misled into thinking that the endemic equilibrium has disappeared. However, this process will indicate that for parameter values close to but more than ϕ_c the approach to the disease-free equilibrium is very slow, warning that in practice one should choose a vaccination rate substantially larger than the critical rate. Another way to determine ϕ_c would be to simulate using a bifurcation program such as AUTO or LOCBIF. We would find that with the given parameters the critical vaccination rate is 17.795, corresponding to an equilibrium $I = 8.55,\ V = 36.68$. Yue Xian Li has pointed out that there is also a Hopf bifurcation leading to periodic solutions for $\phi = 2.425$, corresponding to an equilibrium $I = -2.52,\ V = 50.53$. This equilibrium, of course has no biological significance.

7. Dependence of parameters on infective population size

We have studied the model (5) with parameters which are constant, or which perhaps may drift in response to external effects. However, it would be natural to expect that in the presence of infection individuals might decrease the number of contacts they make in unit time. Thus we might set $\beta = \beta_0 h(I)$, where $h(0) = 1$ and $h'(I) \leqslant 0$ and replace the model (5) by the model

$$\begin{aligned} I' &= \beta_0 h(I)\big[K - I - (1-\sigma)V\big]I - (\mu+\gamma)I, \\ V' &= \phi[K - I] - \sigma\beta_0 h(I)VI - (\mu+\theta+\phi)V. \end{aligned} \tag{17}$$

It is easy to calculate that the basic reproductive number of the model (17) is

$$R(\phi) = \frac{\beta_0 K}{\mu+\gamma} \cdot \frac{\mu+\theta+\sigma\phi}{\mu+\theta+\phi}.$$

Our goals are to obtain a necessary and sufficient condition for the existence of a backward bifurcation and to determine the stability properties of equilibria for this generalization of the original model (5). We write the model (17) in the form

$$I' = If(I, V, \beta), \qquad V' = g(I, V, \beta)$$

with

$$f(I,V,\beta) = \beta\big[K - I - (1-\sigma)V\big] - (\mu+\gamma),$$
$$g(I,V,\beta) = \phi[K-I] - \sigma\beta V I - (\mu+\theta+\phi)V,$$

and $\beta = \beta_0 h(I)$. The determinant of the matrix

$$A = \begin{bmatrix} If_I + \beta_0 f_\beta I h'(I) & If_V \\ g_I + \beta_0 f_\beta h'(I) & g_V \end{bmatrix}$$

of the linearization of (17) at an endemic equilibrium (I, V) is

$$I\big[f_I g_V - f_V g_I + \beta_0 h'(I)(f_\beta g_V - f_V g_\beta)\big].$$

If this determinant is negative the equilibrium is a saddle point.

The bifurcation curve for the model (17) is given by

$$f\big[I, V, \beta_0 h(I)\big] = 0, \qquad g\big[I, V, \beta_0 h(I)\big] = 0. \tag{18}$$

Since $R(\phi)$ is a constant multiple of β_0, we can obtain the sign of the slope of the bifurcation curve by calculating $dI/d\beta_0$. Implicit differentiation of (18) with respect to β_0 gives

$$\det A \cdot \frac{dI}{d\beta_0} = h(I)[f_V g_\beta - f_\beta g_V].$$

Since

$$f_V = -\beta(1-\sigma) < 0, \qquad f_\beta = K - I - (1-\sigma)V > 0,$$
$$g_V = -(\mu+\theta+\phi+\sigma\beta I) < 0, \qquad g_\beta = -\sigma I V < 0,$$

we have $f_V g_\beta - f_\beta g_V > 0$ and thus $dI/d\beta_0$ and $\det A$ have the same sign. This implies that an equilibrium corresponding to a point on the bifurcation curve where the slope is negative is a saddle point, just as for the simpler model (5). Because $f_I < 0$ and $g_V < 0$ it is clear that A has negative trace and thus every equilibrium for which the slope of the bifurcation curve is positive is asymptotically stable. The model extension of allowing the parameter β to be a decreasing function of I cannot destabilize an endemic equilibrium.

Another plausible extension would be to adjust the vaccination rate ϕ in response to the level of infection, that is to replace the constant ϕ by an increasing function $\phi(I)$. In addition, if the vaccination program is an education program designed to influence behavior of susceptibles it would be reasonable to suggest that an increase in the number of infectives might decrease σ, representing a strengthening of the effect of vaccination. Further, an increase in the number of infectives might cause a decrease in the rate θ at which vaccination effects are lost and even an increase in the recovery rate γ by causing more infectives to seek treatment. It is easy to verify that none of these changes can destabilize an endemic equilibrium.

The assumptions that the parameters of the model (17) depend on the size of the infective population is intended to model a situation in which increased levels of infection influence behavior in order to reduce the risk of becoming infected. Another attempt to include this sort of behavior in an SIS model has been the division of the population into a

highly active core group and a less active non-core group with recruitment from the non-core group into the core group which depends on the size of the infective population [2]. It has been shown in [2] that this structure admits the possibility of instability of an endemic equilibrium and oscillatory behavior. The vaccination model (17) does not support this possibility. Thus, the notion of a core group, which has been an important idea in the modeling of sexually transmitted diseases [8], is more general than the vaccination model in the sense of the variety of behavior admitted.

8. Conclusions

We have examined the simplest possible vaccination model and have shown by elementary algebraic means how to analyze the existence of multiple endemic equilibria when the basic reproductive number is less than 1. An equilibrium corresponding to a point on the bifurcation curve with negative slope is unstable, and an equilibrium corresponding to a point on the bifurcation curve with positive slope is asymptotically stable. Our model does not admit the possibility of oscillations about an unstable endemic equilibrium, which is supported by models with core and non-core groups having different contact rates.

We have considered only SIS models with no disease fatalities, which may be formulated as two-dimensional models when vaccination is included. In order to allow disease fatalities or to consider SIR models we would have to use three-dimensional models. The elementary approach used here can be applied to such models to obtain at least partial results.

The models we have examined could also be treated by using center manifold theory and normal forms. However, the required preliminary transformations would be at least as complicated technically as our approach. For models with more compartments, the analysis by elementary means becomes hopelessly complicated and a center manifold approach would be necessary. It would be of considerable interest to determine if the properties we have found in simple examples carry over to more complicated models.

Although the introduction of a vaccination policy may lead to backward bifurcations, we emphasize that it always decreases infective population size. The danger of a vaccination policy is that an unforeseen backward bifurcation may require a larger than expected vaccination fraction to control a disease. If a vaccine can be developed which is completely effective, this possibility does not arise, and a program which decreases the contact rate can also control a disease without leading to backward bifurcations. Nevertheless, a vaccination program, even one which is not fully effective, may be a useful approach in controlling infections.

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