

Letter to the Editor

The reinfection threshold does not exist

Recently, Gomes, White, and Medley (Gomes et al., 2004) have introduced a new concept to mathematical epidemiology, that they call the ‘reinfection threshold’. Gomes et al. claim that the ‘reinfection threshold’ serves to divide sharply the range of R_0 into two distinct regions that have very different epidemiological consequences. They claim that below the ‘reinfection threshold’ levels of infection will be low and that vaccination impact will be high, whereas above the ‘reinfection threshold’ levels of infection will be high and that vaccination programs will fail to protect (Gomes et al., 2004).

Gomes et al. illustrate their new concept for the case of a modified Susceptible–Infectious–Recovered (SIR) model (Eq. (5) in Gomes et al. (2004))

$$\begin{aligned} dS/dt &= e - R_0IS - eS, \\ dI/dt &= R_0I(S + \sigma(1 - S - I)) - I, \end{aligned} \quad (1)$$

where time t is measured in units of average duration of infection. Here e denotes the birth and death rates measured in the same time units ($0 < e < 1$), and σ is a dimensionless factor affecting the degree of partial immunity induced by a previous infection ($0 < \sigma < 1$). Gomes et al. present graphically (Fig. 8 of Gomes et al. (2004)) how the reinfection threshold manifests for the modified SIR model. In particular, they show the variation of the proportion of the population that is infectious at equilibrium versus the basic reproduction ratio (R_0) for three models: (i) the modified SIR model under consideration, (ii) a SIR submodel, and (iii) a Susceptible–Infectious–Susceptible (SIS) submodel. The authors claim that the two submodels are a good fit to the modified SIR model for certain R_0 regions, and thus Gomes et al. conclude that the epidemic thresholds of the two submodels are the same as the epidemic threshold of the modified SIR model. The epidemic threshold of the SIR submodel coincides with the epidemic threshold of the modified SIR model, but the SIS submodel has a different epidemic threshold, $R_0^{SIS} = 1/\sigma$, which Gomes et al. explicitly define as a ‘reinfection threshold’ for their modified SIR model at $R_{0\sigma} \equiv 1/\sigma$. When $R_0 = R_{0\sigma}$, Gomes et al. claim that the reinfection threshold phenomenon occurs.

However, we maintain that the ‘reinfection threshold’ is not a threshold at all. With the variation of a parameter (e.g., R_0), a threshold phenomenon of a given system manifests as follows: If a threshold phenomenon exists, then there exists a critical value of the parameter, at which a dramatic change in the behavior of the system takes place. For parameter values less than the critical value, the system behaves in a certain way, and for parameter values above the critical value, the system has qualitatively different behavior. At the critical parameter value, the system undergoes a discontinuity of some type. For example, the well-known epidemic threshold manifests as follows. For $R_0 < 1$, the proportion infectious at equilibrium is zero, while for $R_0 > 1$, the proportion infectious is positive. At $R_0 = 1$, the derivative of proportion infectious at the stable equilibrium with respect to R_0 is discontinuous. Using the terminology of bifurcation theory, the epidemic threshold of SIR-type models (i.e., that takes place at $R_0 = 1$) is known as a *transcritical bifurcation*. For the modified SIR model proposed by Gomes et al. no discontinuity exists at $R_{0\sigma}$; the threshold $R_{0\sigma} = 1/\sigma$ is extracted from a fit which has no relation to the dynamics of the modified SIR model under discussion. Analysis of the modified SIR model shows that for $R_0 > 1$ there exists a unique endemic equilibrium whose proportion infectious is given by

$$I = \frac{e}{2R_0\sigma} \left[\sqrt{\left(\frac{1 - R_0\sigma}{e} + \sigma\right)^2 + 4(R_0 - 1)\frac{\sigma}{e}} - \left(\frac{1 - R_0\sigma}{e} + \sigma\right) \right]. \quad (2)$$

I is continuous and differentiable at $R_0 = R_{0\sigma}$. The Jacobian matrix of the model evaluated at the endemic equilibrium for $R_0 > 1$ is

$$J = \begin{pmatrix} -R_0I - e & -R_0S \\ R_0I(1 - \sigma) & -\sigma R_0I \end{pmatrix} \quad (3)$$

and it can be verified to have negative trace and positive determinant for all the parameter values given by Gomes et al. (i.e., $0 < e < 1$, $0 < \sigma < 1$, and $R_0 > 1$). Thus, the endemic equilibrium remains stable for $R_0 > 1$, $0 < e < 1$ and $0 < \sigma < 1$. In fact, using Dulac’s criterion

(e.g., Strogatz, 1994) with the function $g(S, I) = 1/(SI)$ for the modified SIR model, one can easily verify that the endemic equilibrium for $R_0 > 1$, $0 < e < 1$ and $0 < \sigma < 1$ is globally stable. The only threshold phenomenon that the endemic equilibrium undergoes for $R_0 > 1$ is a transition from fixed point to spiral. Gomes et al. acknowledge this phenomenon explaining that it occurs when, with increasing R_0 , the eigenvalues of the Jacobian matrix evaluated at the endemic equilibrium become complex. However, it can be verified that this transition does not occur at $R_0 = R_{0\sigma}$. Therefore, $R_{0\sigma}$ does not represent a threshold of the modified SIR model as claimed by Gomes et al. At $R_0 = R_{0\sigma}$, the model behavior does not change abruptly, displaying discontinuity. No threshold phenomenon can be detected at this point.

Since the ‘reinfection threshold’ does not exist, then the claim made by the authors that the ‘reinfection threshold’ acts to divide sharply the range of R_0 into two distinct regions that have very different epidemiological consequences is not valid. The ‘reinfection threshold’ has no implications for public health policy. The modified SIR model behaves the same for R_0 values in the vicinity of $R_{0\sigma}$. No qualitative change in the epidemic spread occurs with decreasing R_0 below $R_{0\sigma}$, instead, what happens is a smooth variation of the endemic equilibrium with R_0 which cannot be characterized by a well-defined value $R_{0\sigma}$. Gomes et al. (2004) show that, if reinfection occurs, prevalence increases in a nonlinear manner as the severity of the epidemic increases (i.e., as R_0 increases). This epidemiological effect of reinfection has previously been reported by Blower et al. (1998) and Feng et al. (2000). Prevalence increases because reinfection serves to

“inflate” the incidence rate (Blower et al., 1998). As the magnitude of R_0 increases both the incidence rate and the “inflation” effect of reinfection on the incidence rate increases, hence prevalence increases in a nonlinear manner with R_0 (Blower et al., 1998; Gomes et al., 2004). Clearly reinfection can play an important role in the epidemiology of some diseases. Reinfection can increase incidence and prevalence; however, it is important to note that (at least for tuberculosis) it has been shown that the higher the susceptibility to reinfection the easier it will be to achieve control and/or eradication (Blower et al., 1998).

References

- Blower, S.M., Porco, T.C., Lietman, T., 1998. Tuberculosis: the evolution of antibiotic resistance and the design of epidemic control strategies. In: Horn, M.A., Simonett, G., Webb, G.F. (Eds.), *Mathematical Models in Medical and Health Sciences*. Vanderbilt University Press, Nashville & London.
- Feng, Z., Castillo-Chavez, C., Capurro, A.F., 2000. A model for tuberculosis with exogenous reinfection. *Theor. Popul. Biol.* 57 (3), 235–247.
- Gomes, M.G.M., White, L.J., Medley, G.F., 2004. Infection, reinfection, and vaccination under suboptimal immune protection: epidemiological perspectives. *J. Theor. Biol.* 228 (4), 539–549.
- Strogatz, S.H., 1994. *Nonlinear Dynamics and Chaos*. Addison-Wesley Publishing Co., New York.

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