Modeling of mixtures of two antibodies with their advantages and disadvantages in infectious diseases: the case of secondary dengue infections

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Abstract

The activity of a single antibody is easier to characterize than that of a mixture of antibodies whose behavior is difficult to predict. In some infectious diseases, such as secondary infection with dengue virus, pre-existing antibodies may cooperate to neutralize the virus (if it corresponds to the same serotype of the first infection) or pre-existing antibodies compete with new neutralizing antibodies and enhance the infection (if it is a different serotype). This phenomenon is called Antibody Dependent Enhancement (ADE). Here we present a mathematical model of the activity of a virus when bound by a mixture of two antibodies that takes into account the fact that the competing antibody pairs bind to distinct or overlapping epitopes of the virus. Hence, we consider three situations: i) purely independent binding, where the binding of one antibody has no effect on the other, ii) purely competitive binding, where the two antibodies cannot bind simultaneously, iii) an intermediate situation, where the two antibodies can bind simultaneously but with a synergistic interaction, i.e., the binding of one alters the binding or potency of the other. We apply this model to study the severity of secondary dengue infection in cooperative antibody (same serotype) and competitive antibody (different serotype) scenarios (we focus particularly on the second case: a mixture of neutralizing and enhancing antibodies). We then use this model to reproduce the dynamics of susceptible and infected target cells and the virus in cooperative or competitive scenarios between the two antibodies. The analytical study of the model (ODE) shows the existence of two equilibria: a disease-free and an endemic equilibrium. Using the concept of the basic reproduction number $\boldsymbol{\mathcal{R}_0}$, we perform the asymptotic stability analysis of the two equilibria.