Trade-off between antiviral and vaccinal effects of passive immunization

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Abstract

Passive immunisation (PI) with antiviral antibodies can induce two major effects. Its classical effect is antiviral drug-like: it reduces the viral load. Recent studies have highlighted a second, vaccinal effect of PI, where it modulates the endogenous humoral response, leading to an increase in the affinity of the antibodies produced for their target antigen. Here, using an *in silico* germinal centre (GC) model, we elucidate a trade-off between these effects. The vaccinal effect has been argued to arise from the preferential presentation of immune complexes formed by high affinity administered antibodies, which increase B cell selection stringency in the GC. Increasing passively administered antibody dosage or their affinity for the target antigen could increase immune complex formation and enhance GC output. Beyond a point, however, a strong antiviral effect could drive a substantial reduction in the target antigen, and hence immune complexes, lowering antigen availability in the GC. This lack of adequate antigen could cause the GC to be extinguished. An optimum dosage thus exists at which the GC output is maximum. We constructed detailed discrete generation Wright-Fisher simulations of the GC reaction to describe affinity maturation against a non-mutating target antigen. In an advance over previous formalisms, we coupled the GC reaction to within-host antigen dynamics, so that the antiviral and vaccinal effects could be explicitly and simultaneously described. The simulations predicted the existence of the trade-off between the two effects. Performing comprehensive parameter scans, we predicted PI dosing protocols that maximized the humoral response.