Impact of Entomological Heterogeneities on Dengue Virus Transmission

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Models of infectious disease often assume that the force of infection is independent of host age. This assumption has been found to be violated for many directly transmitted diseases, such as measles and mumps, but has rarely been examined in vector-borne systems, such as dengue (DEN). Mathematical theory indicates that by taking heterogeneities into account, control can be targeted to those areas or groups at highest risk and, thus, fewer resources overall will be needed to interrupt pathogen transmission. Theoretical analyses of diseases like malaria, canine leishmaniasis, human schistosomiasis, and human sexually transmitted diseases indicate that core groups exist in populations that are responsible for the majority of pathogen production. If cost effective, targeting those groups could result in more effective and efficient disease prevention. This kind of targeted control strategy is not likely to be adequately assessed without incorporating stochastic effects and geographic structure into the analysis.

Data from DNA fingerprinting analyses of mosquito blood meals indicate that the force of DEN and malaria infection may increase with human age; i.e., the biting rate of vectors increases with the age of human hosts. If infection risk correspondingly increases with age, models assuming an age-independent risk will underestimate the parasite's basic reproductive rate, extent to which vector populations need to be reduced to interrupt transmission, and proportion of the population that needs to be vaccinated to prevent disease. To test the importance of heterogeneity in exposure to vector-borne pathogens we are examining risk for DEN seroconversion by human age and its implications for disease prevention, in a cohort of ~ 4,000 schoolchildren and their families in Iquitos, Peru during 1999-2003. For the first 2.5 years, only DEN1 and DEN2 circulated. Those viruses were first detected in Iquitos during 1990 and 1995, respectively. Between introductions acute illness was not detected and 8% of the cohort seroconverted, as indicated by the plaque reduction neutralization test (PRNT). During a dengue epidemic in late 2001, patients clinically ill with DEN1, DEN2, and DEN3 (for the first time) infections were detected. Over 30% of study participants showed evidence of seroconversion by PRNT during the epidemic. To estimate risk for seroconversion by age, logistic regression analysis was performed. Although age was a significant predictor of seroconversion during the interepidemic period [odds ratio for ln(age) = 1.8, $p<0.001$], it was not during the epidemic (odds ratio = 0.9, $p>0.1$). The importance of spatial heterogeneity also varied between different patterns of virus transmission and disease. Quadrants of the city showed no significant difference in seroconversion risk during the interepidemic period (odds ratio = 1.2, $p>0.1$), but did differ during the epidemic (odds ratio = 1.5, $p<0.01$). The significance of these findings to the design and implementation of different dengue prevention strategies will be discussed.