

## VIRAL FACTORS IN DENGUE VIRUS TRANSMISSION

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The four serotypes of dengue virus are responsible for 50-100 million cases of dengue fever globally each year, including 204,000 reported in Brazil in 2005. In this continent, the autochthonous American (AM) genotype of dengue serotype 2 (DENV-2) has been largely replaced by the more virulent Southeast Asian (SEA) genotype, which can cause severe, hemorrhagic dengue. To investigate viral genetic factors contributing to this epidemiologic/ecologic displacement, we infected *Aedes aegypti* mosquitoes with six DENV-2 viruses, three from each of these two genotypes. In the mosquito midgut, SEA viruses produced significantly more viral RNA, measured by RT-PCR, than AM viruses, and SEA viral antigen accumulated at a significantly higher rate, determined by immunofluorescent antibody test. Dissemination to the salivary glands was significantly faster for SEA viruses than AM viruses: 50% of salivary glands were infected by day 7 postinfection with SEA viruses, compared to day 14 for AM viruses. Since virus in the salivary glands is required for transmission to a new host, this reduction in the time to transmission results in up to a 65-fold increase in the number of secondary cases caused by more virulent virus strains. We are now using chimeric dengue virus infectious clones to investigate the contribution of specific nucleotide and amino acids to these differences in dissemination and replication. The increased mosquito dissemination rate, coupled with an increased viral output from infected human cells (resulting in higher viremia), may explain the shifting epidemiology of dengue disease in the Americas.