

Dengue is becoming recognized as one of the most important vector-borne human diseases. It is predominant in tropical and subtropical zones but its geographical distribution is progressively expanding, making it an escalating global health problem of today. The disease is transmitted by mosquitoes, mainly domestic *Aedes aegypti*, that carry infectious virus. It is estimated that approximately 40% of the world's population is at risk of acquiring an infection, leading to millions of infections and one-quarter to one-half million hospitalized cases annually. Dengue disease presents with a wide spectrum of clinical manifestations, ranging from asymptomatic, undifferentiated mild fever, dengue fever, to dengue hemorrhagic fever (DHF) with or without shock (DSS), which is a life-threatening illness characterized by plasma leakage due to increased vascular permeability. Currently, there is no specific antiviral therapy or preventive vaccine available for dengue virus infection and supportive care with vigilant monitoring is the principle course of clinical practice. Since vector control programs have been largely unsuccessful in preventing outbreaks, vaccination seems to be the most viable option for prevention. The pathogenesis of dengue virus infection remains poorly understood, mainly due to the lack of a suitable animal model that can recapitulate the cardinal features of human dengue diseases. Multiple factors have been attributed to the pathological mechanism, mainly derived from in vitro studies, but highly relevant in vivo pathogenic parameters are difficult to obtain and measure. The presentation highlights challenging issues in pathogenic causes of dengue with data obtaining from translational research. With the poor vaccine efficacy in recent clinical phase 2B trials, suggesting that the importance of translational research in pathogenic causes of severe dengue and in dengue vaccine development.