Dengue is a disease that affects millions worldwide. It is caused by four viruses from a family of diverse, widespread viruses known as flaviviruses. Dengue has unique clinical, and potentially life-threatening features that pose the need for accurate and timely diagnosis during acute illness, a time of shifting viral and host prognostic and diagnostic markers. Moreover, these markers may be similar to those present during other viral diseases. Much progress has been made in the last decade, but the field continues to be one of challenges and opportunities for research and public health action.