

DIAGNOSIS (CDC – 1992)

Classical dengue fever may be confused with a variety of febrile illnesses, including influenza, measles, typhoid fever and malaria. DHF may be confused with sepsis, toxic shock and any of the viral hemorrhagic fevers including yellow fever. Diseases with specific treatments, such as bacterial meningitis, sepsis, malaria and Lassa fever, should be ruled out.

Specific diagnosis of dengue infection is made by isolating the virus from the patient's blood. Acute serum samples are inoculated into tissue cultures of mosquito cells or directly into live *Toxorhynchites* or *Aedes* mosquitoes. (66,67) Isolates can be identified from 2 to 7 days after inoculation depending on the actual technique used. (35) Viruses are most likely to be isolated from acute serum samples obtained within 5 days after the onset of illness. (34,35) Specific dengue serotypes can be identified by the indirect fluorescent antibody test, with the use of type-specific monoclonal antibodies on the isolated virus. (67)

Immunodiagnostic methods for determining dengue infection include detection of anti-dengue IgM and IgG by enzyme-linked immunosorbent assay (ELISA) and detection of hemagglutination inhibition antibody. Dengue-induced hemagglutination inhibition antibody cross-reacts broadly with other flaviviruses such as yellow fever and St. Louis encephalitis viruses. (35) Complement fixation and neutralization antibody tests are more specific than hemagglutination inhibition. (35) Most serologic screening for dengue infection is now done with an IgM ELISA. (35,68) With appropriately timed samples, the sensitivity and specificity of this test in diagnosing dengue infection appear to be high. In a review of 131 patients from whom dengue virus was isolated at the Centers for Disease Control, Dengue Branch, 96% of the 76 samples drawn between 7 and 20 days after the onset of illness were positive by IgM capture ELISA (DJ Gubler, G Kuno, I Gomez, et al. unpublished data). A study of the performance of IgM ELISA in Thailand showed the sensitivity of this test in convalescent samples to be 97%, and none of the samples from the 2 groups of noninfected controls (98 soldiers and 39 schoolchildren) were positive. (69)

The pattern of HI response has been used to classify dengue infections as primary or secondary, based on the concept that initial, or primary dengue infections tend to elicit lower HI titers than do secondary infections (subsequent infections with a different dengue serotype or antigenically related flavivirus). (28) IgM:IgG ratios as determined by ELISA may be an alternative method of distinguishing primary from secondary infections. (69,70) The rise in neutralizing antibody in primary infection is believed to be relatively type-specific and can be used to determine the infecting serotype. (35) In secondary infections, because the immunologic cross-reactivity to different flaviviruses and anamnestic responses may result in heterologous titer elevations, the only reliable method for determining the infecting serotype is virus isolation. (35)

In summary diagnosis of dengue infection is best accomplished by obtaining an acute serum sample within 5 days after the onset of illness for virus isolation and antibody testing and a convalescent serum sample 14 to 21 days after illness onset for detecting IgG antibody titer rise and/or the presence of antidengue IgM.