

## Abstract

Yellow fever (YF), dengue fever, and Japanese encephalitis (JE) are the three important reportable diseases belonging to Flavivirus family in Taiwan. It is important to develop a system that is able to differentially diagnose all flavivirus (YF virus, dengue virus, JE virus, and West Nile virus) potentially cause outbreaks in Taiwan. The serological diagnosis of flavivirus virus infection is rather difficult because multiple and sequential flavivirus infections occurred in the regions where two or more flaviviruses are co-circulating and high cross-reactivity of IgG antibodies to homologous and heterologous flavivirus antigens. We have developed a comprehensive serological system using ELISA to rapidly detect and differentiate various flavivirus infections for efficient disease surveillance. These included E/M-specific Capture IgM and IgG ELISA, E/M antigen-coated indirect IgM and IgG ELISA, and NS1-specific indirect IgG ELISA for the analysis of virus-specific antibodies in the convalescent phase sera. For acute phase sera, we have developed Real-time one-step RT-PCR to detect virus-specific nucleotide sequences. In order to setup a flavivirus reference lab with international standard, we have evaluated several commercial rapid test kits of dengue virus infection. Based on the combined analyses of Real-time one-step RT-PCR and E/M-specific Capture IgM and IgG ELISA, 95% of acute phase sera from confirmed cases can be identified as positive or probable cases within 24-48 hours of receiving serum samples. Therefore, we recommend that the insecticide spray will be hold for suspected cases unless laboratory diagnosis comes out positive or probable in areas with no indigenous dengue cases. We have found that serotype of primary dengue virus infection could be correctly identified when convalescent and postinfection sera were analyzed for NS1 serotype-specific IgG. In addition, E/M serotype-specific Capture IgM ELISA and NS1 serotype-specific Capture IgM ELISA can be reliably used to correctly identify dengue serotype from most of primary dengue patients and about 50% of secondary dengue patients. We plan to set up a flavivirus reference laboratory in CDC-Taiwan to play functional roles in the disease surveillance, vector control, serological and molecular diagnoses, and epidemiology. This flavivirus reference laboratory can be operated under the APEC and/or WHO platforms in the future. We will establish international cooperation with other flavivirus laboratories for joined research and information exchange. To start with, we plan to join WHO DengueNet surveillance network for global information exchange of dengue outbreaks in the near future.

**keywords : dengue fever ; NS1 ; Japanese encephalitis ; flavivirus**