登革熱

Dengue Fever

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Dengue is the most important mosquito-borne viral diseases globally, with dramatic increases in incidence in recent decades, placing half of the world's population at risk[1, 2]. It is estimated that 390 million dengue infections per year, of which 96 million manifest clinically[3]. Taiwan experienced the largest dengue fever (DF) outbreak of dengue virus (DENV) serotype 1 genotype 1 in 2014, a new imported dengue strain from Indonesia[4]. During this outbreak, 15,732 cases reported, 136 with dengue hemorrhagic fever (DHF), and 20 deaths (0.13%)[5]. Although the outbreak was coincidental with an accidental petrochemical explosion of gas pipelines in Kaohsiung, climate changes including rainfall and higher temperatures significantly correlated with the outbreak[5].

A revised WHO case classification was introduced in 2009, replacing the traditional 1997 classification of dengue fever and DHF/dengue shock syndrome with dengue with and without warning signs and severe dengue[6, 7]. The revised guidelines seek to enable correct triage and appropriate management by early recognition of warning signs. During the 2014 outbreak in Taiwan, 59 subjects had severe dengue with a mortality rate of 14.7%[8]. In contrasts to other endemic countries, most patients with severe dengue in Taiwan were elderly[8, 9]. Elderly dengue patients present atypically and are at higher risk of DHF, severe dengue and hospital-acquired infections[10]. Patients often manifest with massive gastrointestinal bleeding (33.3%) and bacteremia (25%) prior to death[11].

Current laboratory methods for dengue diagnosis includes direct methods by detection of viral components, such as virus isolation, virus RNA detection (RT-PCR), antigen detection (NS-1 based assays, by ELISA or lateral flow rapid tests) and immunohistochemistry[12]; and indirect methods by serological response, to detect production of immunoglobulins (IgM, IgG and IgA)[12].

Treatment of dengue remains supportive, with particular emphasis on careful fluid management[13, 14]. Development of any warning signs indicate the need for hospitalization[14]. The role of prophylactic platelet transfusion remains controversial[15, 16, 17]. Retrospective data suggested a lack of benefit from prophylactic platelet transfusion for severe thrombocytopenia in dengue patients without bleeding, and

showed potential harm by slowing recovery of platelet count to >50,000/mm3 and increasing length of hospitalization[18]. However, in Taiwan and Singapore, platelet transfusion was given to 13-50% of hospitalized dengue patients. A prospective, randomized study was conducted in Singapore to examine the safety and efficacy of prophylactic platelet transfusion in adults with dengue and severe thrombocytopenia (< 20,000/mm3) without bleeding, results are pending (ClinicalTrials.gov Identifier: NCT01030211).

As of June 2016, the first licensed dengue vaccine, Dengvaxia (CYD-TDV) by Sanofi Pasteur, is approved for use in individuals 9-45 years of age living in endemic areas, including Mexico, Brazil, El Salvador, the Phillipines and Costa Rica[2]. Approximately five additional dengue vaccine candidates are in clinical development, with two candidates (developed by Butantan and Takeda) expected to begin Phase III trials in early 2016 [19]. The dengue vaccine developed by the U.S. NIH confers 80-100% protection from all four serotypes of dengue virus in clinical trials conducted in the U.S., Brazil, Thailand and Bangladesh. The U.S. and Taiwan signed a dengue vaccine development agreement during 2016 World Health Assembly, to conduct clinical trials for the world's first dengue vaccine for the elderly.

In conclusion, dengue fever is a major public health problem with substantial social and economic effect because of increased geographical extension, number of cases, and disease severity[6]. A safe, effective and affordable dengue vaccine against the four strains would represent a major advance for the control of the disease and could be an important tool for reaching the WHO goal of reducing dengue morbidity by at least 25% and mortality by at least 50% by 2020.

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