

ETIOLOGICAL STRUCTURE OF ACUTE ENCEPHALITIS IN CHILDREN AND IMMUNIZATION PROGRAM CONCERNS AT THE NATIONAL HOSPITAL OF PAEDIATRICS IN VIETNAM

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Encephalitis is defined by the presence of an inflammatory process of the brain in association with clinical evidence of neurologic dysfunction. Among the pathogens that are reported to cause encephalitis, the majority are viruses. There are many benefits for the management of encephalitis if the cause is identified. However, despite extensive testing, the etiology of encephalitis remains unknown for the majority of patients. There are several causes of encephalitis that are now considered to be vaccine-preventable, that is, Japanese encephalitis (JE), measles, mumps, polio, rubella, and varicella. Other causes of encephalitis may include autoimmune disease; bacteria, such as Lyme disease, syphilis, and tuberculosis; and parasites, such as roundworms, and cysticercosis. In Vietnam, JE remains the most common cause of encephalitis. This is also one of the common etiologic pathogen of encephalitis in many ASEAN countries, as well as in India and China (Tuan *et al*, 2007; Sunara and Touch, nd).

Our study's research questions included: 1) what is the current etiological structure of viral encephalitis in Vietnamese children, and how has it changed over time?; and 2) has the national vaccination program reduced the number of children

developing encephalitis in Vietnam?

The objectives of the study were to compare the etiological structure of viral encephalitis in children at the National Hospital of Paediatrics, Hanoi, Vietnam in 2012 to the period of 2008-2012 and to analyze the National Immunization Program statistic data of Vietnam (MOH, 2008). The diagnostic criteria used were based on the "Guidelines for diagnosis and treatment of acute viral encephalitis" delivered by the Vietnamese Ministry of Health in 2008 and the guidelines of the Infectious Diseases Society of America (IDSA) (Tuan *et al*, 2007; IDSA, 2008). The etiology of the encephalitis was confirmed by the results of immunological and biomolecular tests on cerebrospinal fluid (CSF) and serum samples, such as polymerase chain reaction (PCR) and enzyme-linked Immunosorbent assay (ELISA) techniques.

During 2012, there were 565 cases admitted to the NHP with the diagnosis of "acute encephalitis." The causative agents were identified in only 147 patients (26%). The causative agents were JE virus 40.8%, herpes simplex virus 31.9%, enterovirus 14.3%, cytomegalovirus 4.8%, Epstein barr virus 4.8%, and mumps 3.4%. The incidence of JE was found to peak during the summer months of June to September

2012. Other causes of encephalitis were found to occur at similar frequencies sporadically all year round.

When comparing the data during 2008-2012, the overall incidence of encephalitis had not reduced over time. JE was still a major cause of encephalitis; however, numbers seemed to be reducing. Encephalitis caused by HSV1 appears to be on the increase. There was an outbreak of rubella in Vietnam in 2011, in which 103 cases were considered as encephalitis caused by this virus. Following this outbreak, all Vietnamese children were vaccinated against rubella, and since then, no case of encephalitis suspected by rubella has been found. Enterovirus (EV) is another virus that appears to be increasing in incidence and has also been found to be the cause of outbreaks of encephalitis.

In Vietnam, the expanded program on childhood immunization followed the World Health Organization recommendations. Children are vaccinated in accordance with the expanded vaccination program with 9-11 vaccines, depending on the epidemic situation of each province. The vaccines that routinely given to all infants are BCG, hepatitis B, diphtheria, tetanus, pertussis, Haemophilus influenzae type, measles-mumps-rubella, Japanese encephalitis, and varicella. Rotavirus, hepatitis A, influenza, and pneumococcal vaccines are recommended based upon the data on incidence and outbreaks in different areas. Meningococcal and typhoid vaccines are also given only in the special circumstances when an outbreak occurs.

In general, vaccine coverage is still inadequate; with significantly lower cover-

age in rural areas, which also depends on the Local Authority governing the vaccination program. Vaccines are obtained from both domestic and overseas sources. In most cases, the vaccines are received on application to receive free vaccines from government. Public opinion has also been found to play an important role in the reduction of disease rates. For example, if deaths follow HBV vaccinations and cause concern among the community, vaccination uptake rates could significantly decrease.

The immunization practices regarding encephalitis are as follows. Vietnam began domestically producing JE vaccines in 1993. The JE vaccine was added to the expanded vaccination program in 1997. In some areas of Vietnam prior to 2012, patients had to pay for vaccinations themselves. Since 2012, all vaccinations for JE for children below 5-years-old have been free of charge. Some problems associated with the vaccination program have been the non-completion of the vaccination course for children who move residence, and/or whose parents are unwilling for them to have the full, 3-injection course (with the misunderstanding that one injection is adequate).

Coverage rates have been found to vary, from 65% to 90%, according to the area. Currently, the EV71 vaccine is not available in Vietnam. However, the government decided to develop the vaccine in-country to address the increasing incidence as well as the morbidities and mortalities from EV71 in the recent past. During the first seven months of 2012, of hand-foot-and-mouth disease reported cases numbered 63,780, despite extensive preventive

efforts. Approximately 58.7% of those and most of the mortalities caused by EV71, emphasizes the need for EV71 vaccine development.

The EV 71 vaccines are still in the preclinical stages in Vietnam. There is excitement about the first inactivated EV71 vaccine that has now reached clinical Phase 3 trials in China (Zhu *et al*, 2013a,b). That study was conducted with more than 10,000 children aged 6-35 months in China. The study indicated vaccine efficacy against EV71-hand-foot-and-mouth disease of 90.0% (95%CI: 67.1-96.9) and against EV-71 associated disease of 80.4% (95% CI: 58.2-90.8) (Zhu *et al*, 2013b).

In summary, 565 cases of children with encephalitis were admitted at the National Paediatric Hospital, Hanoi in 2012. The common causes of encephalitis were JE, HSV1, and EV. The disease predominantly occurs in the summer months, particularly from JE virus. Vietnam's vaccination program needs to be strengthened to decrease encephalitis rates and associated morbidity and mortality rates. Furthermore, other vaccines, which could help prevent encephalitis such as rubella, measles, and mumps, should also be implemented nationwide. The development of the EV71 vaccine in Vietnam remains extremely important and should continue.

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