

87) had nonspecific illnesses of fever, sore throat or gastrointestinal discomfort and only 8% (7/87) had hand, foot and mouth disease.

According to our previous clinical studies, symptomatic enterovirus 71 (EV71) infection can progress through four stages: HFMD/herpangina (Stage 1), CNS involvement (Stage 2), cardiopulmonary failure (Stage 3), and convalescence (Stage 4). Most EV71 cases in those studies stayed at stage 1, some progressed to Stage 2 and a few would advance to the most severe condition, Stage 3. We did autopsy for an EV71 fatal case. The brainstem pathology showed neuronophagia and immune-histochemical stain showed EV71 infected neurons, neuron loss. The most significantly risk factors associated with CNS involvement were fever > 3 days and lethargy. Risk factors for pulmonary edema after CNS involvement are hyperglycemia, leukocytosis, and limb weakness. Hyperglycemia is the most significant prognostic factor for pulmonary edema.

In the follow-up study of severe EV71 cases, 18 (64%) of the 28 cases with cardiopulmonary failure after CNS involvement had limb weakness and atrophy, 17 (61%) required tube feeding, and 16 (57%) required ventilator support. Delayed neurodevelopment was found in only 1 (5%) case with severe EV71 CNS involvement and in 21 (75%) cases with cardiopulmonary failure ($p < 0.001$). Children with cardiopulmonary failure after CNS involvement scored lower on intelligence tests than children with CNS involvement alone ($p = 0.003$). Among patients with CNS involvement alone, children infected at ages younger than 2 had lower verbal comprehension than children infected at older ages ($p = 0.009$). EV71 CNS involvement with cardiopulmonary failure may be associated with neurological sequelae, delayed neurodevelopment and reduced cognitive functioning. Children with CNS involvement without cardiopulmonary failure did well in neurodevelopment. The rate of elevated attention-deficit/hyperactivity disorder-related symptoms among children with enterovirus 71 central nervous system infection was 20%, whereas that rate among matched control subjects was only 3%. They also had more internalizing problems. Enterovirus 71 central nervous system infection may affect long-term regulation of attention and emotion and cause hyperactivity-impulsivity in children.

In conclusion, most EV71 cases are HFMD and recovered. Some (possible 1%) progressed to Stage 2 encephalomyelitis, and 20–30% of cases with encephalomyelitis may progress to cardiopulmonary failure because of brainstem encephalitis and SIRS. Even under modern intensive care, 30% of them would die and many of the survivors would have neurological sequelae. After poliovirus was nearly eradicated by vaccination, EV71 is now considered one of the most important enteroviruses. Therefore, continuous surveillance of its occurrence, investigation of its virulence and its transmission are all warranted to improve the future control. Development of EV71 vaccine are ongoing and we hope for success in the near future.

SYMPOSIUM 11 (SP 11)

EBOLA VIRUS DISEASE

SP 11-1

WHAT WENT WRONG IN WEST AFRICA AND WHERE ARE WE HEADED

Dale Fisher, *Professor of Medicine and Head of the Infectious Diseases Division at the National University Hospital, Singapore*

The Ebola outbreak in West Africa is simply staggering in so many respects. Originating in a rural town Meliandou in Guinea it could have been like any other Ebola outbreak. A single animal to human transmission with some degree of human to human spread most notably at funerals to family members or hospitals to health care workers. Typical outbreaks last months, they are contained fairly locally and eventually controlled by a fairly standard approach rolled out by MSF. However this outbreak is different with never before seen scale in terms of case numbers and deaths. There are many reasons to explain this outcome almost all related to the setting in this part of Africa and human factors.

Movement in this area is not difficult and as people become frightened and witness death it is not surprising that people drive across the country to see family despite being sick and despite the advice. For this reason the geographic spread has been difficult to curtail, although limiting it (by and large) to the 3 most affected countries is a true success story of work done in Mali, Nigeria and other bordering countries.

Infection control, case management and social mobilization efforts have had to likewise geographically pursue the outbreak. Necessarily this has seen the evolution of novel and community based case management strategies as the

community is the regular front line while waiting for treatment units to be established.

There is belief that zero cases can be reached and that Ebola virus disease will not become endemic but that is not guaranteed and ongoing efforts that continuously adapt to circumstances will need to be maintained for some time yet.

SP 11-2

EBOLA BIO-SAFETY AND LABORATORY TESTING

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Ebola outbreak in 2014–2015, the largest in history of Ebola infection, mainly affected a few countries in West Africa. According to the World Health Organization, over 21,700 Ebola cases have been reported in nine countries and over 8,640 people have died. According to the United States Centers for Disease Control and Prevention (CDC), a few imported cases and locally acquired cases in healthcare workers were reported in the US (<http://www.cdc.gov/vhf/ebola/outbreaks/2014-west-africa/index.html>).

CDC provided the infection prevention and control recommendations and guidance for caring hospitalized patients under investigation (PUI) for Ebola Virus Disease (EVD) in U.S. hospitals. It's important to follow standard contact and droplet precautions when caring for a PUI or patient with confirmed EVD. CDC updated personal protective equipment (PPE) portion of the guidance based on the experience of treating patients with EVD in US hospitals including Emory University Hospital. The procedures for putting on (Donning) and removing (Doffing) is posted (<http://www.cdc.gov/vhf/ebola/hcp/procedures-for-ppe.html>).

Procedures that could increase environmental contamination with infectious materials such as body fluid and contaminated medical supplies and equipment or create aerosols should be minimized. CDC lists key components of standard, contact, and droplet precautions recommended for healthcare personnel working in healthcare settings who have the potential for exposure to patients and/or to infectious materials. For patient care considerations, it is best to limit the use of needles and other sharps as much as possible, keep the phlebotomy, procedures, and laboratory testing to the minimum necessary for essential diagnostic evaluation and medical care.

Rapid laboratory tests for diagnosis of Ebola and/or malaria have been developed and used. In addition, rapid tests using point-of-care type analyzers for monitoring electrolytes, respiratory status, liver function, plates are available for patient management.

SP 11-3

FIGHT AGAINST EBOLA: PREPAREDNESS AND PUBLIC HEALTH RESPONSE

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On August 8, 2014, the World Health Organization announced the outbreak of Ebola virus disease (EVD) in West Africa a public health emergency of international concern under the authority of the International Health Regulations (2005) and issued recommendations for affected and non-affected countries regarding preparedness and response against Ebola. Countries without domestic Ebola transmission are requested to establish core capacities to prevent, detect, characterize and respond quickly, efficiently and in a coordinated manner to the EVD threats in order to reduce mortality and morbidity. A comprehensive risk assessment based on well-established criteria would guide countries to determine timing to active the preparedness and response plan.

This talk will address international and domestic preparedness and response against Ebola using the successful story of Nigeria during July 23 to October 20, 2014, as an example. A key element for successful EVD control was the rapid response for activating an Ebola Emergency Operations Center (EOC) by using the Incident Management System (IMS). The EOC effectively coordinated all available public health resources and applied real-time technology in contact tracing and logistics management. Difficult contact tracing was handled with the assistance of psychosocial support team and social mobilization by conducting house-to-house visiting. The alert and rumor surveillance helped discover new cases.

In response to the Ebola outbreak, the Taiwan Centers for Disease Control (TCDC) had issued travel alert and taken measures for preparedness and response since early April, 2014. On August 8, TCDC upgraded the response