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Zika virus and microcephaly: why is this situation a PHEIC?

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When the Director-General of WHO declared, on Feb 1, 2016, that recently reported clusters of microcephaly and other neurological disorders are a Public Health Emergency of International Concern (PHEIC),[1] it was on the advice of an Emergency Committee of the International Health Regulations and of other experts whom she had previously consulted. We are the members of the Emergency Committee, and we were identified by the Director-General from rosters of experts that had been submitted by WHO Member States.

Our advice to declare a PHEIC was not made on the basis of what is currently known about Zika virus infection. During our discussions it became clear that infection with the Zika virus, unlike other arbovirus infections including dengue and chikungunya, causes a fairly mild disease with fever, malaise, and at times a maculopapular rash, conjunctivitis, or both.[2] Additional information from previous outbreaks suggested that about 20% of people infected with Zika virus develop these symptoms, and that the rest are asymptomatic.[2] Fatality from Zika virus infection is thought to be rare.[2] Our advice to declare a PHEIC was rather made on the basis of what is not known about the clusters of microcephaly, Guillain-Barré syndrome, and possibly other neurological defects reported by country representatives from Brazil and retrospectively from French Polynesia that are associated in time and place with outbreaks of Zika infection.[3,4]

The Emergency Committee meeting was convened rapidly by WHO. We were contacted by the Director-General 4 days before the Emergency Committee meeting, and by the time we met WHO had thoroughly prepared the meeting. At the start of the meeting, the WHO legal counsel provided three criteria to help the Emergency Committee decide whether the present situation was a PHEIC. A PHEIC must: (1) constitute a health risk to other countries through international spread; (2) potentially require a coordinated response because it is unexpected, serious, or unusual; and (3) have implications beyond the affected country that could require immediate action.

Representatives from four countries (Brazil, El Salvador, France, and the USA) that have had either outbreaks or importations of Zika virus, and a group of arbovirus specialists, took part in the meeting. Some of them had been working for the past months with the WHO Regional Office in the Americas on the Zika virus outbreaks, and before that on those caused by the dengue and chikungunya viruses. During one country representative's account of Zika virus in French Polynesia, robust and convincing retrospective data were presented about an increase in neurological disorders during the period when there was an outbreak of Zika virus. Other presentations described current clusters of microcephaly and limited information about Zika virus identified in fetuses or infants, pointing out the temporal association with circulation of the Zika virus.

After these country presentations, and comments by the assembled arbovirologists, we were able to discern as a committee, and then agree unanimously in an initial poll, that the clusters of microcephaly and neurological disorders, and their possible association with the Zika virus, constituted a PHEIC. Upon further discussion, it became clear that there was no standard surveillance case definition for microcephaly. The first recommendation of the PHEIC was to call for standardised and enhanced surveillance of microcephaly in areas of known Zika virus transmission. Such surveillance is not only important in countries where there are current and recent outbreaks, but is also retrospectively relevant in African and Asian countries where outbreaks have been occurring since the Zika virus was first identified in 1947.[5,6] Further, we felt that surveillance data should become available within months.

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Our second recommendation under the PHEIC is for increased research into the aetiology of confirmed clusters of microcephaly and neurological disorders to determine whether there is a causative link to Zika virus, other factors, and cofactors. Neurological fetal defects occur with other viral infections such as rubella, which are preventable by vaccine,[7] and could also be caused by factors such as exposure to chemicals or toxins and other environmental factors.[8,9] We understood that this PHEIC recommendation will take much longer to implement than surveillance, and will require accumulation of scientific evidence from post-mortem analyses, case-control studies, and other studies as recommended by experts in microcephaly, obstetric and neonatal medicine, and public health. Part of our discussion also included the need for development of an animal model, and of the possibility of eventually proving Koch's postulates.

After our discussion on the PHEIC, there was unanimous agreement to make recommendations for precautionary measures to prevent arboviral infection. In addition to being good public health practice, which would be intensified should the clusters of microcephaly and other neurological disorders be linked to the Zika virus, they should also result in the prevention of chikungunya and dengue outbreaks.[10–12] Among those recommendations were the need for: stronger surveillance of Zika virus infection with the rapid development and sharing of diagnostics suitable for seroprevalence studies and that do not require antigen presence; improved communication about the risks of outbreaks of Zika and other arboviruses; implementation of vector control measures to decrease exposure to bites from the *Aedes aegypti* mosquito; and guidance to be available to pregnant women so that they better understand the present situation and are empowered to make a decision about personal protection and pregnancy.

We also provided longer-term advice to the Director-General to continue discussions with vaccine developers and regulatory agencies that WHO had already begun, to provide regular and clear guidance on risks associated with travel, and to ensure that all countries share data as they work with WHO to address the recommendations of the PHEIC.

Since the Emergency Committee meeting we have continued to communicate among ourselves, and our hope is that WHO will work in the way that successfully led to control of the outbreak of severe acute respiratory syndrome (SARS) in 2003 when WHO established virtual networks of experts around the world who worked by telephone and the internet to collaborate in surveillance, clinical management, and research.[13–15] The networks established during the SARS outbreak worked in environments that provided the confidentiality and security necessary to freely share data used for improving public health. With policies recently developed by *The Lancet* and other medical journals to accept for publication data that may have previously been shared openly for better outbreak prevention and control, we believe that there should be no excuse for not creating such an environment for sharing of data collected under the PHEIC.[16,17]

Since the Director-General declared the PHEIC on microcephaly and neurological disorders, many of us have had questions about how our recommendation relates to the PHEIC called by the Director-General for the 2014 Ebola outbreaks in west Africa based on the recommendation of a different Emergency Committee. The answer to us is clear. The Director-General declared the Ebola outbreaks a PHEIC because of what science knew about the Ebola virus from many years of research during outbreaks in the past, whereas she declared the current PHEIC because of what is not known about the current increase in reported clusters of microcephaly and other disorders, and how this might relate to concurrent Zika outbreaks.

We were told by the Director-General that she would convene us again within 3 months to reassess the situation, as required under the International Health Regulations. We are confident that virtual meetings will allow us to review global collective action and to learn from WHO about progress in understanding the present situation of microcephaly and neurological disorders and progress in implementation of the precautionary and preparatory measures related to Zika.

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We are all members of the WHO Emergency Committee on Zika virus and observed increase in neurological disorders and neonatal malformations. We declare no competing interests.

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New WHO guidelines on emergency triage assessment and treatment

For many decades WHO has provided invaluable guidelines for the health care of children in low-income and middle-income countries where resources are limited. The principles behind these guidelines are that they use a minimum number of clinical signs to identify the condition in question and classify its severity, are simple to understand and implement, use essential medicines and appropriate technology, and are fit for the context for which they are designed. Historically, the most successful clinical guidelines have been on the use of simple interventions for common diseases, including oral rehydration salts for dehydration from gastroenteritis and antibiotics for pneumonia.[1,2]

Much has changed in the 40 years since the first WHO guidelines for low-income settings. National economies and health-care systems are now more dynamic, heterogeneous, and ambitious. Clinical guidelines are recognised as having an important role in maintaining quality of care in richer nations as well as in low-income countries. And many agencies and professional groups have developed their own guidelines that are easy to access on the internet. Diseases and our understanding of pathophysiology have changed too: pneumonia epidemiology, for example, is developing with the introduction of conjugate vaccines and the increasing prominence of viral syndromes; antimicrobial resistance has emerged for pathogens which cause neonatal sepsis, meningitis, tuberculosis, and malaria; and the International Classification of Diseases 10th Revision now includes more than 69 000 separate diagnoses. These changes to health in the 21st century have led to the development of guidelines for more complex

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