# The Zika virus public health emergency: 6 months on

**This year, the global health community has given top priority ranking on many research and public health fronts to its battle against the spreading Zika virus epidemic. John Maurice reports.**

Feb 1 was a landmark day in the history of the current Zika epidemic. It was the day Margaret Chan, Director-General of WHO, declared to the world that the clusters of microcephaly and other neurological disorders reported by several countries and occurring in the same geographic areas as the epidemic constituted a Public Health Emergency of International Concern (PHEIC). The declaration unleashed a surge of epidemic response activity around the world. This was the fourth public health event to earn PHEIC status, after swine flu in 2009, and polio and Ebola in 2014. Chan made the declaration on the advice of an emergency committee convened to guide her decisions on the epidemic. "The committee recommended the declaration", David Heymann, chair of the committee and head of the Centre on Global Health Security at Chatham House, London, UK, tells *The Lancet*, "because there was an urgent need to know whether there was an epidemiological link between the neurological disorders and the rapidly spreading Zika epidemic".

In early February, Zika virus was circulating in 33 countries. Two of those countries were seeing babies born with undersized (microcephalic) heads and three had a cluster of the normally rare Guillain-Barré syndrome. 6 months on, as of July 21, the virus is present in 63 countries, of which 13 are reporting microcephaly cases and 15, cases of Guillain-Barré syndrome.

## What do we know now?

However, the numbers tell only a part of the story. "The main development since the PHEIC declaration", says Heymann, "is the accumulation of evidence that the cases of microcephaly and other neurological disorders that we're seeing are caused by the Zika virus. The case-control studies that could give absolute, definitive proof are ongoing but will take a long time to complete. However, for the scientific community as a whole, all the circumstantial evidence put together leaves no doubt that the Zika virus is causing these neuropathologies." On April 13, the US Centers for Disease Control and Prevention announced that its scientists had come to the same conclusion.

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Bruce Aylward, Executive Director ad interim of WHO's Outbreaks and Health Emergencies Cluster, looks back on the past 6 months as a period of "great scientific progress in our understanding of the epidemiology and pathogenesis of the virus and in knowing what works and doesn't work in the management of the epidemic. What impresses me most is the short time it took for scientists to reach a consensus that Zika is the culprit. The PHEIC declaration sparked an explosion of scientific work which is filling the gaps in our understanding of the virus and on possible ways of preventing its devastating effects."

Since the PHEIC declaration, scientists have made several unexpected discoveries about the Zika virus. Sexual transmission, for example, can occur from men to women and possibly from women to men. Brain tissue death, eye lesions that threaten blindness, and hearing problems are thought to be more common than microcephaly in affected infants. Births of unusually small babies are also believed to occur more often than births of babies with microcephalic heads in women infected with the Zika virus.

## Unanswered questions

Many knowledge gaps, however, remain. Meetings of WHO's emergency committee on March 8 and June 4 called for data on several points: the genetic sequences and clinical effects of the different Zika virus strains, the neuropathology of microcephaly, the natural history of Zika virus infection, the implications of asymptomatic infection (especially in pregnant women), the persistence of virus excretion, the rates and implications of asymptomatic infection (only 20% of infected people are believed to develop the normally mild symptoms of Zika virus disease), the persistence of viral infection, and the identification of the different strains of *Aedes aegypti* mosquitoes responsible for Zika virus transmission and the sensitivity of these mosquitoes to insecticides. "The research needed to answer these and other questions", says Heymann, "is complex and costly but steady progress is being made".

Aylward has two "extremely frustrating" knowledge gaps. "We know that a pregnant woman infected with the Zika virus runs a risk of having a microcephalic baby but we can't tell her how high that risk is and how it might evolve over the course of

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For the **paper in Science** see http://science.sciencemag.org/content/early/2016/07/13/science.aag0219.full

Associated Press

**A Brazilian mother feeds her son who was born with microcephaly, Feb 4, 2016**

her pregnancy. And we don't know what the full spectrum of the Zika-caused congenital defects will be. Will apparently unaffected children whose mothers had Zika in pregnancy develop normally? Will they be able to walk and talk normally? Will they be mentally impaired or have other problems that only become evident years later?"

Risk assessment occupied a good part of the June emergency committee's agenda, particularly the risks for travellers to the forthcoming Olympic and Paralympic games to be held in Brazil, the country with the highest number of Zika cases. The committee members advised Chan that the risk to an individual of contracting Zika virus disease in an area where the virus is circulating is probably the same whether or not the individual is in a mass gathering such as the Olympics. Moreover, the games are taking place in Rio de Janeiro's winter season, when mosquito vectors of flaviviruses such as Zika are thought to be at their lowest biting levels.

## Weapons against Zika virus

One area where the post-PHEIC scientific "explosion" has produced tangible progress is in research for tools to combat Zika virus. There are currently about 40 vaccines at various stages of development in the pipelines of vaccine developers in Austria, Brazil, Canada, France, India, and the USA. Since June 20, two vaccines have been given regulatory approval by the US Food and Drug Administration to enter phase 1 trials in people. One vaccine has been made by a US–South Korean–Canadian team and a second, by a team from the US National Institute of Allergy and Infectious Diseases.

Most vaccine observers, however, believe it will take anywhere from 2–3 years to have a vaccine that would be used in non-pregnant women, women of childbearing age, and adolescents. Some critics wonder how useful a vaccine will be in 2–3 years, when the Zika endemic is likely to have run its course. A modelling study reported in *Science* on July 14 by a team at Imperial College London, UK, suggests that the current epidemic will "burn itself out" within 1–3 years. "Because the virus is unable to infect the same person twice", team leader Neil Ferguson explains, "the epidemic reaches a stage where there are too few people left to infect for transmission to be sustained". The team's model also predicts that efforts to slow the spread of the epidemic might actually prolong it. "Slowing transmission between people means the population will take longer to reach the level of herd immunity needed for transmission to stop. If our projections are correct, cases will have dropped substantially by the end of next year, if not sooner. This means by the time we have vaccines ready to be tested, there may not be enough cases of Zika in the community to test if the vaccine works."

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Research on vaccines should definitely be pursued, Heymann insists. "Herd immunity would not last indefinitely, and if the Zika virus continues to circulate at low levels, it could periodically cause repeated outbreaks as herd immunity wanes and new susceptible cohorts develop. Rubella caused similar periodic outbreaks before a vaccine was developed. Today, its vaccine prevents infection of pregnant women and the neurological effects on their fetuses."

Diagnostic tests are also needed and several promising tests are emerging from current research. Seven tests are available for laboratory use, 13 have received regulatory approval, and 16 have been submitted to WHO's fast-track assessment procedure. WHO is giving preference to point-of-care tests that detect and differentiate between ongoing and previous Zika infection, and also tests that can detect three closely related flaviviruses: Zika, dengue, and chikungunya.

Attempts to reduce the population of Zika-bearing mosquitoes have had a chequered history. In countries that can afford it, such as the USA, pesticide spraying from aeroplanes has been highly successful, but this is too costly for most resource-strapped countries. Aylward sees only limited progress in developing effective mosquito control methods. "There has definitely been a lot of work done in testing different strategies to battle the mosquito vectors of Zika but none of these strategies has made significant impact to date on the shape of the epidemic and on its tragic consequences. It's clearly going to take a stronger investment in the development of better vector control tools and strategies before we will see real progress in this area."

## Funding shortfall

Another initiative is crying out for financial investment. In February, WHO, together with 23 partner organisations, launched a response strategy aimed mainly at preventing and managing the socioeconomic and medical problems caused by the epidemic and at coordinating research on these problems. The activities covered by the strategy provide women of childbearing age, pregnant women, their partners, households, and communities with the information they need to protect themselves from infection. They also include counselling on sexual and reproductive health and on health education and care. Over its first 6 months the strategy suffered a serious shortfall in funding. US$25 million was needed, but just over $4 million was received. The next 6 months' work will require an estimated $122 million. So far only $3 million has been received. "Why", asks Aylward, "is it so difficult to mobilise the funds needed to mitigate the consequences of such a horrific disease?"

*John Maurice*