

Ebola and Zika: Cautionary tales

The emergence of Zika in the Americas is a stark reminder of how quickly public health challenges of infectious diseases can change. The need for a safe and effective vaccine is immediate. Yet, like the Ebola epidemic 2 years ago, we find ourselves without a vaccine to combat this latest threat.

When surveillance points to a possible emergence of a new infectious disease of potential public health importance, we need procedural and funding mechanisms that can quickly identify candidate vaccines and drive research and development toward licensure and production. Even if such a vaccine is not yet licensed, having it ready for immediate large trials when a regional crisis occurs will be a major advantage over our current reactive system.

Two years ago, amidst the Ebola epidemic in West Africa, the international health community was laser-focused on finding an effective and safe vaccine. By heroic public health actions and luck, the crisis was curtailed without one. Today, hardly a word is mentioned about that crisis or the current status of vaccine development.

Yet tomorrow, we could experience another explosive Ebola epidemic that begins in the slums of one of equatorial Africa's megacities and spreads in deadly waves, where only the availability of an effective vaccine could halt its ruinous progression.

Now, Zika transmission in Florida dominates news in the United States, along with partisan political theater regarding government funding for the country's response. However, we must not take our eye off the most pressing problem of Zika: the explosive transmission in the Americas outside the continental United States. For example, it is estimated that up to 5% of Puerto Rico's population is getting infected with Zika each month, including thousands of pregnant women, for whom infection could result in fetal microcephaly.

I fear the road to a Zika vaccine may be long and bumpy. Despite optimistic predictions, demonstrating safety will be an immense challenge. It likely will be necessary to conduct studies involving many thousands

of participants to determine if Guillain-Barré syndrome (GBS), a serious autoimmune condition caused by natural Zika virus, is also related to vaccine candidates. And recent follow-up of a vaccine efficacy study for dengue, Zika's cousin flavivirus, suggests a diminishing vaccine-induced antibody response over time. This means that antibody-dependent enhancement disease may occur upon infection with a new dengue strain, or possibly even another flavivirus such as Zika or yellow fever.

The handwriting is on the wall regarding the current Zika outbreak in the Americas. High human infection rates in the major impact regions, caused by virus-carrying mosquitoes and human sexual transmission, will continue for several more years. Eventually, the number of cases will drop as more of the community develops immunity. Zika vaccine trials in the Americas may be too late to be tested on the current high number of cases.

The Coalition for Epidemic Preparedness Innovations (CEPI) is a new international effort that includes the Wellcome Trust; Bill & Melinda Gates Foundation; World

Economic Forum; U.S., Indian, and Norwegian governments; GAVI; academic researchers; international vaccine manufacturers; and the World Health Organization. CEPI (www.cepi.net) is the best hope to fill the vaccine preparedness hole.

These experiences demand better answers than our current vaccine research, development, manufacturing, and distribution system has provided. Based on observation, we could, and should, have anticipated that agents like Zika and Ebola virus would emerge as serious pathogens. The 2013 to 2014 Zika outbreak in French Polynesia produced nearly 9000 suspected cases and a strong association with GBS. How much more incentive is needed to develop candidate vaccines? With the growth of megacities in the developing world and prevalence of *Aedes aegypti* mosquitoes in many areas, this disease should not have come as a surprise—nor should the host of others yet to come that we would be foolish not to expect.

—Michael T. Osterholm



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