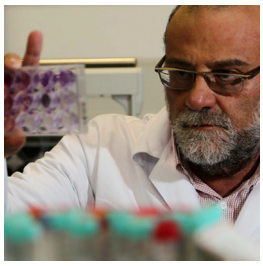
What Will It Take to Respond to the Threat of Zika?

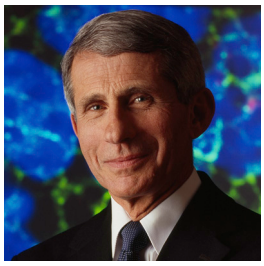
Microcephaly Mystery



Amilcar Tanuri
Federal University of Rio de Janeiro

The Zika virus outbreak, initially regional, is spreading through the Americas, and it does not respect country borders. The virus circulating in Brazil came from French Polynesia. However, the new virus has undergone many changes. The most concerning is its ability to damage the host nervous system. Many other flaviviruses circulate in Brazil, such as dengue, West Nile, and Japanese encephalitis viruses. Occasionally, they cause neuronal damage. Zika, however, seems to have a soft spot for neural tissues. As such, it has been linked to Guillain-Barre syndrome, encephalitis, and myelopathy in infected adults. Recent data suggest that the Brazilian strain can be transmitted vertically through the placenta, and that the virus replicates in cells of the nervous system. The viral damage may explain the abundance of malformations in newborns from infected mothers, in particular the high incidence of microcephaly that has become a hallmark of the current outbreak. Adults seem to recover from the infection, although symptoms may re-emerge a month later and the virus can remain detectable in body fluids many weeks after the acute infection. This could indicate either reinfection or viral reactivation due to incomplete immunological control of the virus. As the burden of Zika in Brazil increases, scientists have doubled their effort to catch up with the virus. We have learned a great deal, but continuous investment in research is critical if we are to understand the disease and control this uninvited guest.

A Dual Research Path



Anthony S. Fauci
National Institute of Allergy and Infectious Diseases

Emerging viral diseases pose ongoing threats, evidenced recently by the outbreaks of Ebola in West Africa and chikungunya and Zika in the Americas. A dual research path is essential to respond effectively to the inevitable and unpredictable emergence of viral diseases. The first path is a robust and sustained basic and clinical research effort in virology, genomics, pathogenesis, and natural history of all important human viruses with the goal of developing interventions. Simultaneously, we must be prepared to respond rapidly to completely unanticipated threats. The recently established Global Health Security Agenda calls for the bolstering of real-time global biosurveillance, rapid reporting, health systems, and global communication networks. Biomedical research also plays an essential role in this endeavor: concomitantly, we must develop vaccine platforms that can be applied immediately to any newly emerging viral infection as well as broad-spectrum antivirals that target common components of multiple viruses, rather than a "one bug/one drug" approach. In addition, multiplex diagnostic assays, which are high-throughput, field-portable, affordable, and require minimal training, are essential to identify and rapidly respond to outbreaks early in their evolution. Emerging viral infections remain a perpetual global health challenge; thus, we must position ourselves at the cutting edge of scientific discovery in order to respond nimbly to unanticipated viral pathogens that will inevitably confront us.

Global Surveillance

Pardis Sabeti
Harvard University

Last year it was Ebola, this year it is Zika and Lassa, and the list will go on—viruses quietly replicating all over the world that could threaten human populations. At any point, a chance event—a new mutation, an encounter with an infected animal—could launch one into a global epidemic. We cannot predict which sparks will ignite, but we can create global surveillance systems to detect the fires as they start. New genomic technologies can transform diagnosis and treatment of infectious diseases, but success requires concerted effort and sustained support. We are more prepared than we were before Ebola, but Zika demonstrates how far we still have to go. We still do not have accessible diagnostic tests for Zika and many other viruses in most of the world, or even in many US states. We still do not know the extent of Zika's genetic diversity and how it might relate to the rising prevalence of microcephaly or impact vaccine development. We have much too little data, and yet people too often work in silos and fail to share samples and information. We can no longer afford business as usual. With so much on the line and with the entire world descending on Brazil this summer, there is not a moment to lose.

Persons, Places, and Time

Cesar Victora
Federal University of Pelotas

Now that the link between Zika virus (ZKV) and microcephaly is beyond doubt, Brazilian epidemiologists need to respond rapidly. The epidemic caught everyone by surprise, and we are unable to quantify the size of the first wave of the ZKV epidemic. The epidemic is moving rapidly from the northeast to the southeast region, where most Brazilians live. Thousands of pregnant women with typical rashes of ZKV infection are being reported. Here are some questions that epidemiologists need to answer soon. What proportion of the population was infected so far? How likely are new waves of the epidemic in affected regions? How many pregnant women were exposed? How does the risk of infection vary according to geographical, social or other risk factors? What proportion of infections during pregnancy result in microcephaly or in brain abnormalities among newborns with normal-sized heads? Are there co-factors—including previous exposure to flaviviruses—that increase the risk of brain abnormalities? What screening criteria should be used to minimize false negatives and false positives—that include many newborns with normally small heads? Does the infection lead to long-lasting immunity? Can the consequences of infection on psychomotor development be reverted? Can health services cope with the increased demand for diagnostic and rehabilitation services? Epidemiology has developed markedly in Brazil in the past 30 years. The ZKV epidemic will put it to a test. Will funding agencies and scientists rise to the occasion?

Following Through

James E. Crowe, Jr.
Vanderbilt University

Responding to massive and rapid instances of emerging infectious diseases, like the current Zika virus outbreak, is becoming situation normal. In the last year, we experienced three major news cycles about chikungunya virus, Ebola virus, and now Zika virus infections. The frequency of such epidemics is accelerating, with frequent world travel, waning vector control, high population density, and increasing human exposure to wild animals. The use of scientific tools to investigate epidemics is accelerating in tandem, and we are seeing large-scale data posted publically in real-time for viral sequences, animal model development, and other important studies. Scientific tools are being used to influence public health interventions in meaningful and new ways. Still, issues of national sovereignty and concerns over intellectual property rights, academic credit, and public recognition inhibit the free exchange of best technologies and human virus and blood samples, slowing the discovery process and development of new diagnostic and therapeutic interventions. The full development of vaccines for emerging infections occurs only after the epidemics have come and gone, and then we lose our drive to finish the job with full force. We still need more commitment to cooperativity in infectious diseases research across the globe. Do we have the will to sustain serious efforts to prevent and treat such infectious diseases when the TV cameras are gone?

Stop the Mosquito

Scott O'Neill
Monash University

Effective options for the control of *Aedes aegypti* mosquitoes, the primary vector for a range of human viruses including dengue, chikungunya, yellow fever, and Zika have for many years been quite limited. They have been focused on the physical removal of breeding sites or the application of insecticides. Unfortunately, these strategies are becoming less and less effective, as evidenced by the growing burden of disease. Things are changing quickly though and not too soon. Novel interventions include the introduction of *Wolbachia* symbionts to prevent virus transmission, the release of genetically modified or irradiated mosquitoes to suppress *Aedes* populations, or the design of new lethal trapping systems. They all show promise and have been under painstaking and methodical development for many years. To date, the most advanced one has only been tested at the scale of small city deployments. Nearly all of these new interventions have been developed with dengue in mind as the principle target disease and none has completed gold standard randomized efficacy trials. Yet modelling predictions and accumulating observational data all point to the potential for large impact of some. To be most efficient, we should consider effectiveness against dengue as a proxy for Zika effectiveness given the similarity of these viruses. It is time to accelerate the most promising interventions and bring them quickly to the scale required to respond to the growing disease problems associated with this mosquito.