

THIS WEEK

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Zika must remain a high priority

Although the evidence suggests that the Olympic Games are safe to proceed, the global health community must not let the Zika virus fade from the research agenda until the threat is wiped out.

Are this summer's Olympic Games under threat from the Zika virus? Or, more importantly perhaps, are the competitors and spectators? Athletes such as US women's soccer goalkeeper Hope Solo have said they will go "begrudgingly", and will barely leave their hotel rooms. Some have called for the event to be cancelled.

This overestimates the risk of Zika to visitors. Although public-health agencies have advised pregnant women to avoid countries with active Zika transmission owing to the threat of birth defects, there are much more pertinent threats to the average visitor to Brazil, including dengue virus and random street violence. Much remains unknown about Zika, but a great deal is known, too, and it suggests that there is no reason to cancel the event.

That we know so much so soon is a victory. When the US Centers for Disease Control and Prevention (CDC) concluded last month that the Zika virus causes birth defects, that marked the conclusion of one of the quickest-ever basic-science investigations into a crucial public-health issue. Some researchers expected it to take years. In the end, it took just six months.

The CDC cited a growing number of studies using a range of approaches, including epidemiological, molecular and pathological, that showed a link between Zika and birth defects. The wisdom of making such a declaration so quickly remains a matter of some debate, but it is noteworthy that the global scientific community was able to organize itself in a relatively rapid fashion. There are three main reasons why this happened, and they offer lessons for research in future outbreaks.

First, Brazil has a substantial amount of research infrastructure. Unlike some regions where outbreaks occur, such as nations in Africa, Brazil has made sizeable investment in research and public health. It is the only country in Latin America that invests more than 1% of its gross domestic product into research, and the country is well supported by foreign research institutes, such as the US National Institutes of Health (NIH). The country spent US\$31.9 billion on research in 2013, for instance.

This meant that when the Zika outbreak arose, there was a highly trained group of researchers ready to investigate the issue. The Oswaldo Cruz Foundation, a federally funded network of research stations across Brazil, has led investigations of the epidemiology and molecular aspects of Zika. And a long-running NIH-funded project on urban slum health in northeastern Brazil quickly adapted to set up large cohort studies to look at the possible link between Zika and birth defects.

Second, there have been significant advances in neuroscience. Some of the most telling evidence for Zika's effects on human brain cells has come from studies of human neural stem cells and organoids — brain-like structures that can be grown in cell culture in the lab. Brain organoids were developed only a few years ago. By using organoids, human stem cells and human fetal tissue, researchers were

quickly able to show that Zika preferentially targets and kills human neural precursors in the brain, offering a plausible explanation for a mechanism through which the virus causes birth defects.

Third, the global health community has acknowledged that its ditheringly slow response to the Ebola epidemic let it grow out of control. Health officials were therefore determined to move more quickly in response to Zika. The World Health Organization declared the outbreak an emergency in February, and in the same month US President Barack Obama

"There should be no complacency."

requested \$1.9 billion for Zika-related activities. Although the US Congress has yet to approve that spending, the CDC said on

13 May that it had found \$85 million to distribute to states to help them prepare for the virus.

There should be no complacency. The quick connection of dots between Zika and birth defects is only the beginning of the necessary mobilization. And we still don't know why only some babies succumb to the devastating effects of Zika, or the most effective way to care for them. The questions will keep coming, and the research community and funders must continue to pursue them — with speed, strength and the highest urgency, as the organizers of the Olympics might say. ■

Second thoughts

Revisiting the past can help to inform ideas of the present.

The thought experiment has a noble place in research, but some thoughts are deemed more noble than others. Darwin and Einstein could let their minds wander and imagine the consequences of certain actions or natural laws. But scientists and historians who try to estimate what might have happened if, say, Darwin had fallen off the *Beagle* and drowned, are often accused of playing parlour games.

Most of these counterfactual thought experiments tend to focus on changes to the lives of historical figures — what would have happened had Hitler never been born, for instance. Dismissed as silly and speculative, such exercises are considered of little academic value, because the results of the experiment tend to align with what the experimenter would have wanted to happen. (One of first such published accounts seems to prove the point: *Napoléon Apocryphe*, published by a supporter in 1841, starts with the emperor surviving the 1812 Russian winter in an unburnt Moscow, conquering Europe, then Asia, Africa and the Americas, while discovering a new planet and inventing a flying car on the way.)