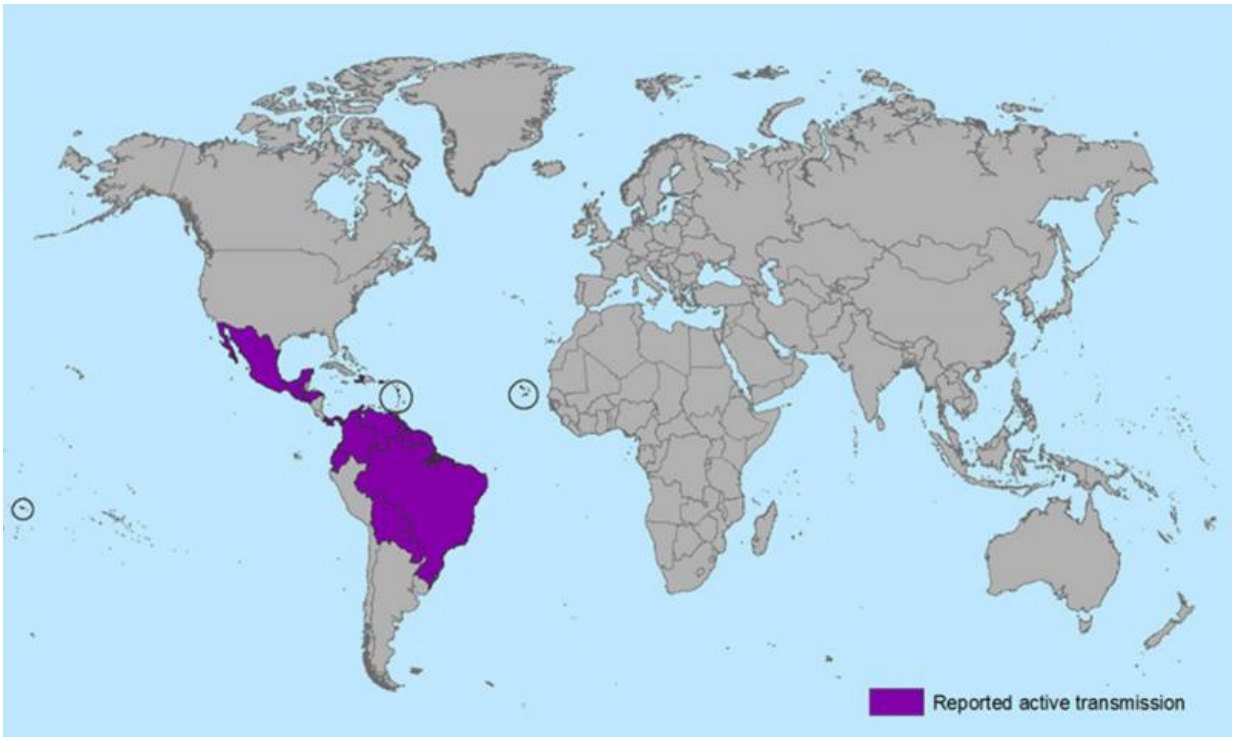
Explainer: Where did Zika virus come from and why is it a problem in Brazil?

January 28 2016, by Amy Y. Vittor, University Of Florida



Countries and territories with active Zika virus transmission. Credit: Centers for Disease Control and Prevention

From October 2015 to January 2016, there were almost 4,000 cases of babies born with microcephaly in Brazil. Before then, there were just 150 cases per year.

The suspected culprit is a mosquito-borne virus called Zika. Officials in Colombia, Ecuador, El Salvador and Jamaica have suggested that women delay becoming pregnant. And the Centers for Disease Control and Prevention has advised pregnant women to postpone travel to countries where Zika is active.

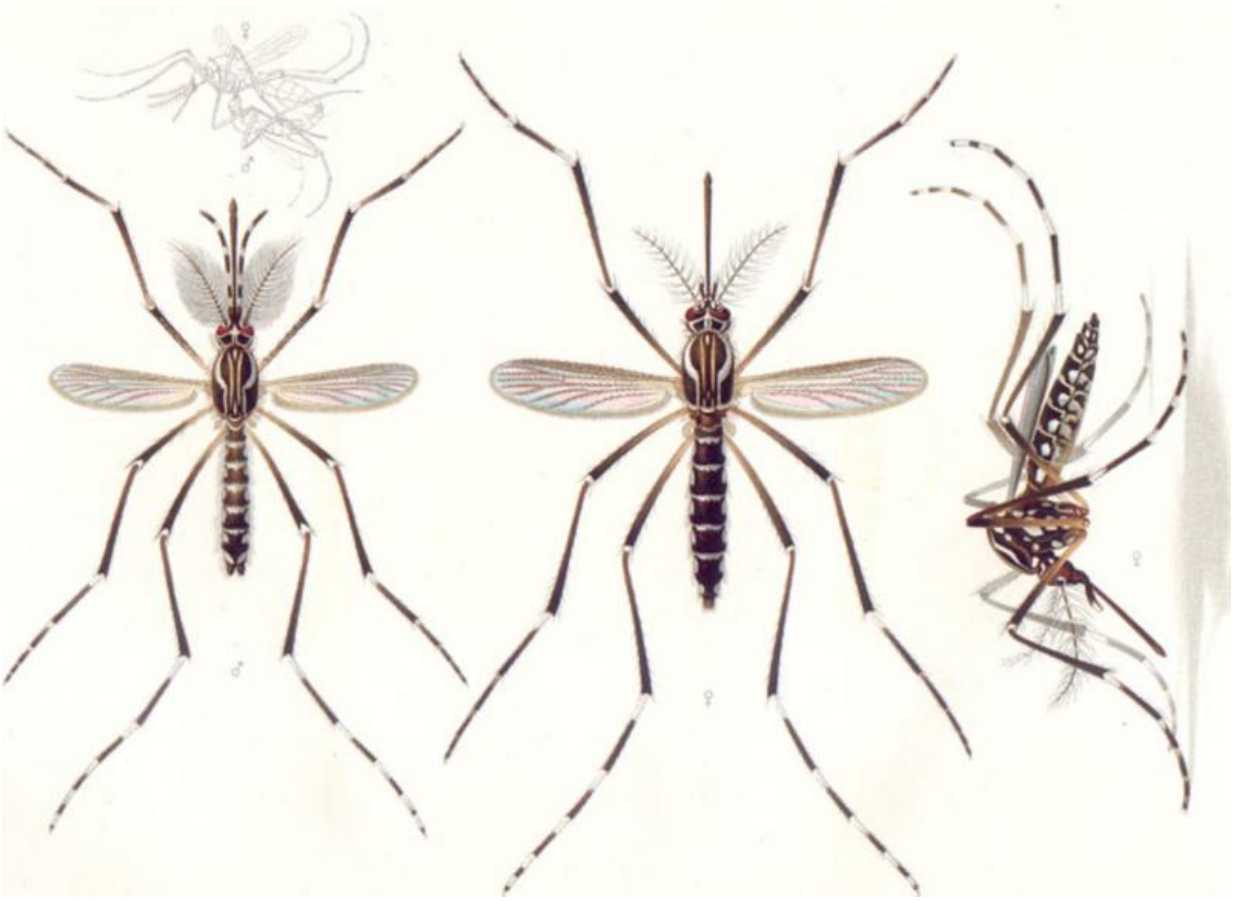
The World Health Organization says it is likely that the virus will spread, as the mosquitoes that carry the virus are found in almost every country in the Americas.

Zika virus was discovered almost 70 years ago, but wasn't associated with outbreaks until 2007. So how did this formerly obscure virus wind up causing so much trouble in Brazil and other nations in South America?

Where did Zika come from?

Zika virus was first detected in Zika Forest in Uganda in 1947 in a rhesus monkey, and again in 1948 in the mosquito *Aedes africanus*, which is the forest relative of *Aedes aegypti*. *Aedes aegypti* and *Aedes albopictus* can both spread Zika. Sexual transmission between people has also been reported.

Zika has a lot in common with dengue and chikungunya, another emergent virus. All three originated from West and central Africa and Southeast Asia, but have recently expanded their range to include much of the tropics and subtropics globally. And they are all spread by the same species of mosquitoes.



Aedes aegypti. Emil August Goeldi (1859-1917). Credit: via Wikimedia Commons.

Until 2007 very few cases of Zika in humans were reported. Then an outbreak occurred on Yap Island of Micronesia, infecting approximately 75 percent of the population. Six years later, the virus appeared in French Polynesia, along with outbreaks of dengue and chikungunya viruses.

How did Zika get to the Americas?

Genetic analysis of the virus revealed that the strain in Brazil was most

similar to one that had been circulating in the Pacific.

Brazil had been on alert for an introduction of a new virus following the 2014 FIFA World Cup, because the event concentrated people from all over the world. However, no Pacific island nation with Zika transmission had competed at this event, making it less likely to be the source.

There is another theory that Zika virus may have been introduced following an international canoe event held in Rio de Janeiro in August of 2014, which hosted competitors from various Pacific islands.

Another possible route of introduction was overland from Chile, since that country had detected a case of Zika disease in a returning traveler from Easter Island.

Most people with Zika don't know they have it

According to research after the Yap Island outbreak, the vast majority of people (80 percent) infected with Zika virus will never know it – they do not develop any symptoms at all. A minority who do become ill tend to have fever, rash, joint pains, red eyes, headache and muscle pain lasting up to a week. And no deaths had been reported.

However, in the aftermath of the Polynesian outbreak it became evident that Zika was associated with Guillain-Barré syndrome, a life-threatening neurological paralyzing condition.

In early 2015, Brazilian public health officials sounded the alert that Zika virus had been detected in patients with fevers in northeast Brazil. Then there was a similar uptick in the number of cases of Guillain-Barré in Brazil and El Salvador. And in late 2015 in Brazil, cases of microcephaly started to emerge.

At present, the link between Zika virus infection and microcephaly isn't confirmed, but the virus has been found in amniotic fluid and brain tissue of a handful of cases.

How Zika might affect the brain is unclear, but a study from the 1970s revealed that the virus could replicate in neurons of young mice, causing neuronal destruction. Recent genetic analyses suggest that strains of Zika virus may be undergoing mutations, possibly accounting for changes in virulence and its ability to infect mosquitoes or hosts.

The Swiss cheese model for system failure

One way to understand how Zika spread is to use something called the Swiss cheese model. Imagine a stack of Swiss cheese slices. The holes in each slice are a weakness, and throughout the stack, these holes aren't the same size or the same shape. Problems arise when the holes align.

With any disease outbreak, multiple factors are at play, and each may be necessary but not sufficient on its own to cause it. Applying this model to our mosquito-borne mystery makes it easier to see how many different factors, or layers, coincided to create the current Zika outbreak.

A hole through the layers

The first layer is a fertile environment for mosquitoes. That's something my colleagues and I have studied in the Amazon rain forest. We found that deforestation followed by agriculture and regrowth of low-lying vegetation provided a much more suitable environment for the malaria mosquito carrier than pristine forest.

Increasing urbanization and poverty create a fertile environment for the

mosquitoes that spread dengue by creating ample breeding sites. In addition, climate change may raise the temperature and/or humidity in areas that previously have been below the threshold required for the mosquitoes to thrive.

The second layer is the introduction of the mosquito vector. *Aedes aegypti* and *Aedes albopictus* have expanded their geographic range in the past few decades. Urbanization, changing climate, air travel and transportation, and waxing and waning control efforts that are at the mercy of economic and political factors have led to these mosquitoes spreading to new areas and coming back in areas where they had previously been eradicated.

For instance, in Latin America, continental mosquito eradication campaigns in the 1950s and 1960s led by the Pan American Health Organization conducted to battle yellow fever dramatically shrunk the range of *Aedes aegypti*. Following this success, however, interest in maintaining these mosquito control programs waned, and between 1980 and the 2000s the mosquito had made a full comeback.

The third layer, susceptible hosts, is critical as well. For instance, chikungunya virus has a tendency to infect very large portions of a population when it first invades an area. But once it blows through a small island, the virus may vanish because there are very few susceptible hosts remaining.

Since Zika is new to the Americas, there is a large population of susceptible hosts who haven't previously been exposed. In a large country, Brazil for instance, the virus can continue circulating without running out of susceptible hosts for a long time.

The fourth layer is the introduction of the virus. It can be very difficult to pinpoint exactly when a virus is introduced in a particular setting.

However, studies have associated increasing air travel with the spread of certain viruses such as dengue.

When these multiple factors are in alignment, it creates the conditions needed for an outbreak to start.

Putting the layers together

My colleagues and I are studying the role of these "layers" as they relate to the outbreak of yet another mosquito-borne virus, Madariaga virus (formerly known as Central/South American eastern equine encephalitis virus), which has caused numerous cases of encephalitis in the Darien jungle region of Panama.

There, we are examining the association between deforestation, mosquito vector factors, and the susceptibility of migrants compared to indigenous people in the affected area.

In our highly interconnected world which is being subjected to massive ecological change, we can expect ongoing outbreaks of viruses originating in far-flung regions with names we can barely pronounce – yet.

This article was originally published on The Conversation. *Read the* original article.

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