

How research is helping kids growing up with congenital Zika syndrome

November 21 2018



Silvia Pinheiro and her daughter Geovanna. As the children with Zika get older, researchers are having to re-evaluate and test their hypotheses. Credit: Silvia Pinheiro

At first, Brazil's Zika emergency was not about Zika.

Signs of a new public health concern emerged late in 2015 with clusters of [microcephaly](#) – babies whose heads were smaller than the normal

range, a condition often associated with developmental delays. Whereas a hospital in Brazil might expect to see a handful of cases of microcephaly a year, some were now diagnosing as many as 20 in a single week. The government declared a public health emergency and, among other actions, set up the Microcephaly Epidemic Research Group (opens in a new tab) to investigate.

"The microcephaly epidemic was something new," says Ricardo Ximenes, Professor of Epidemiology and Infectious Diseases in Recife, where many of the unusual cases of microcephaly were being identified. "And if it was something new, there must have been something new that caused it."

Established links between the Ministry of Health and the national and international research communities enabled research projects to get up and running quickly, with standardised protocols and plans.

"It was a real partnership from the beginning," says Elizabeth Brickley, Assistant Professor of Epidemiology at the London School of Hygiene & Tropical Medicine. "That allowed science to move at the speed of the epidemic, which was really unique."

Early studies focused on the links between microcephaly and possible causes, including the Zika virus. Many women thought the two or three days of itch and rash during their pregnancy had just been a mild form of dengue, nothing to worry about. But it turned out to have been Zika, another virus transmitted by mosquitoes.

First identified in 1947, Zika had not been associated with microcephaly before, but the research has now shown a clear association between an outbreak of Zika earlier in 2015 and the babies being born with microcephaly some months later. Zika was also reported to be linked to Guillain-Barré syndrome, an autoimmune disorder of the nervous

system.

"What we can say at this point is that Zika virus infections in pregnancy are very serious and that the emphasis needs to be on preventing the infection from occurring," says Brickley. "So things like vaccines and vector control are going to be pivotal in the future."

While vector control – reducing people's exposure to mosquitoes – is an ongoing challenge in the fight against many infections, little had been done on developing a Zika vaccine. It just hadn't been considered a priority before.

Good progress has been made since 2015, however, and a number of candidate vaccines have entered early trials – although there is a lot of work still to be done before an effective vaccine will be available.

Over but not ended

In May 2017, the Brazilian government declared the public health emergency over. However, the families affected by Zika still had many questions about their future.

Hannah Kuper, another epidemiologist at the London School of Hygiene & Tropical Medicine, has been working with researchers in Rio and Pernambuco to investigate the impact of Zika on the families, pregnant women, communities and healthcare professionals in Brazil (see video).

As well as looking at the effects on health, including the children's potentially complicated needs and their mothers' mental health, the team is modelling how much it will cost to support these families over the next ten years.

"There's a profound concern about how we will support the communities

that were affected," says Brickley. "Even though the emergency is over, the need for action on Zika has not ended."

Microcephaly is not the only condition that can result from Zika infection during pregnancy. A range of outcomes, many less visible than smaller head sizes, have been identified in research studies, so the term 'congenital Zika syndrome' is now used to describe children who have been affected.

Current studies are looking at patterns in the children's growth, brain development and experiences of epilepsy. By looking across hundreds of cases, researchers have identified other related symptoms that might not otherwise have been considered, such as urinary tract infections.

"When babies are affected in the central nervous system, they can be affected in the function of the kidneys, or be affected by repeat urinary infections," explains Demócrito Miranda-Filho, a physician and Associate Professor in Infectious Diseases at the University of Pernambuco in Recife. Damage in the brain may mean these children have less control over their bladders, increasing the risk of infection.

Nerve damage can also cause dysphagia: problems coordinating the actions involved in swallowing, which can be fatal for these babies. Because many of them also lack a cough reflex, if they breathed in milk by accident when feeding, it could get into their lungs and lead to pneumonia. Knowing this meant mothers could be more alert to the danger.

Lessons for the future

Researchers in the Microcephaly Epidemic Research Group and others are contributing to a range of advice and guidance for the families, from techniques for safe feeding to how to stretch and stimulate the children

as they grow and develop.

But the families are also teaching the researchers. "Every day is different," says Brickley. "As the children get older, we're constantly having to re-evaluate and test our assumptions and hypotheses."

"For us, it's really a new experience," adds Miranda-Filho. "We are still learning every day."

There are wider lessons, too, about preparing for future epidemics, and how to put in place strong systems that will be able to respond quickly and effectively next time. An essential part of that is having laboratories equipped with the right tools, researchers and clinicians learning new skills, and scientific networks growing stronger.

For example, the dozen or so research groups in Brazil working with the families affected by Zika have agreed to combine their data, allowing a more powerful analysis than any single group working alone.

Hopefully, this will help answer the families' questions, which Ximenes says tend to be practical in nature: "What's known about the disease? What has this investigation brought that may help my children? What expectations may I have according to the more recent findings?"

"They are very demanding on translating the scientific findings," he concludes approvingly.

Provided by Wellcome Trust

Citation: How research is helping kids growing up with congenital Zika syndrome (2018, November 21) retrieved 3 July 2024 from <https://medicalxpress.com/news/2018-11-kids-congenital-zika-syndrome.html>

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