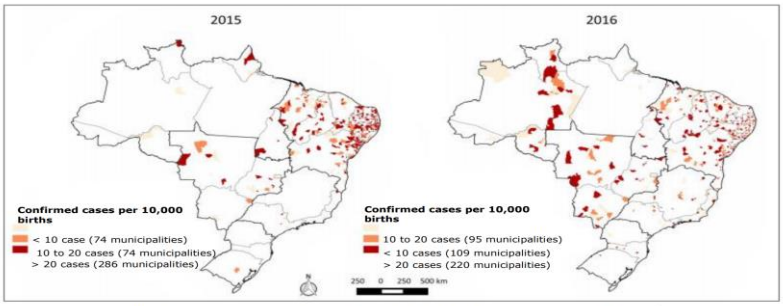
STANDARD DEVIATIONS: ZIKA!? What Zika?

Zounds!

Whatever happened to Zika? It's like this arbovirus has fallen off the radar and is slipping into obscurity.

Zika began spreading in Brazil in April 2015 and the country saw more than 260,000 probable cases in 2016, according to the Health Ministry. Cases of microcephaly, an abnormally small head in babies, and other developmental deficits linked to Zika began surging in 2015, when more than 960 were confirmed; the next year saw more than 1,800.



Source: Data published by the Brazil Ministry of Health and reproduced by PAHO/WHO[12]

As quickly as it spiked, Zika and microcephaly plummeted. In 2017, there were fewer than 18,000 Zika cases and fewer than 300 cases of microcephaly. In the most recent 2018 data, Brazil had seen about 2,200 cases of Zika and 20 cases of developmental abnormalities.

Zika is a flavivirus, an arboviral RNA virus spread primarily by *Aedes* genus mosquitoes. These viruses also include yellow fever virus, dengue virus, Japanese encephalitis virus, and West Nile virus. Eighty percent of Zika infected individuals are asymptomatic or do not report infection or their mild conditions. Affected persons experience fever, rash, headache, red eyes, and joint/muscle pain. The condition lasts a few days to a week. Death is exceedingly rare and rarely requires hospitalization. However, this virus can cross the fetal/maternal, placental bridge and causes birth defects in some children. A pregnant woman who acquires Zika in the first two trimesters is at a higher risk for delivering a baby with microcephaly or other defect.

Zika first appeared in the Zika forest of Uganda, in 1947. An interesting but unremarkable finding, only 14 cases of Zika Fever were documented for 60 years. In 2007, the small remote island of Yap, 1000 miles East of the Philippines, saw an outbreak where 75% of the 6,000 residents became infected. Only 49 cases were confirmed. None of the patients required hospitalization. No hemorrhagic manifestations occurred, and no deaths resulted. In 2013, a small outbreak first noted in French Polynesia was notable for a sudden increase of Guillain-

Barré syndrome (GBS), which is progressive muscle weakness due to damage of the peripheral nervous system, and microcephaly.

In 2015, Zika virus showed up in Brazil; and the story changed. There's a strong case made that Zika was introduced during the 2014 FIFA World Cup. Zika case numbers exploded throughout the country but dengue, chikungunya, and Yellow Fever were endemic diseases with more renown. And then, an increase in **microcephaly was noted in states of NE Brazil**. It seemed that the incidence was suddenly more than twice the expected rate and mothers were testing positive for Zika IgM antibody. This resulted in the WHO declaration of a Public Heath Emergency of International Concern (PHEIC) on February 1, 2016.

Here at home.

In May of 2016, the CDC allocated $85,000,000 for 53 states and territories preparedness and response. State labs, like yours, implemented Emergency Authorization Use (EAU) testing protocols; hiring staff, purchasing reagents and instrumentation for the expected surge of Zika outbreak. We stood up labs across the country in preparation for the onslaught.

Just how bad was it? Ummmm…not that bad?? WHO ended the PHEIC in November 2016. Here's a little table of Zika incidence in the US and territories through 2019:

YEAR	2015	2016	2017	2018	2019 (June 5)
US local	0	224 (FL 218, TX 6)	7 (FL 2, TX 5)	0	0
US imported	62	4897	437	72	2
Territory local	9	36367	665	147	18
Territory imported	1	145	1	1	0

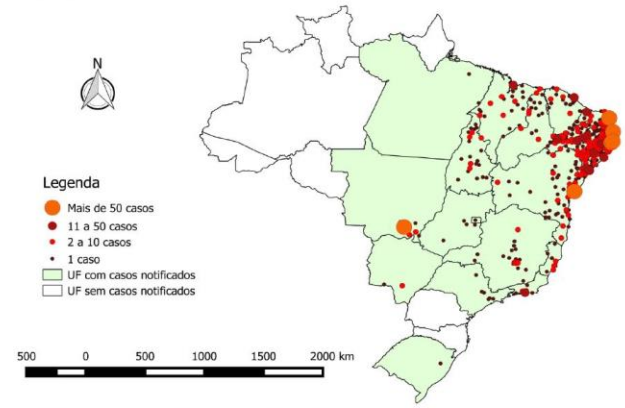
The anticipated crash of Zika, GBS, and microcephaly have not materialized in the US.

In NE Brazil, microcephaly cases never even closely reached projected estimates. Around 1000 cases had been seen in 2015/16 and only 300 followed the next year, and 20 thru 2018.

What happened??

Good question. The distribution of cases is exceptional. This map shows how almost all microcephaly is sequestered in a specific region of Brazil:

Figura 1 – Distribuição espacial dos 549 municípios com casos suspeitos de microcefalia notificados até a semana epidemiológica 49. Brasil, 2015.



Fonte: Ministério da Saúde e Secretarias Estaduais de Saúde (atualizado em 12/12/2015). Dados sujeitos a alteração.

Studies have looked at several possible influences. Was there coinfection with dengue, chikungunya, or Yellow Fever? Studies looked at environmental questions like water quality, population density, and chemicals such as farming pesticides and insecticides. Listen to this, this population had 92% of 8.2 million cases. **The most likely reason why Northeast Brazil reported higher microcephaly rates was because it had more cases of Zika**.

And ecological factors may play a role; there's a strong association between higher microcephaly prevalence and poor living conditions.

A lot of spending has gone into understanding how Zika causes birth defects. What we do know, is that flaviviruses commandeer metabolic pathways in fetal development. Zika has been shown to manipulate glycolysis for its own replication at a critical time in embryology of neural glial cell growth and differentiation in mice. The timing of the disrupted glial cell is why the first two trimesters are significant to disease onset in the mother. Diverting energy from these developing cells that comprise large percentages of brain cause microcephaly. That's it in a nutshell (ouch, horrible pun).

Microcephaly is just one, highly visible, birth defect attributable to Zika. Congenital glaucoma and optical nerve hypoplasia, and optic disc abnormalities are seen in many cases of affected infants, for similar embryonic pathology.

Neural issues from the flaviviruses and alphaviruses (chikungunya) are also implicated and studied in GBS. It's important to remember the growing and adult brain is affected, as well.

Was it 85 million of our dollars well spent? The bulk of this money has been spent in surveillance, research, and diagnosis. What about prevention? Did we throw a bunch of cash into the wind of a passing train?

Zika virus appears to have ridden a singular wave through South and Central Americas. It lacks the ability for transmission to be a threat to most of the US. It's possible that a generation will pass before a congenital anomaly phenomenon like it is observed again.

The costs of preparedness will always be controversial. Our ability to respond to public health emergencies and disease outbreak depends on a commitment to preparedness. We have been testing for arbovirus before Zika. UPHL does surveillance testing for West Nile and other arboviruses, and we've been doing the Zika EUA assay since its release in 2016.

Zika, and the arboviral diseases, in general, pose threats to humans. Another reason the mosquito is our deadliest animal. The adaption of *Aedes* to larger areas of the continent pose a risk to us that Brazil's encounter with Zika has illuminated. The money and resources we have spent on preparedness on for a virus we did not see keeps us ready for the next virus we still do not see.

The same concept applies to how we look at safety and biosafety in the lab; we still spend money and time on preparedness for few and (thankfully) rare events. That understanding and preparedness is probably resources well spent.

Have a great week and be safe,

Bryan

P.s. this marks the end of the first half of 2019. Each week's newsletter began with a subsequent letter of the alphabet, A-Z (Aroma Therapy to Zika) . We'll start again next week, just not sure where.

Have a great 4th of July! Here's a link to the Deseret News list of events around the state.

www.deseretnews.com/article/900076777/60-plus-events-for-utahs-2019-fourth-of-july-celebrations.html

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