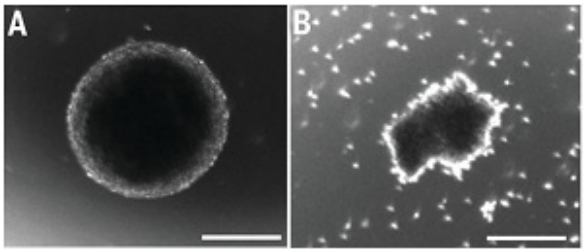
BRINGING OUT THE DEAD: WHAT WE KNOW ABOUT ZIKA VIRUS EFFECT ON HUMAN TISSUE



[(A) Control neurosphere
(B) Zika-infected neurosphere
Source: Science, 13MAY2016
http://science.sciencemag.org/content/352/6287/816.full]

Because unproven claims persist that chemical exposure – specifically the pyridine-based pesticide pyriproxyfen – causes the birth defects seen in children born to women exposed to Zika virus, I am bringing out the dead, laying out the bodies.

By 'bodies' I mean sharing here pictures of cells you see in the embedded photos from a peer-reviewed study published this May.

In these images you'll see the damage done to human tissue in lab conditions.

No pyriproxyfen was present.

How Researchers Studied Zika

This is the methodology researchers used:

1) The researchers used human stem cells to create neurospheres – the kind of cells which turns into nerve and brain tissue in an actual embryo.

2) They set aside control samples of neurospheres which were not infected.

3) They infected test samples neurospheres with Brazilian Zika virus.

4) They observed the changes in the infected neurospheres.

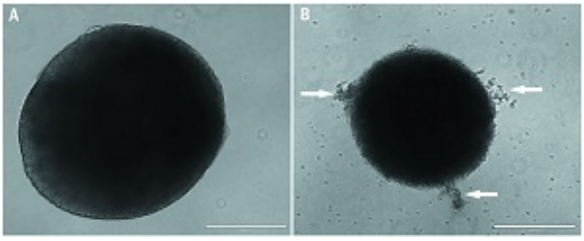
5) They compared them to the uninfected control samples.

6) They wrote and published a report on their findings.

The image above is the best example from their report of the difference between Zika-infected cells and the uninfected test samples.

What Researchers Found in this Study
In short, Zika inhibits, damages, and kills infected neurospheres.

This is what we can expect to happen to a fetus' brain or nerve tissues when infected by Zika under the right conditions during early pregnancy.



[(A) Control mock-infected organoid (B) Zika-infected organoid (damage noted at arrows)]

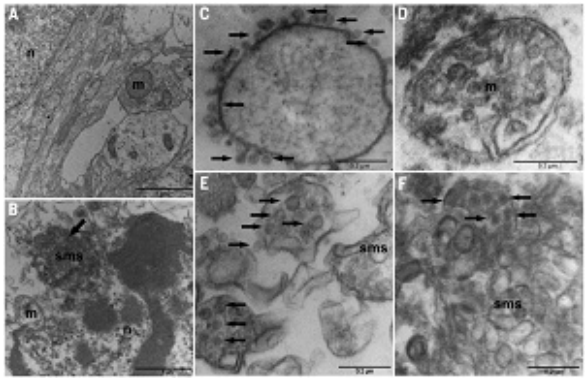
What Else Researchers Found in this Study

The researchers also conducted a very similar test on human brain organoids. These are not single neurospheres but neuro-tissue grown from stem cells so that they form a model like a tiny brain. Not a brain, a tissue-based model

of a brain.

They used the same six steps above using a mock-infected model, a Zika-infected model, and a dengue virus-infected model. (Dengue fever is caused by a flavivirus – the same family of viruses to which Zika and yellow fever belong.) Researchers found Zika virus caused similar destructive damage on these larger models while limiting their growth; they did not find the same damage or destruction in the dengue-infected models and none in the mock-infected control models. Zika alone damaged neurological tissue models.

Researchers also studied neural stem cells (NSCs) – the simplest neuro tissue model – and found similar results in which the Zika virus killed off NSCs. Studying NSCs, neurospheres, and organoids, the researchers observed Zika's actions on different stages of neuro tissue maturity. In each of these models, from the simplest (NSCs) to the most complex (organoids), Zika was destructive.



[ZIKV (Zika virus) induces death in human neurospheres. These micrographs show the ultrastructure of mock- and ZIKV-infected neurospheres after 6 days in vitro.
(A) Mock-infected neurosphere showing cell processes and organelles.
(B) ZIKV-infected neurosphere showing a pyknotic nucleus, swollen mitochondria, smooth membrane structures, and viral envelopes (arrow).
(C) Viral envelopes on the cell surface (arrows).

(D) Swollen mitochondria.
(E) Viral envelopes inside the endoplasmic reticulum (arrows).
(F) Viral envelopes close to smooth membrane structures (arrows).]

Other Research on Zika Using Mouse Tissue

Three other studies published in May this year using mice or mouse tissues likewise showed evidences of neurological tissue and brain damage or growth suppression when infected by Zika virus. The studies came from research facilities in Brazil, China, and the U.S. – and in each study, *pyriproxyfen was not included*. The Zika-infected specimens showed damage and the control specimens did not.

The study from Brazil at the University of São Paulo also included research using human stem cells, comparing a Brazilian strain of Zika against an African strain:

> Beltrão-Braga, Muotri, and their colleagues also grew brain organoids from human stem cells and infected these in vitro models with the Brazilian and African strains of the virus. In the human mini brains, both strains of the virus caused cell death, but the Brazilian strain appeared to also interfere with the formation of cortical layers. The virus didn't replicate in the brain organoids grown from chimpanzee stem cells, suggesting **it may have adapted to human tissue**, the researchers noted in their paper.

Emphasis mine. Research published earlier showed Zika has already mutated rapidly after arriving in Brazil, with at least nine variants found inside the last two years.

What's Next in Zika Research

What researchers don't yet know, for starters: How Zika works – how does it damage or kill cells? When exactly does the virus do the most damage? What mechanisms interfere with Zika's operations and can they be used in vaccines or drug therapy? What makes Zika different from dengue or other flavivirus? What does Zika do to adult neuro tissue to cause Guillain-Barre Syndrome? Which adults are most at risk? Will the different mutations in Brazil respond differently to vaccines? How long can humans carry live Zika virus? Has the virus mutated and become transmissible by bodily fluids or aerosol? These are just a few of the questions we still have about Zika.

There are some good guesses about Zika's mechanisms – like this hypothesis focusing on vitamin A storage in the liver, which also suggests Zika may negatively affect liver cells (yet another avenue of research needed). But will a vaccine targeting this activity work for other flavivirus, too? What if this guess is wrong; are there other approaches we've yet to hear about?

We won't have any of these answers in a reasonable period of time if we don't have adequate funding.

It's not just birth defects we are talking about here, either. Look at the damage in those images again; this virus not only damages fetal nerve and brain tissue, it kills fetuses. Infants born with Zika-related defects may be blind and may lead short, painful lives. And it may kill and maim adults, too, if they develop a serious case of Zika-related Guillain-Barre Syndrome.

Let's not bring out any more Zika dead.

(*Note: Forgive me for the simplistic terms used in this post if you have a background in science. I had to make this as brief and succinct as possible for those who don't have that background.*)

Source:

Zika virus impairs growth in human neurospheres and brain organoids
BY PATRICIA P. GARCEZ, ERICK CORREIA LOIOLA, RODRIGO MADEIRO DA COSTA, LUIZA M. HIGA, PABLO TRINDADE, RODRIGO DELVECCHIO, JULIANA MINARDI NASCIMENTO, RODRIGO BRINDEIRO, AMILCAR TANURI, STEVENS K. REHEN
SCIENCE13 MAY 2016 : 816-818
Zika virus infection in cell culture models damages human neural stem cells to limit growth and cause cell death.
URL:
http://science.sciencemag.org/content/352/6287/816.full

Zika Studies Using Mice:

F. Cugola et al., “The Brazilian Zika virus strain causes birth defects in experimental models,” Nature, doi:10.1038/nature18296, 2016.

C. Li et al., “Zika virus disrupts neural progenitor development and leads to microcephaly in mice,” Cell Stem Cell, doi:10.1016/j.stem.2016.04.017, 2016.

J. Miner et al., “Zika virus infection during pregnancy in mice causes placental damage and fetal demise,” Cell, doi:10.1016/j.cell.2016.05.008, 2016.