

GPA E-Newsletter September 2017

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E-NEWS

Intrauterine Viral Infections with a Focus on Zika

“Never before in history has there been a situation where a bite from a mosquito could result in a devastating malformation.”

*– Dr. Tom Frieden, CDC Director, Press
Telebriefing April 13, 2016*

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In April 2016, we learned conclusively that Zika infection during pregnancy can cause damage to the fetal brain resulting in microcephaly. This association of Zika infection during pregnancy and microcephaly in the offspring was first recognized in Brazil in 2015. In March 2017, the Pan-American Health Organization and WHO reported that, in Brazil, over 10,000 pregnant women were identified as being infected with Zika and over 2,000 cases of Zika-associated microcephaly have

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been identify in their offspring.

In July 2016, the first cases of local mosquito-borne transmission of Zika in the USA were reported from Florida. As of April 1, 2017, 222 cases of Zika transmitted from local mosquitos have occurred in Florida and Texas. As the summer of 2017 approaches and mosquito populations increase, we are concerned that mosquito-borne transmission may spread to Georgia. *(Updated data can be found on the CDC website:*

<https://www.cdc.gov/zika/reporting/pregnancy-outcomes.html>)

We take this opportunity to review intrauterine viral infections with a focus on Zika.

"...the last time an infectious pathogen (rubella virus) caused an epidemic of congenital defects was more than 50 years ago..."

– New England Journal of Medicine, April 13, 2016

Rubella

In the mid 1960's there was a widespread rubella epidemic in the United States which resulted in an estimated 12.5 million cases of rubella infection. There were an estimated 20,000 infants born with prenately acquired Rubella. The symptoms were a result of infection of the central nervous system and affected the brain, eyes, and auditory nerves resulting in developmental delays, intellectual disabilities, visual and hearing impairment, a clinical picture of cerebral palsy with seizure disorders, and behavior problems including autism. Through this experience, we learned that:

1. Mild viral infections in pregnant woman could cause considerable damage to the embryo and developing fetus.
2. Vaccinations not only reduce the risk of childhood infections, but, importantly, prevent women from contracting the infection during

women from contracting the infection during pregnancy.

HIV/AIDS

Approximately 6,500 children are born to HIV-infected mothers each year in the United States. The symptoms of congenital HIV are a result of immune compromise as well as central nervous system consequences with developmental disabilities and other neurological consequences. It is estimated that, by following CDC strategies, the number of perinatally acquired HIV infections have been reduced by over 20,000 between 1994 and 2010.

Cytomegalovirus (CMV)

About one out of every 150 infants in the USA are born with CMV infection, however, only about one in five infants will have long-term consequences. Pregnant women are commonly infected from their toddlers who contract the virus in day care centers or preschool. The risk of transmission is greatest in the third trimester whereas the risk of complications to the infant is greatest if infection occurs during the first trimester. The challenge, however, is how to recognize this common pediatric condition and prevent transmission to the pregnant woman.

Zika

The virus derives its name from the Zika forest in Uganda, where it was first identified in 1947 in a febrile rhesus monkey. Zika is a single-stranded RNA flavivirus related to dengue, yellow fever, Japanese encephalitis, and West Nile viruses. Zika is transmitted to humans via the bite of the *Aedes aegypti* and *Aedes albopictus* mosquito. It is one of the number of viruses that have come out of Africa from primates that include HIV/AIDS and Ebola. Zika infection during pregnancy causes disruption

of fetal brain development and has been identified as a teratogen by the CDC. The Zika virus distinctively infects neural stem cell of the developing fetus thus destroying the lines of development of the stem cells into the neurons, astrocytes and oligodendrocytes resulting in the reduction of the number of brain cells and hence the size of the brain. Infection early in pregnancy results in microcephaly with associated neurological complications including developmental delays and disabilities with intellectual and motor impairment. The impact of Zika on the developing brain in late pregnancy is still being evaluated, and the CDC recommends that all infants born to mothers who were infected with Zika should be tested and closely monitored even if the head size is normal at birth.

Approach to the Obstetrical patient (Combined practice advisory from ACOG and SMFM):

1. Prevention – Avoid travel to areas with documented Zika transmission. If travel to such an area is absolutely necessary, take steps to avoid being bitten including:
 - Cover exposed skin,
 - Treat clothing with permethrin,
 - Stay in air conditioned or screened in areas,
 - DEET is safe in pregnancy. Use it and reapply as directed on product labeling.
 - If the partner frequently travels to an affected area use condoms throughout pregnancy.
2. Monitoring of pregnancy – To determine in a patient qualifies for testing we recommend utilizing the CDC algorithm which is constantly updated.
(www.cdc.gov/zika/pregnancy/widget.html)
Obtain Maternal Fetal- Medicine consultation

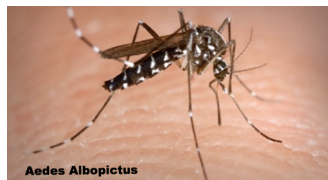
and ultrasounds every 4 weeks to evaluate fetal anatomy and growth. Pros and cons of amniocentesis should be reviewed with patients and unfortunately it is uncertain how the presence of the Zika virus in amniotic fluid will affect neonatal outcome.

3. Birth and immediate neonatal period – Plan vaginal delivery. Perform cesarean section only for obstetrical indication. Submit placental specimens for Zika RNA nucleic acid testing and immunohistochemical staining
4. Breast feeding – There have been no reported cases of transmission of the Zika virus through breast milk and women should be encouraged to breast feed
5. It is very important to provide as much information and support as possible to the families who will have to deal with the long-term consequences of having an infant with a prenatally acquired development disability. For this reason, it is critical to refer the family to an interdisciplinary program where the team can take care of the infant at the same time as provide support to the parents.

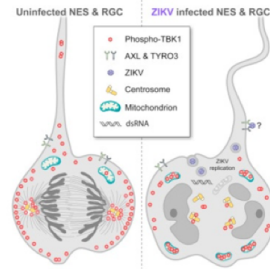
For more information on Zika and pregnancy consult the CDC website

<https://www.cdc.gov/zika/hc-providers/pregnant-women/testing-pregnant-women.html>

The two mosquitos which transmit Zika



Zika Virus Disrupts Mitosis in Human Neuroepithelial Stem Cells



Onorati et al., 2016, Cell Reports 16, 2576–2592

If you...	When to be tested
Traveled to areas with Zika risk that have a CDC Zika travel notice	You should be tested for Zika when you return from travel whether or not you have symptoms.
Traveled to areas with Zika risk but no CDC Zika travel notice	You should be tested if you develop symptoms of Zika or if your fetus has abnormalities seen on ultrasound.
Live in an area with Zika risk that has a CDC Zika travel notice	You are at risk of getting Zika throughout your pregnancy. Test at the first prenatal visit and repeat in the second trimester.

References:

Sonja A. Rasmussen, M.D., Denise J. Jamieson, M.D., M.P.H., Margaret A. Honein, Ph.D., M.P.H., and Lyle R. Petersen, M.D., Zika Virus and Birth Defects — Reviewing the Evidence for Causality M.P.H. N Engl J Med 2016; 374:1981-1987 May 19, 2016 DOI: 10.1056/NEJMSr1604338 Kristina

Zika Epidemiological Report – Brazil

http://www2.paho.org/hq/index.php?option=com_docman&task=doc_view&gid=35221&&Itemid=270

M. Adams Waldorf and Ryan M. McAdams.

Influence of Infection During Pregnancy on Fetal Development Reproduction. 2013 ; 146(5): R151–R162. doi:10.1530/REP-13-0232.

CDC MMWR Progress Toward Control of Rubella

and Prevention of Congenital Rubella Syndrome ---
Worldwide, 2009 October 15, 2010 / 59(40);1307-
1310

CDC HIV Among Pregnant Women, Infants, and
Children

[https://www.cdc.gov/hiv/group/gender/pregnanttwo
men/](https://www.cdc.gov/hiv/group/gender/pregnantwomen/)

CDC CMV and Congenital CMV

[https://www.cdc.gov/cmvp/clinical/congenital-
cmv.html](https://www.cdc.gov/cmvp/clinical/congenital-cmv.html)

Onorati et al., Zika Virus Disrupts Phospho-TBK1
Localization and Mitosis in Human Neuroepithelial
Stem Cells and Radial Glia Cell Reports 2016
16:2576–2592

CDC Zika Virus and Pregnant Women

[https://www.cdc.gov/zika/pregnancy/protect-
yourself.html](https://www.cdc.gov/zika/pregnancy/protect-yourself.html)

CDC Testing of Pregnant Women for Zika

[https://www.cdc.gov/zika/hc-providers/pregnant-
women/testing-pregnant-women.html](https://www.cdc.gov/zika/hc-providers/pregnant-women/testing-pregnant-women.html)

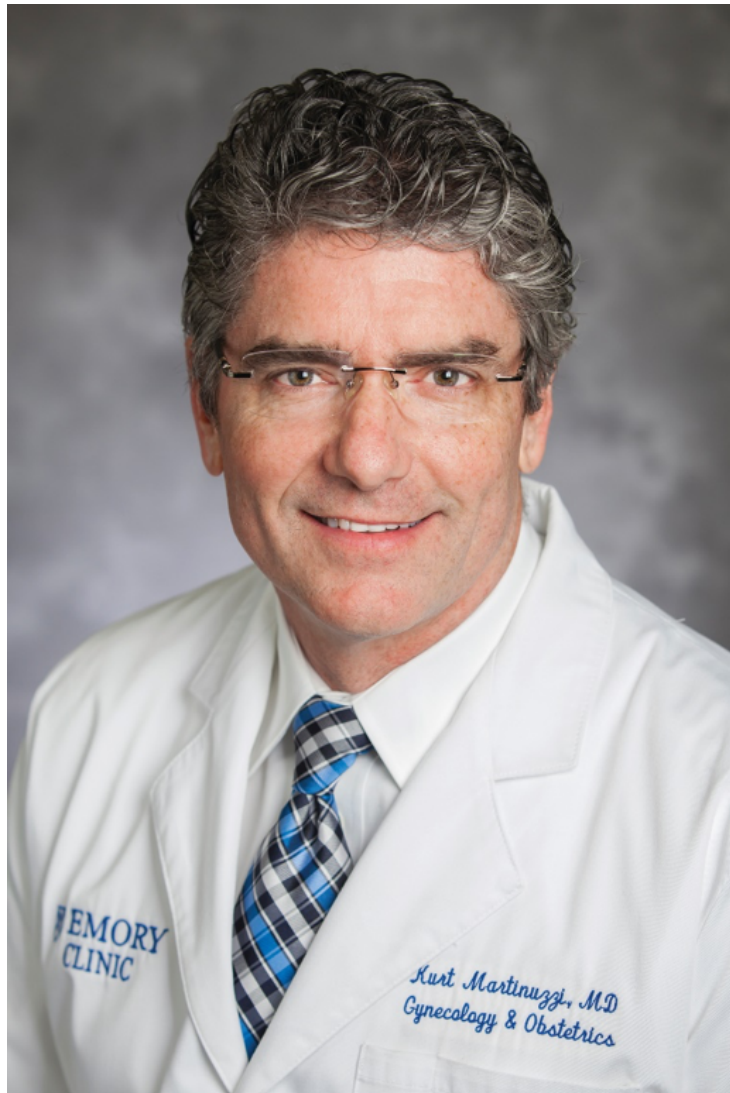
ACOG Practice Advisory on Zika Virus

[http://www.acog.org/About-ACOG/News-
Room/Practice-Advisories/Practice-Advisory-
Interim-Guidance-for-Care-of-Obstetric-Patients-
During-a-Zika-Virus-Outbreak](http://www.acog.org/About-ACOG/News-Room/Practice-Advisories/Practice-Advisory-Interim-Guidance-for-Care-of-Obstetric-Patients-During-a-Zika-Virus-Outbreak)



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