CONGENITAL ZIKA VIRUS SYNDROME

Jan Byrne, M.D.
University of Utah
Maternal-Fetal Medicine
Clinical Genetics
National Birth Defects Prevention Network
UDOH Congenital Zika Collaborative Group

Cortesia Maisa Wanderley
Dr. Byrne has no conflict of interest, financial or otherwise, related to the content of this presentation.
Coming to a neighborhood near you.....
True or False: All blood, body fluids, secretions, excretions (including sweat), nonintact skin and mucous membranes may contain infectious agents.

- A. TRUE
- B. FALSE
True or False: All blood, body fluids, secretions, excretions (including sweat), nonintact skin and mucous membranes may contain infectious agents.

- A. TRUE
- B. FALSE

All blood, body fluids, secretions, excretions (with the exception of sweat), nonintact skin and mucous membranes may contain infectious agents.
When performing procedures including vaginal deliveries, manual placenta removal, bimanual uterine massage and repair of vaginal lacerations, personal protective equipment should include:

- A. Gloves and impermeable gown
- B. Gloves, mask, eye protection and impermeable gown
- C. Gloves, mask, eye protection, impermeable gown and ankle-high impermeable shoe covers
- D. Gloves, mask, eye protection, impermeable gown and knee-high impermeable shoe covers
When performing procedures including vaginal deliveries, manual placenta removal, bimanual uterine massage and repair of vaginal lacerations, personal protective equipment should include:

- A. Gloves and impermeable gown
- B. Gloves, mask, eye protection and impermeable gown
- C. Gloves, mask, eye protection, impermeable gown and ankle-high impermeable shoe covers
- D. Gloves, mask, eye protection, impermeable gown and knee-high impermeable shoe covers
True or False: Zika virus RNA has been detected in body fluids including blood, urine, saliva and amniotic fluid

- A. TRUE
- B. FALSE
True or False: Zika virus RNA has been detected in body fluids including blood, urine, saliva and amniotic fluid

- A. TRUE
- B. FALSE

According to the CDC: “Although there are no reports of transmission of Zika virus from infected patients to health care personnel or other patients, minimizing exposures to body fluids is important to reduce the possibility of such transmission.”
In which scenarios should Standard Precautions be in place? Standard Precautions are necessary in ____________ cases of Zika.

- A. Suspected
- B. Confirmed
- C. Both suspected and confirmed
In which scenarios should Standard Precautions be in place? Standard Precautions are necessary in __________ cases of Zika.

- A. Suspected
- B. Confirmed
- C. Both suspected and confirmed

According to the CDC, Standard Precautions should “be in place at all times, regardless of whether the infection is suspected or confirmed,” because patients with Zika virus infection may be asymptomatic.
When placing a fetal scalp electrode once membranes have already been ruptured or handling newborns before blood and amniotic fluid have been removed from the newborn’s skin, which of the following protective approaches for the health care personnel are recommended?

A. Gloves and impermeable gown
B. Gloves, eye protection and impermeable gown
C. Gloves, mask, eye protection and impermeable gown
When placing a fetal scalp electrode once membranes have already been ruptured or handling newborns before blood and amniotic fluid have been removed from the newborn’s skin, which of the following protective approaches for the health care personnel are recommended?

A. Gloves and impermeable gown
B. Gloves, eye protection and impermeable gown
C. Gloves, mask, eye protection and impermeable gown
According to the CDC, “[p]lacement of a fetal scalp electrode when membranes have already been ruptured or handling newborns before blood and amniotic fluid have been removed from the newborn’s skin require protection of health care personnel’s skin and clothing using gloves and an impermeable gown.

In contrast, when performing procedures where exposure to body fluids is anticipated, such as an amniotomy or placement of an intrauterine pressure catheter, protection of mucous membranes, skin, and clothing are recommended, with a mask and eye protection, in addition to gloves and an impermeable gown.”
What is Zika?
“Never before in history has there been a situation where a bite from a mosquito could result in a devastating malformation...”

T. Frieden, MD, MPH
Director, CDC
in *Fortune*, April 13, 2016
What is Zika?

- Intrauterine viral infections may affect the fetal brain (neurotropic)
- TORCH infections (toxoplasmosis, rubella, CMV, herpes)
- West Nile encephalitis- rare cases of fetal brain abnormalities
What is Zika?

- Member of Flavivirus family
- Mosquito-borne disease closely related to yellow fever, dengue, West Nile and Japanese encephalitis viruses
- First identified in the Zika Valley in Uganda in 1947
- Generally associated with a mild disease (fever, arthralgias, erythema, conjunctivitis)
- Often asymptomatic
- Cases of Guillain-Barré syndrome also reported
What is Zika?

- Spread by bite of female Aedes mosquitoes
  - *Aedes aegypti* and *Aedes albopictus*
- Daytime active
- Same mosquitoes that spread dengue and chikungunya viruses
Why now?

- Cluster of severe microcephaly cases in Brazil corresponding with outbreak of Zika virus in May 2015; incidence of microcephaly 20 times the baseline rate

- Case definition difficulties
  - Revised case definition in June 2016
Why no fetal cases until now?

- First identified in Uganda in 1947
- Underreporting of cases?
- Acquisition of immunity in endemic areas?
- Disease rare until now?
- Genomic changes $\rightarrow$ more virulent strains?
- Possibly the severe cases represent the “tip of the iceberg” and that less severe cases are not recognized at birth $\rightarrow$ underreporting of cases....
Microcephaly
- Generally defined as head circumference > 2 S.D. below the mean for gestation or less than the 3rd %tile
- Many etiologies of microcephaly, including intrauterine viral infections

Intracranial calcifications

Ventriculomegaly

Growth abnormalities

Placentomegaly

Brain destruction rare in viral infection
Ultrasound findings suggestive of Zika virus infection

- Microcephaly
  - Onset often ~24-28 wk gestation
- Intracranial calcifications
  - Usually subcortical rather than more common periventricular
- Ventriculomegaly
  - Often severe, asymmetric
- Brain destruction is significant and affects posterior fossa (cerebellum), brainstem, thalami
- Arthrogryposis- often atypical joint deformations
Symptoms of Zika virus infection at 13 wk gestation
Zika transmission in humans

- Bite of *Aedes aegypti* mosquitoes
- Intrauterine transmission
- Intrapartum transmission from viremic mother
- Sexual transmission
- Blood transfusion
- Laboratory exposure
Possible adverse reproductive outcomes due to congenital Zika infection

- Fetal death - early and late pregnancy loss
- Infant with microcephaly and serious brain anomalies **
- Infant with other birth defects
- Infant with less severe brain anomalies and developmental disabilities
- Infant with developmental disabilities alone
- Other adverse pregnancy outcomes such as preterm birth

** causal relationship established
Potential benefits of prenatal detection of Zika virus infection

- No pre- or postnatal treatment available for an affected fetus
- Diagnosis may allow for a discussion of reproductive options (termination vs. continuation of pregnancy)
- However, late onset / recognition of findings may significantly limit options
Potential benefits of prenatal detection of Zika virus infection

- Coordination of care of the pregnant patient and of the fetus/neonate
- Antenatal diagnosis of allows infants to deliver in appropriate setting - community hospital vs. tertiary care center:
  - Resuscitation issues?
  - Confirmation of diagnosis?
Prenatal Zika virus infection $\rightarrow$
Congenital Zika Syndrome
Severe microcephaly and timing of prenatal Zika virus infection
Destruction of existing CNS tissue & Disruption of future developmental processes

Brain volume loss

Neurologic dysfunction

Hearing, vision, swallowing problems
Global developmental impairment
Limb contractures
Hypertonia, epilepsy, extreme irritability

Recognizable pattern
Congenital Zika syndrome

- Severe microcephaly
- Misshapen skull with overlapping sutures
- Redundant scalp
Congenital Zika Syndrome - Ocular findings

Normal fundus

Fundus of presumed Zika infection
Ventura, et.al. 2016
Congenital Zika Syndrome - Arthrogryposis
Maternal infection → fetal infection?

- Zika can cross the placenta
- Vertical transmission only recently confirmed
- Zika virus RT-PCR can be performed on amniotic fluid, however it is not known how sensitive or specific this is for congenital infection
Maternal infection → fetal infection?

Many unanswered questions:
- How often does maternal infection result in fetal infection?
- What proportion of positive amniotic fluid tests will result in infected fetus/infants?
- What proportion of infected fetus/infants will be severely affected?
- What proportion of asymptomatic infants will have sequelae?
- What are those potential long-term sequelae?
Scope of the problem in the US
as of 12/27/2016

- Total number of pregnant women with laboratory evidence of Zika *
  - 1,292 (states)
  - 2,842 (territories)
- Total completed pregnancies +/- birth defects- 875
  - Total of 36 live born infants with Zika virus related birth defects in the US *
  - 5 pregnancy losses with birth defects *

* Relies on reporting to US Zika Pregnancy Registry
Scope of the problem in the US
as of 12/27/2016

- 2015-2016: 40,281 cases in the entire US **
  - 4,866 in the states/D.C. (all but 217 travel related)
  - 35,415 cases in the territories (all but 135 locally acquired; 98% in Puerto Rico)
  - State of Utah- 20 cases
    - Includes 1 case of possible person to person transmission
    - All other cases travel related

** As of 9/8/16, there were 18,833 cases in US/territories
Number of confirmed and probable Zika virus disease cases reported from United States and territories 2015-2016
Risk stratification

- Consider Zika virus disease in patient with compatible clinical S/Sx and who traveled to or reside in areas with ongoing transmission.
- History of sex without condom with someone who traveled to or resides in those areas- *includes all areas of Florida*.
- All pregnant women should be assessed for possible Zika virus exposure at each prenatal visit.
Offer testing to asymptomatic pregnant women who:

- Traveled to or live in an area with active Zika virus transmission
- Had sex without a condom with someone who traveled to or resides in an area with active Zika virus transmission
Confirmed maternal infection

- Refer to maternal-fetal medicine
- Counsel about reproductive options
- Consider invasive testing (amniocentesis)
- Serial ultrasounds for growth, evaluation of the CNS
- Consider other imaging modalities (e.g. MRI)
  - MRI is **NOT** for screening
- Postnatal evaluation of neonate, placenta-coordinate with health department
Pregnant women or those trying/capable of becoming pregnant should be **counseled against** travel to endemic areas.

If travel unavoidable, **extreme caution** to avoid exposure:
- Insect repellent
- Long sleeves, pants
- Screens on windows
- Air conditioning
“We’re going to Puerto Rico for a wedding- is that ok?”

- Sexual transmission has been documented
- Avoidance of unprotected intercourse for up to 6 months (or for duration of pregnancy) after travel to an endemic area
Imaging in Congenital Zika Syndrome
Thanks to my CDC colleagues

- Cynthia Moore, PhD, MD
  - Director of the Division of Congenital and Developmental Disorders
  - Zika virus response team

- Jan Cragan, MD, MPH
  - Medical officer with the National Center on Birth Defects and Developmental Disabilities

- Sonja Rasmussen, MD, MS
  - Director, Division of Public Health Information Dissemination, Center for Surveillance, Epidemiology, and Laboratory Services
  - Editor-in-chief, Morbidity and Mortality Weekly Report
Questions?