

#### 22<sup>nd</sup> Annual Chicago Infection Control Conference

#### June 9, 2017 Emily Petersen, MD

Lead, US Zika Pregnancy Registry Team Zika Response Centers for Disease Control and Prevention

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#### Learning Objectives

At the conclusion of this course participants will be able to

- Enable the learner to gain knowledge of emerging healthcare-associated infections pathogens.
- Identify effective infection control strategies to mitigate spread of multi-drug resistant organisms.
- Raise awareness of emerging disease threats and identify appropriate diagnostic testing, reporting and prevention methods.
- Raise awareness of local public health issues including opioid epidemic and immigrant health.

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# An Update on Zika Virus as a Cause of Microcephaly and Other Birth Defects

Emily Petersen, MD Lead, US Zika Pregnancy Registry Team Pregnancy & Birth Defects Task Force CDC Zika Virus Response



22<sup>nd</sup> Annual Chicago Infection Control Conference Chicago, Illinois June 9, 2017



U.S. Department of Health and Human Services Centers for Disease Control and Prevention

#### **First Time in History...**

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

– Dr. Tom Frieden, former CDC Director *Fortune,* April 13, 2016

> "...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



#### Where is Zika Now?

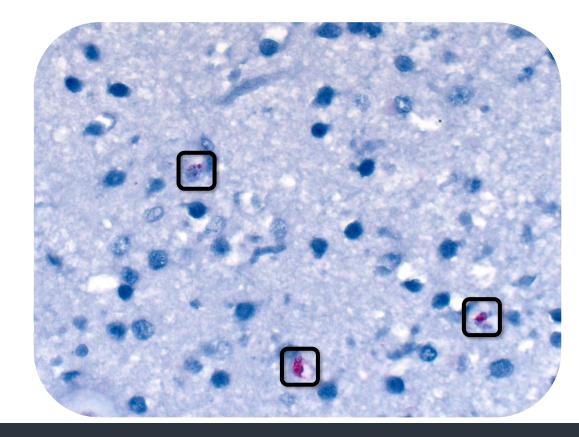


As of June 8, 2017 http://www.cdc.gov/zika/geo/active-countries.html Zika is a risk in 100 countries and territories

This includes areas with Zika travel notices and areas with endemic Zika

#### **Zika Virus Detected in Reproductive Tissues**

- Evidence of Zika virus in
  - Amniotic fluid
  - Placenta
  - Brain
  - Products of conception



### Zika Virus is a Cause of Microcephaly

#### Criteria for Proof of Human Teratogenicity

The NEW ENGLAND JOURNAL of MEDICINE

#### SPECIAL REPORT

Zika Virus and Birth Defects — Reviewing the Evidence for Causality

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., M.P.H.

Criterion		Criterion Met?
1.	Proven exposure to agent at critical time(s) during prenatal development	Yes
2.	Consistent findings by ≥2 high-quality epidemiologic studies	Partially
3.	Careful delineation of clinical cases	Yes
4.	Rare environmental exposure associated with rare defect	Yes
5.	Teratogenicity in experimental animals {important but not essential}	No
6.	Association should make biologic sense	Yes
7.	Proof in an experimental system that the agent acts in an unaltered state	NA

#### **Questions about Zika Virus & Pregnancy**

- Does Zika virus infection cause adverse pregnancy and birth outcomes?
- What is the level of fetal/infant risk of birth defects from a maternal Zika virus infection?
- When during pregnancy does Zika virus infection pose the highest risk to the fetus?
- What is the full range of potential health problems that Zika virus infection may cause?



#### **Surveillance of Pregnant Women, Fetuses, and Infants**



### **US Zika Pregnancy Registry**

#### • Purpose

To monitor pregnancy and infant outcomes in pregnancies with laboratory evidence of possible Zika virus infection and to inform clinical guidance and public health response

- Estimate number of infants with birth defects
- Provide data to inform phenotype of congenital Zika syndrome
- Help ensure infants are linked to care



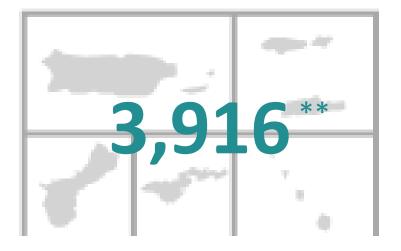
### **US Zika Pregnancy Registry: Inclusion Criteria**

- Who is included:
  - Pregnant women in the United States with laboratory evidence of possible Zika virus infection (regardless of whether they have symptoms) and their exposed infants
  - » Infants with laboratory evidence of congenital Zika virus infection (regardless of whether they have symptoms) and their mothers



## **Pregnancies with Laboratory Evidence of Possible Zika** Virus Infection





Pregnant women with any laboratory evidence of possible Zika virus infection in the **50 US States and DC** 

Pregnant women with any laboratory evidence of possible Zika virus infection in **US Territories** 

\*Includes aggregated data reported to the <u>US Zika Pregnancy Registry</u> as of May 23, 2017 \*\*Includes aggregated data from the US territories reported to the <u>US Zika Pregnancy Registry</u> and data from Puerto Rico reported to the <u>Zika Active Pregnancy Surveillance</u> as of May 23, 2017

### **Pregnancy Outcomes**

- Number of completed pregnancies with or without birth defects:
   1,579
- Of these
  - » 72 liveborn infants born with a birth defect consistent with congenital Zika infection
  - » 8 pregnancy losses affected by a birth defect consistent with congenital Zika infection



### Zika Virus & Pregnancy

- Does Zika virus infection cause adverse pregnancy and birth outcomes?
- What is the level of risk from Zika virus infection during pregnancy?
- When during pregnancy does Zika virus infection pose the highest risk to the fetus?
- What is the full range of potential health problems that Zika virus infection may cause?



Repeated

#### JAMA | Original Investigation

#### Birth Defects Among Fetuses and Infants of US Women With Evidence of Possible Zika Virus Infection During Pregnancy

Margaret A. Honein, PhD: April L. Dawson, MPH: Emily E. Petersen, MD: Abbey M. Jones, MPH: Ellen H. Lee, MD: Mahsa M. Yazdy, PhD: Nina Ahmad, MD: Jennifer Macdonald, MPH: Nicole Evert, MS: Andrea Bingham, PhD: Sascha R. Ellington, MSPH: Carrie K. Shapiro-Mendoza, PhD: Titliope Oduyebo, MD: Anne D. Fine, MD: Catherine M. Brown, DVM: Jamie N. Sommer, MS: Jyoti Cupta, MPH: Philip Cavicchia, PhD: Sally Slavinski, DVM: Jennifer L. White, MPH: S. Michele Owen, PhD: Lyle R. Petersen, MD: Coleen Boyle, PhD: Dana Meaney-Deiman, MD: Denise J. Jamieson, MD: for the US Zika Pregnancy Registry Collaboration

- Among pregnancies in the United States with laboratory evidence of possible Zika virus infection
  - » 6% of fetuses or infants had birth defects potentially related to Zika virus
  - » Similar proportion of pregnancies with birth defects (≈6%) among symptomatic and asymptomatic pregnant women
  - » Among women with infection in the 1<sup>st</sup> trimester of pregnancy, birth defects reported in 11%

Honein MA, Dawson AL, Petersen EE, et al. Birth defects among fetuses and infants of US women with evidence of possible Zika virus infection during pregnancy. JAMA 2017;317:59-68.

Box. Birth Defects Potentially Related to Zika Virus Infection During Pregnancy and Monitored by the US Zika Pregnancy Registry for Enhanced Surveillance

#### **Brain Abnormalities With and Without Microcephaly**

Confirmed or possible congenital microcephaly<sup>a</sup>

Intracranial calcifications

Cerebral atrophy

Abnormal cortical formation (eg, polymicrogyria, lissencephaly, pachygyria, schizencephaly, gray matter heterotopia)

Corpus callosum abnormalities

Cerebellar abnormalities

Porencephaly

Hydranencephaly

Ventriculomegaly/hydrocephaly (excluding "mild" ventriculomegaly without other brain abnormalities)

Fetal brain disruption sequence (collapsed skull, overlapping sutures, prominent occipital bone, scalp rugae)

Other major brain abnormalities including intraventricular hemorrhage in utero (excluding postnatal intraventricular hemorrhage)

Neural Tube Defects and Other Early Brain Malformations

Neural tube defects including anencephaly, acrania, encephalocele, spina bifida

Holoprosencephaly (arhinencephaly)

#### **Eye Abnormalities**

Microphthalmia/anophthalmia

Coloboma

Cataract

Intraocular calcifications

Chorioretinal anomalies involving the macula (eg, chorioretinal atrophy and scarring, macular pallor, gross pigmentary mottling and retinal hemorrhage; excluding retinopathy of prematurity)

Optic nerve atrophy, pallor, and other optic nerve abnormalities

#### **Consequences of Central Nervous System Dysfunction**

Congenital contractures (eg, arthrogryposis, clubfoot, congenital hip dysplasia) with associated brain abnormalities

Congenital deafness documented by postnatal audiological testing

<sup>a</sup> Live births: measured head circumference (adjusted for gestational age and sex) less than the third percentile at birth or, if not measured at birth, within first 2 weeks of life. Pregnancy loss: prenatal head circumference more than 3 SDs below the mean based on ultrasound or postnatal head circumference less than the third percentile. Birth measurements are evaluated using the Intergrowth-21st standards (http://intergrowth21.ndog .ox.ac.uk/) based on measurements within 24 hours of birth.

#### **Vital Signs: Update Previous Estimates**

Morbidity and Mortality Weekly Report

#### Vital Signs: Update on Zika Virus–Associated Birth Defects and Evaluation of All U.S. Infants with Congenital Zika Virus Exposure — U.S. Zika Pregnancy Registry, 2016

Megan R. Reynolds, MPH<sup>1</sup>; Abbey M. Jones, MPH<sup>1</sup>; Emily E. Petersen, MD<sup>2</sup>; Ellen H. Lee, MD<sup>3</sup>; Marion E. Rice, MPH<sup>1,4</sup>; Andrea Bingham, PhD<sup>5</sup>; Sascha R. Ellington, MSPH<sup>2</sup>; Nicole Evert, MS<sup>6</sup>; Sarah Reagan-Steiner, MD<sup>7</sup>; Titilope Oduyebo, MD<sup>2</sup>; Catherine M. Brown, DVM<sup>8</sup>; Stacey Martin, MSc<sup>9</sup>; Nina Ahmad, MD<sup>10</sup>; Julu Bhatnagar, PhD<sup>7</sup>; Jennifer Macdonald, MPH<sup>11</sup>; Carolyn Gould, MD<sup>9</sup>; Anne D. Fine, MD<sup>3</sup>; Kara D. Polen, MPH<sup>1</sup>; Heather Lake-Burger, MPH<sup>5</sup>; Christina L. Hillard, MA<sup>1</sup>; Noemi Hall, PhD<sup>6,12</sup>; Mahsa M. Yazdy, PhD<sup>8</sup>; Karnesha Slaughter, MPH<sup>1</sup>; Jamie N. Sommer, MS<sup>10</sup>; Alys Adamski, PhD<sup>1</sup>; Meghan Raycraft, MPH<sup>1</sup>; Shannon Fleck-Derderian, MPH<sup>4,13</sup>; Jyoti Gupta, MPH<sup>11</sup>; Kimberly Newsome, MPH<sup>1</sup>; Madelyn Baez-Santiago, PhD<sup>1</sup>; Sally Slavinski, DVM<sup>3</sup>; Jennifer L. White, MPH<sup>10</sup>; Cynthia A. Moore, MD, PhD<sup>1</sup>; Carrie K. Shapiro-Mendoza, PhD<sup>2</sup>; Lyle Petersen, MD<sup>9</sup>; Coleen Boyle, PhD<sup>14</sup>; Denise J. Jamieson, MD<sup>2</sup>; Dana Meaney-Delman, MD<sup>13</sup>; Margaret A. Honein, PhD<sup>1</sup>; U.S. Zika Pregnancy Registry Collaboration

Reynolds MR, Jones AM, Petersen EE, et al. Vital Signs: Update on Zika Virus–Associated Birth Defects and Evaluation of All U.S. Infants with Congenital Zika Virus Exposure — U.S. Zika Pregnancy Registry, 2016. MMWR Morb Mortal Wkly Rep 2017;66:366-373.

### **Key Vital Signs Findings**

- 972 completed pregnancies with evidence of Zika in 2016:
  - 5% with possible Zika had birth defects **》**
  - **10%** with confirmed Zika had birth defects **》**
  - **15%** with confirmed Zika in the 1<sup>st</sup> trimester **》** had birth defects



*Vitäl*signs<sup>™</sup>



www.cdc.gov/vitalsigns/zika-babies

### **Baseline Prevalence of Birth Defects Observed with Zika**

- Used data from birth defects surveillance systems in Massachusetts, North Carolina, and Atlanta, Georgia, during pre-Zika outbreak years (2013–2014)
- Compared with data from US Zika Pregnancy Registry
- Prevalence of Zika-related birth defects before Zika outbreak in the Americas:

#### 3 out of every 1,000 births

• Proportion of infants with birth defects among completed pregnancies with confirmed Zika virus infection (2016):

#### 24 out of every 250 completed pregnancies

Estimated **30-fold increase** 

in Zika-related birth defects in pregnancies with confirmed Zika infection compared with pre-Zika years

Cragan JD, Mai CT, Petersen EE, et al. Baseline Prevalence of Birth Defects Associated with Congenital Zika Virus Infection — Massachusetts, North Carolina, and Atlanta, Georgia, 2013–2014. MMWR Morb Mortal Wkly Rep 2017;66:219–222. DOI: <a href="http://dx.doi.org/10.15585/mmwr.mm6608a4">http://dx.doi.org/10.15585/mmwr.mm6608a4</a>

Reynolds MR, Jones AM, Petersen EE, et al. Vital Signs: Update on Zika Virus–Associated Birth Defects and Evaluation of All U.S. Infants with Congenital Zika Virus Exposure — U.S. Zika Pregnancy Registry, 2016. MMWR Morb Mortal Wkly Rep 2017;66:366-373.



Morbidity and Mortality Weekly Report

June 8, 2017

#### Pregnancy Outcomes After Maternal Zika Virus Infection During Pregnancy — U.S. Territories, January 1, 2016–April 25, 2017

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### Zika Virus & Pregnancy

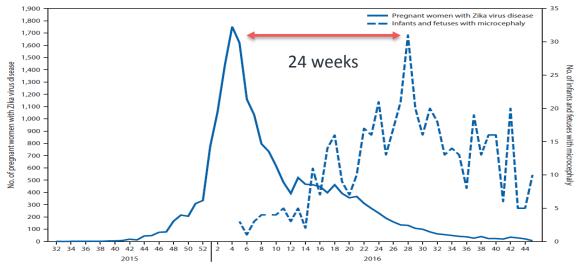
- Does Zika virus infection cause adverse pregnancy and birth outcomes?
- What is the level of risk from a Zika virus infection during pregnancy?
- When during pregnancy does Zika virus infection pose the highest risk to the fetus?
- What is the full range of potential health problems that Zika virus infection may cause?



#### **Period of Highest Risk to the Fetus**

- Remains a key question
- 1<sup>st</sup> and 2<sup>nd</sup> trimester infections have been associated with children with birth defects; unknown if 3<sup>rd</sup> trimester poses lesser or perhaps different risks (growth restriction, stillbirth)

FIGURE 1. Date of symptom onset of reported cases of Zika virus disease among pregnant women\* and date of birth of infants or of pregnancy loss for fetuses with reported microcephaly<sup>+</sup> — Colombia, August 9, 2015 (epidemiologic week 32)–November 12, 2016 (week 45)



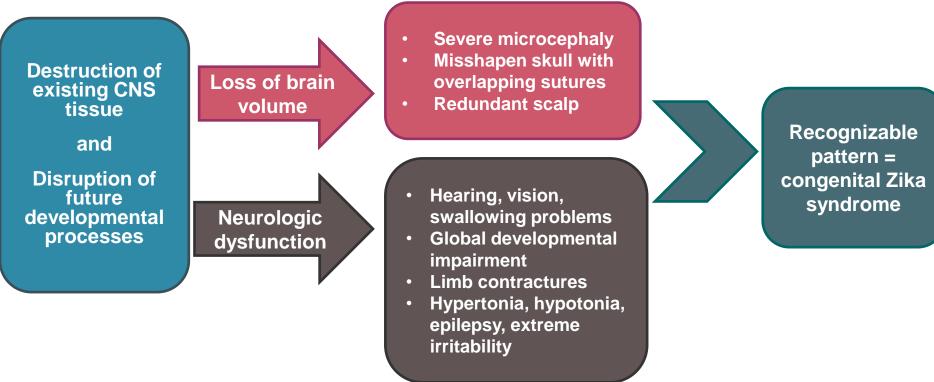
https://www.cdc.gov/mmwr/v olumes/65/wr/mm6549e1.htm ?s cid=mm6549e1 w

### Zika Virus & Pregnancy

- Does Zika virus infection cause microcephaly and other serious birth defects?
- What is the level of risk from a Zika virus infection during pregnancy?
- When during pregnancy does Zika virus infection pose the highest risk to the fetus?
- What is the full range of potential health problems that Zika virus infection may cause?



#### Prenatal Zika Virus Infection – Congenital Zika Syndrome



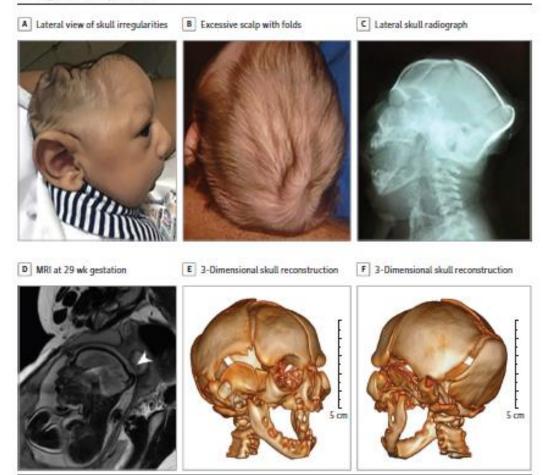
Moore CA, Staples JE, Dobyns WB, et al. Characterizing the pattern of anomalies on congenital Zika syndrome for pediatric clinicians. JAMA Pediatr. 2017;171:288-295.

## **Congenital Zika Syndrome – Components of Unique Pattern**

- Severe microcephaly with partial skull collapse
- Intracranial calcifications in the subcortical region
- Macular scarring and focal pigmentary retinal mottling
- Congenital contractures
- Neurologic abnormalities both pyramidal and extrapyramidal

Moore CA, Staples JE, Dobyns WB, et al. Characterizing the pattern of anomalies on congenital Zika syndrome for pediatric clinicians. JAMA Pediatr. 2017;171:288-295.

Figure 1. Cranial Morphology Supporting Fetal Brain Disruption Sequence Phenotype in Congenital Zika Syndrome

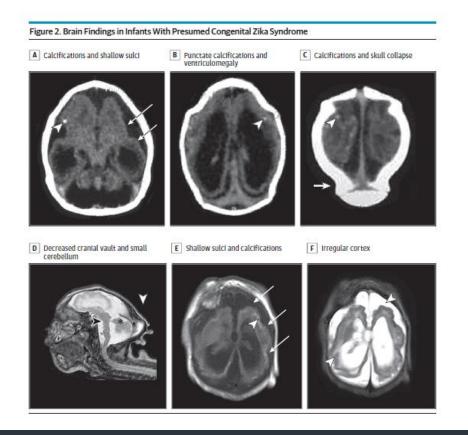


## **Cranial Morphology**

- Features
  - Severe microcephaly (most more than 3 SD below the mean)
  - Partial collapse of the skull with overlapping sutures
  - Occipital bone prominence
  - Small or absent anterior fontanel
  - Scalp rugae

Moore CA, Staples JE, Dobyns WB, et al. Characterizing the pattern of anomalies on congenital Zika syndrome for pediatric clinicians. JAMA Pediatr. 2017;171:288-295.

#### **Congenital Zika Syndrome – Brain Anomalies**

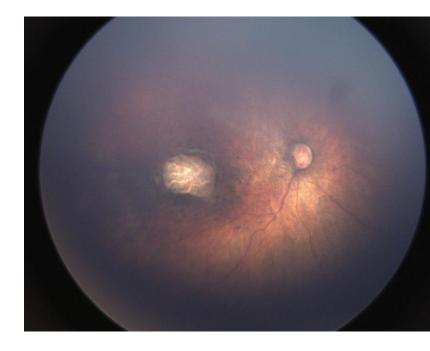


- Features
  - Intracranial calcifications
  - Cerebral volume loss, ventriculomegaly
  - Abnormal gyral development
  - Low forehead and small cranial vault

Moore CA, Staples JE, Dobyns WB, et al. Characterizing the pattern of anomalies on congenital Zika syndrome for pediatric clinicians. JAMA Pediatr. 2017;171:288-295.

#### **Congenital Zika Syndrome – Ocular Findings**

- Structural and anterior eye anomalies
  - » Microphthalmia, coloboma
  - » Cataracts, intraocular calcifications
- Posterior eye anomalies
  - » Optic nerve hypoplasia, atrophy
  - » Chorioretinal atrophy and scarring
  - » Macular pallor
  - » Gross pigmentary anomalies generally in the macular area
- No active chorioretinitis reported to date



Moore CA, Staples JE, Dobyns WB, et al. Characterizing the pattern of anomalies on congenital Zika syndrome for pediatric clinicians. JAMA Pediatr. 2017;171:288-295.

#### **Congenital Zika Syndrome – Congenital Contractures**



Moore CA, Staples JE, Dobyns WB, et al. Characterizing the pattern of anomalies on congenital Zika syndrome for pediatric clinicians. JAMA Pediatr. 2017;171:288-295.

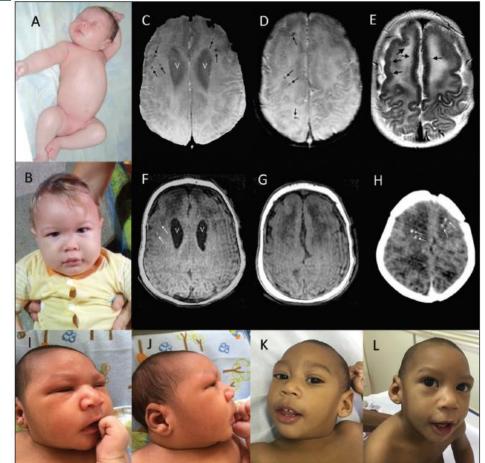
#### **Congenital Zika Syndrome – Other Neurologic Sequelae**

- Information on long-term medical and developmental outcomes or mortality sparse
- Neurologic sequelae reported include the following:
  - » Motor and cognitive disabilities
  - » Epilepsy
  - » Swallowing difficulties
  - » Vision loss and hearing impairment
  - » Hypertonia and spasticity with tremors
  - » Irritability with excessive crying

#### Congenital Zika Syndrome – Postnatal Microcephaly

- Recent report of 13 infants who did not have microcephaly at birth (>-2 SD)
- Had severe findings including
  - All with significant brain abnormalities, 23% with retinal anomalies
  - All with hypertonia
  - 60% with epilepsy
- Head growth slowed and microcephaly diagnosed at ≈ 6 months of age

FIGURE. Clinical photographs and magnetic resonance (MR) and computed tomography (CT) images of two infants with congenital Zika syndrome\* — Brazil, October 2015–October 2016



Van der Linden V, Pessoa A, Dobyns W, et al. Description of 13 infants born during October 2015–January 2016 with congenital Zika virus infection without microcephaly at birth — Brazil. MMWR Morb Mortal Wkly Rep 2016;65:1343-1348.

### **Congenital Zika Syndrome – Expanding the Phenotype**

- Infants with
  - » Brain or eye anomalies but no microcephaly
  - » Sensory/cranial nerve dysfunction only at birth or later
  - » Other neurologic anomalies with origin in the embryonic period
  - » Non-neurologic congenital anomalies
  - » Developmental disabilities
  - » Growth restriction

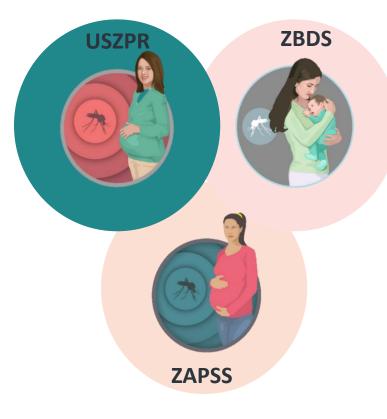
### Congenital Zika Syndrome – Knowledge Limits

- Most available information based on infants with microcephaly and severe phenotype
- Information on long-term medical and developmental outcomes is incomplete
- Majority of reports to date have focused on only one aspect of the phenotype such as neurologic sequelae, eye anomalies, hearing, etc. so information is lacking to describe clustering of anomalies
- Information on mortality rates and causes of death is incomplete

Information is needed by families, healthcare providers, communities, governmental organizations and others to plan for needed services.

#### What Do We Hope to Learn in the Next Year?

- Identify full range of health effects among infants with congenital Zika exposure
- Determine optimal Zika virus testing to identify infants with congenital Zika virus infection
- Understand how neuroimaging will help identify infants with adverse effects of congenital Zika infection
- Assess risk of other adverse outcomes associated with Zika infection during pregnancy
- Use data to inform clinical management of pregnant women with Zika



#### What You Can Do to Help



Ask about Zika

Provide all needed tests and follow-up care

Support infants and families

#### **Educate Families about Zika Virus Prevention**

# Pregnant women should not travel to areas with risk of Zika

#### If a pregnant woman *must* travel, she should

- » Talk with her healthcare provider before she goes
- » Strictly follow steps to prevent mosquito bites during the trip
- » Take steps to prevent sexual transmission
- » Talk with her healthcare provider after she returns, even if she doesn't feel sick



Healthcare Providers Caring for Pregnant Women and Infants Should Ask about Zika Exposure during Pregnancy

Have you traveled to an area with risk of Zika during pregnancy or just before you became pregnant?

Have you had sex without a condom with a partner who lives in or traveled to an area with risk of Zika?

Do you live in or do you frequently travel (daily or weekly) to an area with risk of

Zika?



### Who Should Be Tested for Zika?

#### All pregnant women (regardless of symptoms) who

- » Live in or recently traveled to an area with risk of Zika that has a CDC Zika travel notice, or
- » Had unprotected sex with a partner who lives in or traveled to an area with risk of Zika that has a CDC Zika travel notice

Pregnant women who live in or recently traveled to an area with risk of Zika but <u>without</u> a CDC Zika travel notice

- » If they develop symptoms of Zika, or
- » If their fetus has abnormalities on an ultrasound that may be related to Zika infection

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



### **Testing Infants for Zika**

#### **CDC** recommends laboratory testing for

- » All infants born to mothers with laboratory evidence of Zika virus infection during pregnancy
- » Infants who have abnormal clinical or neuroimaging findings suggestive of congenital Zika syndrome and a mother with a possible exposure to Zika virus, regardless of maternal Zika virus testing results



## Laboratory Testing of Infants with Possible Congenital Zika Virus Infection

#### **Additional Considerations**

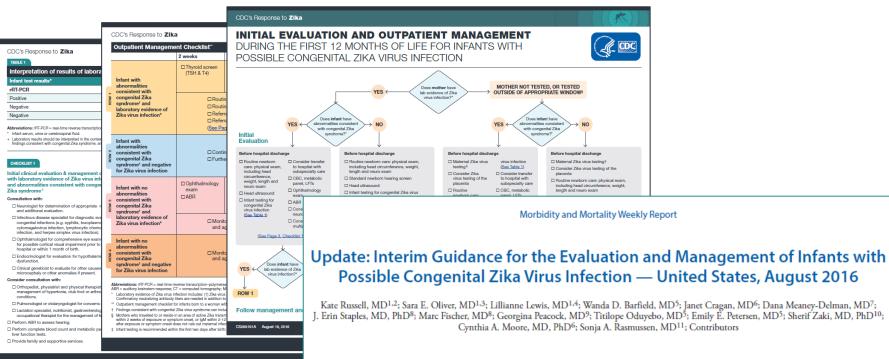
Testing for Zika virus infection should be considered for infants

- Born to mothers with an epidemiologic link for whom
  - » There is concern about infant follow-up care
  - » Maternal testing was not performed before delivery and exposure was >12 weeks before delivery, or
  - » Maternal testing was negative but was performed on a specimen obtained >12 weeks after maternal exposure



\*An epidemiologic link includes travel to or residence in an area with risk of Zika, or sex without a condom with a partner who traveled to or lived in such an area

#### Pediatric Evaluation and Follow-Up: The First 12 Months



On August 19, 2016, this report was posted as an MMWR ongoing psychosocial support and assistance with coordina-

Link to updated infant guidance (April 2017): <u>https://www.cdc.gov/zika/hc-providers/infants-children/evaluation-and-management.html?permalink=https://www.cdc.gov/zika/hc-providers/infants-children/evaluation-and-management.html</u>

### **Contribute to the US Zika Pregnancy Registry**

# Notify health department of pregnant women and/or infants with Zika virus infection

- » More information available on the <u>U.S. Zika Pregnancy Registry</u> website
- » To contact CDC Registry staff, call the CDC Emergency Operations Center watch desk at 770-488-7100 and ask for the Zika Pregnancy Hotline or email <u>ZIKApregnancy@cdc.gov.</u>
- » For non-urgent requests, call 800-CDC-INFO (800-232-4636)





# More information on caring for pregnant women, infants, or children with Zika virus infection is available at <u>CDC's Zika website</u>.

