Pregnancy and Birth Defects
Zika Action Plan Post-Summit Teleconference

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After this teleconference learners will be able to

- Review what we know and don't know about Zika virus infection in pregnancy, and Zika-related pregnancy and infant outcomes.
- Describe CDC's response to the threats posed by the Zika virus, including monitoring pregnancy and infant outcomes.
- Review specific considerations regarding monitoring and response to Zika-associated infant outcomes, and what CDC is doing to support rapid case-finding and referral to services for affected families.

Zika and Pregnancy

Sonja A Rasmussen, MD, MS

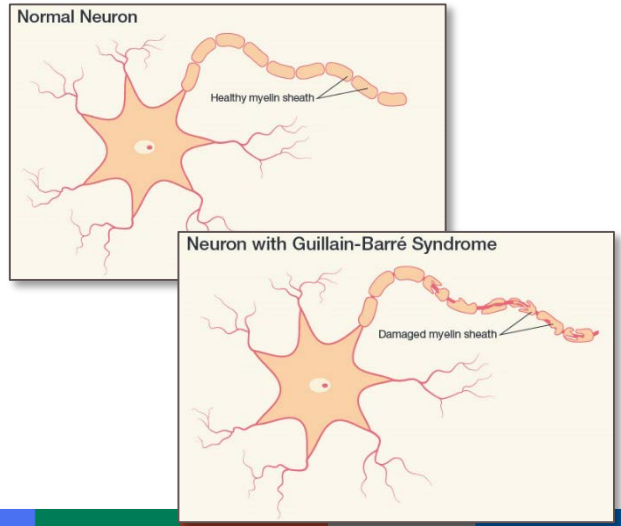
History Making

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

– T. Frieden, *Fortune*–April 13, 2016

Zika Virus Clinical Disease Course and Outcomes: Adults and Children

- Clinical illness usually mild
- Many infections asymptomatic
- When symptoms do occur, they last several days to a week
- Severe disease requiring hospitalization uncommon
- Fatalities are rare
- Guillain-Barré syndrome reported in patients following suspected Zika virus infection

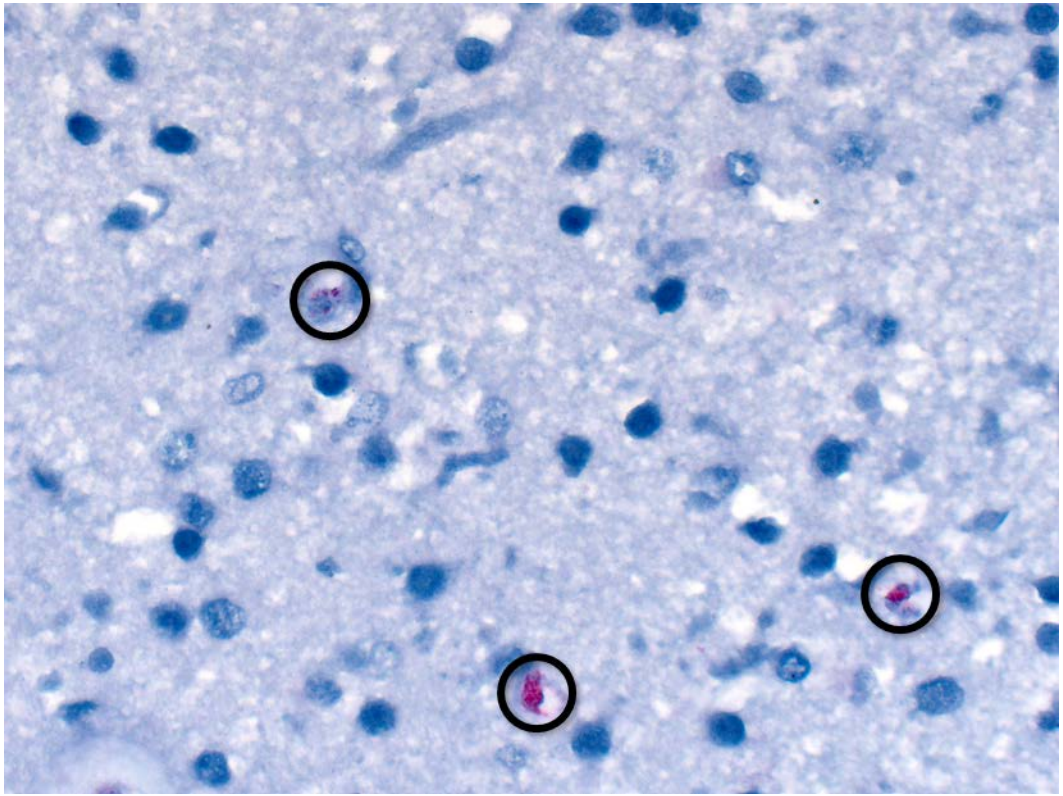


Zika Virus Infection in Pregnant Women

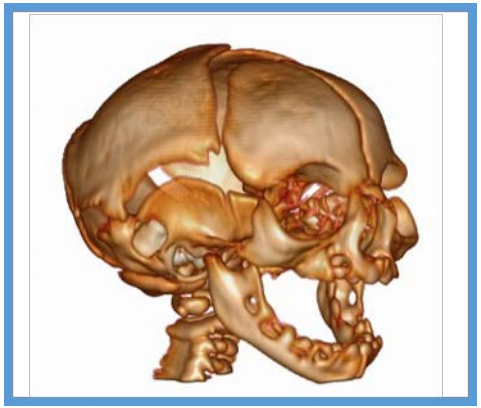
- Pregnant women can be infected
  - Through a mosquito bite
  - Through sex with an infected male
- If infected around conception
  - Zika might present risk to fetus
- If infected during pregnancy
  - Zika can be passed to the fetus during pregnancy or around the time of birth

CDC Lab Confirms Zika In Fetal Tissues

- Evidence of Zika virus has been identified in:
  - Amniotic fluid
  - Placenta
  - Brain
  - Products of conception



Infants with Microcephaly



Images courtesy of
C. Moore and Nova Diagnóstico

Zika is a cause of microcephaly

April 13, 2016

Rasmussen SA, Jamieson DJ, Honein MA, Petersen LR. Zika Virus and Birth Defects– Reviewing the Evidence for Causality. New Engl J Med. 2016 Apr 13.

Many Questions Remain

- What is the level of risk from a Zika virus infection during pregnancy?
- When during pregnancy Zika virus infection poses the highest risk to the fetus?
- What is the full range of potential health problems that Zika virus infection may cause?
- What are other factors (e.g., co-occurring infection) that might affect the risk for birth defects?

Collecting data for action

US Zika Pregnancy Registry

Zika Active Pregnancy Surveillance System (Puerto Rico)

Proyecto Vigilancia de Embarazadas con Zika (Colombia)

US Zika Pregnancy Registry

US Zika Pregnancy Registry : Purpose

- **Purpose of registry:**

  To monitor pregnancy and infant outcomes following Zika virus infection during pregnancy and to inform clinical guidance and public health response

- **How it works:**

  The registry is a supplemental surveillance effort coordinated by CDC and dependent on the voluntary collaboration of the state, tribal, local, a territorial health departments

US Zika Pregnancy Registry

- **Who is included**:

  Pregnant women with laboratory evidence of Zika virus infection and exposed infants born to these women; infants with laboratory evidence of congenital Zika virus infection and their mothers

- **How can you support the registry?**

  Spread the word about the US Zika Pregnancy Registry and assist with health department follow-up for pregnant women and infants who are part of the registry

What CDC is Doing to Respond

- Monitoring spread of Zika virus through public health surveillance
- Increasing laboratory capacity for testing to identify Zika virus infection
- Assisting with the development of tests that can improve detection of previous infection with Zika virus
- Working with partners to improve mosquito control efforts
- Providing recommendations for prevention
- Promoting effective health communication strategies
- Focusing on supporting state, local, tribal, and territorial response efforts
- Building state capacity to identify babies with birth defects

More information: Zika and Pregnancy

- More information is available on the US Zika Pregnancy Registry on CDC's US Zika Pregnancy Registry webpage
- 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 ZIKApregnancy@cdc.gov
- More information on caring for pregnant women, infants, or children with Zika virus infection is available at CDC's Zika website.

Zika and Birth Defects

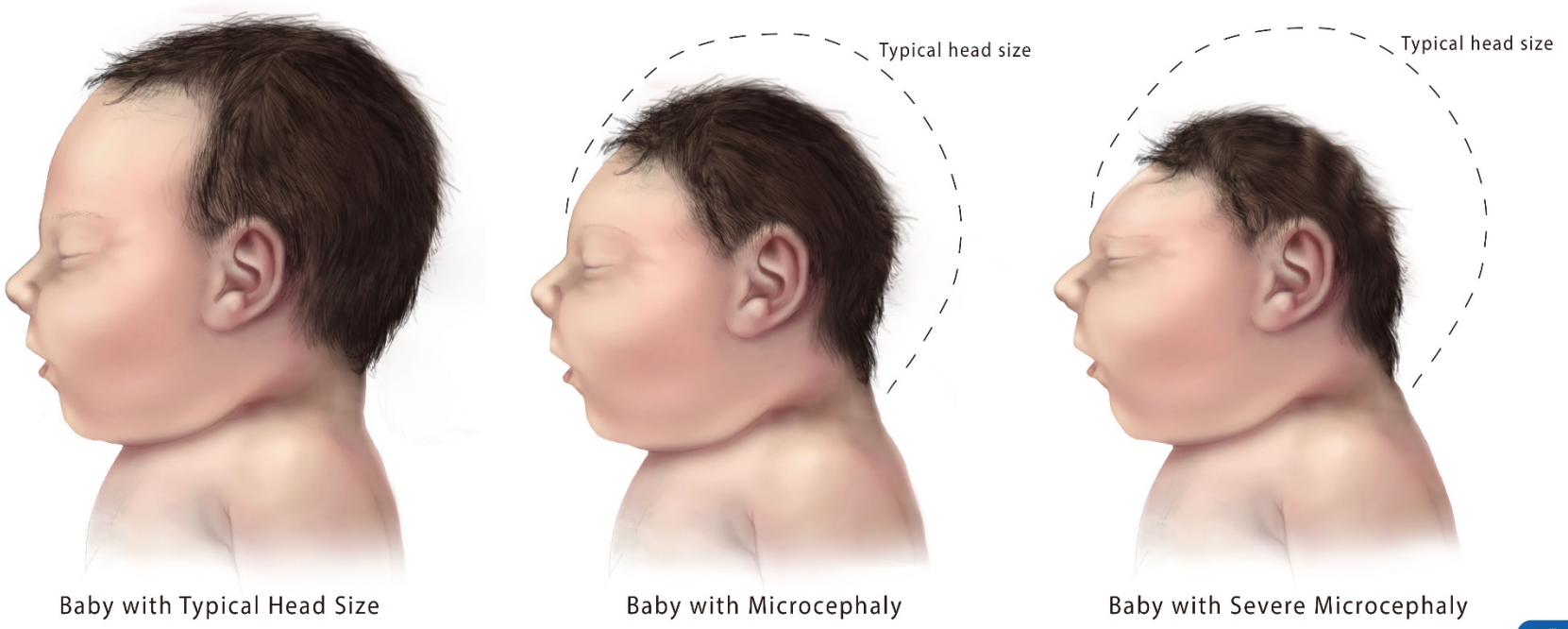
Janet Cragan, MD, MPH

What is Microcephaly?

- Clinical finding of a small head when compared to infants of same sex and age
- Measured by head circumference (HC) or occipitofrontal circumference (OFC)
- Reliable assessment of intracranial brain volume
- Often leads to cognitive and/or neurologic issues
- Difficult birth defect to monitor because of inconsistent definition and use of terminology
  - Clinicians use different cut-points such as less than 3rd, 5th, or 10th percentile for age and sex

Stevenson RE and Hall JG. Human Malformations and Related Anomalies, 2nd ed. Oxford University Press, 2006.

Range of Microcephaly Severity



CDC's microcephaly webpage

Types of Congenital Microcephaly

- Disproportionate - Head is small out of proportion to the weight and length, which may be normal for age and sex
- Proportionate - Head size, weight and length all are small for age and sex but proportional to each other
- “Relative” microcephaly - Head size measures within the normal range for age and sex, but is small out of proportion to the weight and length

Zika-Related Definition of Congenital Microcephaly

Definite

- Live Births
  - Head circumference (HC) at birth <3rd percentile for gestational age and sex, OR
  - If HC at birth is not available, HC <3rd percentile for age and sex within the first 6 weeks of life, adjusted for gestational age if preterm
- Stillbirths and Elective Terminations
  - HC at delivery <3rd percentile for gestational age and sex

Possible

- Live Births
  - If an earlier HC is not available, HC <3rd centile for age and sex beyond 6 weeks of life
- All Pregnancy Outcomes
  - Microcephaly diagnosed or suspected on prenatal ultrasound in the absence of available postnatal HC measurements

Suggested Reference Charts for Head Circumference At Birth by Gestational Age

Gestational Age at Birth	Reference Chart	Web Link
33 to 43 Weeks	INTERGROWTH-21st Newborn Size at Birth Chart	https://intergrowth21.tghn.org/articles/intergrowth-21st-newborn-size-birth-chart/ A tool for calculating percentiles for head circumference for infants 33-42 weeks is available at: https://intergrowth21.tghn.org/global-perinatal-package/intergrowth-21st-comparison-application/
34 to 32 Weeks	INTERGROWTH-21st Very Preterm Size at Birth References	https://intergrowth21.tghn.org/articles/intergrowth-21st-very-preterm-size-birth-references-and-z-scores-standard-deviations/ A tool for calculating percentiles for head circumference for infants 24-32 weeks is also available from this site.
< 24 Weeks	INTERGROWTH-21st Fetal Growth Standards	https://intergrowth21.tghn.org/articles/intergrowth-21st-fetal-growth-standards/ A tool for calculating z-scores for fetal growth standards is also available from this site.

Intergrowth-21st Fetal Growth Standards are based on measurements in utero only. International standards for birth measurements in infants less than 24 weeks gestation are not available. For most elective pregnancy terminations and many stillbirths, accurate postnatal head circumference measurements are not possible.

For a study comparing head circumference measurements in utero to those obtained after birth, see: Melamed N, Yogev Y, Danon D, et al. Sonographic estimation of fetal head circumference: how accurate are we? Ultrasound Obstet Gynecol 2011

Assessing Prevalence

- Subdivide the cases of microcephaly into groups
  - Severity of microcephaly
    - HC <3rd percentile for age and sex
    - HC between 3rd and 5th percentiles for age and sex
    - HC >5th percentile for age and sex
    - HC values missing
  - Known (documented) causes
    - Chromosomal or genetic abnormalities
    - Syndromes (diagnosed or suspected)
    - In utero infections and types (positive culture or antibody titers)
    - Exposure to a known teratogen (e.g., alcohol, hydantoin)
  - No documented cause
- Monitor the relative proportion of each group over time

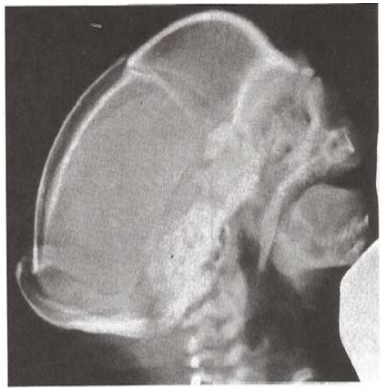
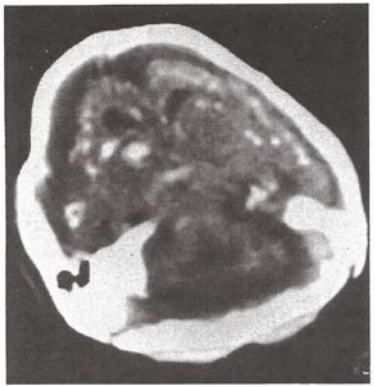
Brain Defects Linked with Zika in the Fetus

- Decreased total brain tissue with resulting microcephaly
- Calcium deposits in the brain indicating brain damage
- Excess fluid in the brain cavities and surrounding the brain
- Absent or poorly formed brain structures
- Abnormal eye development

Karwowski MP, Nelson JM, Staples JE, et al. Zika Virus Disease: A CDC Update for Pediatric Health Care Providers. Pediatrics. 2016;137(5):e20160621

Fetal Brain Disruption Sequence

- First described in 1984 but noted in earlier literature
- Brain destruction resulting in collapse of the fetal skull, microcephaly, scalp rugae and neurologic impairment
- Photos and X-ray from 1990 series;* phenotype appears to be present in affected babies in Brazil

*Moore, et al. J Pediatr 1990;116:383-386.

Adverse Outcomes and Zika Virus

- A range of other problems have been reported:
  - Eye abnormalities
  - Hearing impairment
  - Seizures
  - Swallowing impairment
  - Hypertonicity and posturing
  - Contractures, including club foot and curving of the joints
  - Severe irritability
  - Developmental delay
  - Growth abnormalities, including intrauterine growth restriction and disproportionate growth (head size alone affected)

Karwowski MP, Nelson JM, Staples JE, et al. Zika Virus Disease: A CDC Update for Pediatric Health Care Providers. Pediatrics. 2016;137(5):e20160621

Draft Funding Opportunity Announcement #CDC-RFA-DD16-1605

- Surveillance, prevention, and intervention activities for infants with microcephaly and other adverse outcomes linked with the Zika virus
  - Establish, enhance, and maintain rapid population-based surveillance of microcephaly and other adverse outcomes (especially central nervous system defects) possibly linked to Zika virus infection during pregnancy using an active case-finding methodology
  - Participate in centralized pooled clinical and surveillance data projects
  - Ensure affected infants and families are referred to services
  - Assess health and developmental outcomes of these children
- Additional information is available on the HHS Grants Forecast website at https://forecast.grantsolutions.gov/index.cfm?switch=grant.view&gff_grants_forecastInfoID=100001785

Sources for Data Collection

- Where deliveries occur
  - Birth hospitals, birthing centers/midwifery practices, home births
  - Where elective terminations are performed after prenatal diagnosis of defects
- Where children with microcephaly and central nervous system abnormalities are seen and evaluated
  - Pediatric and family practice clinics
  - Subspecialty clinics (neurology, genetics)
  - Developmental clinics, early intervention programs
- Reporting by healthcare providers and programs
  - May need to revise reporting forms to include information specific to abnormalities of interest

Engage the Healthcare Community

- Need to educate the healthcare community about Zika-related outcomes and why reporting is important
- Provide a letter from the state health commissioner or someone in authority outlining the need for reporting and the circumstances that allow physicians to report patient information
- Collaborate with state professional societies (AAP, AAFP, ACOG, Hospital Association) to inform providers caring for infants and young children
- Provide feedback and ongoing updates to maintain reporting and ascertainment going forward

More information: Zika and Birth Defects

- For clinical questions, please contact ZikaMCH@cdc.gov
- Information about microcephaly, including webinar on conducting surveillance: http://www.cdc.gov/ncbddd/birthdefects/microcephaly.html
- National Birth Defects Prevention Network: http://nbdpn.org/

Thanks to our many collaborators and partners!

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For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov