Objectives

- Become familiar with the origin and history of the Zika Virus (ZIKV), including the modes of transmission

- Know the signs, symptoms and treatments of medical conditions associated with the Zika Virus (ZIKV)

- Understand the methods to control the Zika Virus (ZIKV)
ZIKA VIRUS (ZIKV)

- Single-Stranded RNA Virus
- Genus – *Flavivirus*
- Closely Related to:
  - Yellow Fever Virus
  - Dengue Fever Virus
  - Japanese Encephalitis Virus
  - West Nile Virus
- Primary mode of transmission through the bite of an infected *Aedes* species mosquito
  - *Aedes aegypti*
  - *Aedes albopictus*
ZIKA VIRUS

Aedes aegypti

Aedes albopictus
FACTS

**Aedes aegypti**
- Live in tropical, subtropical and some temperate climates
- Main type of mosquito that spreads ZIKV, dengue, chikungunya, Yellow Fever and other viruses
- Because they live near and prefer to feed on people, more likely to spread these viruses than other types of mosquitoes

**Aedes albopictus**
- Live in tropical, subtropical and temperate climates, but can live in a broader temperature range and at cooler temperatures than the Aedes aegypti
- Because they feed on animals as well as people, they are less likely to spread viruses like ZIKV, dengue, chikungunya and other viruses.
ZIKA VIRUS
Mosquito Distribution - US
Timeline

1947 – Rhesus monkey in the Zika Forest of Uganda acquired an unknown febrile illness

1948 – Virus isolated in *Aedes africanus* mosquitoes from the same forest in Uganda

1954 – First known human case of Zika Virus in Nigeria

1955 to 2006 – Confirmed cases of infection were rare although cases were reported in Africa and Asia during the 1960’s (emerged as two separate lineages)

2007 – Yap Island, Micronesia (first outbreak outside of Africa and Asia: 49 confirmed & 59 probable cases)

2008 – Two American scientists contracted Zika Virus infections in Senegal. First case of “Mosquito-borne STD”.

October, 2013 – Largest outbreak of Zika Virus in French Polynesia, South Pacific (28,000 cases)
Timeline (2015)

- **May 2015** – Pan American Health Organization (PAHO) issued an alert about the first confirmed Zika Virus infections in Brazil (500 cases). Linked to influx of people for 2014 FIFA World Cup.
- **16 October to 12 November 2015** – First reported cases of ZIKV infections in Columbia (578 confirmed, 2654 suspected)
- **12 November 2015** – Surinam authorities report 5 cases of ZIKV
- **24 November 2015** – French Polynesia health authorities reported an unusual increase of 17 cases CNS malformations in fetuses and infants 2014-2015. (Reported from pregnancies during the ZIKA outbreak between September 2013 and March 2014)
- **24 November 2015** – El Salvador reported 3 confirmed cases of ZIKA infections by local transmission. (on 3 Dec they reported a total of 240 ZIKV cases across the country)
- **26 November 2015** – Mexican authorities report 3 ZIKV cases (recently traveled from Columbia)
- **27 November 2015** – Paraguay confirmed 6 ZIKV cases (in town close to Brazil) and Venezuela reported 7 suspected ZIKV cases (local transmission)
- **1 December 2015** – Guatemala reported 17 suspected ZIKV cases (14 of which were in hospital workers)
- **3 December 2015** – Panama’s Ministry of Health reported 3 ZIKV cases in a northeast district (local transmission)
- **26 December 2015** – Island of Martinique becomes the 11th country in the Americas to report ZIKV infections this year and the 12th to report local transmission
- **31 December 2015** – Puerto Rico reports the first case of locally acquired ZIKV infection.
Timeline (2016)

- **16 January 2016** – Barbados, Haiti and Guyana all report confirmed cases of Zika infections in their respective countries
- **17 January 2016** – CDC & P issued a travel advisory for pregnant women to avoid travel to countries with Zika outbreaks in South America and Caribbean countries after a woman in Haiti gave birth to a baby with microcephaly and evidence of Zika virus infection. (she lived in Brazil for most of her pregnancy)
- **1 February 2016** – WHO declares Zika Virus to be a public health emergency of international concern
- **2 February 2016** – First case of Zika Virus transmission in Texas (likely contracted through sexual intercourse with an individual who had traveled to Argentina)
- **18 February 2016** – Group of Brazilian physicians discount ZIKV as the cause for the dramatic increase in microcephaly, instead blame a larvicide introduced in the water supplies in 2014
- **28 February 2016** – CDC&P advised pregnant women and those trying to conceive to avoid travel to outbreak regions, including concern over the Olympic Games being held in Brazil in the summer of 2016. (two US cases now confirmed as sexually transmitted and another 14 under investigation)
- **14 April 2016** – CDC&P confirms a causal relationship between ZIKV infection and microcephaly as well as other birth defects.
ZIKA VIRUS
Active Mosquito Transmission
(48 Countries and Territories)

As of July 14, 2016
TRANSMISSION

Bite of an infected *Aedes* species mosquito (Primary)
- *Ae. Aegypti & Ae. albopictus*
- Lay eggs in and near standing water
  - Flower Pots
  - Buckets
  - Animal Dishes
- Prefer people (*Ae. Albopictus* can also bite animals)
- Aggressive daytime biters, but can also bite at night
- Mosquitos feed on infected person and then can spread ZIKV to another person
ZIKA VIRUS
U.S. Confirmed Cases
(as of 13 July 2016)
All Cases are Lab Confirmed

Locally Acquired assumed to be mosquito-related

CDC&P issued a “Level 2: Practice Enhanced Precautions” for Puerto Rico 1Qtr 2016

<table>
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<tr>
<th></th>
<th>Travel-Associated</th>
<th>Locally Acquired</th>
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<tbody>
<tr>
<td><strong>50 US States</strong></td>
<td>1306</td>
<td>0</td>
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<td>Oklahoma</td>
<td>12 (1%)</td>
<td>0</td>
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<td><strong>US Territories</strong></td>
<td>11</td>
<td>2905</td>
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<tr>
<td>American Samoa</td>
<td>2 (18%)</td>
<td>41 (1%)</td>
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<tr>
<td>Puerto Rico</td>
<td>8 (73%)</td>
<td>2843 (98%)</td>
</tr>
<tr>
<td>US Virgin Islands</td>
<td>1 (10%)</td>
<td>21 (1%)</td>
</tr>
</tbody>
</table>
TRANSMISSION

- **Mother to Child**
  - ZIKV crosses the placenta barrier into the fetus
  - Mother may pass the virus at delivery
  - No reports of ZIKV transmitted via breast feeding
ZIKA VIRUS

TRANSMISSION

Sexual Contact
- Males can spread to sexual partners
- In known sexual cases, transmission can occur:
  - Before symptoms present
  - While symptomatic
  - After symptoms resolve
- ZIKV present in semen longer than in blood
- July 2016 – First case of woman transmitting ZIKV through sexual contact in US.
Laboratory Exposure

- 4 cases reported prior to current outbreak (actual route of transmission unclear)
- As of 15 June 2016, one case of laboratory-acquired Zika Virus disease reported in the US
ZIKA VIRUS

TRANSMISSION

- Theoretical
  - Blood Transfusion
    - No US cases reported
    - Multiple reports of cases in Brazil but not confirmed
    - 2.8% of donors tested positive for ZIKV during French Polynesia outbreak (2013)
  - Organ and Tissue transplants
  - Fertility Treatment
  - Breast Feeding
    - No reports of ZIKV transmission at this time
    - Recommendation is to continue with breast feeding
Animals do not appear to be involved in the spread of ZIKV at this time.

No evidence of ZIKV spread to humans via contact with animals.

No reports of pets or any other animals becoming sick with ZIKV.

Animals in US not at risk of becoming sick with ZIKV.

Apes and monkeys have shown ability to become infected but only research monkeys intentionally exposed to ZIKV have shown any signs of infection, and those were very mild.

Small number of monkeys were reported to have ZIKV from a 2016 study in an area Brazil with high numbers of human illness.

Prevalence of ZIKV in monkeys and other non-human primates is unknown.

More research is needed to understand the potential for monkeys and apes to be reservoirs for ZIKV.
ZIKA INFECTION

- **Incubation**
  - 3 to 14 days from exposure
  - ZIKV remains in semen longer than blood

- **Clinical Course**
  - Clinical illness is typically mild
  - Symptoms remain for several days to a week
  - Severe disease requiring hospitalization is uncommon
  - Fatalities are rare
  - Guillain-Barre Syndrome (GBS) is reported among patients following suspected ZIKV infection
    - Relationship to ZIKV is unknown
ZIKA Infection

- Symptoms
  - Many infections asymptomatic
  - Most common symptoms
    - Acute onset of fever
    - Maculopapular rash
    - Joint pain
    - Conjunctivitis
  - Other symptoms include muscle pain and headache
PREVALENT VIRAL PATHOGENS

- Parvovirus
- Enterovirus
- Adenovirus
- Other alphaviruses
  - Mayaro Virus
  - Ross River Virus
  - Barmah Forest Virus
  - O’nyongnyong Virus
  - Sinbis Virus

PREVALENT BACTERIAL PATHOGENS

- Leptospirosis
- Malaria
- Rickettsia
- Group A Streptococcus
- Rubella
- Measles
## DIAGNOSTIC TESTING FOR ZIKV

- Real time reverse transcriptase-polymerase chain reaction (rRT-PCR) for viral RNA in clinical specimens:
  - Serum collection – less than 7 days after illness onset
  - Urine collection – less or equal to 14 days after illness onset
- Serology for IgM and neutralizing antibodies in serum collected up to 12 weeks after illness onset
- Plaque reduction neutralization test (PRNT) for presence of virus-specific neutralizing antibodies in paired serum samples
- Immunohistochemical staining (IHC) for viral antigens or rRT-PCR on fixed tissues.
- All providers should coordinate with state and local health departments to coordinate testing and interpretation since other flaviviruses can confound results
CDC&P Recommendation for ZIKV Testing

- Symptomatic people living in an active ZIKV transmission area
- Symptomatic people who have recently traveled to an area with ZIKV
- Symptomatic or asymptomatic people who have had unprotected sex with a man who is confirmed to have Zika Virus infection
- Testing blood, semen or urine is not recommended to determine how likely a man is to pass ZIKV through sex (too much remains unknown at this time)
ZIKA Infection

Treatment (Symptomatic)

- Rest
- Fluids
- Acetaminophen for fever and pain
- ASA and NSAIDs should not be used until Dengue is ruled out due to potential for hemorrhage
- No vaccine available (Sabin Institute)
Reporting ZIKV Cases

- Zika Virus disease is a nationally notifiable condition
  - Report all confirmed cases to your state health department
- CDC&P established the **US Zika Pregnancy Registry** to collect information and learn more about pregnant women in the US with Zika and their infants
- CDC&P maintains a 24/7 consultation service for health officials and health care providers caring for pregnant women
  - Call **770-488-7100**
  - Email: [ZIKAMCH@cdc.gov](mailto:ZIKAMCH@cdc.gov)
ZIKV and Pregnancy

What We Know

- Primary way a pregnant woman can contract ZIKV is through a mosquito bite
- A man can spread ZIKV to a pregnant woman through sexual contact
- ZIKV can be passed to her fetus during pregnancy or at time of delivery
- No reports of infants acquiring ZIKV through breast feeding
- No evidence that previous infection will affect future pregnancies once virus has cleared from blood
- From similar infections, once infected with ZIKV, a person is likely to be protected from a future ZIKV infection
ZIKV and Pregnancy

What We **DO NOT** Know

- If pregnant woman is exposed, how likely she is to get ZIKV
- If infected, how virus will affect her or her pregnancy
- How likely ZIKV will pass to fetus
- If fetus infected, how likely are birth defects
- When in pregnancy infection will cause harm to fetus
- If pregnant woman is infected, the likelihood that fetus will have birth defects
- Whether sexual transmission poses greater risk of birth defects than acquiring through sexual contact
Who Should Be Tested During Pregnancy

- Testing for ZIKV not recommended for everyone
- Symptomatic or asymptomatic pregnant woman who has traveled to or lives in an area with ZIKV
- Symptomatic or asymptomatic pregnant woman who has had sex without a condom with a man confirmed to have ZIKV infection
ZIKA VIRUS

CDC's Response to Zika
Updated Interim Guidance:
Testing Algorithm for a Pregnant Woman with Possible Exposure to Zika Virus\(^\text{1}\), Not Residing in an Area with Active Zika Virus Transmission\(^\text{2}\)

Pregnant woman with possible exposure to Zika virus

- Test for Zika virus infection

Positive or inconclusive for Zika virus infection

- Consider serial fetal ultrasounds

Negative for Zika virus infection

- Fetal ultrasound to detect abnormalities consistent with Zika virus disease\(^\text{3}\)

Fetal abnormalities consistent with Zika virus disease

- Retest pregnant woman for Zika virus infection

Fetal abnormalities consistent with Zika virus disease not present

- Routine prenatal care

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\(^\text{1}\) Possible exposure to Zika virus includes travel to an area with active transmission of Zika virus (https://www.cdc.gov/zika/prevention/travel.html), or sexual transmission with a partner who traveled to an area with ongoing transmission of Zika virus, or residence in an area with ongoing transmission of Zika virus.

\(^\text{2}\) Testing is currently only recommended for pregnant women with possible sexual exposure to Zika in areas with known Zika virus transmission in a sexual partner.

\(^\text{3}\) Fetal abnormalities consistent with Zika virus disease include microcephaly, encephalitis, and brain and eye abnormalities. Initial ultrasound might not detect abnormalities until one month into the early third trimester of pregnancy.
Clinical Management of Positive or Inclusive ZIKV Results

- **Antepartum**
  - Consider serial Ultrasounds every 3-4 weeks
  - Referral to maternal-fetus medical specialist

- **Postpartum**
  - Histopathologic exam of placenta and umbilical cord
  - Testing of frozen placental tissue and cord tissue for ZIKV RNA
  - Testing of cord serum for Zika and Dengue virus IgM and neutralizing antibodies
ZIKA VIRUS

CDC's Response to Zika

Interim guidelines for the evaluation and testing of infants whose mothers traveled to or resided in an area with ongoing Zika virus transmission during pregnancy.

Infant whose mother traveled to or resided in an area with Zika virus transmission during pregnancy:

- Microcephaly or intracranial calcifications detected perinatally or at birth:
  - Conduct thorough physical examination and perform Zika virus testing in infant:
    - Positive or inconclusive test for Zika virus infection in infant:
      - Perform additional clinical evaluation, report case, and assess for possible long-term sequelae
    - Negative tests for Zika virus infection in infant:
      - Evaluate and treat for other possible etiologies

- No microcephaly or intracranial calcifications detected perinatally or at birth:
  - Positive or inconclusive test for Zika virus infection in mother:
    - Conduct thorough physical examination and perform Zika virus testing in infant:
      - Negative tests for Zika virus infection in infant:
        - Evaluate and treat for other possible etiologies
      - Positive or inconclusive test for Zika virus infection in infant:
        - Perform additional clinical evaluation, report case, and assess for possible long-term sequelae
  - Negative or no Zika virus testing performed on mother:
    - Routine care of infant, including appropriate follow-up on any clinical findings

*Notes:
- Zika virus transmission are listed on CDC's website at [https://www.cdc.gov/travel/notices](https://www.cdc.gov/travel/notices).
- Microcephaly defined as occipitofrontal circumference less than the third percentile for gestational age and sex based on standard growth curves, not explained by other etiologies.
- Laboratory evidence of Zika virus infection includes 1) detectable Zika virus, Zika virus RNA, or Zika virus antigen in any clinical specimen; or 2) positive Zika virus immunoglobulin M (IgM) with confirmatory neutralizing antibody titer that are 4-fold higher than dengue virus neutralizing antibody titer in serum or cerebrospinal fluid. Testing is considered inconclusive if Zika virus neutralizing antibody titers are <4 fold higher than dengue virus neutralizing antibody titers.
ZIKA VIRUS

- **Evaluation for All Infants with Positive or Inclusive ZIKV Results**
  - Physical exam, measure head circumference, assessment of gestational age
  - Evaluation for neurologic abnormalities, dysmorphic features, enlarged liver or spleen, rash/other skin lesions
  - Cranial Ultrasound
  - Ophthalmologic and hearing evaluation before hospital D/C or within one month after birth
  - Specialty referral for all abnormalities
**ZIKA VIRUS**

- **Long Term Follow-up for Infants with Positive or Inclusive ZIKV Results**
  - Additional hearing screening at 6 months of age with Audiology follow-up for abnormal results
  - Continued evaluation of developmental characteristics and milestones, as well as head circumference, through first year of life
  - Consultation with appropriate medical specialists referral for all abnormalities and any other concerns
Case Definition of Microcephaly

- Definite congenital microcephaly for live births
  - Head circumference (HC) at birth is less than the 3rd percentile for gestational age and sex
  - If head circumference not available, then HC less than the 3rd percentile for gestational age and sex within the first 6-weeks of life

- Definite congenital microcephaly for stillbirths and early terminations
  - Head circumference at delivery is less than the 3rd percentile for gestational age and sex
Measuring head circumference for microcephaly

- Use a measuring tape that cannot be stretched
- Securely wrap the tape around the widest possible circumference of the head
  - Broadest part of the forehead above eyebrow
  - Above the ears
  - Most prominent part of the back of the head
- Take the measurement three times and select the largest measurement to the nearest 0.1 cm
- Optimal measurement at 24-36 hours after birth when molding of the head has subsided

ZIKV and Sexual Contact

What We Know

- Males can spread to sexual partners (male and female)
- In known sexual cases, transmission can occur:
  - Before symptoms present
  - While symptomatic
  - After symptoms resolve
- In known cases, men had vaginal, anal, or oral (mouth-to-penis) sex without a condom
- ZIKV present in semen longer than in blood
- July 2016 – First case of woman transmitting ZIKV through sexual contact in US.
ZIKV and Sexual Contact

What We DO NOT Know

- How often asymptomatic males with ZIKV can have the virus in their semen or if they can pass ZIKV through sex

- How long ZIKV remains in semen – one study showed ZIKV RNA in semen after 62 days after onset of symptoms

- If sexual transmission of ZIKV poses a different risk of birth defects than mosquito-borne transmission

- If a woman with ZIKV can pass the virus to another female through sexual contact
RECOMMENDATIONS

- Pregnant women should **NOT** travel to area with ZIKV
  - If they MUST travel, instructions on how to protect from mosquito bites and steps to protect from sexual transmission during and after travel
RECOMMENDATIONS

MOSQUITO BITE PREVENTION

- Wear long sleeve shirts and long pants (clothing impregnated with repellant)
- Stay and sleep in areas with air conditioning and window and door screens to keep mosquitoes outside
- Vector control inside and outside (remove breeding areas)
- Mosquito bed nets if unable to sleep in enclosed, protected area
- EPA-approved insect repellant
  - Do NOT use on babies under than 2 months old
  - Do NOT use products containing oil of lemon eucalyptus or para-menthane-diol on children younger than 3 years old
RECOMMENDATIONS

**SEXUAL TRANSMISSION PREVENTION**

- Abstinence or correct use of condoms are the best preventive measures.
- Pregnant couples with a male partner who lives in or recently traveled to an area with ZIKV should use a condom from start to finish for every sexual contact during the entire pregnancy.
- Non-pregnant couples with male partner who has recently traveled to ZIKV area:
  - If male has ZIKV diagnosis or has (or had) symptoms then consider abstinence or condom use for at least 6 months after symptoms began.
  - If male does not develop symptoms, then should consider abstinence or condom use for at least 8 weeks following his return.
ZIKA VIRUS

REFERENCES

- World Health Organization (WHO)
  - www.who.int

- Centers for Disease Control & Prevention
  - www.cdc.gov
  - US Zika Pregnancy Registry
  - Health Care Provider consultation service
    - Call: 770-488-7100
    - Email: ZIKAMCH@cdc.gov

- Oklahoma State Department of Health
  - www.ok.gov/health/