

Zika Virus Update

Advisory Council on Blood Stem Cell Transplantation
March 4, 2016

Zika Virus

- Single stranded RNA Virus
- Genus *Flavivirus*, Family *Flaviviridae*
- Closely related to dengue, yellow fever, Japanese encephalitis and West Nile viruses
- Transmitted to humans primarily by *Aedes (Stegomyia)* species mosquitoes

Zika Virus Vectors: *Aedes* Mosquitoes

- *Aedes* species mosquitoes
 - *Ae aegypti* more efficient vectors for humans
 - *Ae albopictus*
- Also transmit dengue and chikungunya viruses
- Lay eggs in domestic water-holding containers
- Live in and around households
- Aggressive daytime biters



Aedes aegypti

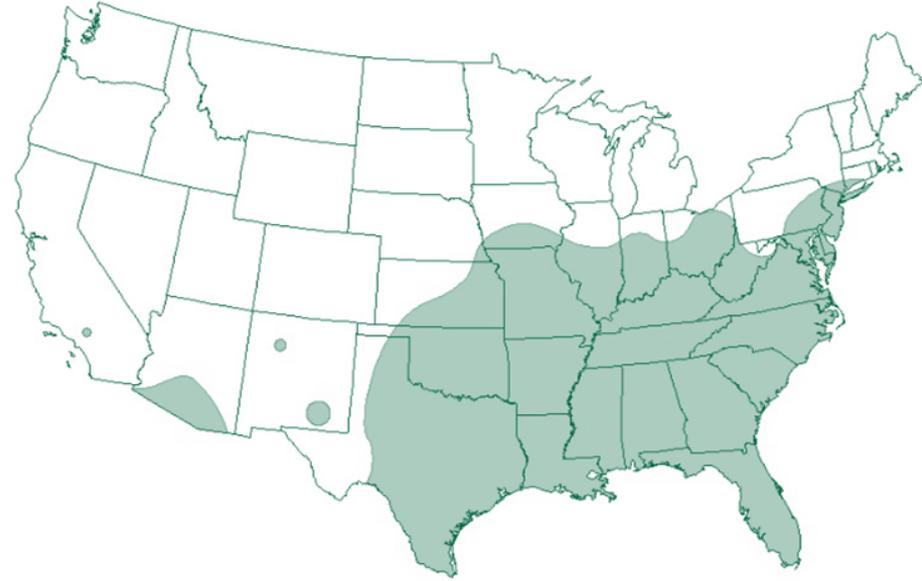


Aedes albopictus

Aedes aegypti and *Aedes albopictus* Mosquitoes: Geographic Distribution in the United States



Aedes aegypti



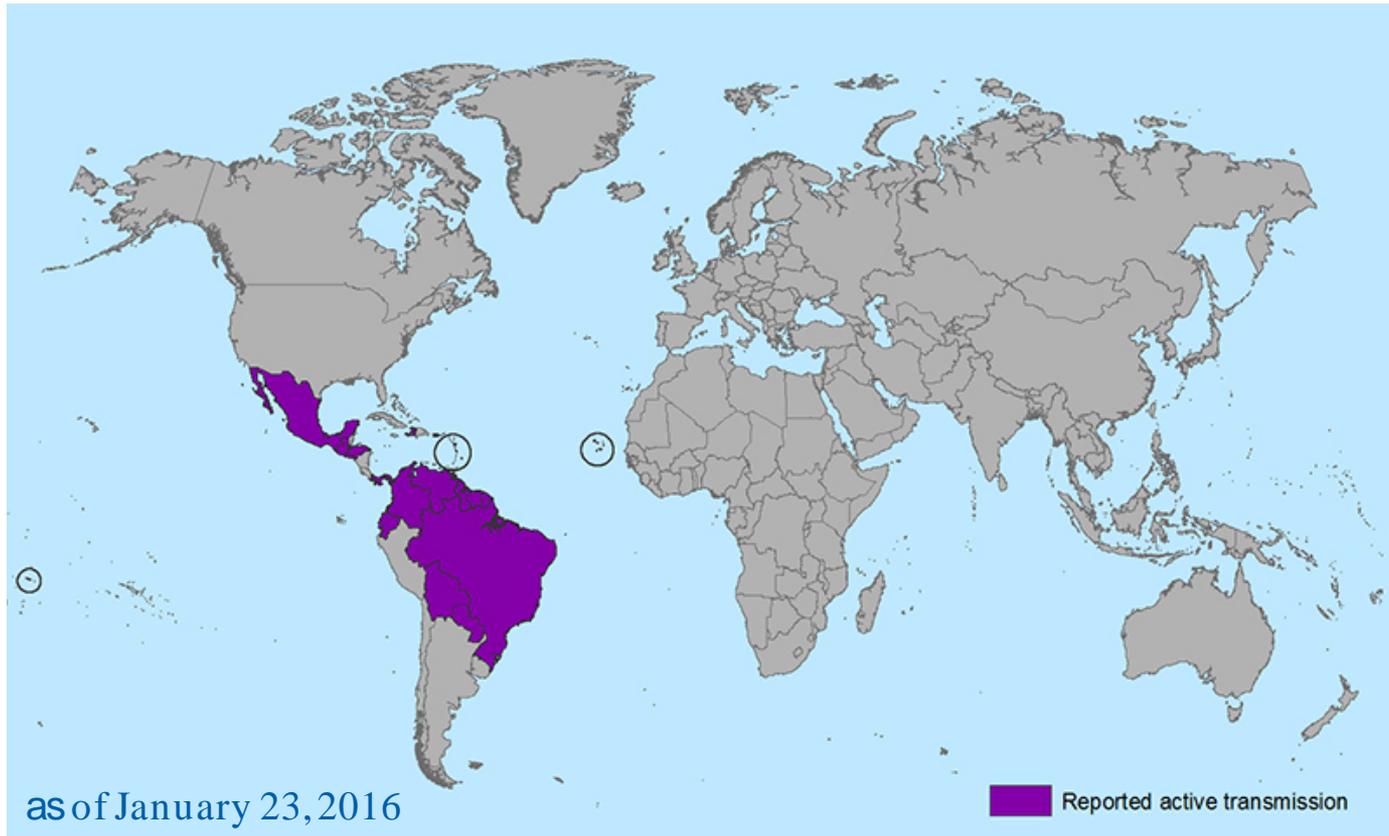
Aedes albopictus

Modes of Transmission

- Mosquito-borne
- Maternal-fetal
 - Intrauterine
 - Perinatal
- Other
 - Sexual
 - **Blood transfusion**
 - Laboratory exposure
- Theoretical (not yet documented)
 - **Organ or tissue transplantation**
 - Breast milk

Zika Virus:

Countries and Territories with Active Zika Virus Transmission



Zika Virus Epidemiology

- First isolated from a monkey in Uganda in 1947
- Prior to 2007, only sporadic human disease cases reported from Africa and southeast Asia
- In 2007, first outbreak reported on Yap Island, Federated States of Micronesia
- In 2013–2014, >28,000 suspected cases reported from French Polynesia*

*<http://ecdc.europa.eu/en/publications/Publications/Zika-virus-French-Polynesia-rapid-risk-assessment.pdf>

Zika Virus in the Americas

- In May 2015, the first locally-acquired cases in the Americas were reported in Brazil
- Currently, outbreaks are occurring in many countries or territories in the Americas, including the Commonwealth of Puerto Rico and the U.S. Virgin Islands
- Spread to other countries likely

Zika Virus in the Continental United States

- Local transmission of Zika virus has not been reported in the continental United States
- Since 2011, there have been laboratory-confirmed Zika virus cases identified in travelers returning from areas with local transmission
- With current outbreaks in the Americas, cases among U.S. travelers will most likely increase
- Imported cases may result in virus introduction and local spread in some areas of U.S.

Zika Virus Incidence and Attack Rates

- Infection rate: 73% (95%CI 68–77)
- Symptomatic attack rate among infected: 18% (95%CI 10–27)
 - estimated 82% asymptomatic
- All age groups affected
- Adults more likely to present for medical care
- No severe disease, hospitalizations, or deaths

Duffy M. N Engl J Med 2009

Note: Rates based on serosurvey on Yap Island, 2007 (population 7,391)

Reported Clinical Symptoms Among Confirmed Zika Virus Disease Cases

Symptoms	N (n=31)	%
Macular or papular rash	28	90%
Subjective fever	20	65%
Arthralgia	20	65%
Conjunctivitis	17	55%
Myalgia	15	48%
Headache	14	45%
Retro-orbital pain	12	39%
Edema	6	19%
Vomiting	3	10%

Yap Island, 2007

Duffy M. N Engl J Med 2009

Differential Diagnosis for Zika Virus Disease

- **Dengue***
- **Chikungunya***
- Leptospirosis
- Malaria
- Rickettsia
- Parvovirus
- Group A streptococcus
- Rubella
- Measles
- Adenovirus
- Enterovirus

* **Similar clinical features**

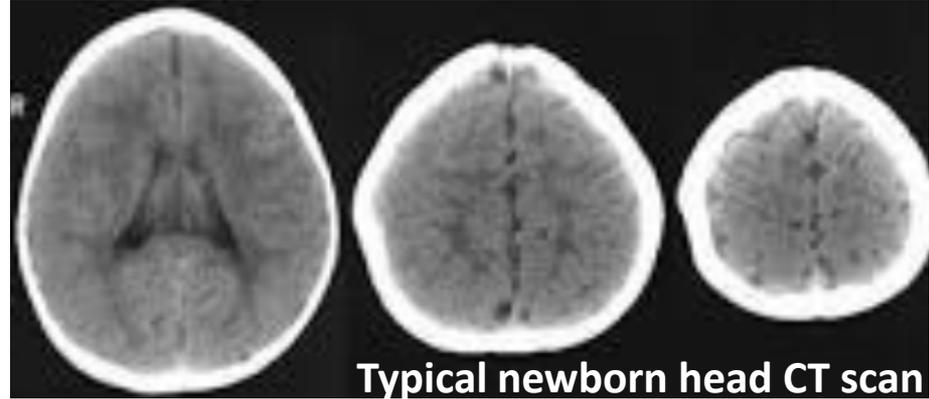
Zika Virus Clinical Disease Course and Outcomes

- Clinical illness usually mild
 - Symptoms last several days to a week, when they occur
 - Severe disease requiring hospitalization uncommon
 - Fatalities are rare
 - Guillain-Barré syndrome reported in patients following suspected Zika virus infection
 - No data on immunosuppressed individuals
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Infants with Microcephaly



AP Photos/Felipe Dana

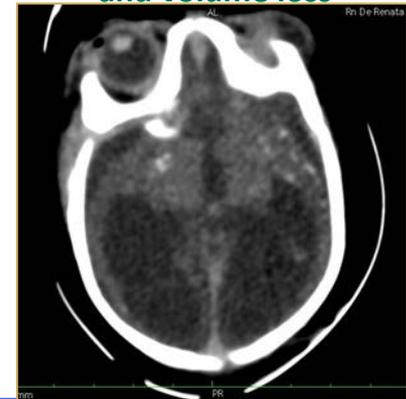


Typical newborn head CT scan

scattered intracranial
calcifications



enlarged ventricles
and volume loss



Zika Virus and Microcephaly in Brazil

- Reports of a substantial increase in number of babies born with microcephaly in 2015 in Brazil; true baseline unknown
 - Zika virus infection identified in several infants born with microcephaly (including deaths) and in early fetal losses
 - Some of the infants with microcephaly have tested negative for Zika virus
- Incidence of microcephaly among fetuses with congenital Zika infection is unknown

Diagnostic Testing for Zika Virus

- Reverse transcriptase-polymerase chain reaction (RT-PCR) for viral RNA in serum collected ≤ 7 days after illness onset
- Serology for IgM and neutralizing antibodies in serum collected ≥ 4 days after illness onset
- Plaque reduction neutralization test (PRNT) for ≥ 4 -fold rise in virus-specific neutralizing antibodies in paired sera
- Immunohistochemical (IHC) staining for viral antigens or RT-PCR on fixed tissues

Treatment

- No specific antiviral therapy
- Treatment is supportive (i.e., rest, fluids, analgesics, antipyretics)
- Suspected Zika virus infections should be evaluated and managed for possible dengue or chikungunya virus infections
- Aspirin and other NSAIDs should be avoided until dengue can be ruled out to reduce the risk of hemorrhage

Zika Virus Preventive Measures

- No vaccine or medication to prevent infection or disease
- Primary prevention measure is to reduce mosquito exposure
- Pregnant women should consider postponing travel to areas with ongoing Zika virus outbreaks
- Advice to infected people for mosquito exposure avoidance during first week of illness to prevent further transmission

Potential for Transmission by Transfusion or Transplantation

- High probability that Zika is transfusion transmitted
 - ~80% of those infected asymptomatic
 - 3% of blood donors with +PCR in French Polynesia outbreak
 - 2 reports of suspected transfusion transmitted infection in Brazil
- High probability of viral persistence in male reproductive tissue; multiple cases of sexual transmission from infected males either confirmed or suspected

Screening for Zika Virus – blood and tissues

- No FDA approved tests for screening donors of blood or tissue
- Screening would most likely first occur under an Investigational New Drug (IND) protocol
- For blood, screening requires high throughput platforms with tests that have been rigorously validated for high sensitivity and specificity

Guidance

- FDA recommendations for blood donor screening, deferral, and product management to reduce the risk of transfusion-transmission of Zika virus (followed bulletin from AABB)
 - blood collection in areas without “active transmission”, donors with history of Zika infection, travel, or sexual contact with a traveler, are deferred for 4 weeks
 - blood collections in areas with “active transmission” required to outsource blood until either laboratory screening or pathogen reduction technology (PRT) are available
- FDA recommendations to prevent tissue transmitted Zika virus infection (human cells, tissues, and cellular and tissue-based products)
 - deceased donors: Ineligible if diagnosis Zika infection in past 6 months
 - living donors: Ineligible if diagnosis Zika infection, travel history, or sex with male with travel history in past 6 months (longer for gestational tissue)



To:	Cord Blood Banks
From:	Merry Duffy Director, Cord Blood, Biorepository, and Affiliated Services

Recommendations (as of Feb 5, 2016)

A cord blood unit should not be collected from an infant with microcephaly.

The assessment of the maternal donor should include any travel to risk areas during the period of pregnancy. Include specific countries, dates of travel, arrival/return date to the US.

The maternal donor should be asked about possible symptoms or diagnosis of Zika virus infection, including when the symptoms occurred, how long symptoms lasted, and were they diagnosed with Zika.

Post-donation donor health information reported within 2 weeks of collection should be evaluated for:

- Diagnosis of Zika infection
- Possible symptoms of Zika infection and reported recent travel to a risk country*

These cord blood units should remain in quarantine until medical evaluation has been completed.

***RISK COUNTRY:** Specific areas where Zika virus transmission is ongoing are often difficult to determine and are likely to change over time. Review the [CDC's Zika Travel Information webpage for the most current information on risk countries](#).

The NMDP/Be The Match Maternal Risk Questionnaire Action Guide will be revised to include these guidelines. We will let you know when that revision is available.

For information about the Zika virus, refer to the [CDC](#).

Zika Virus – More Questions Than Answers

- Incidence of maternal- fetal transmission by trimester?
 - Factors that influence (e.g., severity of infection, maternal immune response)
- Risk of microcephaly and other fetal and neonatal outcomes?
- Risk of Guillain-Barré syndrome?
- Potential for long-term reservoirs of Zika?
 - Reproductive tissue (evidence of virus in semen for months)
 - Studies planned to examine length of time virus is present in blood, urine, saliva, semen, and other body fluids

Summary

- Zika virus continues to spread in the Americas
- Although most infections are symptomatic, suspicion of Zika virus should be high in travelers from active transmission areas with acute fever, rash, arthralgia, or conjunctivitis within 2 weeks after return
- Microcephaly and Guillain-Barré have been reported associated with Zika, but the strength of association and rate in those infected are unclear
- Complications associated with immunosuppressed patients are unknown

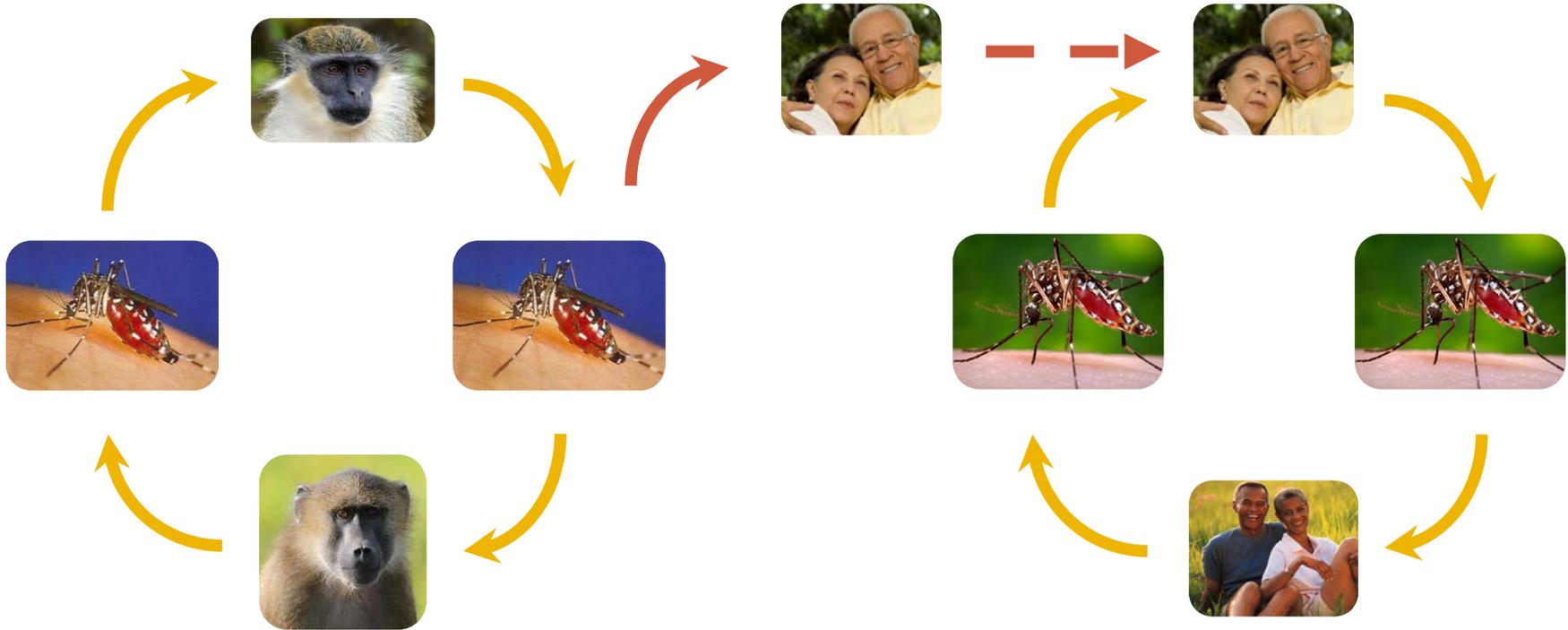
Questions?

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

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.



Zika Virus Transmission Cycles



Sylvatic (jungle) cycle

Epidemic (urban) cycle

Reporting Zika Virus Disease Cases

- As an arboviral disease, Zika virus disease is a nationally notifiable disease
 - Healthcare providers encouraged to report suspected cases to their state health department
- State health departments are requested to report laboratory-confirmed cases to CDC
- Timely reporting allows health departments to assess and reduce the risk of local transmission or mitigate further spread

Possible Future Course of Zika Virus in the Americas

- Virus will continue to spread in areas with competent vectors
 - Transmission increasing in Central America, Mexico, and Caribbean
 - Anticipate further spread in Puerto Rico and U.S. Virgin Islands
- Travel-associated cases will introduce virus to U.S. states
 - Imported cases will result in some local transmission and outbreaks
 - Air conditioning may limit the size and scope of outbreaks
 - Colder temperatures will interrupt and possibly stop further spread
- Experience from dengue might be predictive
 - From 2010–2014, 1.5 million dengue cases reported per year to PAHO
 - 558 travel-related and 25 locally transmitted cases in U.S. states