# **KEY MESSAGES – ZIKA VIRUS DISEASE**

<u>Purpose:</u> This document is for internal and external use. The document contains cleared key messages for use in developing other materials.

## **Updated May 18, 2016**

Updated information is in blue.

# CONTENTS

Outbreak Summary	2
Zika & the Continental United States	2
Local Transmission	2
Travel-Associated Cases	3
Background on Zika	3
Guillain-Barré Syndrome	4
Symptoms	4
Diagnosis	4
Transmission	5
Sexual Transmission	5
Blood Transfusion	7
Zika Virus Blood Screening	7
Puerto Rico Survey of Blood Collection Centers	7
Vector Information	
Vector Control for the General Public	9
Pesticides	10
Risk	10
Prevention	11
Preventing Sexual transmission	11
Insect Repellent	12
Treatment	13
Zika & Pregnancy	
Microcephaly	
Diagnosis	
Laboratory Testing	
Testing for Pregnant Women	

5/18/16	FOR EXTERNAL USE	
Testing for Infants & Children	18	
CDC Guidance & Recommendations	19	
Pregnant Women	19	
Travel	20	
Travel Notices	21	
Obstetrical Healthcare Providers	22	
Zika & Pregnancy	23	
Amniocentesis	24	
Prenatal Diagnosis of Microcephaly	25	
Pediatric Healthcare Providers	25	
Zika Virus Transmission in Infants & Children	26	
Birth Defects	26	
Potential Outcomes & Prognosis	27	
Clinical Guidance	28	
What CDC is Doing	30	
Domestic Activities	30	
International Activities	31	

## **OUTBREAK SUMMARY**

- Before 2015, Zika virus disease (Zika) outbreaks occurred in areas of Africa, Southeast Asia, and the Pacific Islands.
- In May 2015, the Pan American Health Organization (PAHO) issued an alert regarding the first confirmed Zika virus infections in Brazil.
- Since May 2015, CDC has been responding to increased reports of Zika and has assisted in investigations with PAHO and the Brazil Ministry of Health. The first regional travel notices for Zika in South America and Mexico were posted in December 2015.
- Currently, outbreaks are occurring in <u>many countries and territories</u>.
- On January 22, 2016, CDC activated its <u>Emergency Operations Center</u> (EOC) to respond to outbreaks of Zika
  occurring in the Americas and increased reports of birth defects and Guillain-Barré syndrome in areas affected by
  Zika. On February 8, 2016, CDC elevated its EOC activation to a Level 1, the highest level.
- On February 1, 2016, the World Health Organization (WHO) declared a <u>Public Health Emergency of International</u>
   <u>Concern</u> (PHEIC) because of clusters of microcephaly and other neurological disorders in some areas affected by
   7ika
- On February 8, 2016, President Obama announced a request for \$1.8 billion in emergency funds for several agencies to accelerate research into a vaccine and educate populations at risk for disease.

## ZIKA & THE CONTINENTAL UNITED STATES

#### LOCAL TRANSMISSION

• Local transmission means that mosquitoes in the area have been infected with Zika virus and can spread it to people.

- In December 2015, the Commonwealth of Puerto Rico, a United States territory, reported its first confirmed locally transmitted Zika virus case.
- Cases of local transmission have recently been confirmed in two other US territories, the United States Virgin Islands and American Samoa.
  - As of May 11, 2016, US territories had <u>reported</u> 698 locally acquired Zika cases and 3 travel-associated Zika cases to CDC.
    - Of the 701 cases reported, 65 were in pregnant women and 5 had Guillain-Barré syndrome.
- Zika has not been spread by mosquitoes in the continental United States. However, lab tests have confirmed Zika virus in travelers returning to the United States. These travelers have gotten the virus from mosquito bites and some non-travelers got Zika through sex with a traveler.
  - With the recent outbreaks in the Americas, the number of Zika cases among travelers visiting or returning to the United States is increasing.
- CDC monitors and reports to the public cases of Zika, which will help improve our understanding of how and where Zika is spreading.
- CDC is not able to predict how much Zika virus would spread in the continental United States.
  - Many areas in the United States have the type of mosquitoes that can become infected with and spread
     Zika virus. Recent outbreaks in the continental United States of chikungunya and dengue, which are
     spread by the same type of mosquito, have been relatively small and limited to a small area.
  - We will maintain and improve our ability to identify and test for Zika and other mosquito-borne diseases.
- For Zika to cause an outbreak in the continental United States, all of the following must happen:
  - o People infected with the virus enter the United States.
  - o An *Aedes* mosquito in the United States bites the infected person during the period of time when the virus can be found in the person's blood, typically only through the first week of infection.
  - The infected mosquito lives long enough for the virus to multiply and for the mosquito to bite another person.
  - The cycle continues multiple times to start an outbreak.

#### TRAVEL-ASSOCIATED CASES

- A travel-associated (or imported) case means that a person with Zika became infected during travel to an area with active Zika transmission. This includes a traveler becoming infected and anyone infected by that traveler.
  - Zika virus can be sexually transmitted by a man to his partners.
  - Zika virus can be passed from a pregnant woman to her fetus during pregnancy or around the time of delivery.
- As of May 11, 2016, US states had <u>reported</u> a total of 503 travel-associated Zika cases to CDC.
  - o Of these, 48 were in pregnant women, 10 were sexually transmitted, and 1 had Guillain-Barré syndrome.
- Zika is a nationally notifiable disease. State and territorial health departments are encouraged to report laboratory-confirmed cases to CDC through ArboNET, the national surveillance system for arboviral diseases. Healthcare providers should report cases to their local, state or territorial health department according to the laws or regulations for reportable diseases in their jurisdiction.
- CDC continues to work with states to monitor for mosquito-borne diseases, including Zika.

## BACKGROUND ON ZIKA

Zika virus was first discovered in a monkey in the Zika Forest of Uganda in 1947.

• Before 2007, at least 14 cases of Zika had been documented, although other cases were likely to have occurred and were not reported.

- Zika outbreaks have probably occurred in many locations. Because the symptoms of Zika are similar to those of many other diseases, many cases may not have been recognized.
- Mosquitoes that spread Zika virus are aggressive daytime biters, but they can also bite at night.

## **GUILLAIN-BARRÉ SYNDROME**

- The Brazil Ministry of Health has reported an increased number of people who have been infected with Zika virus who also have Guillain-Barré syndrome (GBS). CDC is investigating the link between Zika and GBS.
  - GBS is very likely triggered by Zika in a small proportion of infections, much as it is after a variety of other infections.
- GBS is an uncommon sickness of the nervous system in which a person's own immune system damages the nervous cells, causing muscle weakness, and sometimes, paralysis.
- GBS symptoms include weakness of the arms and legs that is usually the same on both sides of the body.
- These symptoms can last a few weeks or several months. Although most people fully recover from GBS, some people have permanent damage, and in 1 out of 20 cases people have died.
- Researchers do not fully understand what causes GBS. Most people with GBS report an infection before they have GBS symptoms. Rarely, vaccination has also been associated with the onset of GBS (for example, the 1976 Swine influenza vaccine).
- An estimated 3,000 to 6,000 people, or 1-2 cases for every 100,000 people, develop GBS each year in the United States. Most cases of GBS occur for no known reason, and true "clusters" of cases of GBS are very unusual.
- If you want to know more about the number of GBS cases in a certain area, contact the state or local health department in the state where the cases happen. CDC collaborates with state and local health departments to investigate reports of possibly unusually large numbers or "clusters" of GBS cases.

## **SYMPTOMS**

- The most common symptoms of Zika virus disease are
  - o Fever
  - o Rash
  - o Joint pain
  - Conjunctivitis (red eyes)
- Other symptoms include
  - o Muscle pain
  - o Headache
- Many people infected with Zika virus won't have symptoms or will only have mild symptoms.
- The sickness is usually mild with symptoms lasting for several days to a week.
- People usually don't get sick enough to go to the hospital, and they very rarely die of Zika.

## DIAGNOSIS

- To diagnose Zika, your doctor or other healthcare provider will ask you about any recent travel and any signs and symptoms you may have. A blood test can confirm a Zika infection.
- See your doctor or other healthcare provider if you develop symptoms (fever, rash, joint pain, or red eyes) and you live in or have recently traveled to an area with Zika. Tell them that you traveled to an area with Zika.
- Your doctor or other healthcare provider may order blood tests to look for Zika or other similar viral diseases like dengue or chikungunya.

## TRANSMISSION

Zika virus is spread to people primarily through the bite of an infected Aedes species mosquito (Ae. aegypti and Ae. albopictus).

- o Mosquitoes that spread Zika virus are aggressive daytime biters, but they can also bite at night.
- A pregnant woman can pass Zika virus to her fetus during pregnancy or around the time of birth. We are studying how Zika affects pregnancies.
- To date, there are no reports of infants getting Zika through breastfeeding. Because of the benefits of breastfeeding, mothers are encouraged to breastfeed even in areas where Zika virus is found.
- A man with Zika virus can pass it to his female or male sex partners.

#### SEXUAL TRANSMISSION

#### What we know

- o A man with Zika virus can pass it to his female or male sex partners.
  - In the known cases, men had symptoms. Zika can be passed before his symptoms start, while he has symptoms, and after his symptoms end.
  - Men without symptoms may be able to pass the virus to their sex partners, but CDC doesn't have reports of this.
  - In the known cases, the men had vaginal or anal sex without a condom.
  - In some of the known cases, the men also had oral sex (mouth to penis) without a condom.
- o Zika virus can stay in semen longer than in blood, but we don't know exactly how long Zika stays in semen.

#### What we do not know

- o If men with Zika who never develop symptoms have the virus in their semen or if they can pass Zika through sex.
- o If Zika can be passed during oral sex (mouth-to-penis); however, because the virus is in the semen of men with Zika, it may be passed during oral (mouth-to-penis) sex.
- o If a woman with Zika can pass the virus to her sex partners.
- o If Zika can be passed through vaginal fluids during vaginal or oral (mouth to vagina) sex.
- o If Zika can be passed through saliva during kissing.
- If sexual transmission of Zika virus poses a different risk of birth defects than mosquito-borne transmission.
- Live virus (i.e., identified by culture) has been found in semen at least 2 weeks after symptoms of infection began. Virus particles (i.e., identified by RT-PCR) have been found in semen at least 62 days after symptoms of infection began, but presence of virus particles does not confirm the presence of live virus. In all cases, no follow up testing was done to determine when the men no longer had Zika virus in their semen.
- Studies are underway to better characterize how long Zika virus can stay in the semen of infected men, whether the concentration of virus in semen declines consistently or if it is variable, and whether or not there are differences between the semen of men with symptomatic and asymptomatic Zika infection. Differences between the semen of symptomatic and asymptomatic men with Zika infection could include
  - The incidence of the virus shedding in semen
  - o The concentrations of virus in the semen
  - The length of time Zika virus persists in the semen of men who shed it
  - o The pattern of Zika virus shedding in semen
- Not having sex can eliminate your risk of getting Zika from sex.
- Condoms can reduce the chance of getting Zika from sex if used <u>correctly</u> from start to finish, every time you have vaginal, anal, or oral (mouth-to-penis) sex. Condoms also are highly effective in preventing HIV and other STDs.

Only people whose male sex partners have traveled to or live in an area with Zika need to be concerned about
getting Zika virus through sex. The timeframe for using condoms or waiting to have sex will vary based on the
couple's situation and concerns.

- **Couples with a pregnant partner** should use condoms <u>correctly</u> every time they have vaginal, anal, and oral (mouth-to-penis) sex or should not have sex during the pregnancy.
- In addition to condoms, couples who do not want to get pregnant should use the most effective birth control methods that they can use correctly and consistently. Talk to your doctor about available options.
- Anyone who lives in or travels to areas with Zika and not concerned about pregnancy can consider using a condom every time they have vaginal, anal, and oral (mouth-to-penis) sex or not have sex.
  - o For couples with a male partner who has traveled to an area with Zika
    - If the male partner has been diagnosed with Zika or has (or had) symptoms, the couple should consider using condoms or not having sex for at least 6 months after symptoms begin.
    - If the male partner does not developed symptoms, the couple should consider using condoms or not having sex for at least **8 weeks** after the man returns.
  - O For couples with a male partner living in an area with Zika
    - If the male partner has been diagnosed with Zika or has (or had) symptoms, the couple should consider using condoms or not having sex for at least 6 months after symptoms begin.
    - If the male partner has never developed symptoms, the couple should consider using condoms or not having sex while there is Zika in the area.
  - o For couples with a non-pregnant female partner who lives in or has traveled to an area with Zika
    - It is not known if a woman can pass Zika to her sex partners.
    - These couples can also consider using condoms or not having sex.
  - Those considering these options should weigh the personal risks and benefits, including
    - The mild nature of the illness for many people\*
    - Plans for pregnancy (if appropriate)
    - Access to condoms and other contraception
    - Desire for intimacy, including willingness to use condoms or not have sex
    - Ability to use condoms or not have sex
- CDC recommends Zika virus testing for people who may have been exposed to Zika through sex **and** who have Zika symptoms.
- Testing blood, semen, or urine is not recommended to determine how likely someone is to pass Zika virus through
- We have a limited understanding of how to interpret the results of semen tests. Studies are underway to better understand this issue. As we learn more and as tests improve, semen tests may become more helpful for determining the risk of people with Zika passing it through sex.
- CDC has resources on <u>condom effectiveness</u> and <u>using male condoms</u>.
- A case of sexually transmitted Zika in the United States is defined as a person who does not live in or travel to an area with Zika becoming infected with Zika from having sex with an infected man who lives in or travels to an area with Zika.
  - Someone can have a possible sexual exposure to Zika if they have vaginal, anal, or oral (mouth-to-penis) sex without a condom with a man infected with Zika virus, including a man who lives in or traveled to an area with Zika.
  - On February 23, 2016 CDC issued a <u>Health Alert Network (HAN)</u> to alert health departments, healthcare providers, and the public that sexual transmission of Zika may be more common than previously

considered. People are encouraged to follow CDC's <u>Interim Guidance for Prevention of Sexual</u> Transmission of Zika Virus.

\*In many cases, Zika does not cause any symptoms or causes only mild symptoms lasting several days to a week. Severe disease requiring hospitalization is uncommon.

## **BLOOD TRANSFUSION**

- To date, there have been no confirmed blood transfusion-transmission cases in the United States.
- There is a strong possibility that Zika virus can be spread through blood transfusions.
  - Because many people infected with Zika virus don't have any symptoms, blood donors may not know they
    have been infected.
  - There have been suspected cases of Zika transmission through blood transfusion in Brazil. These reports
    are currently being investigated. During the Zika virus outbreak in French Polynesia in 2013-2014, 2.8% of
    blood donors tested positive for Zika. In previous outbreaks elsewhere, the virus has also been found in
    blood donors.
- Zika virus currently poses a low risk to the blood supply in the continental United States, but this could change depending on how many people become infected with the virus.
- On February 16, 2016, the Food and Drug Administration (FDA) released <u>Recommendations for Donor Screening</u>, <u>Deferral and Product Management to Reduce the Risk of Transfusion-Transmission of Zika Virus</u>, which include specific steps for blood collection organizations.
- In areas of active transmission, FDA recommends that blood either be screened by laboratory testing, subjected to pathogen reduction technology (PRT), or outsourced from other areas.

## ZIKA VIRUS BLOOD SCREENING

- Blood donor screening on the basis of a questionnaire, without a laboratory test, is insufficient for identifying Zikainfected donors in areas with active mosquito-borne transmission of Zika virus due to the high rate of asymptomatic infection.
- Although there is no FDA-licensed test for Zika virus, on April 3, 2016, testing for Zika became available through an Investigational New Drug (IND) application for blood collected in Puerto Rico.
- Zika virus testing may become available in the continental U.S. through the IND, if areas become affected by active mosquito-borne transmission of Zika virus.
- Specific questions about the test screening process and IND protocol should be directed to the test manufacturer,
   Roche Molecular Systems, Inc.

## PUERTO RICO SURVEY OF BLOOD COLLECTION CENTERS

- The Puerto Rico <u>survey of blood collection centers</u> was conducted February 10-24, 2016.
- The results of this survey were used to guide a federally supported coordinated effort to address the blood supply
  and safety challenges in Puerto Rico. This effort included importing all blood components from the continental
  United States at a volume sufficient to meet the demand projected from the 2015 estimates, beginning March 5,
  2016, until a nucleic acid screening test was implemented under IND protocol beginning April 4, 2016.
- Efforts to implement PRT for apheresis platelets and plasma collections in Puerto Rico are currently under way, and evaluation trials to determine safety and efficacy of investigational PRT for red blood cells (RBCs) are in planning stages.
- Lessons learned from the experience in Puerto Rico can inform blood safety interventions in areas of the United
   States where Aedes species mosquitoes are found and where similar issues might arise if Zika virus transmission

occurs. These interventions could include outsourcing of blood components, implementation of nucleic acid testing of donations, and implementation of PRT.

- Because of the potential for local Zika virus transmission in areas with a competent mosquito vector, other areas of the United States should develop plans to ensure local blood safety and adequacy.
- Blood collection organizations and public health agencies should collaborate to prepare for blood safety and supply adequacy challenges that might arise if Zika virus transmission spreads in the continental United States.

## **VECTOR INFORMATION**

- A mosquito can transmit Zika virus through bites. Not all people who are infected will get sick.
- There are many species of *Aedes* mosquitoes. Not all *Aedes* species spread Zika virus. At this time, we don't know if there are other non-*Aedes* mosquito species that could spread Zika virus.
  - Aedes aegypti mosquitoes live in tropical, subtropical, and in some temperate climates. They are the
    primary vector of Zika, dengue, chikungunya, and other arboviral diseases. Because Aedes aegypti
    mosquitoes live near and prefer to feed on people, they are considered highly efficient at spreading these
    diseases.
  - Aedes albopictus mosquitoes live in tropical, subtropical, and temperate climates. They have adapted to survive in a broader temperature range and at cooler temperatures than Aedes aegypti. Because these mosquitoes feed on people and animals, they are less likely to spread viruses like Zika, dengue, or chikungunya. The strain of Ae. albopictus in the United States came from northern Japan in 1985 and is capable of living in more temperate climates.
- To produce eggs, the female mosquito bites people to feed on blood. When feeding, a mosquito will pierce the skin (like a needle) and inject saliva into a person's skin. This allows the disease-causing germ (for example, the Zika virus) into the site.
- In addition to Zika, the most common viruses and parasites transmitted through mosquito bites are:
  - Chikungunya
  - o Dengue
  - Eastern equine encephalitis
  - Filariasis, including dirofilaria, which causes dog heartworm
  - Jamestown Canyon virus disease
  - Japanese encephalitis
  - LaCrosse encephalitis
  - o Malaria
  - o Rift Valley fever
  - Ross River virus disease
  - o St. Louis encephalitis
  - o Venezuelan equine encephalitis
  - Western equine encephalitis
  - Yellow fever
- Once a mosquito is infected with Zika virus, it will remain infected for life. A mosquito lifespan is up to 30 days. There is no evidence that a mosquito infected with Zika will have a shorter than expected lifespan.
- Spread of Zika virus from an infected female mosquito to her eggs has not been well studied, but researchers think the likelihood is generally very low.
- Changes in the environment caused by climate change can influence the spread of mosquitoes
  - These changes can affect
    - How quickly viruses replicate in mosquitoes
    - The life cycle of mosquitoes
    - The distribution of viruses, mosquitoes, or animal hosts

Natural disasters in the continental United States have rarely been accompanied by outbreaks of viruses spread by mosquitoes. Flooding immediately washes away existing mosquito larvae populations.
 Following the disaster, mosquito eggs hatch and develop and mosquito populations surge (this takes about a week). New adult mosquitoes are not infected with virus until they bite an infected person or animal.

- Mosquitoes cannot survive high winds; they dry out and die. There is no evidence that high winds can successfully carry mosquitoes into new areas where they will survive.
- There are no data to link genetically modified (GM) mosquitoes released by Oxitec and the Zika outbreak or cases of microcephaly in Brazil. Oxitec released mosquitoes in only a few towns in Brazil. Occurrence of the Zika outbreak and cases of microcephaly have been reported from most states in Brazil.
  - Before Oxitec could release genetically modified mosquitoes in communities, the Brazilian government had to approve. These genetically modified mosquitoes have not been associated with or expected to cause any harmful effects in people.
- Though their role in mosquito control has not yet been determined, CDC sees the use of GM mosquitoes as a promising new method for controlling mosquitoes that can transmit viruses like dengue, chikungunya, and Zika.
  - o GM mosquitoes cannot replace traditional integrated mosquito management methods, including:
    - Mosquito surveillance,
    - Control of adult and young (larvae and pupae) mosquitoes,
    - Insecticide resistance monitoring, and
    - Personal protection (people protecting themselves from mosquito bites).
  - o Though GM mosquitoes have a role in mosquito control, release of these mosquitoes will not have an immediate effect on a local mosquito population.
  - Therefore, in an epidemic, it is more important to immediately kill infected adult mosquitoes that are spreading viruses.
  - For more information on integrated mosquito management, see: http://www.cdc.gov/zika/pdfs/vectorcontrolaedesmosquitoes.pdf
- Flies do not spread Zika. Only a small number of fly species will bite people. When a fly bites, it creates a wound and laps blood up from the site. When a fly bites, it does not directly inject saliva into the bite site like a mosquito does.
  - o Flies spread some diseases but fewer germs than mosquitoes because their feeding habits are different.

#### VECTOR CONTROL FOR THE GENERAL PUBLIC

- Here's what you can do outside of your home:
  - o **Install or repair and use window and door screens**. Do not leave doors propped open.
  - Once a week, empty and scrub, turn over, cover, or throw out any items that hold water like tires, buckets, planters, toys, pools, birdbaths, flowerpot saucers, or trash containers. Mosquitoes lay eggs near water.
    - Tightly cover water storage containers (buckets, cisterns, rain barrels) so that mosquitoes cannot get inside to lay eggs.
    - For containers without lids, use wire mesh with holes smaller than an adult mosquito.
    - Use larvicides to treat large containers of water that will not be used for drinking and cannot be covered or dumped out.
  - Use an outdoor flying insect spray where mosquitoes rest. Mosquitoes rest in dark, humid areas like under patio furniture, or under the carport or garage. When using insecticides, always follow label instructions.
  - o **If you have a septic tank,** repair cracks or gaps. Cover open vent or plumbing pipes. Use wire mesh with holes smaller than an adult mosquito.
- Here's what you can do inside your home:

- Use air conditioning when possible.
- Keep mosquitoes from laying eggs inside your home. Once a week, empty and scrub, turn over, cover, or throw out any items that hold water like vases and flowerpot saucers.
- Kill mosquitoes inside your home. Use an indoor flying insect fogger\* or indoor insect spray\* to kill
  mosquitoes and treat areas where they rest. These products work immediately, but may need to be
  reapplied. Always follow label directions. Only using insecticide will not keep your home free of
  mosquitoes.
  - Mosquitoes rest in dark, humid places like under the sink, in closets, under furniture, or in the laundry room.
  - Use an indoor fogger\* or indoor insect spray\* to reach and treat areas were mosquitos rest inside the home.
- Do-it-yourself products\*:

Product	Active ingredient	Brand name examples**	How long it works
Indoor flying insect spray	Imidacloprid, β-	Home Pest Insect Killer, Raid,	7-10 days
	Cyfluthrin	Ortho, HotShot, EcoLogic	
Indoor flying insect fogger	Tetramethrin,	Hot Shot, Raid, Real Kill,	Up to 6 weeks
	Cypermethrin	Spectracide	
**Inserticide brand names are provided for your information only. The Centers for Disease Control and Prevention and the			

<sup>\*\*</sup>Insecticide brand names are provided for your information only. The Centers for Disease Control and Prevention and the U.S. Department of Health and Human Services cannot recommend or endorse any name brand products.

#### **PESTICIDES**

- Several media reports in February 2016 suggested that a pesticide called pyriproxyfen might be linked with
  microcephaly. These media reports appear to be based on a February 3 publication authored by an Argentine
  physicians' organization, which claims that the use of pyriproxyfen in drinking water in Brazil is responsible for the
  country's increase in microcephaly cases.
- The World Health Organization (WHO) has approved the use of pyriproxyfen for the control of disease-carrying mosquitoes.
- Pyriproxyfen is a registered pesticide in Brazil and other countries, it has been used for decades, and it has not been linked with microcephaly.
- Exposure to pyriproxyfen would not explain recent study results showing the presence of Zika virus in the brains of infants born with microcephaly.
- In a published study, CDC scientists concluded that Zika virus infection during pregnancy is a cause of microcephaly and other severe fetal brain defects. Scientists continue to study the full range of other potential health problems that Zika virus infection during pregnancy may cause.

## RISK

- Anyone who lives in or travels to an area where Zika virus is found and has not already been infected with Zika virus can get it from mosquito bites.
- A man with Zika virus can pass it to his female or male sex partners. Condoms can reduce the chance of getting Zika from sex if used correctly from start to finish, every time you have vaginal, anal, or oral (mouth-to-penis) sex.
- Based on information about similar infections, once you have been infected with Zika virus, you are likely to be protected from future infections.
- Zika virus testing has been recommended to establish a diagnosis of infection. Testing blood or semen is not recommended to determine the risk of sexual transmission of Zika virus.
  - Because Zika virus can remain in semen longer than blood, someone might have a negative blood test but a positive semen test. The results of the tests are difficult to interpret.

 Studies are underway to better understand the performance of these tests and how best to interpret the results. As additional information becomes available, CDC will share it.

Recommendations for condom use among pregnant couples do not change if a man with possible Zika virus
exposure tests negative for Zika virus infection. Pregnant couples should use a condom every time they have sex or
should not have sex during the pregnancy. To be effective, condoms must be used <u>correctly</u> (warning: this link
contains sexually graphic images) from start to finish, every time you have sex. This includes vaginal, anal, and oral
(mouth-to-penis) sex.

## **PREVENTION**

- There is no vaccine to prevent Zika virus disease.
- The best way to prevent diseases spread by mosquitoes is to protect yourself and your family from mosquito bites.
  - Wear long-sleeved shirts and long pants.
  - Stay in places with air conditioning and window and door screens to keep mosquitoes outside.
  - o Treat your clothing and gear with permethrin or buy pre-treated items.
  - Use <u>Environmental Protection Agency (EPA)-registered insect repellents</u>. Always follow the product label instructions.
    - When used as directed, these insect repellents are proven safe and effective even for pregnant and breastfeeding women.
    - Do not use insect repellents on babies younger than 2 months old.
    - Do not use products containing oil of lemon eucalyptus or para-menthane-diol on children younger than 3 years old.
    - Mosquito netting can be used to cover babies younger than 2 months old in carriers, strollers, or cribs to protect them from mosquito bites.
  - Sleep under a mosquito bed net if air conditioned or screened rooms are not available or if sleeping outdoors.
- During the first week of infection, Zika virus can be found in a person's blood and can pass from an infected person to a mosquito through mosquito bites. An infected mosquito can then spread the virus to other people.
  - To help prevent others from getting sick, strictly follow steps to prevent mosquito bites during the first week of illness.
- Even if they do not feel sick, travelers returning to the United States from an area with Zika should take steps to prevent mosquito bites for 3 weeks so they do not pass Zika to mosquitoes that could spread the virus to other people.
- If you have a baby or child
  - o Do not use insect repellent on babies younger than 2 months old.
  - Do not use products containing oil of lemon eucalyptus or para-menthane-diol on children younger than 3
    years old.
  - Dress your child in clothing that covers arms and legs
  - Cover crib, stroller, and baby carrier with mosquito netting.
  - o Do not apply insect repellent onto a child's hands, eyes, mouth, and cut or irritated skin.
  - o Adults: Spray insect repellent onto your hands and then apply to a child's face.

#### PREVENTING SEXUAL TRANSMISSION

- Only people whose male sex partners have traveled to or live in an area with Zika need to be concerned about
  getting Zika virus through sex. The timeframe for using condoms or waiting to have sex will vary based on the
  couple's situation and concerns.
- Not having sex can eliminate your risk of getting Zika from sex.

• Couples with a pregnant partner should take steps to protect their pregnancy. Because Zika can cause birth defects, these couples should

- o Use a condom every time they have sex or not have sex during the pregnancy.
- o To be effective, condoms must be used <u>correctly</u> from start to finish, every time you have vaginal, anal, and oral (mouth-to-penis) sex.
- Anyone concerned about the sexual transmission of Zika and not concerned about pregnancy can consider using a
  condom every time they have vaginal, anal, and oral (mouth-to-penis) sex or not have sex. To be effective,
  condoms must be used <u>correctly</u> from start to finish, every time during sex.
  - o For couples with a male partner who has traveled to an area with Zika
    - If the male partner has been diagnosed with Zika or has (or had) symptoms, the couple should consider using condoms or not having sex for at least 6 months after symptoms begin.
    - If the male partner does not developed symptoms, the couple should consider using condoms or not having sex for at least 8 weeks after the man returns.
  - For couples with a male partner living in an area with Zika
    - If the male partner has been diagnosed with Zika or has (or had) symptoms, the couple should consider using condoms or not having sex for at least 6 months after symptoms begin.
    - If the male partner has never developed symptoms, the couple should consider using condoms or not having sex while there is Zika in the area.
  - o For couples with a non-pregnant female partner who lives in or has traveled to an area with Zika
    - It is not known if a woman can pass Zika to her sex partners.
    - These couples can also consider using condoms or not having sex.
  - o Those considering these options should weigh the personal risks and benefits, including
    - The mild nature of the illness for many people\*
    - Plans for pregnancy (if appropriate)
    - Access to condoms and other contraception
    - Desire for intimacy, including willingness to use condoms or not have sex
    - Ability to use condoms or not have sex

## **INSECT REPELLENT**

- CDC recommends using <u>EPA-registered insect repellents</u> with one of the following active ingredients: DEET, picaridin, IR3535, oil of lemon eucalyptus, or para-menthane-diol. Choosing an EPA-registered repellent ensures the EPA has evaluated the product for effectiveness.
- Insect repellents registered by the EPA repel the mosquitoes that spread Zika and other viruses like dengue, chikungunya, and West Nile.
- When used as directed, EPA-registered insect repellents are proven safe and effective even for pregnant and breastfeeding women.
- Always follow the product label instructions.
- Reapply insect repellent as directed.
- Do not spray repellent on the skin under clothing.
- If you are also using sunscreen, apply sunscreen before applying insect repellent.
- Treat clothing and gear with permethrin or buy permethrin-treated items.
  - The EPA has reviewed scientific studies on the use of permethrin-treated clothing. Based on EPA's review, there is no evidence of reproductive or developmental effects to mother or child following exposure to permethrin.

<sup>\*</sup>In many cases, Zika does not cause any symptoms or causes only mild symptoms lasting several days to a week. Severe disease requiring hospitalization is uncommon.

 Treated clothing remains protective after multiple washings. See product information to learn how long the protection will last.

- o If treating items yourself, follow the product instructions carefully.
- Do **NOT** use permethrin products directly on skin. They are intended to treat clothing.
- We do not know the effectiveness of non-EPA registered insect repellents, including some natural repellents.
  - Some natural insect repellents, often made with natural oils, have not been tested for effectiveness.
     Homemade insect repellents may not protect you from mosquito bites.
- Some natural products are EPA-registered.
  - o These natural products with EPA registration include para-menthane-diol and oil of lemon eucalyptus.
- Do not use insect repellents on babies younger than 2 months old.
- Do not use products containing oil of lemon eucalyptus or para-menthane-diol on children younger than 3 years old.
- To protect your child from mosquito bites:
  - Dress your child in clothing that covers arms and legs
  - Cover crib, stroller, and baby carrier with mosquito netting.
  - o Do not apply insect repellent onto a child's hands, eyes, mouth, and cut or irritated skin.
  - Adults: Spray insect repellent onto your hands and then apply to a child's face.

## TREATMENT

- There is no specific medicine or vaccine for Zika virus.
- Treat the symptoms.
  - o Get plenty of rest.
  - Drink fluids to prevent dehydration.
  - o Take medicine such as acetaminophen (Tylenol®) to reduce fever and pain.
  - O Do not take aspirin or other non-steroidal anti-inflammatory drugs (NSAIDS) until dengue can be ruled out to reduce the risk of bleeding.
  - o If you are taking medicine for another medical condition, talk to your doctor or other healthcare provider before taking additional medication.
- During the first week of infection, Zika virus can be found in a person's blood. The virus can be passed from an infected person to a mosquito through mosquito bites. An infected mosquito can then spread the virus to other people.
  - To help prevent others from getting sick, strictly <u>follow steps to prevent mosquito bites</u> during the first week of illness.

## **ZIKA & PREGNANCY**

- CDC issued new guidance and information to prevent Zika virus transmission and negative health outcomes, including <u>updated interim guidance for healthcare professionals</u> for counseling patients about pregnancy planning and the timing of pregnancy after possible exposure to Zika virus.
  - For women and men who have been diagnosed with Zika virus disease or who have symptoms of Zika (fever, rash, joint pain, or red eyes) after possible exposure to Zika virus, CDC recommends that healthcare providers
    - Advise women to wait at least 8 weeks after their symptoms first appeared before trying to get pregnant.
    - Advise men to wait at least 6 months after their symptoms first appeared before trying to get their partner pregnant.

 Men should correctly and consistently use condoms for vaginal, anal, and oral (mouth-to-penis) sex or not have sex during this time period if they are concerned about the possibility of transmitting Zika virus to their sex partners.

- For men and women without symptoms of Zika virus but who had possible exposure to Zika from recent travel or sexual contact, healthcare providers should recommend their patients wait at least 8 weeks after their possible exposure before trying to get pregnant.
- Men and women without symptoms of Zika virus who live in an area with active Zika transmission should talk with their healthcare providers about their pregnancy plans during a Zika virus outbreak, the potential risks of Zika, and how they can prevent Zika virus infection during the pregnancy.
- For healthcare professionals: Decisions about pregnancy planning are deeply personal and very complex.
   Circumstances for women and their partners will vary, and these circumstances are best discussed as part of clinical care for a woman and her partner during a visit with a trusted healthcare professional.
- CDC has established the <u>US Zika Pregnancy Registry</u> to learn more about pregnant women in the United States
  with confirmed Zika virus infection and their infants and is collaborating with state, tribal, local, and territorial
  health departments to collect information about pregnancy and infant outcomes following Zika virus infection
  during pregnancy.
  - o CDC also developed a similar system, the Zika Active Pregnancy Surveillance System, in Puerto Rico.
- CDC maintains a 24/7 consultation service for health officials and healthcare providers caring for pregnant women. To contact the service, call 770-488-7100 or email ZIKAMCH@cdc.gov.
- Zika virus can pass from a pregnant woman to her fetus during pregnancy or around the time of birth. We do not know how often this occurs.
- Zika virus infection during pregnancy is a cause of microcephaly and other severe fetal brain defects. Scientists are
  investigating the full range of other potential health problems that Zika virus infection during pregnancy may
  cause.
- In addition to microcephaly, other problems have been detected in pregnancies and among fetuses and infants infected with Zika virus before birth, such as miscarriage, stillbirth, absent or poorly developed brain structures, defects of the eye, hearing deficits, and impaired growth. Although Zika virus has been linked with these other problems in infants, there is more to learn. Researchers are collecting data to better understand the extent of Zika virus' impact on mothers and their children.
- We expect that pregnant women who develop Zika will have similar illness to people who are not pregnant. No
  evidence exists to suggest that pregnant women are more susceptible or experience more severe disease during
  pregnancy.
- We do not know if pregnant women are more likely to develop symptoms compared to the general population.
- We do not know if pregnant women are more likely to get Guillain-Barré syndrome.
- Pregnant women should talk to a doctor or other healthcare provider if they or their male sex partners recently traveled to an area with Zika, even if they don't feel sick.
- Pregnant women should see a doctor or other healthcare provider if they develop a fever, rash, joint pain, or red eyes during their trip or within 2 weeks after traveling to a country where Zika has been reported. They should tell the doctor or other healthcare provider where they traveled.
- Because Zika infection is a cause of microcephaly, pregnant women should strictly follow <u>steps to prevent</u> <u>mosquito bites</u>.
- If a pregnant woman has a male sex partner who lives in or has traveled to an area with Zika, she should use a condom every time she has sex or should not have sex with that partner during the pregnancy. To be effective, condoms must be used <u>correctly</u> (warning: this link contains sexually graphic images) from start to finish, every time you have sex. This includes vaginal, anal, and oral (mouth-to-penis) sex.

#### **MICROCEPHALY**

Zika is a cause of <u>microcephaly</u>, a severe birth defect that is a sign of a problem with brain development.
 Microcephaly is a condition in which a baby's head is much smaller than expected. During pregnancy, a baby's head grows because the baby's brain grows. Microcephaly can occur because a baby's brain has not developed properly during pregnancy or has stopped growing after birth.

- CDC concluded that Zika virus infection is a cause of microcephaly.
  - More lab testing and other studies are planned to learn more about the risks of Zika virus infection during pregnancy.
  - o CDC scientists announced that enough evidence has accumulated to conclude that Zika virus infection during pregnancy is a cause of microcephaly and other severe fetal brain defects. This means that a Zika virus infection in pregnancy increases the chances of poor pregnancy outcomes. However, Zika virus infection in a mother does not definitely mean a poor pregnancy outcome will occur.
- We do not know if a newborn who gets Zika at birth will develop microcephaly after birth, which is called acquired microcephaly.
  - o Babies can acquire microcephaly if their head growth slows or fails to develop after birth.
  - o There have been no reports of Zika infection around the time of birth and acquired microcephaly.
  - All reports of microcephaly so far have been congenital microcephaly, meaning the microcephaly occurred before birth.
- Currently, there is no evidence to suggest that past Zika virus infection poses an increased risk of birth defects for future pregnancies.
- Zika virus usually remains in the blood of an infected person for about a week. There is no evidence that the virus will cause infection in a pregnancy that occurs after the virus is cleared from the mother's blood. The virus can be present in semen longer than in blood.
  - A woman thinking about pregnancy and recently recovered from Zika infection, should talk to her doctor or other healthcare provider about planning her pregnancy.
- Babies with microcephaly can have a range of other health problems, depending on how severe their microcephaly
  is. These problems can range from mild to severe and are often lifelong. In some cases, these problems can be lifethreatening.
  - Seizures
  - Developmental delay, such as problems with speech or other developmental milestones (like sitting, standing, and walking)
  - o Intellectual disability (decreased ability to learn and function in daily life)
  - Problems with movement and balance
  - o Feeding problems, such as difficulty swallowing
  - Hearing loss
  - Vision problems
- Because it is difficult to predict at birth what problems babies will have from microcephaly, they often need close follow-up through regular check-ups with a doctor or other healthcare provider to track their growth and development.

## **DIAGNOSIS**

- During pregnancy, microcephaly can sometimes be diagnosed during an ultrasound (which creates pictures of the baby).
- Microcephaly might not be detectable until late in the second or early in the third trimester of pregnancy.
- CDC has interim guidelines for testing and evaluating an infant with possible congenital Zika virus infection.

• The accuracy of the test varies depending on the type of test, the timing of the test during pregnancy, the specific equipment used for the test, and the person conducting the test.

• CDC <u>provides information on diagnosing birth defects</u> both during pregnancy and after birth. Some tests need to be done during a particular time in pregnancy, but others such as an ultrasound can be done at any time during pregnancy. High resolution ultrasounds (also known as Level 2 ultrasounds) are used to look in more detail for possible birth defects and are usually completed between weeks 18 and 22 of pregnancy. They can also be performed later if risks are detected later in pregnancy.

## LABORATORY TESTING

- Laboratories processing clinical specimens for Zika virus diagnostic testing should, at a minimum, adhere to BSL2
   (biosafety level 2) precautions. All laboratories should perform a risk assessment to determine if there are certain
   procedures or specimens that may require higher levels of biocontainment. Suspicion that the specimen may
   contain a pathogen that requires BSL3 precautions (e.g., chikungunya virus), should be considered a significant risk
   factor.
- On February 26, 2016, the Food and Drug Administration (FDA) issued an <a href="Emergency Use Authorization (EUA)">Emergency Use Authorization (EUA)</a> for a diagnostic tool for Zika virus that is being distributed to qualified laboratories and, in the United States, those that are certified to perform high-complexity tests.
  - The test, called the CDC Zika IgM Antibody Capture Enzyme-Linked Immunosorbent Assay (Zika MAC-ELISA), is intended to be used on serum and cerebrospinal fluid samples from people with a history of symptoms associated with Zika and/or people who have recently traveled to an area with Zika.
  - CDC has and continues to distribute the test to qualified laboratories in the <u>Laboratory Response Network</u> (<u>LRN</u>). The test is not available in US hospitals or primary care settings.
- On March 17, 2016, FDA <u>issued an EUA</u> for a diagnostic tool for the qualitative detection and differentiation of RNA from Zika virus, dengue virus, and chikungunya virus in human sera or cerebrospinal fluid, and for the qualitative detection of Zika virus RNA in urine and amniotic fluid.
  - The test, called the Trioplex Real-time RT-PCR Assay (Trioplex rRT-PCR), is intended to be used on specimens collected from people with a recent history of symptoms associated with Zika and/or people who have lived in or traveled to an area with Zika.
  - Testing is being performed by qualified laboratories designated by CDC and, in the United States, certified to perform high-complexity tests.
  - Because Trioplex rRT-PCR combines three tests (for Zika, dengue, and chikungunya) into one, it reduces
    costs and increases efficiency. Trioplex rRT-PCR has been adapted to be run on equipment that is common
    in public health labs in the United States and abroad.
- On April 28, 2016, FDA issued an EUA for a commercial assay for the qualitative detection of Zika virus RNA.
  - This test is the Focus Diagnostics, Inc., Zika Virus RNA Qualitative Real-time RT-PCR for use on acute serum only.
  - Unlike the Trioplex assay which tests for three viruses, the Focus Diagnostics RT-PCR is for the detection of Zika RNA only.
- Zika virus testing is performed at CDC and some state and territorial health departments. Healthcare providers should contact their state and local health department to facilitate testing. See the <u>Diagnostic Testing webpage</u> for information on how to obtain Zika testing.
- Healthcare providers should work closely with the state or local health department to ensure that the appropriate test is ordered and interpreted correctly.
- In the United States, none of the commercially available testing products are FDA-cleared. CDC is working to expand diagnostic testing capacity with both public and commercial partners in the United States.

 CDC is aware of these products, but CDC doesn't have information on the reliability of these commercially available Zika virus kits.

- Recently, CDC published interim guidance on the use of urine for Zika virus testing.
  - o Currently, it is recommended that Zika virus rRT-PCR be performed on urine collected <14 days after onset of symptoms in patients with suspected Zika virus disease. Zika virus rRT-PCR testing of urine should be performed in conjunction with serum testing. A matching serum specimen should always be collected when urine is collected; the serum should be tested for Zika IgM followed by plaque-reduction neutralization testing (PRNT) if indicated.</p>

#### Tests

- o During the first week of illness, Zika virus disease can often be diagnosed by performing reverse transcription-polymerase chain reaction (RT-PCR) on serum and urine.
  - A negative Zika virus RT-PCR does not always rule out Zika virus infection. During the first 7 days of symptom onset, viral RNA can often be identified in serum, and RT-PCR is the preferred test. Zika virus rRT-PCR should be performed on urine collected <14 days after onset of symptoms in patients. However, as viremia decreases over time, a negative RT-PCR collected after symptom onset does not preclude Zika virus infection. Serologic testing should be performed.</p>
- Serology assays can also be used to detect Zika virus-specific IgM and neutralizing antibodies, which
  typically develop toward the end of the first week of illness.
  - A positive IgM result does not always indicate Zika virus infection and can be difficult to interpret
    because cross-reactivity can occur with related flaviviruses (e.g., dengue, Japanese encephalitis,
    West Nile, yellow fever).
  - A positive Zika virus IgM result may reflect previous vaccination against a flavivirus; previous infection with a related flavivirus; or current infection with a flavivirus, including Zika virus.
- Plaque-reduction neutralization testing (PRNT) can be performed to measure virus-specific neutralizing antibodies to confirm primary flavivirus infections and differentiate from other viral illnesses.
  - PRNT can be performed to measure virus-specific neutralizing antibodies to Zika virus, but neutralizing antibodies may still yield cross-reactive results in a person who was previously infected with another flavivirus, such as dengue, or has been vaccinated against yellow fever or Japanese encephalitis.
- Each clinical scenario is unique, and healthcare providers should consider all available information when ordering a test for Zika virus infection including patient travel history, history of flavivirus infection, vaccination history, ultrasound findings, and the presence of symptoms. They should work with their state, local, and territorial health departments for assistance ordering laboratory tests and interpreting test results.

#### **TESTING FOR PREGNANT WOMEN**

- Laboratory evidence of maternal Zika virus infection can include Zika virus RNA detected by RT-PCR in any clinical specimen or positive Zika virus IgM with confirmatory neutralizing antibody titers that are ≥4-fold higher than dengue virus neutralizing antibody titers in serum by PRNT. Testing would be considered inconclusive if Zika virus neutralizing antibody titers are < 4-fold higher than dengue virus neutralizing antibody titers.</li>
  - Zika virus RT-PCR and serology assays can be performed on maternal serum or plasma. Zika virus RT-PCR can also be performed on amniotic fluid. Other testing that can be performed includes the following: 1) histopathologic examination and immunohistochemical staining of the placenta and umbilical cord, 2) Zika virus testing of frozen placental tissue and cord tissue, and 3) IgM and neutralizing antibody testing of cord blood.

## For Asymptomatic Pregnant Travelers

 Testing can be offered from 2 to 12 weeks after pregnant women return from travel to areas with Zika virus. Information about serologic testing of asymptomatic persons is limited; on the basis of experience

with other flaviviruses, we expect that antibodies will be present from 2 weeks after virus exposure and can persist for up to 12 weeks.

- Pregnant women with possible exposure to Zika virus up to 8 weeks before the start of pregnancy (or 6 weeks before the woman's last menstrual period) can be offered testing for Zika within 2 to 12 weeks after the possible exposure.
- Although data on the performance of IgM serologic testing in asymptomatic persons is limited, on the
  basis of experience with other flaviviruses, when performed 2 to 12 weeks after travel to areas with Zika
  virus, a negative (IgM) result suggests that infection did not occur and could remove the need for serial
  ultrasounds.
- For pregnant women who had sex without a condom with a male partner who had possible exposure to Zika virus, testing is recommended if:
  - o The woman has at least one symptom of Zika virus infection OR
  - o Her male partner is diagnosed with Zika virus disease or has symptoms consistent with Zika virus infection

## • For Pregnant Women in Areas with Ongoing Transmission

- Pregnant women who reside in areas with Zika virus are at ongoing risk of maternal Zika virus infection throughout their pregnancy; therefore, symptomatic pregnant residents should be tested for Zika virus infection.
  - For pregnant women with symptoms consistent with Zika virus disease, testing is recommended during the first week of illness.
- Asymptomatic pregnant residents may be offered screening with serologic testing at the initiation of prenatal care and mid-second trimester. Local health officials should determine when to implement testing of asymptomatic pregnant women on the basis of information about local levels of Zika virus transmission and laboratory capacity.
  - For asymptomatic pregnant women, IgM testing is recommended at the initiation of prenatal care with follow-up IgM testing mid-second trimester.
- o If new symptoms consistent with Zika virus infection develop, a prior negative test for Zika virus does not rule out current infection. If new symptoms develop, a pregnant woman should be retested. During the first 7 days after symptom onset, viral RNA can often be identified in serum, and RT-PCR is the preferred test to detect this. However, viremia decreases over time, and a negative RT-PCR on serum collected 5-7 days after symptom onset does **not** exclude Zika virus infection.

## **TESTING FOR INFANTS & CHILDREN**

- Zika virus infection can be diagnosed by reverse transcriptase-polymerase chain reaction (RT-PCR) or through detection of Zika virus-specific IgM and neutralizing antibodies.
  - It has not been established which test is most reliable for a diagnosis in infants. Therefore, RT-PCR and IgM tests should both be performed. Plaque-reduction neutralization testing (PRNT) may also need to be performed to measure virus-specific neutralizing antibodies to differentiate Zika virus from infection with or vaccination for other flaviviruses.
  - If cerebrospinal fluid (CSF) specimens are available, Zika virus RT-PCR should be performed; however, CSF specimens should not be collected for the sole purpose of Zika virus testing.
  - Histopathologic evaluation of the placenta and umbilical cord, immunohistochemical staining on fixed tissue, and Zika virus RT-PCR on fixed and frozen tissue can be performed.
- Zika virus infection can be confirmed in infants and children by performing reverse transcriptase-polymerase chain reaction (RT-PCR) on serum within 7 days of symptoms onset.
  - Serologic assays can also be used to detect Zika virus-specific IgM and neutralizing antibodies 4 or more days after symptoms onset.

 Evaluation of infants and children for acute Zika virus infection should include testing of serum and may include cerebrospinal fluid (CSF) testing for Zika viral RNA, if samples were obtained as part of routine care. A CSF sample collected for the sole purpose of Zika RT-PCR testing is not recommended.

- Zika virus testing is performed at the CDC Arbovirus Diagnostic Laboratories and at some state and territorial health departments.
- Healthcare providers should contact their state and local health department to facilitate testing.
  - o See the <u>Diagnostic Testing webpage</u> for information on how to obtain Zika testing.
- Laboratory evidence of Zika virus infection in an infant or child would include, in any clinical specimen, detectable Zika virus in culture, Zika virus RNA (by RT-PCR) or antigen, or a clinical specimen positive for Zika virus IgM with confirmatory neutralizing antibody titers ≥4-fold higher than dengue virus neutralizing antibody titers. If Zika virus antibody titers are <4-fold higher than dengue virus antibody titers, test results for Zika virus would be considered inconclusive.
- Zika virus testing in newborns has several challenges.
  - o RT-PCR tests may not detect Zika virus RNA in an infant or child who had Zika virus infection *in utero* if the period of viremia has passed.
  - Serologic tests for Zika virus can often be falsely positive because of cross-reacting antibodies against related flaviviruses (e.g., dengue and yellow fever viruses).
  - Plaque-reduction neutralization testing (PRNT) can be performed to measure virus-specific neutralizing antibodies to Zika virus, but neutralizing antibodies may still yield cross-reactive results in newborns due to maternal antibodies that were transferred to the infant.
  - It is important to work closely with state or territorial health departments to ensure the appropriate test is ordered and interpreted correctly.

## CDC GUIDANCE & RECOMMENDATIONS

- CDC has developed guidance and recommendations on Zika for travelers, healthcare workers, and other groups. As new guidance and recommendations are developed and updated, they are posted on CDC's <u>Zika website</u>.
- CDC has <u>interim guidelines</u> for pregnant women and women of reproductive age with possible Zika virus exposure.
   Because there are limited data and experience with Zika virus in pregnancy, CDC continually evaluates any new or emerging data that may inform future recommendations. As more information becomes available, we will update the <u>CDC Zika website</u>.
  - CDC has <u>additional Q&As</u> about Zika virus for healthcare providers.
- CDC has <u>interim guidelines</u> for healthcare providers caring for infants and children with possible Zika virus exposure. <u>Q&As</u> on these guidelines are also available.
- CDC has updated interim guidance for prevention of sexual transmission of Zika virus.
- CDC has released two Health Alert Network messages on Zika for partners.

#### PREGNANT WOMEN

- Until more is known, CDC recommends special precautions for the following groups:
  - Pregnant women
    - Should not travel to any area where Zika virus is spreading.
    - If you must travel to one of these areas, talk to your doctor or other healthcare provider first and strictly follow <u>steps to prevent mosquito bites</u> during the trip.
    - If you have a male partner who lives in or has traveled to an area where Zika is spreading, use a condom every time you have sex or do not have sex during the pregnancy. To be effective,

condoms must be used <u>correctly</u> (warning: this link contains sexually graphic images) from start to finish, every time you have sex. This includes vaginal, anal, and oral (mouth-to-penis) sex.

- Women trying to get pregnant
  - Before you or your male partner travel, talk to your doctor or other healthcare provider about your plans to become pregnant and the risk of Zika virus infection.
  - You and your male partner should strictly follow <u>steps to prevent mosquito bites</u> during the trip.
- For women and men considering conceiving who have been diagnosed with Zika virus disease or who
  have symptoms of Zika virus infection, including fever, rash, joint pain or red eyes, after possible exposure
  to Zika virus, CDC recommends:
  - Women wait at least 8 weeks after their symptoms first appeared before trying to get pregnant.
  - Men wait at least 6 months after their symptoms first appeared to try to get their female partner pregnant
  - Men should correctly and consistently use condoms for vaginal, anal, and oral (mouth-to-penis) sex or not have sex during this time period if they are concerned about the possibility of transmitting Zika virus to their sex partners.
- For both men and women considering conceiving without symptoms of Zika virus but who had possible
   exposure to Zika from recent travel or sexual contact, CDC recommends waiting at least 8 weeks after the
   last possible exposure before trying to get pregnant.
- Pregnant women who have recently traveled to an area with Zika should talk to a doctor or other healthcare provider about their travel even if they don't feel sick.
- Pregnant women should see a doctor or other healthcare provider if they develop a fever, rash, joint pain, or
  conjunctivitis (red eyes) during their trip or within 2 weeks after traveling to a country with Zika. They should tell
  the doctor or other healthcare provider where they traveled. CDC has developed interim guidelines for pregnant
  women for Zika. The doctor or other healthcare provider may order specialized blood tests to look for Zika or other
  similar viral diseases like dengue or chikungunya.
  - Pregnant women should also talk to their doctor or other healthcare provider if their male sex partner recently traveled to an area with Zika.
  - o Pregnant women who have a fever should take acetaminophen (for example, Tylenol®) for fever control.
- CDC has guidance to help healthcare providers decide which tests are needed for pregnant women who may have been exposed to Zika.
- A woman who is planning or thinking about pregnancy and has recently traveled to an area where Zika is spreading should talk to her doctor or other healthcare provider after returning. She should also talk to her doctor or other healthcare provider if her male sex partner lives in or has traveled to an area with Zika.
- If you are pregnant and worried that you might have had Zika, talk to your doctor or other healthcare provider. Tell them about your recent travel and any symptoms of Zika you experienced. The most common symptoms of Zika are fever, rash, joint pain, and conjunctivitis (red eyes). Your doctor may order specialized blood tests to look for Zika or other similar viral diseases, like dengue or chikungunya.
- Women should talk to their doctor or other healthcare provider about any concerns regarding Zika infection.

### TRAVEL

- Travelers who go to places with outbreaks of Zika can be infected with Zika virus.
  - o Travelers can protect themselves by <u>preventing mosquito bites</u>.
- Some travelers become infected while traveling abroad but do not get sick until they return home. Be aware of any illness or symptoms during your trip or after you return home. Tell your doctor or other healthcare provider where you have traveled and when you were there.

• Even if they do not feel sick, travelers returning to the United States from an area with Zika should take steps to prevent mosquito bites for 3 weeks so they do not spread Zika to uninfected mosquitoes.

- The mosquitoes that spread Zika usually do not live at elevations above 6,500 feet (2,000 meters). Travelers who plan to be only in areas above this elevation are at a very low risk of getting Zika from a mosquito.
- Sexual transmission of Zika virus from a male partner is possible, so travelers are encouraged to use condoms or not have sex.
- Until more is known, CDC recommends the following:
  - o Pregnant women
    - Should not travel to any area below 6,500 feet (2,000 meters) where Zika virus is spreading.
    - If you must travel to one of these areas, talk to your doctor or other healthcare provider first and strictly follow steps to prevent mosquito bites during the trip. If your itinerary is limited entirely to areas above 6,500 feet, there is minimal risk of getting Zika from a mosquito.
    - If you have a male partner who lives in or has traveled to an area where Zika is spreading, use a condom every time you have sex or do not have sex during the pregnancy. To be effective, condoms must be used <u>correctly</u> (warning: this link contains sexually graphic images) from start to finish, every time you have sex. This includes vaginal, anal, and oral (mouth-to-penis) sex.
  - Women trying to get pregnant
    - Before you or your male partner travel, talk to your doctor or other healthcare provider about your plans to become pregnant and the risk of Zika virus infection.
    - You and your male partner should strictly follow steps to prevent mosquito bites during the trip.
    - For women and men who have been diagnosed with Zika virus disease or who have symptoms of Zika virus infection, including fever, rash, joint pain or red eyes, after possible exposure to Zika virus, CDC recommends:
      - Women wait at least 8 weeks after their symptoms first appeared before trying to get pregnant.
      - Men wait at least **6 months** after their symptoms first appeared before trying to get their partner pregnant.
      - Men should correctly and consistently use condoms for vaginal, anal, and oral (mouthto-penis) sex or not have sex during this time period if they are concerned about the possibility of transmitting Zika virus to their sex partners.
    - For men and women without symptoms of Zika virus but who had possible exposure to Zika from recent travel or sexual contact, CDC recommends waiting at least 8 weeks after the last possible exposure before trying to get pregnant.
- There are no restrictions for travelers entering the United States who have contracted Zika virus. CDC is not conducting enhanced entry screening of arriving travelers for Zika at this time.
  - Because most people who have Zika do not have symptoms, entry screening will not work to prevent imported cases. CDC and Customs and Border Protection are working together to assess the situation and determine necessary measures.
  - CDC has routine steps to detect sick travelers entering the United States, including requirements for ships and airplanes arriving in the United States to report certain illnesses to CDC. State and territorial health departments routinely notify CDC when cases of Zika are detected in the United States.

## TRAVEL NOTICES

- CDC has issued a <u>travel notice</u> (level 2 alert, "practice enhanced precautions") for people traveling to places where Zika virus is spreading.
  - o Specific areas where Zika is spreading are often difficult to determine and are likely to change over time.

• As more information becomes available, CDC's <u>Zika travel notices</u> will be updated. Please check back frequently for the most up-to-date recommendations.

- CDC regularly issues level 2 alert travel notices when recommending special precautions for travelers because of a specific outbreak or situation.
  - Special precautions might mean getting a certain vaccine or taking a certain medicine that would not
    usually be recommended for that destination. Sometimes the special precaution is that a certain group
    should avoid travel.
- Countries and territories where Zika is spreading are included in the travel notice.
  - Local transmission means that mosquitoes in affected areas have been infected with Zika virus and are spreading it to people.
  - Countries and territories with imported cases are not included in the travel notice. Imported cases occur
    when people are infected with Zika during travel to an affected area and then return to their home
    countries.
  - Countries with past Zika transmission are not included. CDC has had Zika travel notices in the past for several other countries, but those were removed as outbreaks ended.
- CDC has issued guidance for travel to the 2016 Summer Olympic and Paralympic Games in Brazil.
- CDC has posted notices that include maps that show elevation levels in countries with Zika.
- CDC has posted <u>maps</u> that show elevation levels in countries with Zika.
- The mosquitoes that spread Zika usually do not live at elevations above 6,500 feet (2,000 meters). Travelers whose itineraries are limited **entirely** to areas above this elevation are at minimal risk of getting Zika from a mosquito.

#### **OBSTETRICAL HEALTHCARE PROVIDERS**

- CDC issued new guidance and information to prevent Zika virus transmission and negative health outcomes, including <u>updated interim guidance for healthcare professionals</u> for counseling patients about pregnancy planning and the timing of pregnancy after possible exposure to Zika virus. <u>Updated interim guidance</u> was also issued for preventing sexual transmission with information about how long men and women should consider using condoms or not having sex after possible exposure or infection.
  - o <u>For men who traveled to or live in an area with Zika and have a pregnant partner, CDC recommends using condoms every time they have sex or not having sex during the pregnancy. To be effective, condoms must be used correctly, every time during sex. This includes vaginal, anal, and oral (mouth-to-penis) sex.</u>
  - For non-pregnant women and men who have been diagnosed with Zika virus or who have symptoms of Zika including fever, rash, joint pain or red eyes after possible exposure to Zika virus, CDC recommends
    - Women wait at least 8 weeks after their symptoms first appeared before trying to get pregnant.
    - Men wait at least 6 months after their symptoms first appeared to have unprotected sex.
  - For non-pregnant women and men who traveled to an area with Zika but did not develop symptoms of Zika, consider using condoms or not having sex for at least 8 weeks after return in order to minimize risk of sexual transmission of Zika.
  - Couples with men who live in an area with Zika but have not developed symptoms might consider using condoms or not having sex while there is active Zika transmission in the area.
- CDC has <u>Interim Guidelines for Health Care Providers Caring for Pregnant Women and Women of Reproductive</u>
  Age with Possible Zika Virus Exposure.
  - CDC updated its guidelines to include a new recommendation to offer serologic testing to asymptomatic
    pregnant women (women who do not report clinical illness consistent with Zika virus disease) who have
    traveled to areas with Zika virus.
  - The updated guidance includes a recommendation to offer IgM antibody testing for Zika virus to
    asymptomatic pregnant women. Although we have limited information about antibody testing of
    asymptomatic patients, data from related viruses suggest that this testing may be useful when timeframe
    of exposure is known. Thus, testing may provide useful information for pregnant women and their

healthcare providers. A negative IgM test result 2-12 weeks after known exposure suggests that a recent Zika virus infection did not occur, which may remove the need for serial ultrasounds. Local health officials should determine when to implement testing of asymptomatic pregnant women on the basis of information about levels of Zika virus transmission and laboratory capacity.

- The updated guidance also provides recommendations for female residents in areas with Zika virus.
- CDC released a <u>new report</u> emphasizing the importance of healthcare personnel following practices, called Standard Precautions, to prevent the spread of infectious diseases such as Zika when caring for all patients, including pregnant patients in labor and delivery settings. Currently, there are no reports of Zika spreading from an infected patient to a health care provider or other patients. However, in labor and delivery units where health care personnel might come in contact with high volumes of body fluids, Standard Precautions to minimize contact with body fluids are important to reduce the possibility of spreading infectious diseases such as Zika.
- CDC continues to evaluate all available evidence and to update recommendations as new information becomes available. CDC's updated guidelines have been informed by our close collaboration with clinicians, professional organizations, state, tribal, local, and territorial health departments, and many other stakeholders.
- The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine (SMFM) have issued a <u>Practice Advisory</u> directed to obstetric providers about prevention strategies and clinical management of pregnant women.

#### **ZIKA & PREGNANCY**

## • Counseling Pregnant Women

- o Pregnant women should not travel to an area with Zika virus.
- Pregnant women considering travel to an area with active Zika virus transmission should talk to their healthcare provider. If a pregnant woman does travel, she should strictly follow steps to avoid mosquito bites during the trip.
- O Given the potential risks of maternal Zika virus infection, pregnant women whose male partners lived in or traveled to an area with Zika should use a condom every time they have sex or not have sex during the pregnancy. To be effective, condoms must be used <u>correctly</u> (warning: this link contains sexually graphic images) from start to finish, every time you have sex. This includes vaginal, anal and oral (mouth-to-penis) sex.
  - Recommendations will be updated as more information becomes available.

## Counseling Women Who are Considering Pregnancy

- For non-pregnant women and men who have been diagnosed with Zika virus or who have symptoms of Zika virus disease, including fever, rash, joint pain or red eyes, after possible exposure to Zika virus, CDC recommends
  - Women wait at least 8 weeks after their symptoms first appeared before trying to get pregnant.
  - Men wait at least 6 months after their symptoms first appeared to try to get their female partner pregnant.
  - Men should correctly and consistently use condoms for vaginal, anal, and oral (mouth-to-penis) sex or not have sex during this time period if they are concerned about the possibility of transmitting Zika virus to their sex partners.
- For both non-pregnant women and men who traveled to an area with Zika but did not develop symptoms
  of Zika, consider using condoms or not having sex for at least 8 weeks after return in order to minimize
  risk of sexual transmission of Zika virus.

## • Counseling Women of Reproductive Age in Areas with Local Zika Virus Transmission

 A preconception counseling guide for healthcare providers counseling couples who are interested in conceiving and who live in an area with active Zika virus transmission is available <u>online</u>.

 Women of reproductive age with current or previous laboratory-confirmed Zika virus infection should be counseled that

- CDC recommends waiting at least 8 weeks after their symptoms first appeared before trying to get pregnant.
- There is no evidence that prior Zika virus infection poses an increased risk of birth defects in future pregnancies.
- Zika virus usually remains in the blood of an infected person for about a week. There is no evidence that the virus will cause infection in a pregnancy that occurs after the virus is cleared from the mother's blood. The virus can be present in semen longer than in blood.
- A woman thinking about pregnancy and recently recovered from Zika infection should talk to her doctor or other healthcare provider about planning her pregnancy.
- Healthcare providers should discuss reproductive life plans, including pregnancy intentions and timing with women of reproductive age in the context of the potential risks of Zika virus transmission.
  - A reproductive life plan helps a woman think about her goals for having or not having children
    and how to achieve these goals. A woman's plan depends on her personal goals. Reproductive
    life plan worksheets are available online.
- Healthcare providers should discuss strategies to prevent unintended pregnancy, including counseling on family planning and the correct and consistent use of effective contraceptive methods. Additionally, when choosing a contraceptive method, the prevention of sexually transmitted infections should also be considered, including the correct and consistent use of condoms.
- For women planning to become pregnant, healthcare providers should discuss the potential risk of Zika virus infection in pregnancy, the signs and symptoms associated with Zika virus disease, and when to seek care if the patient develops symptoms of Zika virus disease. They should also emphasize strategies to prevent mosquito bites.

#### **AMNIOCENTESIS**

- Consideration of amniocentesis should be based on the patient's clinical circumstances. Healthcare providers should discuss the risks and benefits of amniocentesis with their patients.
- While amniocentesis is a relatively safe test, risks and benefits of amniocentesis should always be considered and discussed thoroughly with a healthcare provider. An amniocentesis can be used to provide additional clinical information.
  - For example, a laboratory test result positive by RT-PCR on amniotic fluid would be suggestive of
    intrauterine infection and potentially useful to pregnant women and their healthcare providers to assist in
    determining clinical management (e.g., antepartum testing, scheduling serial ultrasounds, delivery
    planning).
- Amniocentesis is not recommended until after 15 weeks of gestation.
- Amniocentesis performed ≥15 weeks of gestation is associated with lower rates of complications than those
  performed at earlier gestational ages (≤14 weeks of gestation).
- The exact timing of amniocentesis should be individualized based on the patient's clinical circumstances. Referral to a maternal-fetal medicine or infectious disease specialist with expertise in pregnancy management may be warranted. Risks and benefits of performing the amniocentesis should be discussed with the patient.
- A positive Zika virus RT-PCR result from amniotic fluid would be suggestive of intrauterine infection. This
  information would be useful for pregnant women and their healthcare providers to assist in determining clinical
  management (e.g., antepartum testing, decision-making, delivery planning). A negative Zika virus RT-PCR result
  from amniotic fluid may prompt a work-up for other causes of microcephaly (e.g., other infections, genetic
  disorders).

#### PRENATAL DIAGNOSIS OF MICROCEPHALY

- Microcephaly and intracranial abnormalities have been demonstrated in pregnancies with known Zika virus infection. Hence, additional ultrasounds might provide an opportunity to identify findings consistent with fetal Zika virus infection and offer pregnant women the option of amniocentesis to test for Zika virus RNA.
- Microcephaly can be diagnosed during pregnancy with ultrasound. Microcephaly is most easily diagnosed by ultrasound in the late second trimester or early third trimester of pregnancy.
- Fetal ultrasound is generally performed in pregnancies between 18-20 weeks of gestation to assess fetal anatomy as part of routine obstetrical care.
- Although microcephaly and intracranial calcifications are typically detected during ultrasounds in the late second
  and early third trimester of pregnancy, these findings might be detected as early as 18-20 weeks gestation.
   However, detection by prenatal ultrasound can be challenging at this gestational age due to fetal position and fetal
  motion artifact.
- The optimal time to perform ultrasound screening for fetal microcephaly is not known. In the absence of microcephaly, the presence of intracranial calcifications before 22 weeks gestation might suggest a risk for the future development of microcephaly.
- Zika virus infection is a cause of severe fetal brain defects. Brain abnormalities reported in infants with laboratory-confirmed congenital Zika infection include microcephaly and disrupted brain growth. Some infants with possible Zika virus infection have been found to have intracranial calcifications and abnormalities of the eye.
  - o In one published report of two infants with Zika virus RNA detected by RT-PCR, brain anomalies detected on ultrasound included corpus callosal and vermian dysgenesis, enlarged cisterna magna, severe unilateral ventriculomegaly, agenesis of the thalami, cataracts, intracranial and intraocular calcifications.
- Ultrasound is performed during pregnancy when medical information is needed. It has been used during pregnancy for many years and has not been associated with adverse maternal, fetal, or neonatal outcomes.
  - Ultrasound operators are trained to use the lowest power for the minimum duration of time to obtain the needed information. There is consensus among various national and international medical organizations (American College of Radiology, American College of Obstetricians and Gynecologists, and the Society for Maternal Fetal Medicine) that ultrasound is safe for the fetus when used appropriately.
- The accuracy of ultrasound to detect microcephaly in the setting of maternal Zika virus is not known and will depend on many factors, such as the timing of maternal infection relative to the timing of screening, severity of microcephaly, patient factors (e.g., obesity), gestational age, the equipment used, and the expertise of the person performing the ultrasound.
  - Because the absence of fetal microcephaly and intracranial calcifications on ultrasound at one point in pregnancy does not exclude future microcephaly, additional ultrasounds may be considered at the discretion of the healthcare provider. As we get more information specifically related to Zika virus infection and microcephaly, we expect that more specific guidance for women and their healthcare providers will be developed.
- The sensitivity of prenatal ultrasound for detection of microcephaly depends on a range of factors (e.g., timing of
  ultrasound screening, severity of microcephaly, patient factors). In a study of fetal microcephaly not caused by Zika
  virus infection, prenatally ultrasound-diagnosed microcephaly correlated with neonatal microcephaly
  approximately 57% of the time.
- Fetal MRI is not a screening tool and should be used only to answer specific questions raised by ultrasound or used
  in occasional specific high-risk situations. Interpretation of fetal MRI requires specialized expertise and has limited
  availability and accessibility in the United States.

#### PEDIATRIC HEALTHCARE PROVIDERS

• CDC has updated its interim guidelines for healthcare providers in the United States caring for infants and children with possible congenital or perinatal Zika virus infection.

- Update: Interim Guidelines for Healthcare Providers Caring for Infants and Children with Possible Zika
   Virus Infection United States, February 2016
- These guidelines include recommendations for the evaluation, testing, and management of infants and children with possible Zika virus infection. These interim guidelines will be updated as more information becomes available.
- Updated guidelines contain a new recommendation to provide routine care to infants with no abnormal findings
  on prenatal or postnatal ultrasound, normal physical examination and whose mothers were not previously tested
  for Zika virus infection. Updated guidelines also contain new recommendations for the care of infants and children
  with possible acute Zika virus disease.
- An infant or child who has traveled to or resided in an area with Zika virus is at risk for Zika virus infection. Additionally, an infant whose mother was infected with Zika virus during pregnancy is at risk for Zika virus infection in utero. Infants can also be infected perinatally if the mother traveled to or resided in an area with Zika virus transmission within 2 weeks of delivery.
- The baseline prevalence of congenital microcephaly is difficult to determine because of underreporting, and the inconsistency of clinical criteria used to define microcephaly. Although population-based estimates of congenital microcephaly in Brazil vary, the number of infants with microcephaly currently being reported in Brazil is greater than would be expected.
- Although Zika virus RNA has been detected in breast milk, transmission of Zika infection through breastfeeding has
  not been documented. Based on available evidence, the benefits of breastfeeding infants outweigh any theoretical
  risk. CDC encourages mothers with Zika virus infection and mothers living in areas with Zika to breastfeed their
  infants.
- We do not know if a newborn who gets Zika virus at birth will develop microcephaly after birth. Babies can develop microcephaly after birth if their head growth slows or fails to develop after birth. There have been no reports of Zika virus infection around the time of birth leading to microcephaly in infants.
- The prognosis for infants with congenital Zika virus infection is not known.

## ZIKA VIRUS TRANSMISSION IN INFANTS & CHILDREN

- Zika virus can be transmitted from a pregnant woman to her fetus during pregnancy or around the time of birth. We do not know how often Zika transmission occurs during pregnancy or around the time of birth.
- Congenital or intrauterine transmission of Zika virus occurs when a woman is infected with Zika virus during her pregnancy, but before delivery, and the virus passes to the fetus.
- Perinatal transmission of Zika virus occurs when a woman is infected with the Zika virus within 2 weeks of delivery, and the virus passes to the infant at or around the time of delivery.
- When an infant acquires Zika virus disease perinatally, the infant may develop symptoms such as maculopapular rash, conjunctivitis, arthralgia (joint symptoms), and fever.
- Zika virus RNA has been identified in breast milk. No evidence of Zika virus infection associated with breastfeeding has been reported.
  - Current evidence suggests that the benefits of breastfeeding outweigh the theoretical risks of Zika virus infection transmission through breast milk. CDC encourages mothers with Zika virus infection and mothers living in areas with Zika virus to breastfeed their infants.

**BIRTH DEFECTS** 

• In a published review of existing evidence, CDC scientists concluded that Zika virus infection during pregnancy can cause microcephaly and other severe fetal brain defects. Scientists continue to study the full range of other potential health problems that Zika virus infection during pregnancy may cause.

- No treatment is currently available for Zika virus infection. Care for these infants is focused on diagnosing and
  managing conditions that are present, monitoring the child's development over time, and addressing problems as
  they arise.
- From what we know about severe <u>microcephaly</u>, a range of neurologic sequelae have been reported (e.g., intellectual disability, hearing loss, vision loss, and seizures). These problems can range from mild to severe, are often life-long, and in some cases can be life-threatening.
- Microcephaly is diagnosed when an infant's head is smaller than expected as compared to infants of the same age
  (or gestational age) and sex. Although a universally accepted definition of microcephaly does not exist,
  microcephaly is most often defined as head circumference (occipitofrontal circumference) greater than 2 standard
  deviations below the mean, or less than the 3<sup>rd</sup> percentile based on standard growth charts.
  - o For infants diagnosed with microcephaly, head size correlates with underlying brain size. However, these measurements do not consistently predict long-term sequelae.
  - Neurologic sequelae may include seizures, vision or hearing problems, and developmental disabilities.
     Sequelae vary with the extent of brain disruption.
  - Causes of congenital microcephaly may include genetic conditions such as chromosomal abnormalities or maternal exposures (e.g., alcohol, mercury, or radiation) during pregnancy. Other maternal infections that have been associated with microcephaly include cytomegalovirus (CMV), herpes simplex virus, rubella virus, lymphocytic choriomeningitis virus (LCMV), *Treponema pallidum* (i.e., syphilis), and *Toxoplasma* gondii.
- Head circumference (HC) and occipitofrontal circumference (OFC) are the same. These terms can be used interchangeably.
  - The shape of the head after delivery can affect the accuracy of the OFC/HC measurement as an estimate of brain volume due to molding of the head from the birth canal. The optimal time to measure HC is at 24-36 hours after birth when molding of the head has subsided.
  - Head circumference measurements should be taken using a tape measure that cannot be stretched. The tape is securely wrapped around the widest possible circumference of the head, 1-2 finger widths above the eyebrow on the forehead and at the most prominent part of the back of the head. It may be helpful to have the parent or nurse hold the infant's arms. Ideally, the measurement should be taken 3 times and the largest measurement to the nearest 0.1 cm should be used.

#### POTENTIAL OUTCOMES & PROGNOSIS

- There is limited information on neurocognitive outcomes in neonates if they are exposed to Zika virus during labor and delivery or after birth.
  - o Perinatal transmission of Zika virus infection has been reported. However information is limited to two cases: one of these infants was asymptomatic and the other had thrombocytopenia and a diffuse rash.
  - Evidence from other flaviviruses, such as West Nile virus and dengue virus, indicate that transmission has
    resulted in findings in the neonate ranging from no symptoms to severe illness (including fever,
    thrombocytopenia, and hemorrhage).
  - The spectrum of clinical features that might be observed in infants who acquire Zika virus during the perinatal period is currently unknown.
- The prognosis for infants with congenital Zika virus infection is not known.
- For infants with congenital Zika virus infection, care is focused on diagnosing and managing conditions that are present, monitoring the child's development over time, and addressing problems as they arise.

• Information on long-term outcomes among infants and children with acute Zika virus disease is limited. Thus, until more evidence is available to inform recommendations, routine pediatric care is advised for these infants and children.

- Most children infected with Zika virus are asymptomatic or have mild illness, similar to the findings seen in adults with Zika virus infection.
  - Treatment is supportive; this includes rest and fluids to prevent dehydration.
  - Non-steroidal anti-inflammatory drugs (NSAIDS) should not be used until dengue is ruled out as a cause of illness and should be avoided in children aged < 6 months.</li>
  - o Aspirin is not recommended for use with acute viral illnesses due to the risk of Reye's syndrome.
- In general, the risk for Guillain-Barré syndrome from any cause appears to increase with increasing age. GBS has been reported following Zika virus infection, although a causal link has not been established.
  - It is unclear how often GBS following Zika virus infection has occurred in children; one report from Brazil
    refers to 6 patients, aged 2–57 years, with neurologic syndromes (4 with GBS and 2 with acute
    disseminated encephalomyelitis) after laboratory-confirmed Zika virus infection; no further data are
    available.
  - o Deaths due to Zika virus infection appear to be very rare at all ages.

#### CLINICAL GUIDANCE

- Testing for Zika virus infection is recommended for infants born to women potentially infected with Zika during pregnancy and
  - Who were diagnosed with microcephaly at birth, intracranial calcifications detected prenatally or at birth, or other brain or eye abnormalities consistent with congenital Zika virus infection

or

o If the mother's possible Zika exposure occurred within 2 weeks of delivery and the infant develops fever, rash, conjunctivitis (red eyes) or joint pain within 2 weeks of birth

or

- When the mother had a positive or inconclusive Zika virus test result
- Because information on the effects of congenital Zika virus infection is limited, healthcare providers should
  exercise clinical judgment in the assessment of newborns with abnormalities other than microcephaly or
  intracranial calcifications who were born to mothers who traveled to or resided in an area with active Zika virus
  transmission during pregnancy.
  - For these infants, healthcare providers should consider testing the mother before testing the infant.
     Healthcare providers should notify their local, state or territorial health departments to arrange testing.
- Acute Zika virus disease should be suspected in an infant or child aged <18 years who</li>
  - 1) traveled to or resided in an area with Zika virus within the past 2 weeks and
  - 2) has ≥1 of the following manifestations: fever, rash, conjunctivitis, or arthralgia.
- Because transmission of Zika virus from mother to infant during delivery is possible, acute Zika virus disease should
  also be suspected in an infant during the first 2 weeks of life
  - o 1) whose mother traveled to or resided in an affected area within 2 weeks of delivery and
  - 2) who has ≥1 of the following manifestations: fever, rash, conjunctivitis, or arthralgia.
- Arthralgia can be difficult to detect in infants and young children and can manifest as irritability, walking with a limp (for ambulatory children), difficulty moving or refusing to move an extremity, pain on palpation, or pain with active or passive movement of the affected joint.
- For infants with microcephaly or intracranial calcifications and whose mothers have a history of travel to or who reside in areas with Zika virus, Zika virus testing is recommended within 48 hours of birth, if possible. Healthcare providers should work with their local, state or territorial health departments to arrange testing.

• For infants without evidence of microcephaly or intracranial calcifications, Zika virus testing is recommended under the following circumstances: (1) if the mother tested positive (e.g. RT-PCR, IgM) for Zika virus, (2) if the mother had inconclusive Zika virus test results, (3) if the mother traveled to or resided in an affected area within 2 weeks of delivery and the infant develops fever, rash, conjunctivitis, or arthralgia within the first 2 weeks of life. For infants without evidence of microcephaly or intracranial calcifications and whose mothers either tested negative for Zika virus or were not tested for Zika virus, testing is not recommended. The infant should receive routine care.

- For infants born to mothers who were potentially exposed to Zika virus but the mother was not tested for Zika virus infection during pregnancy, the results of previous prenatal ultrasounds and maternal Zika virus testing should be reviewed and a thorough newborn physical examination, with careful measurement of head (occipitofrontal) circumference, length, and weight, should be performed.
  - o Infants without evidence of microcephaly or intracranial calcifications whose mothers have negative Zika virus test results or who were not tested for Zika virus should receive routine care.
  - Because information on the effects of congenital Zika virus infection is limited, healthcare providers should exercise clinical judgment in the assessment of newborns with abnormalities other than microcephaly or intracranial calcifications who were born to mothers who traveled to or resided in an area with active Zika virus transmission during pregnancy. For these infants, healthcare providers should consider testing the mother before testing the infant.
- If an infant has positive or inconclusive Zika virus test results, a thorough physical examination should be
  performed, including careful measurement of the head circumference, length, weight, and assessment of
  gestational age.
  - Cranial ultrasound is recommended unless it was performed as part of prenatal screening in the third trimester and clearly showed no abnormalities of the brain.
  - Ophthalmologic evaluation is recommended as well as newborn hearing screen. An evaluation for neurologic abnormalities, dysmorphic features, splenomegaly, hepatomegaly, and rash or other skin lesions is also recommended.
  - Full body photographs and any rash, skin lesions, or dysmorphic features should be documented. If an abnormality is noted, consultation with an appropriate specialist is recommended.
- If an infant has positive or inconclusive test results and microcephaly or intracranial calcifications, consultations are recommended with a clinical geneticist or dysmorphologist, a pediatric neurologist, and a pediatric infectious disease specialist.
  - A complete blood count, platelet count, and liver function tests should also be conducted. Testing for other congenital infections is also recommended. If any additional congenital anomalies are identified through clinical examination and imaging studies, genetic and other teratogenic causes should be considered.
- For infants with a negative test result and without suspected abnormalities, healthcare providers should continue with routine pediatric care including measurement of growth and development, and appropriate evaluation and follow-up for any clinical findings that arise.
  - If the newborn has abnormal findings on examination, diagnostic testing for other causes of the newborn's conditions should be performed including testing for other congenital viral infections if indicated.
- If a mother had Zika virus infection during pregnancy but the newborn tests negative for Zika virus:
  - If the newborn does not have abnormal findings on examination, the infant should receive routine pediatric care including measurement of growth and development, and appropriate evaluation and follow-up for any clinical findings that arise.
  - If the newborn has abnormal findings on examination, diagnostic testing for other causes of the newborn's conditions should be performed including testing for other congenital viral infections if indicated.

## WHAT CDC IS DOING

CDC's <u>Emergency Operations Center</u> (EOC) was activated January 22, 2016, and moved to a level 1 activation—the
highest level – on February 8, 2016. The EOC is the command center for monitoring and coordinating the
emergency response to Zika, bringing together CDC scientists with expertise in arboviruses like Zika, reproductive
health, birth defects, developmental disabilities, and travel health. Their work includes:

- Developing laboratory tests to diagnose Zika.
- o Conducting studies to learn more about learn more about Zika and its effects during pregnancy and the potential link between Zika and Guillain-Barré syndrome.
- Conducting a study to evaluate persistence of Zika virus in semen and urine among male residents of the United States.
- Monitoring and reporting cases of Zika, which will help improve our understanding of how and where Zika
  is spreading.
- o Providing guidance to travelers and Americans living in areas with current outbreaks.
- Providing on-the-ground support in American Samoa, Brazil, Colombia, Guam, the Marshall Islands,
   Panama, Puerto Rico, Trinidad and Tobago, and the US Virgin Islands.
- CDC's EOC is currently home to hundreds of CDC staff working in collaboration with local, national, and international response partners to analyze, validate, and efficiently exchange information about the outbreak.
- The EOC has resources to rapidly transport diagnostic kits, clinical specimens that will be tested for Zika virus, and personnel.
  - The EOC is serving as CDC's command center for monitoring and coordinating the emergency response to Zika, including sending CDC staff and the procurement and management of all equipment and supplies that CDC responders may need during deployment.
  - CDC is sending staff to assist with the response senior leaders, vector control, emergency management, logistician, epi/surveillance, data entry, pregnancy and birth defects, blood safety specialists, etc.

## **DOMESTIC ACTIVITIES**

- CDC has been aware of Zika for some time and has been preparing for its possible introduction into the United States. Laboratories in many countries, including the United States, have been trained to test for chikungunya and dengue, and these laboratories are prepared for Zika testing.
- CDC is working with public health partners and with state health departments to
  - Alert healthcare providers and the public about Zika.
  - o Post travel notices and other travel-related guidance.
  - o Provide state health laboratories with diagnostic tests.
  - Monitor and report cases of Zika.
  - Publish and disseminate guidelines to inform testing and treatment of people with suspected or confirmed Zika.
  - o Publish and disseminate conclusions on the causal association between Zika and microcephaly.
- On April 1, 2016, CDC hosted the Zika Action Plan Summit for state and local health officials. The Summit aimed to
  - o Provide officials with information and tools to improve Zika preparedness and response within their states and jurisdictions.
  - o Increase knowledge on the latest Zika science, including implications for pregnant women.
  - o Increase knowledge of best communication practices, including crisis and risk communication principles.
  - Accelerate readiness for local Zika transmission through training and technical assistance to states to help establish and support surveillance and share best practices for vector control.
  - Identify possible gaps in preparedness and response at the federal, state, and local levels, and to help begin to address possible gaps.

• CDC released guidance documents to assist in preparedness and response planning for state, local, and territorial public health officials.

- o Zika Virus Risk-Based Preparedness and Response Guidance for States
- o Zika Communication Planning Guide for States
- o Interim CDC Recommendations for Zika Vector Control in the Continental United States
- The arrival of Zika in the Americas demonstrates the risks posed by this and other exotic viruses. CDC's health security plans are designed to effectively monitor for disease, equip diagnostic laboratories, and support mosquito control programs both in the United States and around the world.
- CDC is creating and distributing Zika Prevention Kits for affected US territories (Puerto Rico, US Virgin Islands, and American Samoa).

#### INTERNATIONAL ACTIVITIES

- CDC is working in laboratories and in dozens of countries, with ministries of health, and with partners around the
  world to develop a deeper understanding of Zika virus. We are also helping to prevent, control, and respond to the
  Zika outbreak, along with outbreaks of other diseases like chikungunya, dengue fever, malaria, yellow fever, and
  other vector-borne diseases. CDC is working through our country offices, Field Epidemiology and Lab Training
  Programs, Global Disease Detection Centers overseas, Global Disease Detection Operations Center at CDC
  headquarters, Division of Parasitic Diseases and Malaria, and with international partners to
  - Alert healthcare providers and the public about Zika.
  - Post travel notices and other travel-related guidance.
  - o Provide health laboratories with diagnostic tests. Through the CDC's Emergency Operations Center, CDC is assisting countries with Zika testing by supplying them with reagents for molecular diagnostic lab testing.
  - Monitor and report cases of Zika, which will help improve our understanding of how and where Zika is spreading.
  - Learn more about Zika and its effects during pregnancy as well as potential link between Zika and Guillain-Barré syndrome.
- CDC is committed to global health security. We help build the capacity of even the most vulnerable countries to detect, prevent, and respond to public health emergencies within their own borders.
- CDC staff are providing essential lab assistance, including
  - Organizing and triaging requests for Zika virus PCR reagents, needed for Zika diagnostics testing, from CDC's 10 Global Disease Detection Regional Centers and more than 30 countries
  - Standing up and operating regional Zika virus laboratory diagnostic capabilities at two of the most critical Global Disease Detection Regional Centers - the Central America Regional Center in Guatemala and the SE Asia Regional Center in Thailand
  - Developing a next-generation diagnostics card for acute febrile illness that tests samples of up to 8 people for 30 pathogens simultaneously, including Zika, delivering results in less than 3 hours
- Through its 24/7 Global Disease Detection Operations Center, regional Global Disease Detection Centers, Country Offices, and global Field Epidemiology and Laboratory Training Programs, CDC is working with governments, ministries of health, and international partners to conduct rigorous surveillance for new and emerging infections, identify and characterize new pathogens, develop and evaluate new laboratory methods, and train disease detectives in the countries in which they operate.
- CDC's Global Disease Detection (GDD) Operations Center operates 24/7 and is continually carrying out event-based surveillance to monitor this outbreak globally.
  - This center, in collaboration with Zika subject matter experts and international partners and governments, has been conducting event-based surveillance to monitor spread of Zika from Brazil to other areas in the Americas since May 2015, sharing this information to coordinate the response.
  - o The GDD program, launched in 2004, was one of the first ways CDC systematically began helping countries build the systems they need to prevent, detect and respond to health threats. Its regional centers are

currently working with governments and international partners to provide data from the field back to CDC's Global Disease Detection Operations Center for global surveillance.

- Because of this work we are able to know:
  - Where Zika is spreading
  - Where (in what regions) we are seeing increased numbers of microcephalic babies
  - Where there are significant upticks in Guillain-Barré syndrome.
- CDC's GDD Center, part of the Central America Region office located in Guatemala City has been critical in:
  - Ensuring that emergency operations centers in countries with Zika in Central America and beyond are equipped and ready to activate and perform, and that different government agencies in each country know how to collaborate across programs and agencies on the response.
  - Helping Colombia, El Salvador, Guatemala, Honduras, and Panama with lab testing for Zika and chikungunya.
  - Instituting four functions vital to disease detection and surveillance in the countries it serves:
    - Developing a common testing platform and protocol for influenza;
    - Drafting and testing of national emergency action plans;
    - Training field epidemiologists and lab technicians through the Field Epidemiology and Lab Training Programs (FETP and FELTP)
  - Strengthening laboratory capabilities by:
    - Supporting Zika virus testing in Guatemala, laboratory diagnostic training in South and Central America, and specimen transport in the Latin American region; and sharing protocols and procedures with labs in Lima, Peru to strengthen overall ability to accurately and quickly test for selected diseases.
    - Supporting countries with Zika in vector surveillance, control strategies, and insecticide resistance testing in coordination with the Pan American Health Organization (PAHO)
- In an effort to better understand Zika and its effects during pregnancy, the Brazilian Ministry of Health (MOH) and PAHO are investigating.
  - o PAHO invited CDC to provide technical assistance to the Brazil MOH for its investigation of microcephaly and the possible association with Zika virus infection by collaborating on studies.
  - CDC regularly communicates with representatives from PAHO and the Brazil MOH to discuss the investigation and laboratory testing options.
  - CDC has offered to test samples from the microcephaly cases for serologic evidence of Zika virus infection until in-country capacity can be established.
- CDC's FETP and FELTP programs provide real-time training to capable "disease detectives" and laboratory specialists in these countries who can identify and target disease.
- CDC's Central America Field Epidemiology Training Program (CA FETP) includes national field epidemiology training programs in Belize, Costa Rica, Dominican Republic, El Salvador, Haiti, Guatemala, Honduras, and Panama.
  - These countries are coordinated through REDCEC (Red Centroamericana de Epidemiologia de Campo;
     Central American Network of Field Epidemiology), under the umbrella organization of the Council of
     Health Ministers of Central America and the Dominican Republic (COMISCA).
  - Brazil, Mexico, Colombia, and additional South American countries have independent FETPs.

## CDC FOUNDATION

• At CDC's request, the CDC Foundation activated two funds on February 10, 2016, to help with the Zika response: the U.S. Emergency Response Fund and the Global Disaster Response Fund.

• These funds allow CDC to better prepare for and respond to crisis situations, such as Zika, by providing flexibility to meet needs that would not otherwise be met through federally appropriated funds.

- Financial support raised through these funds will enhance CDC's response in a number of ways, such as extend the agency's ability to alert healthcare providers and the public about Zika; fund Zika prevention kits with educational materials for pregnant women in Puerto Rico and other high-risk areas; protect travelers with guidance and information; support state health laboratories with diagnostic tests; and detect and report cases to help prevent further spread.
- The CDC Foundation recently <u>announced a partnership</u> with CDC and multiple donors to create Zika prevention kits for pregnant women in the US territories of the Commonwealth of Puerto Rico, the US Virgin Islands (USVI), and American Samoa. The purpose of these Zika prevention kits is to inform pregnant women about Zika, its risks, and how to avoid infection, while providing an initial supply of prevention tools. The initial donations included mosquito repellent, mosquito dunks, and condoms.
- Walgreens also <u>recently announced</u> a collaboration with CDC and the CDC Foundation on Zika education and prevention in Puerto Rico. In addition, Walgreens made a \$100,000 donation to the CDC Foundation to aid its Zika education and prevention efforts.
- On April 1, 2016, the CDC Foundation, along with Bayer and SC Johnson, provided donor support for the Zika Action Summit at CDC, which was attended by federal and state government representatives as well as representatives from associations, philanthropies, and the private sector.

33