KEY MESSAGES – ZIKA VIRUS DISEASE

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

Updated March 16, 2016

Updated information is in blue.

CONTENTS

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 many countries and territories.
- On January 22, 2016, CDC activated its Emergency Operations Center (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 Public Health Emergency of International Concern (PHEIC) because of clusters of microcephaly and other neurological disorders in some areas affected by Zika.
- 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.
- 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 a few non-travelers got Zika through sex.
    - 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:
    - People infected with the virus enter the United States.
    - An *Aedes* mosquito in the United States bites the infected person during the relatively short time that the virus can be found in the person's blood.
    - The infected mosquito lives long enough for the virus to multiply and for the mosquito to bite another person.

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 at delivery.
- As of March 9, 2016, US states had reported a total of 193 travel-associated Zika cases to CDC.
- Zika is a nationally notifiable disease. Healthcare providers are required to report suspected cases to their state or local health departments to facilitate diagnosis and reduce the risk of local transmission.
    - State health departments are encouraged to report laboratory-confirmed cases to CDC through ArboNET, the national surveillance system for arboviral diseases.
- 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 working with Brazil to study the possibility of a 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 nerve 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
  - Fever
  - Rash
  - Joint pain
  - Conjunctivitis (red eyes)
- Other symptoms include
  - Muscle pain
  - Headache
- Most people infected with Zika virus won't even know they have the disease because they won't have 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 healthcare provider will ask you about any recent travel and any signs and symptoms you may have. A blood test is the only way to confirm a Zika infection.
- See your doctor 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 your doctor that you traveled to an area with Zika.
- Your doctor 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 (*A. aegypti* and *A. albopictus*).
  - 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. 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.

- Although mosquito bites are the main way that Zika virus is spread, Zika virus can also spread when an infected man has sex with his partners.

SEXUAL TRANSMISSION

- What we know
  - Zika virus can be sexually transmitted by a man to his partners.
  - In the known cases of likely sexual transmission, the men developed Zika symptoms, but the virus can be transmitted before, during, and after symptoms develop.
  - The virus can be present in semen longer than in blood.
- What we do not know
  - How long the virus can stay in the semen of men who have had Zika.
  - If infected men who never develop symptoms can have Zika virus in their semen.
  - If infected men who never develop symptoms can transmit Zika virus through sex.
  - If a woman can transmit Zika virus to her sex partners.
  - If Zika can be spread through oral sex.
    - Although there are no known cases of Zika transmission from mouth-to-penis oral sex, Zika is known to be spread from semen.
    - It is not known if Zika can be spread from other body fluids that may be exchanged during oral sex, including saliva and vaginal fluids.
  - If sexual transmission of Zika virus poses a different risk of birth defects than mosquito-borne transmission.
- One report found the virus in semen at least 2 weeks after symptoms of infection began. Another report found the virus in semen at least 62 days after symptoms of infection began. In both cases, no follow up testing was done to determine when the men no longer had Zika virus in their semen.
- For men who live in or traveled to an area with Zika virus
  - If the man's partner is pregnant, the couple should either use condoms (warning: this link contains sexually graphic images) the right way every time they have vaginal, anal, and oral (mouth-to-penis) sex, or not have sex during the pregnancy.
    - Condoms can also help prevent getting HIV and other sexually transmitted diseases.
  - Men who live in or are traveling to an area with Zika transmission should also take steps to prevent mosquito bites.
  - If a man develops symptoms of Zika virus illness during his travel or within 2 weeks after he returns, he should see his doctor to see if he has Zika virus or another illness.
- If a woman thinks her male partner may have or had Zika, she should talk to her doctor about his travel history, including how long he stayed, whether or not he took steps to prevent getting mosquito bites, and whether or not she had sex without a condom since his return.
- Anyone concerned about getting Zika from sex can use condoms (warning: this link contains sexually graphic images) the right way every time they have vaginal, anal, or oral (mouth-to-penis) sex.
- Not having sex is the best way to be sure that someone does not get sexually transmitted Zika virus.
  - If a person is sexually active, using latex condoms the right way every time they have vaginal, anal, or oral (mouth-to-penis) sex can reduce the chance that they can get Zika virus from sex.
- Only people whose male sex partners have traveled to or live in an area with Zika need to be concerned about potential sexual transmission of Zika virus.
- There are tests to detect Zika virus in semen but they are not widely available. The results of the tests are difficult to interpret, so testing of semen is not recommended at the present time. We may change this recommendation as we learn more.

- CDC has resources on condom effectiveness and using male condoms (warning: this link contains sexually graphic images).
- A case of sexually transmitted Zika means that a person who does not live in or travel to an area with Zika gets Zika from having sex with an infected man who lives in or travels to an area with Zika.
    - Someone is considered to be potentially exposed to Zika if they had sex without a condom with a man who has traveled to an area with Zika and has shown symptoms of the virus during travel or within 2 weeks of his return.
    - In all of these cases, the infected man had symptoms of Zika, and reported having sex without a condom with their partners.
    - On February 23, 2016 CDC issued a Health Alert Network (HAN) to alert health departments, healthcare providers, and the public that sexual transmission of Zika may be more common than previously considered. The HAN reminds people to follow CDC's Interim Guidelines for Prevention of Sexual Transmission of Zika Virus.

BLOOD TRANSFUSION

- There is a strong possibility that Zika virus can be spread through blood transfusions. Because most people infected with the Zika virus don't show any symptoms, they may not know they have been infected.
- Multiple reports of Zika virus being spread through transfusions in Brazil are being investigated.
- To date, there have not been any confirmed cases of transmission caused by blood transfusion in the United States.
- Zika virus currently poses a low risk to the US blood supply, but this could change depending on how many people in the United States become infected with the virus.
- Currently, there are no Food and Drug Administration (FDA)-licensed blood donor laboratory screening tests available to detect Zika virus in blood. Therefore, the best way to protect the US blood supply is to screen blood donors using a donor history questionnaire and ask about recent travel to areas where Zika is spreading.
- FDA released Recommendations for Donor Screening, Deferral and Product Management to Reduce the Risk of Transfusion-Transmission of Zika Virus.
    - The newly released FDA guidance recommends steps for screening, deferral, and product management to reduce the risk of Zika virus spreading through blood transfusions.
- CDC is working with partners to learn more about Zika and blood safety.

VECTOR INFORMATION

- A mosquito can transmit Zika virus through bites. Not all people who are infected will get sick.
- 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.
- 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.
    - Flies spread some diseases but fewer germs than mosquitoes because their feeding habits are different.
- In addition to Zika, the most common viruses and parasites transmitted through mosquito bites are:
    - Chikungunya
    - Dengue
    - Eastern equine encephalitis
    - Filariasis, including dirofilaria, which causes dog heartworm
    - Jamestown Canyon virus disease

  - Japanese encephalitis
  - LaCrosse encephalitis
  - Malaria
  - Rift Valley fever
  - Ross River virus disease
  - St. Louis encephalitis
  - Venezuelan equine encephalitis
  - Western equine encephalitis
  - Yellow fever
- There are many species of *Aedes* mosquitoes. Not all *Aedes* species spread Zika virus. *Aedes aegypti* mosquito species, found throughout most tropical countries, most commonly transmit Zika virus. *Aedes albopictus* mosquito species can also transmit Zika virus. At this time, we don't know if there are other non-*Aedes* mosquito species that could spread Zika virus.
- 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.
- There are no data to link genetically modified 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.

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.
- 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.
- CDC is working closely with international partners to study infants with microcephaly to better understand what role various factors, including Zika virus, may play in this birth defect.

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.
- Zika can also be spread during sex from a man who has Zika in his semen to his sex partners. Using condoms (warning: this link contains sexually graphic images) the right way every time you have vaginal, anal, and oral (mouth-to-penis) sex can reduce the chance that you can get Zika from 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.

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.
    - Treat your clothing and gear with permethrin or buy pre-treated items.
    - Use Environmental Protection Agency (EPA)-registered insect repellents. 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.
- If you are a man who lives in or has traveled to an area with Zika:
    - If your partner is pregnant, either use condoms (warning: this link contains sexually graphic images) the right way every time you have vaginal, anal, and oral (mouth-to-penis) sex, or don't have sex during the pregnancy.
    - Men who have traveled to an area with Zika should consider using condoms the right way, every time they have sex to protect their partners.
- If you are concerned about getting Zika from a male sex partner
    - You can use condoms (warning: this link contains sexually graphic images) the right way every time you have vaginal, anal, and oral (mouth-to-penis) sex. Condoms also prevent HIV and other STDs. Not having sex is the best way to be sure that you do not get Zika from sex.
- If you have a baby or child
    - 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.
    - 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.

INSECT REPELLENT

- CDC recommends using EPA-registered insect repellents 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.
    - Treated clothing remains protective after multiple washings. See product information to learn how long the protection will last.
    - 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.
    - 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.
    - 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.
    - Get plenty of rest.
    - Drink fluids to prevent dehydration.
    - Take medicine such as acetaminophen (Tylenol®) to reduce fever and pain.
    - Do not take aspirin or other non-steroidal anti-inflammatory drugs (NSAIDS) until dengue can be ruled out to reduce the risk of bleeding.
    - If you are taking medicine for another medical condition, talk to your 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 follow steps to prevent mosquito bites during the first week of illness.

ZIKA & PREGNANCY

- CDC released a new report that summarizes preliminary findings on reported cases of laboratory-confirmed Zika virus infection among pregnant women in the United States with travel histories to areas with Zika. As of February 17, 2016, nine pregnant travelers with Zika virus infection had been identified after returning to the United States. Among these women
    - No Zika virus-related hospitalizations or deaths were reported.
    - Two experienced early pregnancy losses, two chose to undergo elective terminations of pregnancy (abortions), three infants were born (two healthy infants and one infant with severe microcephaly), and two pregnancies are continuing without known complications.
- CDC has established a registry to learn more about pregnant women in the United States with confirmed Zika virus infection and their infants.
- CDC maintains a 24/7 consultation service for health officials and healthcare providers caring for pregnant women. To contact the service, call the CDC Emergency Operations Center at (770) 488-7100 or email ZIKAMCH@cdc.gov.
- We do not know if pregnant women are more likely to develop symptoms compared to the general population.
- Zika virus can pass from a pregnant woman to her fetus during pregnancy. We do not know how often this occurs.
- We know that Zika and microcephaly are associated, although we do not yet have definitive proof that Zika virus infection causes microcephaly. There have been reports of microcephaly in babies of mothers who were infected with Zika virus while pregnant. The link between Zika and microcephaly is being investigated.
- In addition to microcephaly, other problems have been detected among fetuses and infants infected with Zika virus before birth, such as 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 Zika virus' impact on mothers and their children.
- We do not know if pregnant women are more likely to get Guillain-Barré syndrome.
- 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.
- Pregnant women who have recently traveled to an area with Zika should talk to a doctor about their travel even if they don't feel sick.
- Pregnant women should see a doctor 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 where they traveled.
- Because of the association between Zika infection and microcephaly, pregnant women should strictly follow steps to prevent mosquito bites.
- If a pregnant woman has a male sex partner who lives in or has traveled to an area with Zika, she should either use condoms (warning: this link contains sexually graphic images) the right way every time she has vaginal, anal, and oral (mouth-to-penis) sex, or not have sex during the pregnancy.

MICROCEPHALY

- Zika is linked to microcephaly, a severe birth defect that is a sign of incomplete brain development. Microcephaly is a condition where 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.

- There have been reports of microcephaly in babies of mothers who were infected with Zika virus while pregnant.
    - Brazil has been having a significant outbreak of Zika virus since May 2015. Officials in Brazil have also noted an increase in the number of babies with congenital microcephaly during that time.
    - Health authorities in Brazil, with assistance from the Pan American Health Organization, CDC, and other agencies, have been investigating the link between Zika virus infection and microcephaly.
- CDC is investigating the link between Zika and microcephaly.
    - More lab testing and other studies are planned to learn more about the risks of Zika virus infection during pregnancy.
- We do not know if a newborn who gets Zika at birth will develop microcephaly after birth, which is called acquired microcephaly.
    - Babies can acquire microcephaly if their head growth slows or fails to develop after birth.
    - 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 a 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 healthcare provider.
- 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 life-threatening.
    - Seizures
    - Developmental delay, such as problems with speech or other developmental milestones (like sitting, standing, and walking)
    - Intellectual disability (decreased ability to learn and function in daily life)
    - Problems with movement and balance
    - 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 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 provides information on diagnosing birth defects 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.

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. Pregnancy, as well as suspicion that the specimen may contain a pathogen that requires BSL3 precautions (e.g., Chikungunya virus), should be considered a significant risk factor.
- On Feb. 26, 2016, the Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for a diagnostic tool for Zika virus that will be 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 blood samples from people with a history of symptoms associated with Zika and/or people who have recently traveled to an area with Zika.
    - CDC will distribute the test to qualified laboratories in the Laboratory Response Network. The test will not be available in US hospitals or primary care settings.
- Zika virus testing is performed at the CDC Arbovirus Diagnostic Laboratory and select state health departments. Healthcare providers should contact their state and local health department to facilitate testing. See the Diagnostic Testing webpage 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 for diagnostic purposes. 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 Zika virus kits.
- Tests
    - During the first week of illness, Zika virus disease can often be diagnosed by performing reverse transcriptase-polymerase chain reaction (RT-PCR) on serum.
        - 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. However, viremia decreases over time, and a negative RT-PCR on serum collected 5-7 days after symptom onset does not preclude Zika virus infection. Serologic testing should be performed.
    - 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.
    - 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.
    - Although data on the performance of IgM serologic testing in asymptomatic persons is limited, on the basis of experience with other flaviviruses, when performed from 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 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.
    - 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.
- There are no commercially available tests for Zika virus. Zika virus testing is performed at the CDC Arbovirus Diagnostic Laboratory and at some state and territorial health departments. Healthcare providers should contact their state and local health department to facilitate testing.
    - See the Diagnostic Testing webpage 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.
    - 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 Zika website.
- CDC has interim guidelines 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 CDC Zika website.
    - CDC has additional Q&As about Zika virus for healthcare providers.

- CDC has interim guidelines for healthcare providers caring for infants and children with possible Zika virus exposure. Q&As on these guidelines are also available.
- CDC has interim guidelines 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
        - Postpone travel to any area where Zika virus is spreading.
        - If you must travel to one of these areas, talk to your doctor first and strictly follow steps to prevent mosquito bites during the trip.
        - If you have a male partner who lives in or has traveled to an area where Zika is spreading, either use condoms (warning: this link contains sexually graphic images) the right way every time you have sex, or do not have sex during your pregnancy.
    - Women trying to get pregnant
        - Before you or your male partner travel, talk to your doctor 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.
- Pregnant women who have recently traveled to an area with Zika should talk to a doctor about their travel even if they don't feel sick.
- Pregnant women should see a doctor 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 where they traveled. CDC has developed interim guidelines for pregnant women for Zika. The doctor 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 doctors if their male sex partner recently traveled to an area with Zika.
    - Pregnant women who have a fever should take acetaminophen (for example, Tylenol®) for fever control.
- CDC has guidance to help doctors 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 after returning. She should also talk to her doctor 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. Tell your doctor 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 doctors about any concerns regarding Zika infection.

TRAVEL

- Travelers who go to places with outbreaks of Zika can be infected with Zika virus.
    - Travelers can protect themselves by preventing mosquito bites.
- 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 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:
    - 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 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, either use condoms (warning: this link contains sexually graphic images), or do not have sex during your pregnancy.
    - Women trying to get pregnant
        - Before you or your male partner travel, talk to your doctor 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.
    - Men who have traveled to an area with Zika should use condoms to protect their sex partners. Men who have traveled to an area with Zika and who have a pregnant partner should use condoms or not have sex (vaginal, anal, or oral) during the pregnancy.
- 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 travel notice (level 2 alert, “practice enhanced precautions”) for people traveling to places where Zika virus is spreading.
    - 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 Zika travel notices 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 get 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 maps that show elevation levels in countries with Zika.

OBSTETRICAL HEALTHCARE PROVIDERS

- CDC has Interim Guidelines for Health Care Providers Caring for Pregnant Women and Women of Reproductive 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 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 and local health departments, and many other stakeholders.
- The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine (SMFM) have issued a Practice Advisory directed to obstetric providers about prevention strategies and clinical management of pregnant women.

ZIKA & PREGNANCY

- **Counseling Pregnant Women**
  - Pregnant women should not travel to an area with Zika virus.
  - Pregnant women considering travel to one of these areas should talk to their healthcare provider. If a pregnant woman does travel, she should strictly follow steps to avoid mosquito bites during the trip.
  - Given the potential risks of maternal Zika virus infection, pregnant women whose male partners have or are at risk for Zika virus infection should consider using condoms (warning: this link contains sexually graphic images) or not having sex during the pregnancy. Recommendations will be updated as more information becomes available.
- **Counseling Women of Reproductive Age in Areas with Local Zika Virus Transmission**
  - Women of reproductive age with current or previous laboratory-confirmed Zika virus infection should be counseled that there is no evidence that prior Zika virus infection poses a risk of birth defects in future pregnancies.
    - This is because the viremia is expected to last approximately one week in patients with clinical illness. There is no evidence that a fetus conceived after Zika virus has cleared from the blood would be at risk for fetal infection.

- 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 provide preconception care and emphasize strategies to prevent mosquito bites and provide preconception care, which should include a discussion about the potential risk of Zika virus infection in pregnancy, the signs and symptoms associated with Zika virus disease, and when to seek care.

AMNIOCENTESIS

- Amniocentesis should be offered to pregnant women with recent travel to an area with Zika virus transmission, reporting 2 or more symptoms within 2 weeks of travel and a positive or inconclusive maternal serum test.
- For pregnant women with recent travel to an area with Zika virus transmission and ultrasound findings of microcephaly or intracranial calcifications, amniocentesis may also be considered. Consultation with a maternal-fetal medicine (high-risk obstetrics) specialist should be considered.
- 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 positive RT-PCR result on amniotic fluid would be suggestive of intrauterine infection and potentially useful to pregnant women and their healthcare providers to guide decisions about timing of delivery and the level of neonatal care at delivery sites.
- 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 late in the 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.
- 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. It is not known if Zika virus infection caused any of these abnormalities.
    - 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 of Maternal and 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 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.
- Zika virus infections have been confirmed in several infants with microcephaly from Brazil. The time frame and geographic location of reports of infants with microcephaly coincides with the outbreak of Zika virus infections in Brazil.
- 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, but attempts to culture the virus have been unsuccessful. No evidence of Zika virus infection associated with breastfeeding have 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

- Brain abnormalities reported in infants with microcephaly and laboratory-confirmed congenital Zika infection include microcephaly and disrupted brain growth.
    - A report of 35 infants with microcephaly who were born during an outbreak of Zika virus infection in Brazil in 2015 described the following brain abnormalities: intracranial calcifications, ventriculomegaly, and neuronal migration disorders (lissencephaly and pachygyria). Other anomalies included congenital contractures and clubfoot. An important distinction is that neither these infants nor their mothers had laboratory-confirmed Zika virus. However, most of the mothers (≈75%) reported symptoms consistent with Zika virus disease.

- Some infants with possible Zika virus infection have been found to have intracranial calcifications and abnormal eye findings. It is not known if Zika virus infection caused any of these abnormalities.
- 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 microcephaly, 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 3rd percentile based on standard growth charts.
    - 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. 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.
    - 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.
    - 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.
    - 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 who traveled to or lived in an area with Zika virus during pregnancy who were
    - Diagnosed with microcephaly or intracranial calcifications detected prenatally or at birth
      or
    - Who have mothers with positive or inconclusive test results for Zika virus infection
- 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
    - 1) traveled to or resided in an area with Zika virus within the past 2 weeks and
    - 2) has ≥2 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
    - 1) whose mother traveled to or resided in an affected area within 2 weeks of delivery and
    - 2) who has ≥2 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, or (2) if the mother had inconclusive Zika virus test results. 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.
    - 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 Emergency Operations Center (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
    - Conducting studies to learn more about the link between Zika and microcephaly and Guillain-Barré syndrome
    - Monitoring and reporting cases of Zika, which will help improve our understanding of how and where Zika is spreading.
    - Providing guidance to travelers and Americans living in areas with current outbreaks
    - Providing on-the-ground support in Puerto Rico, Brazil, Colombia, American Samoa, the US Virgin Islands, and Panama
- CDC's EOC is currently home to more than 300 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.
    - Post travel notices and other travel-related guidance.
    - 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.
    - Study what might be responsible for the reported rise in microcephaly.
- 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: Zika prevention kits arrived and distribution scheduled for today, Monday, February 29, 2016.
    - American Samoa: Zika prevention kits have shipped.
    - US Virgin Islands: Zika prevention kits have shipped.

INTERNATIONAL ACTIVITIES

- CDC has been aware of Zika for some time and has been helping countries prepare for outbreaks like Zika. CDC uses the multi-national Global Health Security Agenda to enhance disease surveillance, equip diagnostic

laboratories, improve emergency response, and extend the public health workforce in the United States and around the world.

- 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, and with international partners to
    - Alert healthcare providers and the public about Zika.
    - Post travel notices and other travel-related guidance.
    - 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.
    - Study the potential link between Zika and microcephaly 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.
- 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 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.
- CDC's Global Disease Detection (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 (in what regions) we are seeing microcephaly
        - Where there are significant upticks in Guillain-Barre syndrome. This includes cases reported in Honduras, El Salvador, and Colombia.
- CDC's Latin American regional GDD Center in Guatemala has been critical in:
    - Ensuring that emergency operating centers in these countries are equipped and ready to activate and perform, and that different government agencies in each country know how to collaborate across programs 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:
        - A common test platform and protocol for detecting influenza;
        - Emergency action plans;
        - Trained epidemiologists and lab technicians through the Field Epidemiology and Lab Training Programs (FETP and FELTP)
    - Enhanced lab capabilities including:

        - Supporting Zika virus testing in Guatemala, 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 disease.
- In an effort to better understand what might be responsible for the rise in microcephaly cases, the Brazilian Ministry of Health (MOH) and the Pan American Health Organization (PAHO) are investigating.
    - 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 Regional Program includes 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).
    - At this time, we don't know how many FETP graduates are involved in Zika activities.
    - Brazil, Mexico, Colombia, and additional South American countries have independent FETPs.
    - The Central America FETP is in discussion about potential studies related to Zika.
        - Estimation of baseline microcephaly rate, most easily conducted by medical records review of facility deliveries or review of CLAP data or both;
        - Evaluation of congenital malformations surveillance system, if one exists; if not, scoping of potential data sources leading to a proposal of one;
        - Evaluation of acute febrile syndrome surveillance system. This is most feasible in places with surveillance sites such as ViCo (Integrated Community Surveillance) in Guatemala, which has been active since 2007;
        - Entomologic surveillance at sites with acute febrile syndrome surveillance;
        - Pregnant women and offspring cohort (prospective or retrospective) study assessing impact of acute febrile illness on birth outcomes and achievement of early developmental milestones, most feasible in Social Security health systems due to relatively captive population and better health information systems.

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 announced a partnership 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 recently announced 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.

GLOBAL MESSAGES

Messages in this section differ from those used for US audiences.

- 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. Here's how:
  - Wear clothes that cover as much of the body as possible, such as long-sleeved shirts and long pants.
  - Stay in places with air conditioning or that use window and door screens to keep mosquitoes outside.
  - Use a repellent with one of the following active ingredients: DEET, picaridin, IR3535, oil of lemon eucalyptus, or para-menthane-diol. This includes women who are pregnant and breastfeeding. See CDC's website for a table of recommended active ingredients and their common names. We do not know the effectiveness of many natural insect repellents.
    - 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.
    - 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.
    - Treated clothing remains protective after multiple washings. See product information to learn how long the protection will last.
    - If treating items yourself, follow the product instructions carefully.
    - Do **NOT** use permethrin products directly on skin. They are intended to treat clothing.
- If you have a baby or child
  - Do not use insect repellent on babies younger than 2 months of age.
  - 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.
  - 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.
- Treat the symptoms of Zika:
  - Get plenty of rest.
  - Drink fluids to prevent dehydration.
  - Take medicine such as acetaminophen (Paracetamol or Tylenol®) to reduce fever and pain.
  - Avoid ibuprofen, aspirin, or aspirin-containing drugs until dengue can be ruled out to reduce the risk of bleeding.

- If you are taking medicine for another medical condition, talk to your healthcare provider before taking other medicines.

- Protect others: During the first week of infection, Zika virus can be found in a person's blood and can pass from an infected person to another mosquito through mosquito bites. An infected mosquito can then spread the virus to other people. To help prevent others from getting sick, avoid mosquito bites during the first week of illness by strictly following steps to prevent mosquito bites.
- If you are a man who lives in or has traveled to an area with Zika
  - If your partner is pregnant, either use condoms (warning: this link contains sexually graphic images) the right way every time you have vaginal, anal, and oral (mouth-to-penis) sex, or do not have sex during the pregnancy.
- If you are concerned about getting Zika from a male sex partner
  - You can use condoms (warning: this link contains sexually graphic images) the right way every time you have vaginal, anal, and oral (mouth-to-penis) sex. Condoms also prevent HIV and other STDs. Not having sex is the best way to be sure that you do not get sexually transmitted Zika.