Zika – Background and Testing

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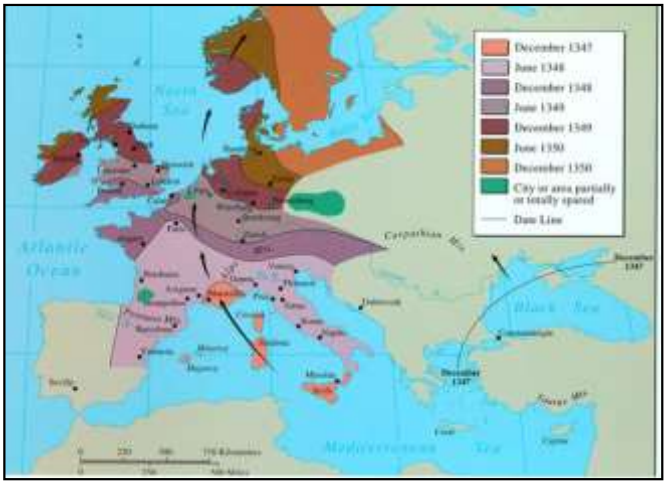
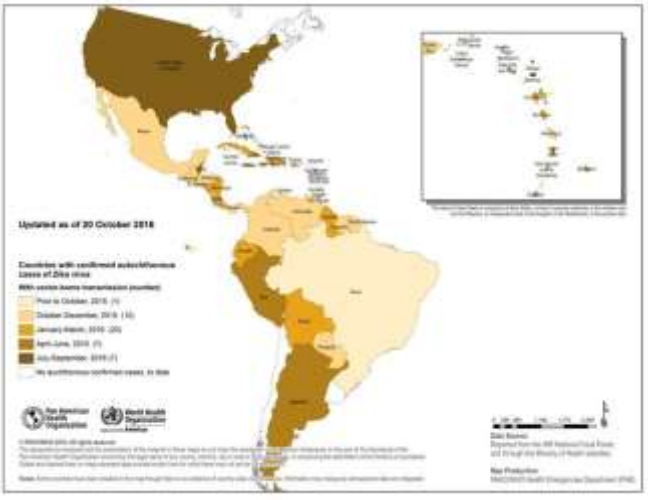
Black Death 1347-1350



Spread through Western Hemisphere



Zika Virus (ZIKV)

Named for Ugandan forest first isolated 1947

First major recognized outbreak – 2007

- Yap Islands
- >70% infected

Western hemisphere – 2014

Brazil – May 2015

CDC issues another travel advisory for Brazil, this time due to Zika virus

Posted by Robert Herriman on June 9, 2015 // 3 Comments

Less than **two months after issuing a travel notice for Brazil because of the dengue fever outbreak**, the Centers for Disease Control and Prevention (CDC) today issued another because of a different mosquito borne virus, Zika virus.

Image/CIA

This follows **a report last month of 16 confirmed, locally transmitted cases of Zika**. Cases have been reported in the states of Bahia and Rio Grande do Norte.

Zika is an illness caused by a virus that is spread to humans through mosquito bites, specifically the Aedes mosquito, the same that transmits dengue fever, chikungunya and yellow fever, all found in Brazil.

Symptoms of Zika may include fever, headache, red eyes, rash, muscle aches, and joint pains. The illness is usually mild, lasting 4–7 days.

There is currently no vaccine or medicine to prevent Zika. Travelers can protect themselves by preventing mosquito bites (see the CDCs 'Avoid bug bites page).

Related: Dominican Republic records 1st Zika virus case in Puerto Plata child

Are Mosquitoes Behind an Increase in Brazilian Babies Born with Abnormally Small Heads?

By Donna Bowater

November 13, 2015 | 2:40 pm

The Brazilian ministry of health has declared a nationwide public health emergency while doctors investigate whether a mosquito-borne disease that is new to the country is behind a sudden spike in the number of babies born with abnormally small heads.

November 13, 2015

PAHO issues Zika virus alert

Filed Under: Zika
Lisa Schnirring | News Editor | CIDRAP News | Dec 01, 2015

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In a move that signals growing concerns over the spread of Zika virus and its neurologic complications, the Pan American Health Organization (PAHO) today issued an alert about the threat, urging countries in the region to be on the lookout for the disease and to watch for unusual patterns in newborns.

For the past few weeks health authorities have voiced strong suspicions about an unusual rise in microcephaly in Brazil's hardest-hit Zika virus regions, and in today's update, PAHO said Brazil's health ministry is reporting a 20-fold increase in microcephaly cases compared with previous years.

Marco Silva/ iStock

December 1, 2015

Local Transmission

Florida – 227

Texas – 6

April 12, 2017

Zika Cases Reported in US

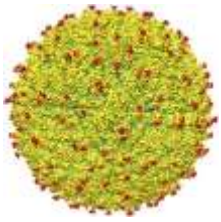
CDC as of 4/12/17

NJ – 244 Travel Related

Zika Virus

Flavivirus

- West Nile virus
- Dengue virus
- Tick-borne encephalitis virus
- Yellow fever virus
- Japanese encephalitis virus

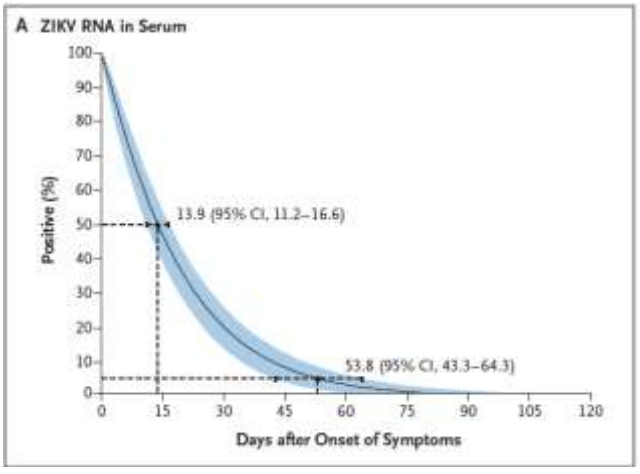


Zika Virus in Bodily Fluids

Zika virus detected in:

- **Blood**
- Urine
- **Semen**
- Saliva
- CSF
- **Amniotic fluid**
- Breast milk
- **Vaginal fluid**

Zika Virus in Blood



Persistence of Zika Virus in Body Fluids – Preliminary Report; Paz-Bailey et al, NEJM; 2/17

Transmission of ZIKV

DOCUMENTED	PLAUSIBLE
▪ *Aedes aegypti/albopictus*	▪ Tissue transplantation
▪ Intrauterine/perinatal	▪ Breast milk
▪ Sexual transmission	
▪ Laboratory exposure	
▪ Blood transfusion	
▪ Close contacts	

Sexual Transmission - Known

ZIKV found in semen and vaginal fluids

Male/female to partners

- Vaginal, anal, and possibly oral (fellatio) sex

Virus lasts longer in semen than blood

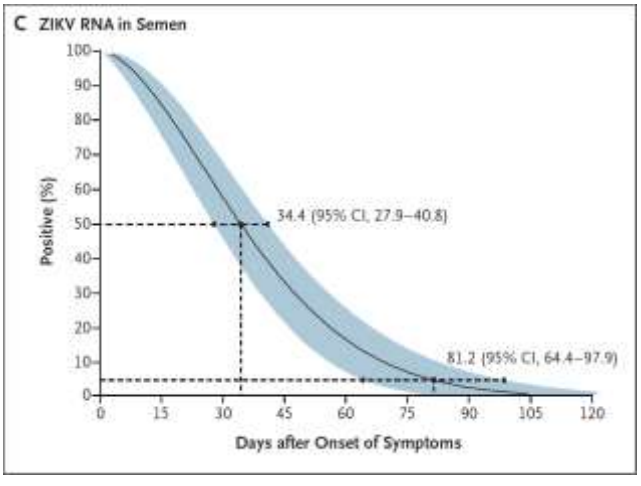
- Testis are immunologically privileged

Minor mode of transmission

- Most cases mosquito borne

Asymptomatic men have been shown to transmit

Zika Virus - Semen



Persistence of Zika Virus in Body Fluids – Preliminary Report; Paz-Bailey et al, NEJM; 2/17

Mosquitos - Most Important Vector

Aedes Mosquitos

Females need blood meal to reproduce

- Sip feeder
- Black/white stripes on legs

Daytime biter

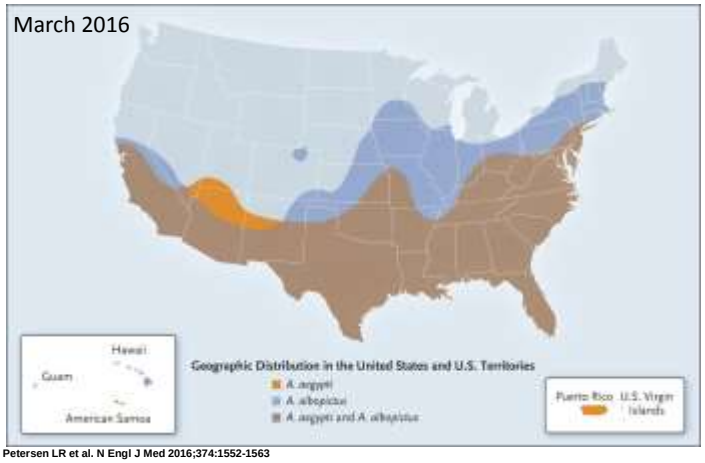
Urban dweller

- Close proximity to humans
- Standing H_2O

Aedes aegypti

Aedes albopictus

Approx Ranges *A. aegypti and albopictus*



Petersen LR et al. N Engl J Med 2016;374:1552-1563

Clinical Presentation

75-80% asymptomatic

Incubation period

- Typically 2-7 days
- ? Long end of ~14 days

Mild illness

Symptoms resolve 2-7 days

Clinical Presentation

Fever

- Acute/low grade (37.8-38.5^{o}C)

M/P rash

- Typically pruritic/descending

Arthralgia

- Typically small joints hands and feet

Conjunctivitis (non-purulent)

Other Manifestations

Myalgias
Headache
Retro-orbital pain
Asthenia
GI

- Abdominal pain, nausea, diarrhea, mucus membrane ulcers

Pruritus
Thrombocytopenia (case reports)

By FRED - Own work, CC BY-SA 3.0, https://commons.wikimedia.org/w/index.php?curid=30734915

By Cramunhao - Own work, CC BY-SA 4.0, https://commons.wikimedia.org/w/index.php?curid=39873314

Differential Diagnosis

Dengue fever

- *Flavivirus, aedes* mosquito

Chikungunya

- *aedes* mosquito

Parvovirus, rubella, measles, leptospirosis, malaria, rickettsial infection, group A *Strep*

Clinical features: Zika virus compared with dengue and chikungunya

Features	Zika	Dengue	Chikungunya
Fever	++	+++	+++
Rash	+++	+	++
Conjunctivitis	++	–	–
Arthralgia	++	+	+++
Myalgia	+	++	+
Headache	+	++	++
Hemorrhage	–	++	–
Shock	–	+	–

Reproduced from: Centers for Disease Control and Prevention. Zika virus - What clinicians need to know? Clinician Outreach and Communication Activity (COCA) Call, January 26, 2016. Available at: http://emergency.cdc.gov/coca/ppt/2016/01_26_16_zika.pdf (Accessed February 1, 2016).

UpToDate®

Differential Diagnosis

Rule out Dengue, Chikungunya

- Clinical history/exam often not definitive
- Testing for dengue, chikungunya

Testing Guidelines
Pregnant Women

With/without symptoms who either while pregnant or during the 8 weeks prior to conception (6w prior to LMP):

- Traveled to Zika area OR
- Had unprotected sex with partner with travel history

Asymptomatic test 2-12w following travel/exposure

Testing Guidelines
Symptomatic Non-Pregnant Individuals

≥1 Zika compatible sign/symptom AND

- Fever
- Rash
- Arthralgia
- Conjunctivitis

Exposure (Travel OR Unprotected sex with traveler) AND

Symptoms began within 2w of exposure AND

Specimens collected <12w after symptom onset

Testing Guidelines
Assessing Risk of Asymptomatic Sexual Transmission

Serum testing NOT recommended
- Accuracy of IgM testing unknown

Semen testing NOT recommended
- Only available through CDC
- Accuracy unknown
- Possibility of intermittent shedding

Criteria for Testing
Infants

Microcephaly, intracranial calcifications, brain/eye abnormalities whose mothers had potential exposure OR

Born to mothers with positive/inconclusive testing while pregnant

Criteria for Testing
Others

Guillain-Barré syndrome

- Exposure history
- No other suspected cause

NAT Testing

Serum/Urine – ≤14 days post onset symptoms

Amniotic*, CSF*, placental* – special circumstances

Trioplex*

- Zika, dengue, chikungunya

Positive = Positive

- Negative – may have missed window

*Only available via NJDOH – contact local health department for approval

IgM Antibodies

IgM (Zika MAC-ELISA)

- Begins to turn positive after ~ 4 days
- Declines after 12 weeks
- Cross reacts with other *Flaviviruses*
  - Dengue
  - WNV
  - YF, Japanese encephalitis infection or vaccination

PRNT

Plaque-reduction neutralization testing (PRNT)

- Measures titer of neutralizing antibodies in serum and determines the level of protective antibodies towards flaviviruses
- Used when IgM is positive
- Still may be inconclusive

Commercial vs PH Lab

COMMERCIAL LAB	PUBLIC HEALTH LAB
ZIKV NAT ▪ Serum, urine ZIKV IgM ▪ Positive reflex CDC Easier to order More expensive More complicated to order	Trioplex PCR ▪ Serum, urine, other ZIKV IgM, PRNT Need PH approval No cost for test ▪ May be drawing fee

Prevention
All Travelers

Be aware of current risk areas and notices

- http://wwwnc.cdc.gov/travel/page/zika-information

Avoid mosquito bites

- Insect repellant
- Long-sleeved shirts, long pants
  - Permethrin
- Air conditioning, screens

Prevention
Pregnant/Trying to Conceive

EPIDEMIC AREAS	ENDEMIC AREAS
Avoid travel 	Southeast Asia ▪ Consider postponing travel Other areas ▪ Strict mosquito precautions

Prevention
Pregnant/Trying to Conceive

Cautionary Areas
- Consider postponing Travel

Prevention - Pregnant

If partner has traveled to Zika areas

- Abstinence
- Consistent condom use

Planning Pregnancy

Suggested timeframe to wait before trying to get pregnant	
Possible exposure via recent travel or sex without a condom with a partner infected with Zika	
Women	Men
Wait at least 8 weeks after symptoms start or last possible exposure	Wait at least 6 months after symptoms start or last possible exposure

WHO recommends 6 months for women and men

Outbreak in NJ?

A. albopictus

- Competent but…

Air conditioning

Screens

Mosquito control

No natural animal reservoir

- Unlike WNV

Sporadic and sexually transmitted possible

Vector Control

Outside

- Install/repair screens
- Empty (larvicide) standing water weekly
- Outdoor flying insect spray where mosquitos rest

Inside

- Air conditioning
- Empty standing water (vases) weekly
- Kill mosquitos
  - Flying insect fogger
  - Indoor insect spray

What is NJ Doing?

NJDOH is communicating with doctors:
- Health alert messages
- Conference calls
- Grand rounds

Facilitating Zika testing for doctors

Public Awareness Campaign

Collaborating with mosquito control

Questions?

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New Jersey Department of Health

The Emerging Threat of Zika Virus: Assessing Impact and Designing a Response

With a lot more questions than answers and adapting to constantly changing guidance…

Thomas Westover MD
Assistant Professor Maternal Fetal Medicine
Cooper Medical School
Rowan University
Camden NJ

The American College of Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

Society for Maternal-Fetal Medicine

About This Practice Advisory

Zika virus continues to be an area of evolving care and practice. Recommendations below are based on limited data. Fellows should check periodically for revisions and updates on ACOG's Practice Advisories web page and Zika virus web pages (www.acog.org/zika and http://immunizationforwomen.org/providers/Zika-Virus-Updates), CDC's web site, and SMFM's web site. ACOG and SMFM will communicate important changes and updates to this guidance.

This Practice Advisory represents the current information available regarding Zika virus. When new information becomes available, the entire Practice Advisory is reviewed and individual sections are updated as needed and dated accordingly.

Click here to view this Practice Advisory in Spanish.

In the Zika Practice Advisory

- Background (Updated: December 19, 2016)
- Travel Restrictions (Updated: April 3, 2017)
- Prevention (Updated: October 18, 2016)
- Reproductive Counseling (Updated: October 18, 2016)
- Testing (Updated: April 3, 2017)
- Clinical Management of a Pregnant Woman with Suspected Zika Virus Infection (Updated: December 19, 2016)
- Postnatal Management (Updated: December 19, 2016)
- Neonatal Outcomes and Evaluation (Updated August 22, 2016)
- Reporting and the U.S. Pregnancy Registry (Updated: August 3, 2016)
- Infection Control Considerations (Updated: August 3, 2016)
- Zika Virus and Blood Transfusion (Updated: September 14, 2016)
- References (Updated: April 3, 2017)

Zika Virus

- ACOG's Practice Advisory on Zika Virus, updated April 4
- ACOG's Zika webpage
- ACOG Zika Toolkit, including patient education video, infographic, and assessment web tool endorsed by CDC
- CDC's Pregnancy and Zika Testing Clinical Algorithm
- CDC Zika Virus Website
- CDC's April 'Vital Signs' Report on Zika
- State Health Department Contact list for ob-gyns (members only) for questions on CDC's Zika Registry
- State Health Department Contact list for ob-gyns (members only) for questions on testing
- **CDC Zika Pregnancy Hotline for Healthcare Providers:** Obstetrician-gynecologists can contact the CDC Zika Pregnancy Hotline at **770-488-7100** or email ZikaPregnancy@cdc.gov for any concerns related to clinical management or the US Zika Pregnancy Registry.
- Office of Population Affairs' Zika Toolkit

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Background

(Updated: December 19, 2016)

Zika virus was reported in May 2015 in South America and since then has spread throughout the Americas, including the U.S. The CDC and Pan American Health Organization (PAHO) web sites maintain and update the list of areas where Zika virus transmission has been identified, including a list of U.S. states and territories where active mosquito-borne Zika virus transmission is found (for current locations, see Travel Restrictions).

The virus spreads to humans primarily through infected Aedes species mosquitoes (Ae. aegypti and Ae. albopictus), from mother to her fetus during pregnancy, and through sexual contact, although Zika virus transmission may also occur through blood transfusion and through laboratory exposure. Zika virus disease is defined as having at least one of the following signs or symptoms: acute onset of fever, rash, arthralgia, conjunctivitis and laboratory confirmation of Zika virus infection. It appears that only about one in five infected individuals will exhibit these symptoms and most of these will have mild symptoms. Once a person is infected, the incubation period for the virus is approximately 3–14 days. This time frame is suggested based on limited experience from Zika virus cases as well as extrapolation from data on other flaviviruses. Possible Zika virus exposure is defined as travel to or residence in an area of active Zika virus transmission (http://www.cdc.gov/zika/geo/index.html), or sex without a condom with a partner who traveled to or lived in an area of active transmission. Anyone who lives or travels to an area where Zika virus is found and has not already been infected with Zika virus is at risk of contracting Zika virus. Once a person has been infected, he or she is likely to be protected from future infections, although this is based on limited data and experience from other flaviviruses and has not been confirmed.

It is not known if pregnant women are at greater risk of Zika virus transmission than non-pregnant individuals. However, there is demonstrated causation between Zika virus infection during pregnancy and adverse pregnancy outcomes such as pregnancy loss, microcephaly, and other brain and eye abnormalities. Transmission of Zika virus to the fetus has been documented in all trimesters; Zika virus RNA has been detected in fetal tissue from early missed abortions, amniotic fluid, term neonates, and the placenta. However, much is not yet known about Zika virus in pregnancy. Uncertainties include the incidence of Zika virus infection among pregnant women in areas of Zika virus transmission, the rate of vertical transmission, and the rate with which infected fetuses manifest complications such as microcephaly or demise. However, one study utilizing modeling based on the Zika virus outbreak in French Polynesia (Cauchemez 2016) suggested microcephaly would occur in 1%–13% of babies born to mothers infected in the first trimester, and a recent cohort study from Brazil (Brasil 2016) found abnormal outcomes including stillbirth, growth restriction, and microcephaly and other sonographic abnormalities in 29% of fetuses of Zika virus–infected mothers in all trimesters.

- **Travel Restrictions**
- *(Updated: April 3, 2017)*
- Pregnant women should not travel to any area where there is a risk of Zika virus infection, including areas where the virus has been newly introduced or reintroduced and local mosquito-borne transmission is ongoing; areas where the virus was present before 2015 (endemic) and there is no evidence transmission has stopped; and areas where the virus is likely to be circulating but has not been documented. Because Zika infection in a pregnant woman can cause severe birth defects, pregnant women should not travel to these areas. To help pregnant women and others identify areas of Zika risk, see CDC's interactive World Map of Areas with Zika Risk to search for location-specific Zika information and travel recommendations. CDC updates Zika travel guidance regularly. Fellows should check CDC's Zika Travel Notices periodically for updates.

- Pregnant women and their partners who must travel to one of these areas should strictly follow steps to prevent mosquito bites during the trip and decrease the risk for sexual transmission (see Prevention).

- **Prevention**
- *(Updated: October 18, 2016)*
- Avoiding exposure is best:
- When traveling to areas where Zika virus has been reported, women should take all precautions to avoid mosquito bites including the use of EPA-approved bug spray with DEET, covering exposed skin, staying in air-conditioned or screened-in areas, and treating clothing with permethrin.
- Providers should specifically communicate to pregnant women that when used as directed on the product label, EPA-registered insect repellents, particularly those with DEET and permethrin, can be used safely during pregnancy.
- These protective measures should be followed both day and night as the Aedes aegypti mosquito (which carries Zika virus) bites primarily during the day as well as at dusk and dawn. Reapplication of insect repellant should be practiced as directed on the product label.
- Consistently and correctly using condoms during sex or abstaining from sex for the duration of the pregnancy is recommended if you have a sex partner that has traveled to or lives in an area with active Zika virus transmission.
- View additional resources on the prevention of Zika virus.

- **Reproductive Counseling**
- *(Updated: October 18, 2016)*
- Obstetrician–gynecologists and other health care providers should discuss pregnancy intentions and reproductive options with all women of reproductive age for shared decision making.
- Preconception care should include a discussion of the signs and symptoms and the potential risks of Zika virus infection. Health care providers should discuss their patients' reproductive life plans in the context of potential Zika virus exposure. View CDC's guide for preconception counseling in context of Zika.

- Sexual transmission
- Pre-Pregnancy Counseling; Contraception vs preg planning
- Antenatal screening/testing

Suggested timeframe to wait before trying to get pregnant	
Possible exposure via recent travel or sex without a condom with a partner infected with Zika	
Women	**Men**
Wait at least 8 weeks after symptoms start or last possible exposure	Wait at least 6 months after symptoms start or last possible exposure

http://www.cdc.gov/zika/pregnancy/women-and-their-partners.html

No instances of Zika virus transmission during fertility treatment have been documented, but transmission through gametes or embryos is theoretically possible. Recommendations for sexually intimate couples with Zika virus infection or possible Zika virus exposure undergoing fertility treatment with their own gametes and embryos should follow the testing and timing recommendations as described above; recommendations might need to be adjusted depending on individual circumstances. The Food and Drug Administration has issued guidance to reduce the risk of Zika virus transmission by donated human cells, tissues, and cellular and tissue-based products, including reproductive tissues.

View additional resources on reproductive counseling and the Zika virus.

Testing

(Updated: April 3, 2017)

All pregnant women in the U.S. and U.S. territories should be assessed for possible Zika virus exposure at each prenatal care visit. Sexual exposure includes vaginal, anal, or oral sex, and the sharing of sex toys without a barrier method. Testing for asymptomatic, non-pregnant sexual partners (with or without potential Zika exposure) of pregnant women is not currently supported by the CDC guidelines.

Routine Zika virus testing is not currently recommended for women or men with possible Zika virus exposure without clinical illness who are attempting pregnancy. Additional research is needed to determine if semen culture can reliably detect presence of infectious virus in semen.

Testing of specimens to assess risk for sexual transmission is currently not recommended. However, Zika virus testing of serum and urine is recommended for persons who have had possible sexual exposure to Zika virus and who develop signs or symptoms consistent with Zika virus disease (http://www.cdc.gov/zika/laboratories/lab-guidance.html).

Non-pregnant women and all men with Zika virus exposure and symptoms consistent with Zika virus should be tested.

Non-pregnant women and all men with Zika virus exposure but without symptoms consistent with Zika virus exposure should not be tested.

Pregnant women with Zika virus exposure should be tested following Figure 1 regardless of symptom status.

ZIKA SCREENING TOOL FOR PREGNANT WOMEN

(To be administered by nurse, check-in receptionist, or other healthcare provider)

All pregnant women should be assessed for possible Zika virus exposure[1] at each prenatal care visit. Use this tool to evaluate pregnant women for exposure to Zika virus and for signs and symptoms of Zika virus disease to determine whether testing is indicated.

NOTE: If your pregnant patient has questions about Zika testing, educational factsheets are available on CDC's website: http://www.cdc.gov/zika/hc-providers/pregnant-woman.html

Assess for Possible Exposure[1] to Zika Virus Infection

(See references on back for more information.)

Circle response:

Do you live in or do you frequently travel (daily or weekly) to an area with active Zika virus transmission[2]?	YES | NO
Have you traveled to an area with Zika[2] during pregnancy or just before you became pregnant [8 weeks before conception or 6 weeks before your last menstrual period]?	YES | NO
Have you had sex (vaginal, anal, or oral sex) without a condom or shared sex toys with a partner(s) who lives in or has traveled to an area with Zika[2]?	YES | NO

➡ If your pregnant patient answered **"NO"** to ALL questions, she is at low risk for exposure to Zika.

If Pregnant Patient Answered "Yes" to Any Question, Assess for Signs and Symptoms of Zika Virus Disease

Circle response:

Do you currently have or have you had (in the last 12 weeks) fever, rash, joint pain, or conjunctivitis (red eyes)?	YES | NO

➡ If your pregnant patient answered **"YES"** to having any of these signs or symptoms, she might have symptomatic Zika virus infection. Test in accordance with CDC guidance for symptomatic persons[3].

➡ If your pregnant patient answered **"NO"** to having any signs or symptoms, she has been exposed and might have an asymptomatic Zika virus infection. Test in accordance with CDC guidance for asymptomatic pregnant women[3].

References:

1. Possible exposure to Zika virus that warrants testing includes one or more of the following:
   a. Living in an area with active transmission
   b. Travel to an area with active transmission
   c. Sex (vaginal, anal, and oral sex) without a condom or the sharing of sex toys with a person who traveled to or lives in an area with Zika

3. **Please see the algorithm on the back from CDC's Updated Interim Guidance for Health Care Providers Caring for Pregnant Women with Possible Zika Virus Exposure to guide testing and interpretation of results.** (http://www.cdc.gov/mmwr/volumes/65/wr/mm6529e1.htm?s_cid=mm6529e1_e)

CDC U.S. Department of Health and Human Services

CDC's Response to **Zika**

ZIKA VIRUS TESTING FOR ANY PREGNANT WOMAN NOT LIVING IN AN AREA WITH ZIKA

CDC understands that a pregnant woman may be worried and have questions about Zika virus infection (Zika) during pregnancy. Learn more about Zika virus testing for a pregnant woman and what you might expect if you have Zika during your pregnancy.

How Zika spreads.

A pregnant woman who does not live in an area with Zika can catch the virus from a mosquito bite while visiting an area where mosquitoes are spreading Zika. She can also get Zika through sex with an infected partner. For more information on transmission of Zika, visit www.cdc.gov/zika/transmission.

What CDC knows about Zika virus and pregnancy.

- Zika virus can spread from mother to fetus during pregnancy and around the time of birth.
- Zika virus can cause birth defects and has been linked with other problems in infants.

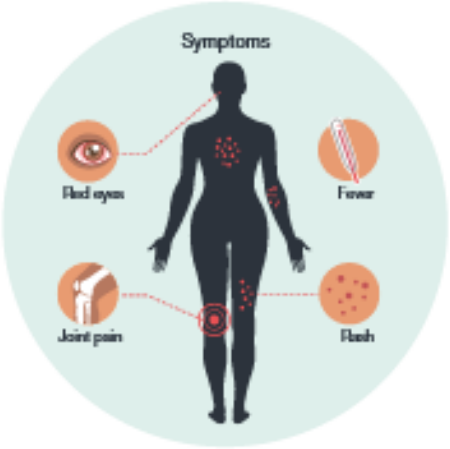
What CDC doesn't yet know about Zika virus and pregnancy and is researching quickly to find out.

If a woman is infected during pregnancy, we don't know

- How likely it is that the virus will affect her or her pregnancy.
- How likely it is that the virus will be passed to the fetus.
- How likely it is that the fetus, if infected, will have birth defects.
- When in pregnancy the infection might harm the fetus.

How can a pregnant woman find out if she has Zika?

- If a pregnant woman gets infected with Zika, the virus will be in her blood and urine for up to two weeks. If she gets sick with a fever, joint pain, rash, or red eyes, doctors or other healthcare providers can test small amounts of her blood and urine and test them for Zika virus.
- If she never feels sick, or if more than two weeks have gone by since possible exposure to Zika (through travel or sexual contact with an infected partner), doctors can order a different test to look for evidence of Zika infection.



What do the test results mean?

What happens if samples from a pregnant woman test positive?

If a woman has a positive test result for Zika during pregnancy, it signals to her doctor or other healthcare provider to watch her pregnancy more closely, meaning the provider might do more ultrasounds or other tests to check the growth and development of her fetus and check for any signs of Zika virus infection. CDC recommends steps for doctors or other healthcare providers to help care for pregnant women.

What happens if a pregnant woman's test results are inconclusive (not positive or negative)?

Sometimes, if the tests aren't clearly positive or negative, the results are considered inconclusive. If the test results are inconclusive, her doctor may follow the CDC recommendations for a positive test result, meaning he or she might do more ultrasounds or other tests to monitor your pregnancy.

What happens if a pregnant woman tests negative?

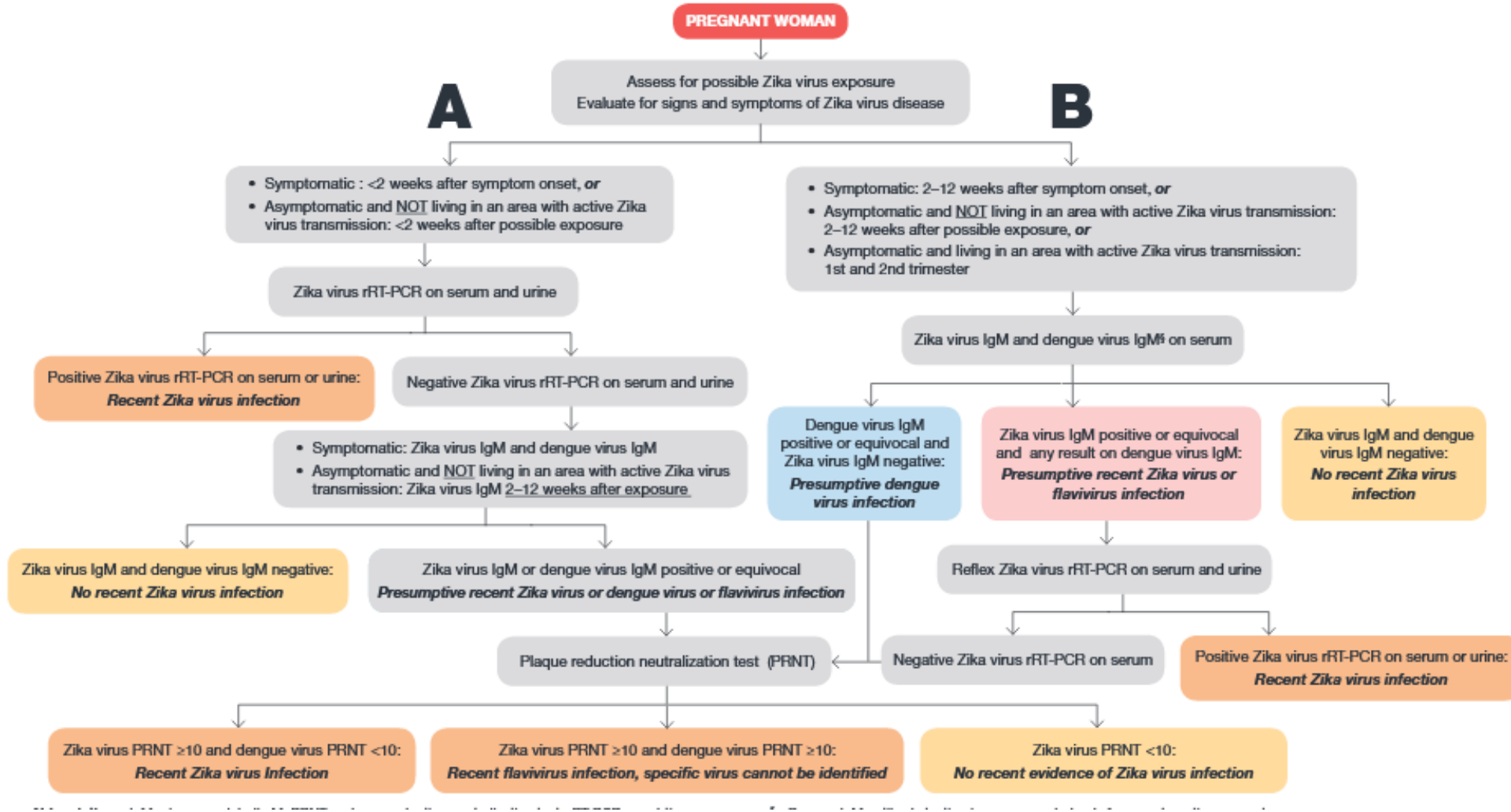
If she tests negative, her doctor may check the growth and development of the fetus during an ultrasound and check for any signs of Zika virus infection. If there are no signs of Zika virus infection, routine prenatal care is recommended. If her doctor sees signs of Zika virus infection during an ultrasound, then the doctor may do additional tests.

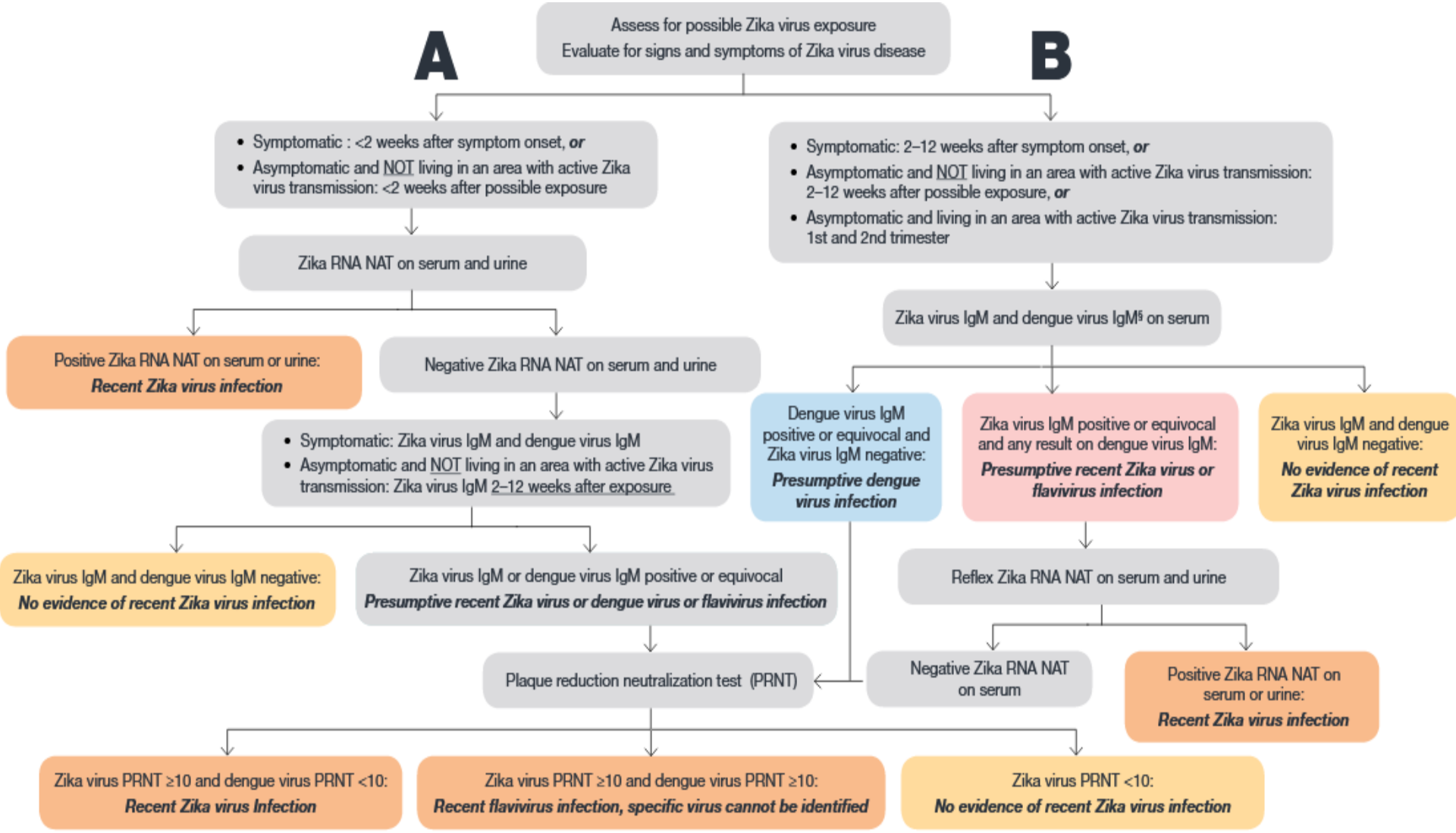
www.cdc.gov/zika

CDC's Response to **Zika**

UPDATED INTERIM PREGNANCY GUIDANCE:

Testing and interpretation recommendations*†‡§¶ for a pregnant woman with possible exposure to Zika virus — United States (including U.S. territories**




Assess for possible Zika virus exposure
Evaluate for signs and symptoms of Zika virus disease
A
B
• Symptomatic : <2 weeks after symptom onset, or
• Asymptomatic and NOT living in an area with active Zika virus transmission: <2 weeks after possible exposure
Zika RNA NAT on serum and urine
Positive Zika RNA NAT on serum or urine: Recent Zika virus infection
Negative Zika RNA NAT on serum and urine
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Zika virus IgM and dengue virus IgM negative: No evidence of recent Zika virus infection
Zika virus IgM or dengue virus IgM positive or equivocal Presumptive recent Zika virus or dengue virus or flavivirus infection
Plaque reduction neutralization test (PRNT)
Zika virus PRNT ≥10 and dengue virus PRNT <10: Recent Zika virus Infection
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Zika virus IgM and dengue virus IgM§ on serum
Dengue virus IgM positive or equivocal and Zika virus IgM negative: Presumptive dengue virus infection
Zika virus IgM positive or equivocal and any result on dengue virus IgM: Presumptive recent Zika virus or flavivirus infection
Zika virus IgM and dengue virus IgM negative: No evidence of recent Zika virus infection
Reflex Zika RNA NAT on serum and urine
Negative Zika RNA NAT on serum
Positive Zika RNA NAT on serum or urine: Recent Zika virus infection

Symptom Status	Timing[b]	Ongoing Exposure	First Test	Follow-On Test	Comments
Symptomatic	< 2 weeks	No or Yes (Applies to patients with or without ongoing exposure)	Zika RNA NAT (urine, serum, whole blood)[L,M]	If ZIKV RNA NAT negative, IgM for Zika and dengue[d]	IgM done (preferably same sample as ZIKV RNA NAT or ideally sample drawn at same time as ZIKV RNA NAT)
Symptomatic	2–12 weeks	No or Yes (Applies to patients with or without ongoing exposure)	IgM for Zika and dengue[e]	If Zika IgM positive or equivocal, Zika RNA NAT (preferably same sample) [c,k] If Zika IgM negative but dengue IgM positive or equivocal, PRNT[N] testing.	If ZIKV RNA NAT negative, do PRNT[N] on same ZIKV RNA NAT sample
Asymptomatic[f]	< 2 weeks	No	Zika RNA NAT (urine, serum, whole blood)[L,M]	If ZIKV RNA NAT negative, IgM for Zika ONLY[d]	IgM done (different sample drawn at a later date, 2 and 12 weeks after exposure)
Asymptomatic[f]	2–12 weeks	No	IgM for Zika[e]	If Zika IgM positive or equivocal, Zika RNA NAT (preferably same sample) [c,k]	If ZIKV RNA NAT PCR negative, do PRNT[N] on same ZIKV RNA NAT sample
Symptomatic OR asymptomatic[f]	> 12 weeks[g]	No	***Consider*** IgM[h]	ZIKV RNA NAT (serum and urine) if fetal abnormalities	***Consider*** serial ultrasound[i]

Clinical Management of a Pregnant Woman with Suspected Zika Virus Infection

(Updated: December 19, 2016)

The many uncertainties about Zika highlight the challenges of managing and counseling about preg exposure/infection. Referral to MFM/peds ID.

Given that serology can be difficult to interpret, particularly in previously infected/vaccinated pts, preg pts with lab evidence of recent flavivirus infection are considered to have possible Zika virus infection and should be monitored frequently.

Pregnant women with confirmed or possible Zika virus infection and women with presumptive recent Zika or flavivirus infection should be managed Table 2. While the clinical implications of prolonged detection of Zika virus RNA in serum are not known, repeat ZIKV RNA NAT has been performed in some cases. Currently, there is insufficient info to make recommendations regarding repeat ZIKV RNA in preg pts.

It is important that maternal Zika virus exposure and testing information be available and communicated to the pediatric team so that appropriate infant testing and management can be implemented in accordance with existing guidance. It is particularly important that this information be conveyed while neonates are hospitalized after birth to allow for collection of infant specimens within 2 days of birth.

Interpretation of laboratory results**	Prenatal management
Recent Zika virus infection Recent flavivirus infection specific virus cannot be identified Presumptive§ recent Zika virus infection¦ ¦	Consider serial ultrasounds every 3–4 weeks to assess fetal anatomy and growth. † Decisions regarding amniocentesis should be individualized for each clinical circumstance. ? Consider serial ultrasounds every 3–4 weeks to assess fetal anatomy and growth.† Amniocentesis might be considered;
Presumptive§ recent flavivirus infection¦ ¦	decisions should be individualized for each clinical circumstance.
Recent dengue virus infection No evidence of Zika virus or dengue virus infection	Clinical management in accordance with existing guidelines.¶ A prenatal ultrasound to evaluate for fetal abnormalities consistent with congenital Zika virus syndrome.† *Fetal abnormalities present*: repeat Zika virus rRT–PCR# and IgM test; base clinical management on corresponding laboratory results. *Fetal abnormalities absent*: base obstetric care on the ongoing risk for Zika virus exposure risk to the pregnant woman.

Fetal Evaluation:

Prenatal US is recommended for all preg pts tested for Zika, regardless of lab findings.

Serial US > assess fetal anatomy, particularly CNS, and to monitor growth > intracranial calcifications, microcephaly, ventriculomegaly, arthrogryposis, eyes; The International Society of Ultrasound in Obstetrics and Gynecology offers a tutorial .

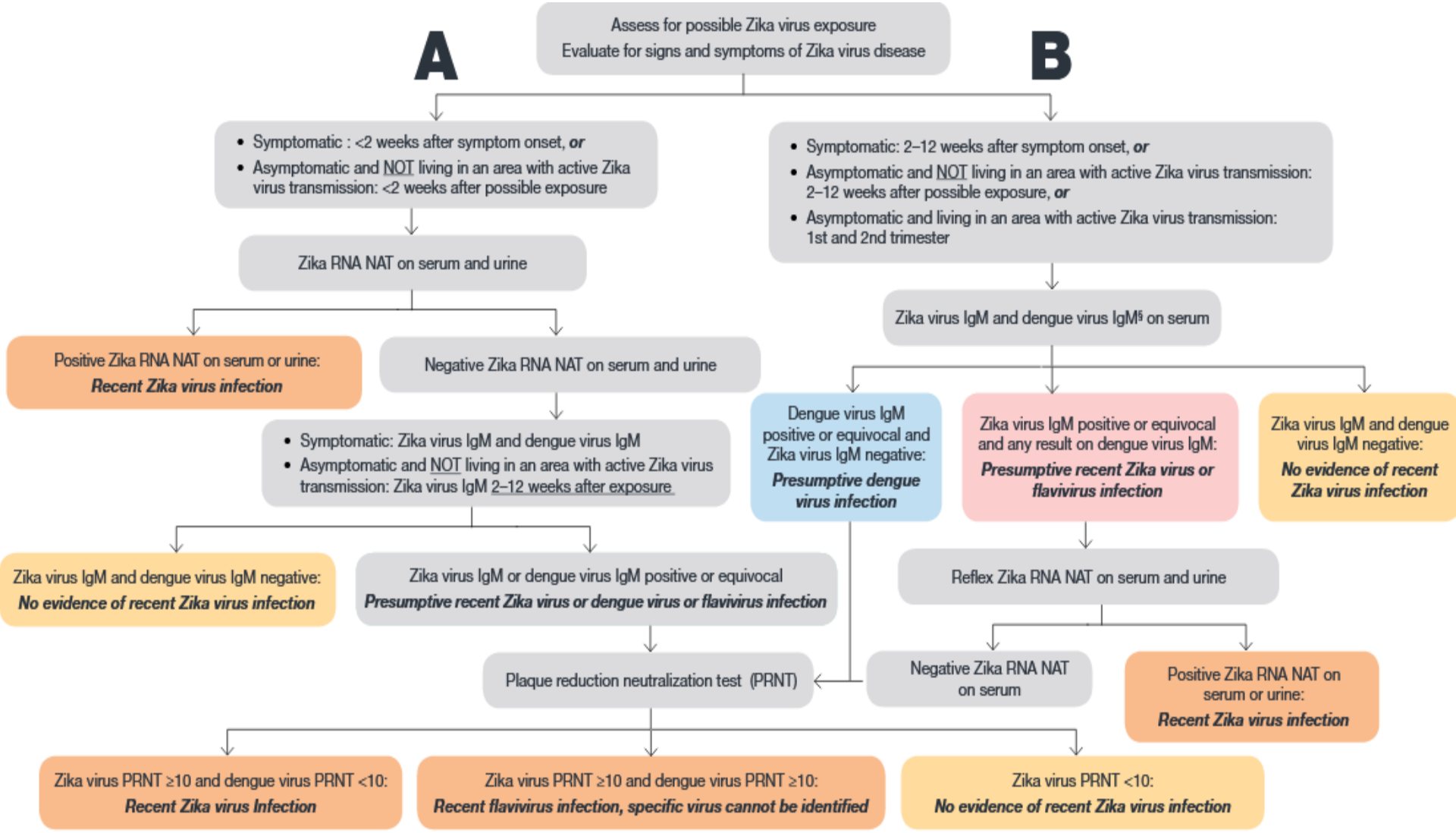
Ultrasound examinations, may not preclude later manifestations, and cases with delayed findings have been reported. These reports include infants without microcephaly at birth who later exhibited head growth deceleration occurring to the point of microcephaly after birth. Many of these infants had abnormal brain imaging after birth by CT or MRI, and many exhibited varying degrees of abnormalities, including dysphagia, seizures, and hypertonia/dystonia. Only three infants were reported to have a history of prenatal ultrasound examination abnormalities consistent with congenital Zika virus infection. Of note, data suggest that severe adverse outcomes appear to be more common but are not limited to women infected in the first trimester. Additional data suggest that severe adverse outcomes are not limited to symptomatic pregnant women.

Repeat imaging should be considered if Zika testing suggests infection. If maternal testing does not suggest infection and exposure is not ongoing, serial ultrasound examinations are unlikely to be needed (BUT almost all Obgyns will order them!).

When imaging raises suspicion for fetal infection, amniocentesis for Zika virus testing of amniotic fluid may be considered While it is assumed that assay performance on amniotic fluid is similar to that with maternal serum, this is not certain. Nor is it known how long after a pregnant woman becomes infected she can transmit the virus to the fetus, for what duration amniotic fluid will be ZIKV RNA NAT positive, or what the ability of the test is to determine the presence of fetal injury.

Prenatal counseling uncertainties

- There is much that is still unknown about the effects of Zika virus on a fetus. .
- All pregnant women infected or presumptively infected with Zika virus should be offered comprehensive options counseling, including a thorough discussion of pregnancy continuation, termination of pregnancy, and adoption. As with all patient counseling, health care providers should not seek to impose their personal beliefs upon their patients nor allow personal beliefs to compromise patient health, access to care, or informed consent.
- There is a demonstrated causation between antenatal Zika and adverse pregnancy outcomes. However, there are still many uncertainties regarding the degree of transmission from woman to fetus and the degree with which infected fetuses manifest complications such as microcephaly, demise, or congenital Zika syndrome.
- Testing for Zika can result in false-positives and false-negatives >difficult to exclude infection.
- US exams, may not preclude later manifestations (cases with delayed findings)
- Patients should be counseled about the limitations of US (as in all fetal imaging)
- Congenital Zika syndrome — a recently recognized pattern of congenital anomalies including microcephaly, intracranial calcifications or other brain/eye anomalies among others — may present after birth. Therefore, normal fetal US do not preclude neonatal sequelae (?? developing or ??manifesting after birth)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- **Breastfeeding:**

- Although the presence of Zika virus in breast milk has been reported, there are no reports of infants getting Zika virus through breastfeeding. Infection through oral intake is not known. The benefits of breastfeeding likely outweigh the potential neonatal risks. Therefore, the recommendation is that women should continue to breastfeed, even in areas where Zika virus is found.
- **Reporting:**
- Obstetrician–gynecologists will need to report pregnant women with any laboratory evidence of Zika virus infection (positive or inconclusive test results) as well as any adverse outcomes to the state health department (see U.S. Zika Pregnancy Registry for details).

Table 3. Postnatal management of a pregnant woman and their neonates with suspected Zika virus infection

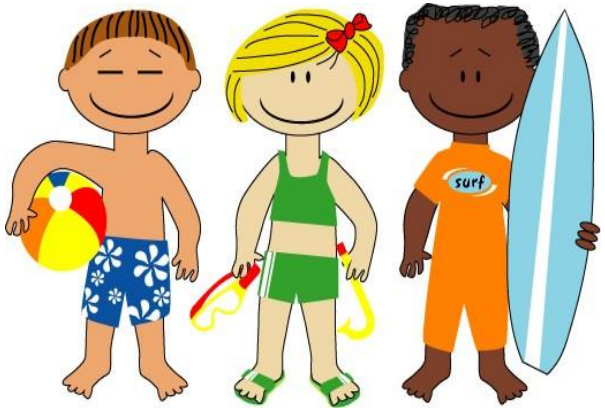
	Maternal Testing*	Fetal or Infant Testing*
Maternal laboratory evidence of Zika virus infection† (live birth)	No further maternal laboratory testing Submit placental specimens for ZIKV RNA NAT and IHC staining	Infant serum IgM and ZIKV RNA NAT, infant urine ZIKV RNA NAT. (See CDC Guidance for details)
Presumptive maternal Zika virus infection ‡ (live birth)	PRNT if indicated Consider Zika virus placental testing	Infant serum IgM and ZIKV RNA NAT, infant urine ZIKV RNA NAT. (See CDC Guidance for details)
No maternal testing performed (livebirth) §, ¶	Maternal Zika virus testing§, ¶, ** Consider Zika virus placental testing	Infant with findings consistent with congenital Zika syndrome: infant serum, urine, or cerebrospinal fluid# ZIKV RNA NAT and IgM testing. (See CDC Guidance for details) Infant without findings consistent with congenital Zika syndrome: infant testing should be considered.**, †† If maternal IgM testing is performed outside the recommended testing window (> 12 weeks from symptom onset or exposure), negative maternal testing may not rule out maternal infection. In this circumstance infant testing may be more informative than maternal testing.
No lab evidence of Zika virus infection on Maternal testing performed outside of appropriate window (live birth)	Consider Zika virus placental testing	Infant with findings consistent with congenital Zika syndrome: infant serum, urine, or cerebrospinal fluid# ZIKV RNA NAT and IgM testing. (See CDC Guidance for details) Infant without findings consistent with congenital Zika syndrome: infant testing should be considered.** Negative maternal testing may not rule out maternal infection. In this circumstance infant testing may be more informative than maternal testing.
Maternal laboratory evidence of Zika virus infection† (live birth)	PRNT, if indicated	Recommended to submit fetal tissues for ZIKV RNA NAT and IHC staining.
Presumptive‡ maternal Zika virus infection (fetal loss)	Consider Zika virus placental testing	Consider submitting fetal tissues for ZIKV RNA NAT and IHC staining.

Clinical management of a pregnant woman with suspected Zika virus infection

Interpretation of Laboratory Results*	Prenatal Management	Postnatal Management
Recent Zika virus infection	• Consider serial ultrasounds every 3–4 weeks to assess fetal anatomy and growth† • Decisions regarding amniocentesis should be individualized for each clinical circumstance§	**LIVE BIRTHS:** • Infant serum and infant urine should be tested for Zika RNA NAT. Infant serum should be tested for Zika IgM. If CSF is obtained for other reasons, it can also be tested.** • Zika RNA NAT and IHC staining of umbilical cord and placenta is recommended.¶ **FETAL LOSSES:** • Zika RNA NAT and IHC staining of fetal tissues is recommended.¶
Recent flavivirus infection; specific virus cannot be identified		
Presumptive recent Zika virus infection***	• Consider serial ultrasounds every 3–4 weeks to assess fetal anatomy and growth† • Amniocentesis might be considered; decision should be individualized for each clinical circumstance§	**LIVE BIRTHS:** • Infant serum and infant urine should be tested for Zika RNA NAT. Infant serum should be tested for Zika IgM. If CSF is obtained for other reasons, it can also be tested. ** • Zika RNA NAT and IHC staining of umbilical cord and placenta should be considered.¶ **FETAL LOSSES:** • Zika RNA NAT and IHC staining of fetal tissues should be considered.¶
Presumptive recent flavivirus infection***		
Recent dengue virus infection	• Clinical management in accordance with existing guidelines (http://apps.who.int/iris/bitstream/10665/44188/1/9789241547871_eng.pdf).	
No evidence of Zika virus or dengue virus infection	• Prenatal ultrasound to evaluate for fetal abnormalities consistent with congenital Zika virus syndrome.† ◆ Fetal abnormalities present: repeat Zika RNA NAT and IgM test; base clinical management on corresponding laboratory results. ◆ Fetal abnormalities absent: base obstetric care on the ongoing risk of Zika virus exposure to the pregnant woman.	

Thank you!

Zika Virus: Managing the Newborn



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Disclosure

- I have no financial disclosures.
- I do not plan to discuss off label uses of medications.

Objective

- Evaluate a newborn of a mother who was infected with Zika virus during her pregnancy

Current Surveillance

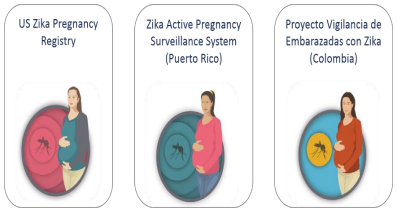
Collecting data for action

US Zika Pregnancy Registry

Zika Active Pregnancy Surveillance System (Puerto Rico)

Proyecto Vigilancia de Embarazadas con Zika (Colombia)

Zika in Pregnancy



Data as of March 14, 2017

- United States: 1617 pregnant women
  - Outcomes: 1228 completed pregnancies
  - 54 newborn with birth defects
  - 7 fetal losses with defects
- US Territories: 3363 pregnant women
  - Outcomes information not available

Pregnancy Outcomes

- Any evidence of possible recent Zika: 51/972 (5%); microceph. 43, other 8
- Confirmed Zika infection: 24/250 (10%); microceph. 18, other 6
- Zika infection in first trimester: 15/60 (15%); microceph. 8, other 1
- Postnatal studies: imaging in only 25%, Zika virus testing in 65%

www.cdc.gov/mmwr/early_release.html April 4, 2017

Mother to Fetus

- Zika virus RNA detected in placenta, amniotic fluid and fetal tissues
- Fetal loss, stillborn, brain abnormality
- Frequency and risk unknown
- Peripartum transmission reported
- Registry: ZikaPregnancy@cdc.gov

www.cdc.gov/zika/hc-providers/registry.html

Fetal Infection

- Virus is neurotropic and destroys brain
- Microcephaly, fetal brain disruption, ocular abnormalities
- In utero ultrasounds: calcification
- Zika confirmed in fetal brain tissue*
- Highest risk in 1st trimester

*DOI:10.1056/NEJMoa1600651

Effects of Zika on the Fetus

- Microcephaly: fetal brain disruption
- Imaging: calcification, abnormal gyri, decreased brain volume, +
- Hypertonia, hypotonia, spasticity, irritability, seizures
- Eyes: chorioretinal atropy, optic disc hypoplasia, pallor and cupping

www.cdc.gov/mmwr/volumes/65/wr/mm6533e2.htm?s_cid=mm6533e2_w

Management of the Baby

Laboratory testing recommended:

- Infants born to mother with evidence of Zika virus infection during pregnancy
- Infants with abnormal clinical or imaging findings and maternal epidemiologic link

rRT-PCR (serum, urine) and IgM for Zika

www.cdc.gov/mmwr/volumes/65/wr/mm6533e2.htm?s_cid=mm6533e2_w

Baby of Zika + Mother

- Postnatal head ultrasound
- Zika virus testing: rRT-PCR, IgM within 2 days; if CSF obtained, test it as well
- Comprehensive physical examination
- Neurologic examination
- Standard hearing screen
- Report to the registry

www.cdc.gov/mmwr/volumes/65/wr/mm6533e2.htm?s_cid=mm6533e2_w

Interpretation of Tests

- Positive infant serum or urine rRT-PCR confirms congenital Zika virus infection
- +Zika IgM, -rRT-PCR indicates probable congenital Zika virus infection; PRNT (plaque reduction neutralization test)
- -Zika IgM, -rRT-PCR means not infected
- Report Positives to Public Health

www.cdc.gov/mmwr/volumes/65/wr/mm6533e2.htm?s_cid=mm6533e2_w

Confirmed Congenital Zika

- By 1 month: Comprehensive ophthalmologic exam and hearing by Auditory brainstem response (ABR)
- Follow up depends on whether abnormalities are present

Baby With Abnormalities

- CBC, metabolic panel (liver function)
- Coordinated evaluation by multiple specialists within first month of life
- Assess vision, hearing, feeding , growth, neurodevelopment and endocrine function in first year

www.cdc.gov/zika/hc-providers/infants-children/zika-evaluation.html

Baby With Abnormalities

- Consultation: Neurology (imaging), ID (r/o other), Ophthalmologist, Genetics, Endocrine (hypothalamus, pituitary)
- Others: orthopedics, rehabilitation, pulmonary, lactation, nutritionist, GI, speech, occupational therapy
- Psychosocial support; coordinated care
- My opinion: palliative care essential

www.cdc.gov/zika/hc-providers/infants-children/zika-evaluation.html

Baby With Abnormalities

- Multidisciplinary team and medical home
- Monthly visits X 6: growth, development, immunize, guidance, support
- Neurologic exam at ages 1 and 2 months
- Refer to developmental specialist and early intervention services

www.cdc.gov/zika/hc-providers/infants-children/zika-evaluation.html

Baby With Abnormalities

- Repeat eye exam at 3 months
- Repeat ABR testing at 4-6 months, refer if abnormal
- Repeat thyroid studies (TSH, T4) at 2 weeks and 3 months, refer if abnormal
- Provide family and supportive services

www.cdc.gov/zika/hc-providers/infants-children/zika-evaluation.html

Baby Without Abnormalities

- Medical home: growth, developmental screen at each visit, anticipatory guide
- Standardized devel. screen at 9 mos
- Repeat hearing test, 4-6 mos
- Provide family and supportive services

www.cdc.gov/zika/hc-providers/infants-children/zika-evaluation.html

Anticipatory Guidance

- Encourage breastfeeding
- Watch for poor suck, swallowing difficulty, reflux, aspiration
- Sleep problems, excess irritability
- Monitor family for depression
- Social stigma, financial stress

www.cdc.gov/mmwr/volumes/65/wr/mm6533e2.htm?s_cid=mm6533e2_w

Zika Prevention

- Avoid exposure: travel precautions
- Avoid mosquitoes
- Sexual transmission: abstinence or condoms
- Stay tuned for more information
- www.cdc.gov/zika/

The End