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)

Abbreviations: IgM = immunoglobulin M; PRNT = plaque reduction neutralization test; rRT-PCR = real-time reverse transcription–polymerase chain reaction.

* A pregnant woman is considered symptomatic if one or more signs or symptoms (fever, rash, arthralgia, or conjunctivitis) consistent with Zika virus disease is reported whereas a pregnant woman is considered asymptomatic if symptoms are NOT reported.

† Testing includes Zika virus rRT-PCR on serum and urine samples, Zika virus and dengue virus Immunoglobulin M (IgM), and plaque reduction neutralization test (PRNT) on serum samples. PRNT results that indicate recent flavivirus infection should be interpreted in the context of the currently circulating flaviviruses. Refer to the laboratory guidance for updated testing recommendations (http://www.cdc.gov/zika/laboratories/lab-guidance.html). Because of the overlap of symptoms in areas where other viral illness are endemic, evaluate for possible dengue or chikungunya virus infection.

‡ Dengue IgM antibody testing is recommended only for symptomatic pregnant women.

§ If Zika virus rRT-PCR testing is requested from laboratories without IgM antibody testing capacity or a process to forward specimens to another testing laboratory, storing of additional serum samples is recommended for IgM antibody testing in the event of a rRT-PCR negative result.

** Possible exposure to Zika virus includes travel to or residence in an area with active Zika virus transmission (http://wwwnc.cdc.gov/travel/notices/), or sex (vaginal sex (penis-to-vagina sex), anal sex (penis-to-anus sex), oral sex (mouth-to-penis sex or mouth-to-vagina sex), and the sharing of sex toys) without a barrier method to prevent infection (male or female condoms for vaginal or anal sex, male condoms for oral sex (mouth-to-penis), and male condoms cut to create a flat barrier or dental dams for oral sex (mouth-to-vagina) with a partner who traveled to, or lives in an area with active Zika virus transmission.

A

Assess for possible Zika virus exposure
Evaluate for signs and symptoms of Zika virus disease

• 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 virus rRT-PCR on serum and urine

Positive Zika virus rRT-PCR on serum or urine:
Recent Zika virus infection

Negative Zika virus rRT-PCR on serum and urine

Zika virus IgM and dengue virus IgM§ on serum

B

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

Plaque reduction neutralization test (PRNT)

Zika virus PRNT ≥10 and dengue virus PRNT <10:
Recent Zika virus infection, specific virus cannot be identified

Zika virus PRNT ≥10 and dengue virus PRNT ≥10:
Recent flavivirus infection, specific virus cannot be identified

Zika virus PRNT <10:
No recent evidence of Zika virus infection

Positive Zika virus rRT-PCR on serum or urine:
Recent Zika virus infection

Symptomatic: 2–12 weeks after symptom onset, or
Asymptomatic and NOT living in an area with active Zika virus transmission: 2–12 weeks after possible exposure, or
Asymptomatic and living in an area with active Zika virus transmission: 1st and 2nd trimester

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

Plaque reduction neutralization test (PRNT)

Zika virus PRNT ≥10 and dengue virus PRNT <10:
Recent Zika virus infection, specific virus cannot be identified

Zika virus PRNT ≥10 and dengue virus PRNT ≥10:
Recent flavivirus infection, specific virus cannot be identified

Zika virus PRNT <10:
No recent evidence of Zika virus infection

Positive Zika virus rRT-PCR on serum or urine:
Recent Zika virus infection

Symptomatic: Zika virus IgM and dengue virus IgM
Asymptomatic and NOT living in an area with active Zika virus transmission: Zika virus IgM 2–12 weeks after exposure

Zika virus IgM and dengue virus IgM negative:
No recent Zika virus infection

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 virus rRT-PCR on serum and urine

Negative Zika virus rRT-PCR on serum and urine

Zika 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, specific virus cannot be identified

Zika virus PRNT ≥10 and dengue virus PRNT ≥10:
Recent flavivirus infection, specific virus cannot be identified

Zika virus PRNT <10:
No recent evidence of Zika virus infection

Positive Zika virus rRT-PCR on serum or urine:
Recent Zika virus infection

Symptomatic: Zika virus IgM and dengue virus IgM
Asymptomatic and NOT living in an area with active Zika virus transmission: Zika virus IgM 2–12 weeks after exposure

Zika virus IgM and dengue virus IgM negative:
No recent Zika virus infection

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 virus rRT-PCR on serum and urine

Negative Zika virus rRT-PCR on serum and urine

Zika 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, specific virus cannot be identified

Zika virus PRNT ≥10 and dengue virus PRNT ≥10:
Recent flavivirus infection, specific virus cannot be identified

Zika virus PRNT <10:
No recent evidence of Zika virus infection

Positive Zika virus rRT-PCR on serum or urine:
Recent Zika virus infection

Symptomatic: Zika virus IgM and dengue virus IgM
Asymptomatic and NOT living in an area with active Zika virus transmission: Zika virus IgM 2–12 weeks after exposure

Zika virus IgM and dengue virus IgM negative:
No recent Zika virus infection

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 virus rRT-PCR on serum and urine

Negative Zika virus rRT-PCR on serum and urine

Zika 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, specific virus cannot be identified

Zika virus PRNT ≥10 and dengue virus PRNT ≥10:
Recent flavivirus infection, specific virus cannot be identified

Zika virus PRNT <10:
No recent evidence of Zika virus infection

Positive Zika virus rRT-PCR on serum or urine:
Recent Zika virus infection

Symptomatic: Zika virus IgM and dengue virus IgM
Asymptomatic and NOT living in an area with active Zika virus transmission: Zika virus IgM 2–12 weeks after exposure

Zika virus IgM and dengue virus IgM negative:
No recent Zika virus infection

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 virus rRT-PCR on serum and urine

Negative Zika virus rRT-PCR on serum and urine

Zika 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, specific virus cannot be identified

Zika virus PRNT ≥10 and dengue virus PRNT ≥10:
Recent flavivirus infection, specific virus cannot be identified

Zika virus PRNT <10:
No recent evidence of Zika virus infection

Positive Zika virus rRT-PCR on serum or urine:
Recent Zika virus infection

Symptomatic: Zika virus IgM and dengue virus IgM
Asymptomatic and NOT living in an area with active Zika virus transmission: Zika virus IgM 2–12 weeks after exposure

Zika virus IgM and dengue virus IgM negative:
No recent Zika virus infection

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 virus rRT-PCR on serum and urine

Negative Zika virus rRT-PCR on serum and urine

Zika 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, specific virus cannot be identified

Zika virus PRNT ≥10 and dengue virus PRNT ≥10:
Recent flavivirus infection, specific virus cannot be identified

Zika virus PRNT <10:
No recent evidence of Zika virus infection
### Clinical management of a pregnant woman with suspected Zika virus infection

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

**Abbreviations:** CSF = cerebrospinal fluid; IgM = immunoglobulin M; IHC = immunohistochemical; PRNT = plaque reduction neutralization test; rRT-PCR = real-time reverse transcription–polymerase chain reaction.

* Refer to the previously published guidance for testing interpretation (http://www.cdc.gov/mmwr/volumes/65/wr/mm6521e1.htm).

† Fetal abnormalities consistent with congenital Zika virus syndrome include microcephaly, intracranial calcifications, ventriculomegaly, arthrogryposis, and abnormalities of the corpus callosum, cerebrum, cerebellum, and eyes.

§ Health care providers should discuss risks and benefits of amniocentesis with their patients. It is not known how sensitive or specific rRT-PCR testing of amniotic fluid is for congenital Zika virus infection, whether a positive result is predictive of a subsequent fetal abnormality, and if it is predictive, what proportion of infants born after infection will have abnormalities.

¶ Refer to pathology guidance for collection and submission of fetal tissues for Zika virus testing for detailed information on recommended specimen types (http://www.cdc.gov/zika/laboratories/test-specimens-tissues.html).

** rRT-PCR or PRNT should be performed for positive or equivocal IgM results as indicated. PRNT results that indicate recent flavivirus infection should be interpreted in the context of the currently circulating flaviviruses. Refer to the laboratory guidance for updated testing recommendations (http://www.cdc.gov/zika/laboratories/lab-guidance.html). Because of the overlap of symptoms and areas where other viral illnesses are endemic, evaluate for possible dengue or chikungunya virus infection.