

Center for Family Health

Contents

Center for Infectious Diseases

Comprehensive Zika Virus Information for Healthcare Providers

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Zika Fundamentals for Health Care Providers

Identifying Patients at Risk

All pregnant women, women planning pregnancy, and patients who have symptoms consistent with Zika virus disease should be assessed for potential Zika virus exposures.

Criteria for possible exposure to Zika virus include:

- 1. Recent travel to an area with risk of Zika, or
- 2. Recent unprotected sexual contact (oral, vaginal, or anal sex) with a male who has traveled within the prior 3 months to an area with risk of Zika or with a female who has traveled within the prior 2 months to an area with risk of Zika

To identify geographic areas with risk of Zika, the California Department of Public Health (CDPH) recommends providers use the <u>CDC Zika Travel Recommendation</u> <u>Map</u> (https://wwwnc.cdc.gov/travel/page/zika-information).

CDPH recommendations for identifying persons at risk of Zika infection are based on U.S. Centers for Disease Control and Prevention (CDC) guidance, regional epidemiology of Zika cases, and travel patterns of Californians.

Clinical Features

Primary symptoms compatible with Zika virus disease include:

- maculopapular rash
- fever over 100.4F/38C
- arthralgia
- conjunctivitis

Other potential symptoms include myalgia and headache, but these symptoms alone are not considered sufficient to qualify as a suspect case due to non-specificity.

Symptom onset should be within 2 weeks of travel or last known exposure.

Assessing Patient Risk and Shared Decision-Making

Multiple clinical variables are likely to influence the level of risk of disease in any given clinical setting, and therefore will influence the positive and negative predictive value of laboratory testing. Both the CDC and CDPH emphasize the importance of **shared decision-making** between providers and patients in deciding whether or not to test in a given clinical situation, based upon individualized risk factors. Remaining questions in such situations may be directed to local health departments. Risk factors that may prompt testing include:

- 1. Locally-transmitted Zika infections reported in the region of travel at the time of the possible exposure
- 2. Sexual partner with travel to a Zika-risk area and unprotected (e.g., without use of male or female condom or dental dam) sexual exposure
- 3. Longer duration of travel (e.g., over four weeks) or multiple sexual exposures
- 4. Engagement in higher risk activities (e.g., outdoor recreation as opposed to indoor activities) while in an area with risk of Zika transmission
- 5. Known mosquito bites in an area with risk of Zika transmission
- 6. Lack of use of protective clothing and insect repellent on a regular basis in an area with risk of Zika transmission
- 7. Compromised integrity of housing in an area with risk of Zika transmission (e.g., lack of window screens or air conditioning)
- 8. Other household members diagnosed with Zika virus infection
- 9. High risk patient occupation (e.g., potential laboratory or needle stick exposure)
- 10. Patient is recipient of recent transfusions or transplants, especially in an area with risk of Zika transmission and there is not reliable testing of blood supply for Zika virus. The U.S. routinely tests blood donations for Zika virus.
- 11. Patient undergoing fertility treatment and is a recipient of a recent semen or egg donor in an area with a risk for Zika transmission and there was no screening done at the time of donation.

Testing Guidance for Zika Infection

Laboratory testing for Zika should be considered for the following patients with travel or sexual exposure to Zika:

- 1. Pregnant patients who have at least one of the four primary symptoms of Zika (see <u>above</u>) within two weeks of potential exposure
- 2. Pregnant women who have a fetus with prenatal ultrasound findings consistent with congenital Zika virus infection who live in or traveled to areas with a risk of Zika during her pregnancy

Routine Zika testing is **NOT** recommended for:

1. Asymptomatic pregnant women living in or with recent travel to the U.S. and its territories

- 2. Asymptomatic pregnant women living in or with recent travel to <u>an area with risk</u> <u>of Zika</u> outside the U.S. and its territories
 - a. Zika virus testing is **NOT** routinely recommended, but NAT testing may still be considered.
- 3. Symptomatic non-pregnant patients
 - a. Refer to testing guidance for <u>dengue</u>. Zika testing is **NOT** currently recommended for this group based on the current epidemiology of these viruses.
- 4. Asymptomatic non-pregnant patients
 - a. Zika virus testing should **NOT** be performed as part of preconception screening.

For details regarding specimen collection and test selection, see Laboratory Testing.

Reported Zika Cases and Aedes Mosquitoes in California

The CDPH Zika website is regularly updated with the number of <u>confirmed and probable</u> Zika cases by California county

(https://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/TravelAssociatedCasesofZikaVirusinCA.pdf).

To date, there has been no local mosquito-borne transmission of Zika virus in California. Thus far, Zika virus infections have been documented only in persons exposed through travel to a Zika-affected area, sexual contact with a traveler, or through congenital transmission.

View an <u>updated map of California counties where *Aedes* vector mosquitoes are present (https://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/Aedes DistributionMap.pdf).</u>

View an <u>interactive map</u> with more detailed information about the distribution of *Aedes* vector mosquitoes in California

(http://cdphdata.maps.arcgis.com/apps/webappviewer/index.html?id=57367199287a4d1 8a2cecf107854255b).

General Patient Education and Prevention Messaging

Pregnant women in any trimester of pregnancy should be advised not to travel to any area where there is an outbreak of Zika. See the most current <u>CDC Zika Travel Recommendation</u> <u>Map</u>.

If patients are planning travel to <u>areas with risk of Zika</u> (including those areas with current or past transmission but no current outbreak), the potential risks of travel should be discussed. If deciding to travel, patients should be advised of strict precautions to protect themselves from mosquito bites and sexual transmission:

- 1. Apply EPA-registered mosquito repellents; wear long-sleeved shirts and long pants; and use air conditioning or window/door screens to keep mosquitoes outside, or use a mosquito bed net.
- 2. Use condoms/barriers correctly every time they have sex, or abstain from sex.

After returning from an area with risk of Zika, *use mosquito repellent for 3 weeks* to prevent spreading Zika to California mosquitoes and the community.

People who have Zika infection or have been potentially exposed to Zika virus (through travel or sexual contact) should abstain from sex or use condoms (male or female) and dental dams to prevent transmitting the virus to their sexual partner, as follows:

- Pregnant couples in which either partner is exposed or infected should abstain from sexual contact or use barrier protection for the duration of the pregnancy.
- **Non-pregnant women** should abstain from sexual contact or use barrier protection and effective contraception to prevent pregnancy for **2 months** after last exposure or symptom onset.
- **Males** should abstain from sexual contact or use barrier protection for **3 months** after last exposure or symptom onset.

Zika Outreach & Education Material Toolkits are available. Toolkits address Zika and -Pregnancy, -Travel, -Family Planning, -Sex, and -Men and contain posters (in English and Spanish), discussion points, and social media posts. They are available on the <u>CDPH Zika</u> <u>Outreach & Education Materials website</u>

(https://www.cdph.ca.gov/Programs/CID/DCDC/Pages/ZikaOutreachandEducationMaterials.aspx)

General Population

Zika virus testing is indicated for <u>symptomatic</u> pregnant women who have been <u>exposed</u> to Zika within 2 weeks of symptom onset. Symptomatic pregnant women should undergo testing for Zika virus according to <u>Laboratory Testing</u>, below. For asymptomatic pregnant women living in or with recent travel to an area with risk of Zika outside the U.S. and its territories, Zika virus testing is **NOT** routinely recommended, but NAT testing may still be considered. Use the <u>CDC Updated</u> <u>Zika Testing Guidance</u> as a quick reference for testing recommendations. Symptomatic non-pregnant patients should refer to testing guidance for dengue. Zika testing is **NOT** currently recommended for this group based on the current epidemiology of these viruses.

Evaluation for Possible Local Transmission: The risk of local Zika virus transmission in California is low. However, mosquitoes that can transmit Zika virus are present in some parts of California.¹ To rule out a possible case of locally transmitted Zika infection in a California region with a local *Aedes* vector mosquito population, lab testing for Zika may be considered in consultation with the local public health department and CDPH if Zika virus infection is suspected in a symptomatic patient <u>without</u> recent travel or sexual exposure history, including newborns with findings consistent with congenital Zika syndrome and no maternal exposure history.

Pregnant Patients and Their Sexual Partners

Pregnancy Outcomes

Zika virus infection during pregnancy has been linked to problems such as miscarriage, stillbirth, birth defects, and other developmental delays that may be revealed as we continue to follow these infants.

Zika causes microcephaly and other serious brain anomalies in infants. *Zika-associated birth defects* include microcephaly, calcium deposits in the brain indicating possible brain damage, thin cerebral cortices with enlarged ventricles and excess fluid in the brain cavities and surrounding the brain, absent or poorly formed brain structures (i.e. corpus callosum, cerebellum, cerebellar vermis, and ventral cord), abnormal gyral patterns, abnormal eye development (e.g. microphthalmia, coloboma, intraocular calcifications, optic nerve hypoplasia/atrophy, macular scarring with focal pigmentary retinal mottling), or other problems resulting from damage to brain that affects nerves, muscles and bones, such as clubfoot or other limb contractures, and sensorineural hearing loss. Other reported neurologic sequelae include abnormalities of tone or movement, dysphagia, and epilepsy. Some infants without structural eye lesions may have cortical visual impairment.

¹ See <u>a map of California counties where these mosquitoes are present</u> or view a <u>more detailed interactive map</u> <u>about the distribution of *Aedes* mosquitoes in California</u>.

Congenital Zika syndrome is unique to fetuses and infants infected with Zika virus before birth and is described by a spectrum of features, including:

- Severe microcephaly in which the skull has partially collapsed
- Decreased brain tissue with a specific pattern of brain damage, including subcortical calcifications
- Damage to the back of the eye, including macular scarring and focal pigmentary retinal mottling
- Congenital contractures, such as clubfoot or arthrogryposis
- Hypertonia restricting body movement soon after birth

In 2016, about 5% of fetuses and infants born to women with laboratory evidence of recent possible Zika virus infection in the U.S. territories had possible Zika-associated birth defects, comparable to the percentage reported in the 50 U.S. states during 2016. Among women with confirmed recent Zika virus infection in the *first trimester*, between 8% (U.S. territories) and 15% (50 U.S. states and DC) had a fetus or infant with Zika-associated birth defects. The discrepancy between populations may be attributed in part to the laboratory definition of "confirmed" infection, with U.S territories using NAT (e.g. RT-PCR) only whereas the 50 U.S. states/DC confirmed infection using either NAT or serology.

Based on data from the U.S. Territories and Associated States in <u>an August 10,</u> <u>2018, MMWR Vital Signs report</u>, among children ages 1 year or older born to women with laboratory evidence of confirmed or possible Zika virus infection, 6% had at least one Zika-associated birth defect, 9% had at least one neurodevelopmental abnormality possibly associated with congenital Zika virus infection, and 1% had both.

Many unknowns related to Zika virus infection in pregnancy remain. The full spectrum of defects caused by Zika virus infection in pregnancy continues to evolve, and factors that contribute to a woman's risk of adverse pregnancy or birth outcomes continue to be a subject of research.

Among infants with prenatal exposure to Zika virus, absence of microcephaly at birth does not exclude congenital Zika virus infection or the presence of Zika-related brain and other abnormalities.

Prevention

Pregnant women in any trimester or within 2 months of anticipated pregnancy should not travel to areas with an outbreak of Zika. Before traveling to other areas with risk of Zika (which may include areas with current or past transmission but not current outbreaks), pregnant women should talk to a healthcare provider about potential risks and should follow strict precautions to prevent mosquito bites and sexual exposure to Zika if deciding to travel.

If pregnant women or their sexual partners who have lived in or traveled to an area with Zika are unable to abstain from sex for the duration of the pregnancy, they should use

condoms (male or female) and dental dams from start to finish every time they have sex (oral, vaginal, or anal) during the pregnancy. This includes same-sex couples and applies even if the pregnant woman's partner does not have symptoms of Zika or feels sick. Pregnant women should not share sex toys throughout the entire pregnancy.

Women should avoid exposure to Zika virus within 2 months of anticipated pregnancy. If exposure occurs, follow the testing <u>recommendations</u> for women exposed during pregnancy.

Screening for Exposure History

- 1. Health care providers should ask all pregnant women at *every* prenatal visit about their residence in and travel history to areas with risk of Zika² and the residence/travel history of their sexual partners.
- 2. Providers should ask about exposure *before* and *during* the current pregnancy including place, duration, and type of travel in order to understand the potential intensity of exposure.

Pediatricians and primary care providers should ask about possible maternal Zika exposure, Zika virus test results, special testing or evaluation, examinations or diagnoses by pediatric subspecialists, signs of congenital Zika syndrome, or any additional concerns about the baby during newborn care. Pediatricians should be aware that clinical signs of congenital Zika syndrome may develop or become evident after birth, including post-natal onset microcephaly, post-natal onset hydrocephalus in infants born with microcephaly, neurologic status, development, and vision impairment.

Zika Virus Testing for Pregnant Patients

CDPH, CDC, ACOG and the Society for Maternal Fetal Medicine recommend that all pregnant women should be evaluated for possible Zika virus exposure during each prenatal care visit. This evaluation should include an assessment of signs and symptoms of Zika virus disease, a travel history to an area with risk of Zika virus transmission², and a woman's sexual partner's potential exposure.

Symptomatic Pregnant Women with possible Zika virus exposure² and symptoms (acute onset of fever, rash, arthralgia, or conjunctivitis) of Zika virus disease should be tested for Zika virus as soon as possible:

- 1. Concurrent dengue and Zika virus NAT testing on a serum specimen, and Zika virus NAT on a urine specimen, and IgM testing *for dengue only*.
- 2. Zika virus IgM testing is **NOT** recommended for symptomatic pregnant women.
 - a. Zika IgM antibodies can persist for months to years following infection. Therefore, detecting Zika IgM antibodies might not indicate a recent infection.

² Refer to the <u>CDC Zika Travel Recommendation Map</u>.

- b. There is notable cross-reactivity between dengue IgM and Zika IgM antibodies in serologic tests. Antibodies generated by a recent dengue virus infection can cause the Zika IgM to be falsely positive.
- 3. If the Zika NAT is positive on a single specimen, the Zika NAT should be repeated on newly extracted RNA from the same specimen to rule out false-positive Zika NAT results. If the dengue NAT is positive, this provides adequate evidence of a dengue infection and no further testing is indicated.
- 4. If the IgM antibody test for dengue is positive, this is adequate evidence of a dengue infection and no further testing is indicated.

Asymptomatic Pregnant Women *living in or with recent travel to the U.S. and its territories* are **NOT** currently recommended for routine Zika virus testing.

- For asymptomatic pregnant women living in or with recent travel to an area with risk of Zika² outside the U.S. and its territories, Zika virus testing is NOT routinely recommended, but NAT testing may still be considered. Risk factors that may prompt testing include:
 - a. Locally-transmitted Zika infections reported in the region of travel at the time of the possible exposure
 - b. Sexual partner with travel to Zika-risk areas or unprotected (e.g., without use of male or female condom or dental dam) sexual exposure
 - c. Longer duration of travel (e.g., over four weeks) or multiple sexual exposures
 - d. Engagement in higher risk activities (e.g., outdoor recreation as opposed to indoor activities) while in an area with risk of Zika transmission
 - e. Known mosquito bites in areas with risk of Zika transmission
 - f. Lack of use of protective clothing and insect repellent on a regular basis in an area with risk of Zika transmission
 - g. Compromised integrity of housing in an area with risk of Zika transmission (e.g., lack of window screens or air conditioning)
 - h. Other household members diagnosed with Zika virus infection
 - i. High risk patient occupation (e.g., potential laboratory or needle stick exposure)
 - j. Patient is recipient of recent transfusions or transplants, especially in an area with risk of Zika transmission and there is not reliable testing of blood supply for Zika virus (the U.S. routinely tests blood donations for Zika virus)
 - k. Patient preferences and decision-making
- 2. Zika virus serologic testing is **NOT** recommended for asymptomatic pregnant women.
 - a. Zika IgM antibodies can persist for months to years following infection. Therefore, detecting Zika IgM antibodies might not indicate a recent infection.

b. There is notable cross-reactivity between dengue IgM and Zika IgM antibodies in serologic tests. Antibodies generated by a recent dengue virus infection can cause the Zika IgM to be falsely positive.

Pregnant women who have recent possible Zika virus exposure and who have a fetus with prenatal ultrasound findings consistent with congenital Zika syndrome should receive Zika virus testing to assist in establishing the etiology of the birth defects.

- 1. Zika virus NAT and IgM testing should be performed on maternal serum and NAT on maternal urine.
- 2. If the Zika virus NATs are negative and the IgM is positive, confirmatory PRNTs should be performed against Zika and dengue.
- 3. If amniocentesis is being performed as part of clinical care, Zika virus NAT testing of amniocentesis specimens should also be performed and results interpreted within the context of the limitations of amniotic fluid testing. It is unknown how sensitive or specific RNA NAT testing of amniotic fluid is for congenital Zika virus infection or what proportion of infants born after infection will have abnormalities.
- 4. Testing of placental and fetal tissues may also be considered (see guidance for Collecting and Submitting Specimens at Time of Birth for Zika virus Testing).

Reporting to Public Health

Pregnant patients with laboratory evidence of Zika virus infection or suspect cases with Zika-associated birth defects should be **reported immediately to the local health department**.

Providers who are using the CalREDIE Provider Portal may enter the information directly into CalREDIE. Otherwise, providers should check with their local health department on how to report cases.

Reporting of these patients will enable patient tracking and expedite testing and reporting of results.

See <u>contact list for local health department communicable disease reporting</u> (https://www.cdph.ca.gov/Programs/CCLHO/Pages/LHD%20Contact%20Informa tion.aspx)

Management and Monitoring Recommendations for Zika-infected Pregnant Patients

Ultrasound: Pregnant women with laboratory evidence of Zika virus infection should be monitored during pregnancy. Prenatal, Perinatal and Pediatric providers are referred to the <u>ACOG</u> and the <u>AAP</u> Zika Virus websites for recommendations of the specialty organizations. All pregnant women are recommended to receive a comprehensive ultrasound exam to evaluate fetal anatomy at 18-22 weeks' gestation.

• **Pregnant women with confirmed or probable Zika virus infection** should be counseled and monitoring considered with serial fetal ultrasounds every 3–4 weeks to assess fetal anatomy, particularly neuroanatomy, and to monitor growth. Data to guide timing of serial ultrasounds are limited. Obstetric providers may consider extending the interval between ultrasounds based on patient preference and clinical judgement.

- Exposed mothers without laboratory evidence of possible Zika infection should receive routine ultrasound monitoring.
- For pregnant women with an exposure more than 12 weeks prior to seeking prenatal care or with ongoing exposure, decisions for serial ultrasound monitoring beyond standard prenatal care should be made on a case by case basis, taking into consideration the individual circumstances of the exposure and patient preferences. Any abnormalities identified by prenatal ultrasound should be followed with repeat imaging.
- Major ultrasound findings that have been associated with congenital Zika syndrome include microcephaly, intracranial calcifications, ventriculomegaly, arthrogryposis, and abnormalities of the corpus callosum, cerebrum, cerebellum, and eyes.

Amniocentesis: Amniocentesis should be individualized for each clinical circumstance in accordance with the recommendations of clinical specialists.

- It is unknown how sensitive or specific NAT (e.g. RT-PCR) testing of amniotic fluid is for congenital Zika virus infection or whether a positive test is predictive of subsequent fetal abnormalities.
- A negative test result on amniotic fluid cannot rule out congenital Zika virus infection.

The CDC provides <u>counseling guidance and clinical tools</u> online (https://www.cdc.gov/zika/hc-providers/pregnant-woman.html). However, it should be noted, in keeping with the discretion extended to states to apply regional epidemiology as described above, that CDPH recommendations may deviate slightly from recommendations applied to the U.S. population in general.

Counseling Recommendations

Free and confidential counselors speaking English and Spanish are available at **MotherToBaby** to talk to families about Zika virus infection or diagnosis during pregnancy. Contact information: Phone 1-866-626-6847, Text 1-855-999-3525, or <u>contact information webpage</u> (http://mothertobaby.org/contact-expert/).

Visit the <u>CDC's Zika patient counseling webpage</u> for more information and specific counseling suggestions (https://www.cdc.gov/pregnancy/zika/testing-follow-up/patient-counseling-pregnant-women.html).

Patients who Traveled to Areas with Risk of Zika Prior to Conception

For women or men with or without <u>symptoms</u> of Zika virus disease who meet criteria for Zika <u>exposure</u> or have been diagnosed with Zika virus disease, CDC recommends that healthcare providers:

• Advise women to wait at least 2 months after return from travel or

symptom onset before trying to get pregnant.

- Advise men to wait **at least 3 months** after return from travel or symptom onset before trying to get pregnant with their partner.
- People with possible Zika exposure should not have sex (vaginal, oral, or anal) during this time period or should use condoms (male or female) and dental dams to avoid infecting their partners. To be effective, condoms must be used every time, from start to finish during vaginal, anal, and oral sex, and there should be no sharing of sex toys.

The relationship between the time of conception and maternal Zika virus viremia and the ultimate effects of disease on the fetus remains under study, but Zika infection earlier in pregnancy (e.g., during first trimester) appears to increase the likelihood of more severe neurodevelopmental sequelae in the infant.

Zika virus testing for the purpose of assessing the risk of sexual transmission is of uncertain value because the current understanding of the duration and pattern of shedding in the male and female genitourinary tract is limited. Therefore, testing of specimens to assess risk for sexual transmission is currently *not* recommended.

Patients who are Not Pregnant but Planning Pregnancy

<u>CDC recommends</u> that women trying to get pregnant and their male partners talk to their healthcare provider before traveling to areas with risk of Zika.

Healthcare providers should discuss pregnancy intention and reproductive options with women of reproductive age. For women traveling to areas with Zika risk (See <u>Screening for Exposure History</u>), preconception care should include a discussion (ideally before travel) about mosquito bite prevention, signs and symptoms of Zika virus infection, and the potential risks associated with travel and Zika virus infection.

Health care providers should assist patients to access highly effective contraceptive methods (e.g. long acting reversible contraception) if they would like to delay pregnancy.

Patients should consider several factors regarding risk:

- Risk of acquiring vector-borne Zika depends on the duration and extent of exposure to infected mosquitoes and the steps taken to prevent mosquito bites.
- Most Zika virus infections are asymptomatic when they occur.

If patients do travel, because sexual transmission is possible, both men and women should strictly follow steps to prevent mosquito bites during the trip. See <u>CDPH Zika + Family Planning for discussion points</u> to share with patients.

Patients Undergoing Fertility Treatment

Zika virus transmission through assisted reproductive technology has not been reported; however, transmission through gametes or embryos is theoretically possible.

Fertility treatment for sexually active couples using their own gametes and embryos should follow the timing recommendations for persons attempting conception, although recommendations may need to be adjusted depending on individual circumstances (see above recommended waiting periods).

The Food and Drug Administration (FDA) has developed guidance for donated tissues in the context of a Zika virus outbreak, including donated sperm, oocytes, and embryos. The guidance states that living donors will be deemed ineligible for anonymous donation if they have any of the following risk factors:

- 1. Medical diagnosis of Zika virus infection in the past 6 months
- 2. Residence in or travel to an area with risk of Zika within the past 6 months
- 3. Within the past 6 months, had sex with a male partner who, during the 6 months before sexual contact, either 1) received a diagnosis of or experienced an illness consistent with Zika virus disease or 2) had traveled to an area with risk of Zika

FDA Tissue Donor Screening Recommendations

(https://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatory Information/Guidances/Tissue/UCM488582.pdf)

Infants

See the CDPH Information for California Birthing Hospitals

Zika Testing

Indications for Zika Virus Testing at Birth:

- 1. Infants with clinical findings suggestive of congenital Zika syndrome and possible maternal Zika virus exposure during pregnancy, regardless of maternal testing results.
- 2. Infants born to mothers with laboratory evidence of possible Zika virus infection during pregnancy.

Note: Birthing hospitals may consider collecting infant specimens for concurrent Zika virus testing if maternal testing is being done at delivery. If infant testing is being conducted but maternal infection is not yet confirmed, consider concurrent maternal testing to inform infant Zika test result interpretation.

Laboratory Testing of Infants for Congenital Zika Virus Infection:

- 1. Zika virus NAT testing should be performed on both infant serum and urine and Zika virus IgM antibody testing should concurrently be performed on infant serum. If non-negative IgM and negative Zika NAT, confirm with PRNT.
- 2. For infants with clinical findings consistent with congenital Zika syndrome, testing CSF for Zika virus NAT and IgM antibodies should be considered, especially if

serum and urine testing are negative and another etiology has not been identified.

3. If CSF is collected for other purposes, NAT and IgM antibody testing should be performed on CSF.

Newborn Specimen Collection:

- 1. Newborn specimens should be collected within 2 days of delivery, if possible. If testing is performed later, distinguishing between congenital, perinatal, and postnatal infection is difficult. If timing of infection cannot be determined, infants should be managed as if they have congenital Zika virus infection.
- 2. Testing cord blood is not recommended because of issues with precision and accuracy.

See <u>CDC Evaluation and Testing for Congenital Zika Virus Infection</u> for additional information.

Placental Testing:

Pathology testing of placental tissues for Zika virus infection may be considered to aid in maternal diagnosis for women with an exposure history/epidemiologic link to an area with risk of Zika, as appropriate.

 Placental Zika virus testing may be considered on a case-by-case basis in consultation with public health and is prioritized for: 1) symptomatic mothers with probable (unspecified flavivirus) Zika virus infection; and 2) mothers with an infant or fetus with possible Zika virus-associated birth defects but no definitive diagnosis of Zika virus infection during pregnancy. See the <u>CDPH Information for</u> <u>California Birthing Hospitals</u>.

Fetal Loss and Testing:

If a pregnant woman with laboratory evidence of Zika virus infection experiences a fetal loss, CDC recommends consideration of fetal and placental pathology testing for Zika virus infection on a case-by-case basis to aid in fetal or maternal Zika diagnosis. Hospitals should work with their <u>local health department</u> regarding specimen collection details.

See CDC Interim Guidance for Zika Virus Testing of Formalin-Fixed, Paraffin-Embedded Placental, Fetal, or Infant Autopsy Tissues for additional guidance and CDC Collecting and Submitting Placental and Fetal Tissue Specimens for Zika Virus Testing for tissue collection details.

Infant Evaluation

Newborn Evaluation and Management for Possible Congenital Zika Virus Infection:

Conduct Recommended Clinical Evaluation of All Newborn Infants Born to Mothers with Possible Zika Virus Exposure

See the <u>CDC algorithm</u>, Evaluation for Infants with Possible Congenital Zika Virus Infection (https://www.cdc.gov/pregnancy/zika/testing-follow-up/documents/pediatric-evaluation-follow-up-tool.pdf) and the <u>CDPH Information for California Birthing</u>

Hospitals.

Pediatricians, primary care providers and neonatologists should ask about possible maternal Zika virus exposure or possible congenital Zika syndrome during newborn care. Maternal exposure history and maternal and infant Zika test results should be shared with pediatric providers caring for the infant as an outpatient. In addition to Zika virus testing as outlined above and in <u>Laboratory Testing</u>, below, see recommendations below for the care of infants born to mothers with possible Zika virus exposure.

Infants with abnormalities consistent with congenital Zika syndrome

Regardless of maternal Zika virus test results, infants should have:

- 1. Routine newborn care with comprehensive physical exam, including <u>standardized measure of head circumference</u>
- 2. Zika virus testing
- 3. Head ultrasound by age 1 month
- 4. Comprehensive ophthalmologic exam by 1 month
- 5. Newborn hearing screen, preferably automated auditory brainstem response (ABR). If not ABR for newborn screen then ABR by 1 month
- 6. Evaluate for other causes of congenital anomalies
- 7. Refer to developmental specialist and <u>early intervention</u> services
- 8. Provide family support services.
- 9. Consider additional consultation with infectious disease specialist, clinical geneticist, neurologist, and others based on clinical findings

Further neuroimaging (MRI, CT) in consultation with a neurologist may be considered. Transfer to a hospital with subspecialty care typically is not necessary unless there is an urgent clinical need.

Infants with normal exams

Born to mothers with *laboratory evidence of possible Zika virus infection during pregnancy* should have:

- 1. Routine newborn care with comprehensive physical exam, including <u>standardized measurement of head circumference</u>
- 2. Zika virus testing
- 3. Head ultrasound by 1 month of age to detect subclinical brain findings
- 4. Comprehensive ophthalmologic exam by 1 month of age to detect subclinical eye findings
- 5. Newborn hearing screen, preferably automated ABR by 1 month of age
- 6. If findings suggestive of congenital Zika syndrome are identified

at any time, evaluation should follow recommendations for infants with clinical findings of congenital Zika syndrome with referral to appropriate specialists and further evaluation

Born to mothers with <u>no</u> laboratory evidence of Zika virus infection should have:

- 1. Routine newborn care with comprehensive physical exam, including <u>standardized measurement of head circumference</u>
- 2. Newborn hearing screening
- 3. Further clinical evaluation for congenital Zika virus infection is not routinely indicated but health care providers can consider additional evaluation in consultation with families, taking into account infant's complete physical exam with emphasis on neurologic findings, risk of screening (e.g., identification of incidental findings), and maternal risk factors for Zika infection (e.g., presence and timing of symptoms, and type, location and length of possible Zika virus exposure)
- 4. If findings suggestive of congenital Zika syndrome are identified at any time, evaluation should follow recommendations for infants with clinical findings of congenital Zika syndrome with referral to appropriate specialists and further evaluation

In-hospital Level of Care for Newborn:

See <u>CDPH Information for California Birthing Hospitals</u>. Unless otherwise medically necessary, newborns with findings consistent with congenital Zika syndrome are not required to be transferred to the neonatal intensive care unit (NICU) for infant examinations, evaluations, or specimen collection. Health care providers should consider both the immediate needs of the infant and the potential negative impact of possible separation from his or her family. Rooming-in with mother is recommended when possible. Transfer to a facility with access to pediatric subspecialty care typically is not necessary unless there is an urgent clinical need.

In addition, free and confidential counselors speaking English and Spanish are available at <u>MotherToBaby</u> to talk to families about Zika virus infection during pregnancy.

Neonatal Evaluation for Acute Perinatal Zika Virus Infection:

Maternal-infant transmission of Zika virus is possible during delivery. Acute Zika virus disease should be suspected in a symptomatic infant within the first 2 weeks of life whose mother was potentially exposed to Zika virus within approximately 2 weeks of delivery. Infant symptoms in acute infection include one or more of the following: fever, rash, conjunctivitis, or arthralgia. (See under *Postnatal Zika Virus Infection* on the CDC's Congenital Zika Virus Infection Evaluation & Testing webpage.)

Infant Follow-up

Arrange Follow-up Evaluation and Management Prior to Hospital Discharge for ALL

Infants:

All infants, including those without findings of congenital Zika syndrome, should have an established medical home to receive routine pediatric preventive care, to include comprehensive physical exams, growth parameters (e.g., head circumference, weight, and length), immunizations, developmental monitoring and screening using <u>validated</u> <u>screening tools recommended by the American Academy of Pediatrics</u>, and <u>vision</u> <u>screening as recommended by the American Academy of Pediatrics</u>.

For normal-appearing infants with mothers with laboratory evidence of Zika infection, a head ultrasound, comprehensive ophthalmologic exam and ABR should be done by 1 month of age if not done at the birthing hospital.

The hospital medical record, including Zika testing and evaluation results for both the mother and infant, should be shared with the outpatient pediatric care provider(s) caring for the infant after discharge, including monitoring for signs of postnatal-onset congenital Zika syndrome.

Additional Follow-up Care of Infants with Findings Consistent with Congenital Zika Syndrome:

Infants with clinical findings consistent with congenital Zika syndrome require a multidisciplinary team and an established medical home for coordination of care to ensure abnormal findings are addressed. Follow-up appointments with specialists and services recommended during hospital evaluation should be made prior to discharge. Decisions on further evaluation should be guided by clinical findings and made in consultation with the family. Follow-up visits with specialists will be based on the specialist(s) recommendations. Birthing hospitals and primary care providers may consider using <u>Zika Care Connect</u>, which provides a searchable network of healthcare specialists who care for patients affected by Zika.

- 1. Pediatric providers should maintain vigilance for additional clinical findings:
 - Neurologic status and delays in development
 - Post-natal onset microcephaly
 - Signs of increasing intracranial pressure (e.g., vomiting, mental status changes) should prompt brain imaging to assess for hydrocephalus after birth
 - Visual impairment
 - Signs of dysphagia or problems with swallowing
 - Consider diaphragmatic paralysis among infants with respiratory distress
- All infants with congenital Zika syndrome should be referred to a developmental specialist and <u>Early Start</u> early intervention services through their <u>local Regional</u> <u>Center</u>.

For referral to the California Children's Services (CCS) program, contact <u>your local</u> <u>county CCS office</u>. California Children's Services (CCS) is a state program for children with certain diseases or health problems. Eligible children will be referred to providers knowledgeable in the care of children with special health care needs.

Family Support:

Families should be connected with family supportive services in the community prior to hospital discharge.

Postpartum Patients and Breastfeeding

Although Zika virus RNA has been detected in breast milk, transmission of Zika infection through breastfeeding has not been documented.

Mothers are encouraged to breastfeed infants even in areas where Zika virus is found, as available evidence indicates the benefits of breastfeeding outweigh any theoretical risks associated with Zika virus infection transmission through breast milk. (See <u>CDC</u> <u>MMWR</u>, February 26, 2016)

There are no current recommendations to test breast milk.

There is no current evidence that Zika virus infection in one pregnancy poses a risk of infection or birth defects in future pregnancies.

Patients with Guillain-Barré Syndrome

Patients who have **both** a diagnosis of Guillain-Barré Syndrome and meet criteria for <u>exposure</u> to Zika virus should undergo testing for Zika virus according to <u>Laboratory Testing</u>, below.

Laboratory Testing

Testing Recommendations by Patient Population for Exposed Patients

Testing for Non-Pregnant Symptomatic Individuals:

Symptomatic non-pregnant patients should refer to testing guidance for <u>dengue</u>. Zika testing is **NOT** currently recommended for this group based on the current epidemiology of these viruses.

Testing for Symptomatic Pregnant Women:

- 1. Concurrent dengue and Zika virus NAT testing on a serum specimen, and Zika virus NAT on a urine specimen, and IgM testing for dengue only.
- 2. Zika virus IgM testing is **NOT** recommended for symptomatic pregnant women.
 - a. Zika IgM antibodies can persist for months to years following infection. Therefore, detecting Zika IgM antibodies might not indicate a recent infection.
 - b. There is notable cross-reactivity between dengue IgM and Zika IgM antibodies in serologic tests. Antibodies generated by a recent dengue virus infection can cause the Zika IgM to be falsely positive.
- 3. If the Zika NAT is positive on a single specimen, the Zika NAT should be repeated on newly extracted RNA from the same specimen to rule out false-positive Zika NAT results. If the dengue NAT is positive, this provides adequate evidence of a dengue infection and no further testing is indicated.
- 4. If the IgM antibody test for dengue is positive, this is adequate evidence of a dengue infection and no further testing is indicated.

Testing for Asymptomatic Pregnant Women:

For asymptomatic pregnant women *living in or with recent travel to the U.S. and its territories*, routine Zika virus testing is **NOT** currently recommended.

- 1. For asymptomatic pregnant women living in or with recent travel to <u>an area with</u> <u>risk of Zika</u> *outside the U.S. and its territories*, Zika virus testing is **NOT** routinely recommended, but NAT testing may still be considered.
- 2. Zika virus serologic testing is **NOT** recommended for asymptomatic pregnant women.
 - a. Zika IgM antibodies can persist for months to years following infection. Therefore, detecting Zika IgM antibodies might not indicate a recent infection.
 - b. There is notable cross-reactivity between dengue IgM and Zika IgM antibodies in serologic tests. Antibodies generated by a recent dengue virus infection can cause the Zika IgM to be falsely positive.

Testing for Pregnant Women with Prenatal Findings Consistent with Congenital Zika Virus Disease in the Infant:

- 1. Zika virus NAT and IgM testing should be performed on maternal serum and NAT on maternal urine.
- 2. If the Zika virus NATs are negative and the IgM is positive, confirmatory PRNTs should be performed against Zika and dengue.
- 3. If amniocentesis is being performed as part of clinical care, Zika virus NAT testing of amniocentesis specimens should also be performed and results interpreted within the context of the limitations of amniotic fluid testing. It is unknown how sensitive or specific RNA NAT testing of amniotic fluid is for congenital Zika virus infection or what proportion of infants born after infection will have abnormalities.
- 4. Testing of placental and fetal tissues may also be considered (see guidance for Collecting and Submitting Specimens at Time of Birth for Zika virus Testing).

Testing for Infants with Possible Congenital Exposure to Zika Virus Should Occur *Ideally* within the First Two Days Following Delivery:

- 1. Zika virus NAT testing should be performed on both infant serum and urine and Zika virus IgM antibody testing should concurrently be performed on infant serum.
 - a. The plaque reduction neutralization test (PRNT), which measures virusspecific neutralizing antibodies, can be used to help identify false-positive results. If the infant's initial sample is IgM non-negative and NAT negative, but PRNT was not performed on the mother's sample, PRNT for Zika and dengue viruses should be performed on the infant's initial sample. If Zika virus PRNT is negative, this suggests that the infant's Zika virus IgM test is a false positive.
 - b. Birthing hospitals may consider collecting infant specimens for concurrent Zika virus testing if maternal testing is being done at delivery. If infant testing is being conducted but maternal infection is not yet confirmed, consider concurrent maternal testing to inform infant Zika test result interpretation.
- 2. If CSF is collected for other purposes, NAT and IgM antibody testing should be performed on CSF.
- 3. For infants with clinical findings consistent with congenital Zika syndrome, testing CSF for Zika virus NAT and IgM antibodies should be considered, especially if serum and urine testing are negative and another etiology has not been identified.

Test Performance by Specimen Type

Zika NAT Testing

- 1. NAT testing can most reliably detect Zika virus in serum during the first two weeks following onset of symptoms or infection and in urine or whole blood for the first three weeks following onset of infection.
- 2. Recent evidence suggests that Zika virus RNA can be detected for a long period of time in serum (Oduyebo T et al, July 2017) and perhaps longer in whole blood versus the serum of infected persons. There are documented cases in which Zika virus RNA has been detected in various samples for longer periods of time than originally determined. Zika virus RNA has been shown to be detectable in whole blood and urine for longer periods of time than in serum. While a positive NAT test beyond 14 days from onset of symptoms or infection is significant, a negative NAT test, regardless of the timing of testing, does not rule out a recent Zika virus infection.

Zika IgM Testing

- Zika antibody may be detected as early as a few days following onset of infection, but a negative IgM test result on a specimen collected <2 weeks after onset does not rule out a recent Zika virus infection (i.e., IgM may be falsely negative). IgM testing should be performed on specimens collected between 2 weeks and 12 weeks following onset of infection.
- IgM tests may remain positive for significantly longer than 12 weeks. Because of this, the interpretation of timing of infection for a positive result during pregnancy is unreliable unless the timing of seroconversion is documented (see <u>May 5</u>, <u>2017, CDC Health Advisory</u>, https://emergency.cdc.gov/han/han00402.asp).
- 3. Positive or equivocal Zika IgM results require confirmatory testing because IgM tests for Zika virus may give false positive results. The main reason for false positive results is that there is serologic cross reactivity among related flaviviruses including dengue, West Nile, yellow fever, and Japanese encephalitis viruses. Previous exposure to or vaccination against a flavivirus could result in a false positive Zika virus IgM. Some false positives may be due to other non-specific reactions without prior virus exposure.
- 4. Information that may help to interpret a potentially false positive IgM result by influencing pretest probability include:
 - a. History of other virus infection or vaccination
 - b. Symptoms of acute infection and timing related to exposure
 - c. Confirmed Zika infection in a sexual partner or household member
 - d. Other evidence of congenital Zika infection or complication, such as fetal microcephaly or intracranial calcifications
 - e. Duration and quality of travel exposure

Confirmatory PRNT Testing

- 1. Confirmatory PRNT testing results could come back as:
 - a. Evidence of a recent infection with Zika virus
 - b. Evidence of a recent infection with another virus (such as dengue)
 - c. Evidence of infection with a flavivirus of undetermined type (positive for more than one virus)
 - d. No evidence of infection (preliminary IgM test is false positive)

For symptomatic and asymptomatic pregnant women with possible Zika virus exposure who seek care >12 weeks after symptom onset or possible exposure, NAT testing (e.g. RT-PCR testing) should be performed on maternal serum and whole blood and urine, if submitted.

Because IgM antibody and viral RNA levels decline over time, negative testing conducted greater than 12 weeks after symptom onset or possible exposure may be a false negative result and does not rule out recent Zika virus infection. Therefore, when testing beyond 12 weeks after symptom onset or possible exposure, serial fetal ultrasounds should be considered during prenatal care.

Specimen Collection, Storage, and Submission

See VRDL Testing Guidance for Arboviruses

Amniotic fluid, if collected, should be collected in a CSF collection tube. The sample should be frozen (-70C) and shipped on dry ice.

If whole blood is submitted, it will require an EDTA whole blood specimen in addition to serum for a potential subsequent IgM test and, if elected, a urine specimen.

Test Turn Around Time

The time required for results of testing to be reported varies depending upon specimen transport, sample type submitted, timing of sample collection from symptom onset, the lab performing testing, and the type of test being performed. Some tests are rapid while others take up to 7 days to complete.

Zika virus testing by detection of viral RNA (nucleic acid testing, NAT) or serology (IgM antibody testing) is available in commercial clinical laboratories throughout California and, as is typical of screening for other infectious diseases, can be directed to commercial laboratory resources. Specimens should be submitted to commercial laboratories for processing using regular clinical testing protocols.

Some local public health labs may conduct Zika virus testing. Contact your local public health department to see if testing is available locally. CDPH Viral and Rickettsial Disease Laboratory (VRDL) performs confirmatory Zika virus testing as necessary to accurately monitor the incidence of Zika virus disease in California. PRNT testing for confirmation of positive Zika IgM test results is only conducted in California at VRDL at this time.

The U.S. Zika Pregnancy and Infant Registry (USZPIR)

The purpose of the USZPIR is to provide data to further elucidate the full range of potential outcomes for fetuses and infants of mothers with Zika virus infection during pregnancy; to anticipate and plan to meet the needs of pregnant women and their families for clinical and public health services; and to inform updates to clinical guidance for managing pregnant women and their affected infants.

The USZPIR includes both asymptomatic and symptomatic pregnant women with laboratory evidence of possible Zika virus infection whose pregnancies are completed on or before March 31, 2018 and follow up on their infants up to 2 years of age. The USZPIR also includes infants with laboratory evidence of congenital Zika virus infection and their mothers.

- CDPH is the point of contact for USZPIR data submission for California to CDC. Providers and local health departments should submit data forms to CDPH for compilation and submission to CDC. <u>Instructions for data submission</u> are available on the CDPH US Zika Pregnancy and Infant Registry website (https://www.cdph.ca.gov/Programs/CID/DCDC/Pages/USZikaPregnancyRegistry.aspx).
- Local health departments or CDPH may be in contact with health care providers to assist with data collection.
- Potential data collection points in the USZPIR include: the time of maternal diagnosis; second trimester; third trimester; at delivery; and infant follow-up at 2, 6, 12, 18, and 24 months of age.
- Data collection for the Zika Pregnancy and Infant Registry is intended to capture existing information in the medical record at the above milestones.
- For questions about enrolling affected pregnant patients and their infants with the USZPIR, contact us at <u>ZikaOutcomes@cdph.ca.gov</u> or call (510) 620-3151.

Prevention of Transmission

Protection Against Mosquito Vector Transmission

The best way to prevent the spread of Zika through mosquito bites is by:

- Using <u>Environmental Protection Agency (EPA)-registered insect repellents</u> as directed by the product label. If also using a sunscreen, apply insect repellent **after** having applied sunscreen.
- Wearing long sleeved shirts and long pants
- Treating your clothing and gear with permethrin or buying pre-treated items
- Covering the crib, stroller, and baby carrier with mosquito netting
- Staying in places with air conditioning and window and door screens to keep mosquitoes outside
- Sleeping under a mosquito bed net if air conditioned or screened rooms are not available or if sleeping outdoors
- See <u>CDPH mosquito control information</u> (https://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Libra ry/MosquitoControlFAQs.pdf) and an <u>insect repellent guide for pregnant</u> <u>women</u> (https://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Libra ry/InsectRepellentandPregnancyGuideFinal.pdf)

Special precautions for infants and children younger than 3 years old:

- Do not use insect repellent on babies younger than 2 months old
- Caregivers/adults should spray insect repellent onto their own hands and then apply to a child's face
- Do not apply insect repellent onto a child's hands, eyes, mouth, or cut or irritated skin
- Do not use products containing oil of lemon eucalyptus or para-menthanediol on children younger than 3 years old

California residents exposed to Zika virus through travel to an area at risk for Zika or through sexual contact with a person with exposure should apply mosquito repellent and avoid mosquito exposure for three weeks after return to California to prevent potentially transmitting the virus to local mosquitoes. This is especially important for residents of California counties known to be habitat for the vector mosquitoes, *Aedes aegypti* and *Aedes albopictus*. See a map of California counties where these mosquitoes are present.

View an <u>interactive map</u> with more detailed information about the distribution of *Aedes* vector mosquitoes in California.

Protection Against Sexual Transmission

If patients are planning travel to areas where Zika is present, they should be advised to abstain from sex or use condoms (male or female) and dental dams correctly every time they have sex during travel.

People who have Zika infection or have been potentially exposed to Zika (through travel or sexual contact) should abstain from sex or use condoms (male or female) and dental dams to prevent transmitting the virus to their sexual partner, as follows:

- Pregnant women should abstain from sexual contact or use barrier protection for the duration of the pregnancy.
- **Non-pregnant females** should abstain from sexual contact or use barrier protection for **2 months** after last exposure or symptom onset.
- **Males** should abstain from sexual contact or use barrier protection for **3 months** after last exposure or symptom onset.

Protection Against Transmission in Healthcare Settings

Standard precautions are recommended to prevent the spread of Zika virus in healthcare settings.

The U.S. Food and Drug Administration posted new guidance for the screening of donated blood for Zika virus on August 26, 2016 under Title 21 of the Code of Federal Regulations (CFR) 630.3(h)(2).

The potential for transmission of Zika virus to the recipient of transplanted tissue is possible, but the magnitude of the risk of Zika transmission by solid organ transplantation is unknown at this time. It is recommended by organ procurement organizations that donor deferral should be considered for recipients who are women of childbearing age or pregnant if there is history of donor travel to Zika-endemic areas in the 28 days prior to donation. In the case of potential living donors with Zika infection, donation should be deferred where possible. See <u>Organ Procurement and Transplantation Network's guidance on Zika virus</u> (https://optn.transplant.hrsa.gov/news/guidance-on-zika-virus/).

Useful Resources

Patient Education Toolkits

CDPH has created various educational materials that you can use for patient outreach. These materials are organized into four toolkits for <u>Zika and Pregnancy</u>, <u>Zika and Travel</u>, <u>Zika and Family Planning</u>, <u>Zika and Men</u>, and <u>Zika and Sex</u>.

Each toolkit contains educational posters in English and Spanish, talking points for healthcare providers and educators, and social media posts that you can use on your social media sites.

All of these materials are available for free download on the CDPH Zika webpage, and printed posters are available for order while supplies last.

CDPH Zika Website

http://www.cdph.ca.gov/Zika

Public Q & A

See the CDPH Zika Questions and Answers resource for the public.

Quick References and Tools

<u>CDPH: Assessment and Testing for Zika Virus Infection in Pregnant Women and their</u> <u>Newborns: Information for California Birthing Hospitals</u>

https://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/CABirthing HospitalsInfo.pdf

CDC: Evaluation for Infants with Possible Congenital Zika Virus Infection:

https://www.cdc.gov/pregnancy/zika/testing-follow-up/documents/pediatric-evaluation-follow-up-tool.pdf

<u>CDC Interim guidance: Evaluation and Testing of Infants with Possible Congenital Zika</u> <u>Virus Infection</u>: http://www.cdc.gov/zika/pdfs/zika_peds.pdf

VRDL Zika Virus Information:

https://www.cdph.ca.gov/Programs/CID/DCDC/Pages/Zika_VRDL.aspx

VRDL Laboratory Testing Guidance for Arboviruses: https://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/ZIKV-CHIKV-DENV-TestingGuidance.pdf

<u>CDC Zika Virus Information for Healthcare Providers</u>: https://www.cdc.gov/zika/hc-providers/index.html

American College of Obstetricians and Gynecologists Committee Opinion – Management of Patients in the Context of Zika Virus:

https://www.acog.org/Clinical-Guidance-and-Publications/Committee-Opinions/Immunization-Infectious-Disease-and-Public-Health-Preparedness-Expert-Work-Group/Management-of-Patients-in-the-Context-of-Zika-Virus

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