Zika Hospital Toolkit for Los Angeles County

March 20, 2018

REVISED

County of Los Angeles Public Health

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A PDF of this toolkit is available on our website: ph.lacounty.gov/ZikaProviders

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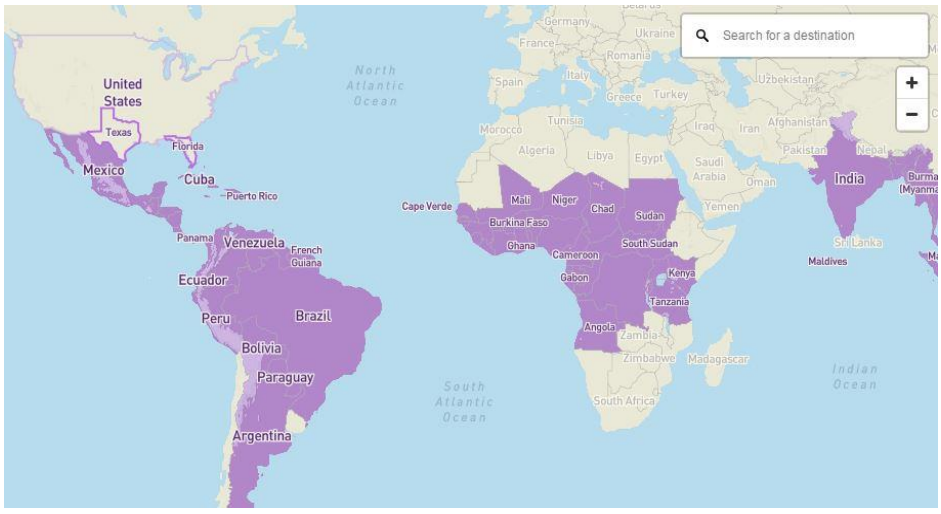
BACKGROUND

Zika virus belongs to the Flavivirus genus in the *Flaviviridae* family, and is closely related to other globally important flaviviruses, including dengue, yellow fever, Japanese encephalitis, West Nile, and tick-borne encephalitis viruses.[1] Zika virus is primarily transmitted to humans through Zika-infected *Aedes* sp. mosquitos but can also be transmitted through sex and blood products. Zika virus is the first mosquito-borne infection linked to congenital birth defects and is associated with microcephaly, intrauterine growth retardation, ocular defects, other serious brain abnormalities, and fetal death.

Before 2015, Zika virus disease outbreaks have occurred in areas of Africa, Southeast Asia, and the Pacific Islands.[2] Since May 2015, the CDC has responded to increased reports of Zika in the Americas.[3] Currently, Zika is a risk in many countries and territories. The Los Angeles County (LAC) population is highly mobile and frequently travels to areas of ongoing Zika virus transmission for family visits, business, and leisure. This population includes pregnant women at risk of acquiring Zika while abroad or via sexual transmission from male partners with Zika virus infection. The risk of local mosquito-borne Zika transmission is compounded by the presence and expansion of *Aedes albopictus* and *A. aegyptii* mosquitoes within LAC. On September 29, 2017, the CDC deactivated its emergency response for Zika virus to transition efforts to normal program operations.[4]

The CDC has created an interactive map at https://wwwnc.cdc.gov/travel/page/world-map-areas-with-zika where people preparing to travel may check to see if it is safe to travel (Figure 1). The highlighted purple areas in the map below indicate areas of risk of Zika infection.

Figure 1: World Map of Areas with Zika Risk



[1] Shan, C., Muruato, A. E., Jagger, B. W., Richner, J., Nunes, B. T., Medeiros, D. B., Shi, P., et al. (2017). A single-dose live-aĀenuated vaccine prevents Zika virus pregnancy transmission and tesĀs damage. *Nature Communications, 8*(676), 1-9. doi:10.1038/s41467-017-00737-8
[2] CDC. (2017, September 18). Key Messages Zika Virus Disease. Retrieved from hĀps://www.cdc.gov/zika/pdfs/zika-key-messages.pdf
[3] CDC. (2017, September 18). Key Messages Zika Virus Disease. Retrieved from hĀps://www.cdc.gov/zika/pdfs/zika-key-messages.pdf
[4] CDC. (2017, September 29). CDC Is DeacĀvaĀng the Emergency OperaĀons Center for the Zika Response. Retrieved from hĀps://www.cdc.gov/media/releases/2017/p0929-eoc-deacĀvaĀon-zika.html

As of January 5, 2018, there have been 634 travel-associated Zika virus infections in California.[5] Of this total, 136 travel-associated cases were reported in LAC.[6] There have been no locally acquired mosquito-borne cases of Zika Virus reported in California to date. The following statistics were gathered for pregnant women in LAC who were infected with Zika virus in 2015-2016:

- 90% were born outside the United States
- 60% have Spanish as their first language
- 50% report owning a residence in the country they traveled to
- 25% were visiting family
- 75% of Zika-affected pregnant women have deep ties to Mexico or the Central American country where they generally stayed over one month. The most frequented countries or territories of Zika exposure for California Zika cases overall include Mexico, Nicaragua, Guatemala, El Salvador, the Dominican Republic, Costa Rica, Puerto Rico, and Honduras.

Healthcare providers who care for pregnant and reproductive age women should be vigilant in screening women for Zika exposure and advising pregnant women and women planning pregnancy to avoid travel to areas with local Zika transmission. This is especially important due to the fact that 80% of people infected with Zika virus are asymptomatic.[7,8] Women with unavoidable travel exposure or sexual exposure to partners who have traveled to areas with Zika transmission should delay pregnancy by abstaining or using the most effective contraceptive method available, use male or female condoms or other barrier protections to prevent sexual transmission, and protect themselves against mosquito bites during travel.[9]

Data from the United States (U.S.) and U.S. territories reports about 5% of fetuses or infants had birth defects potentially related to Zika virus among women with possible Zika virus infection during pregnancy.[10,11] The pattern of congenital anomalies associated with Zika virus infection is called Congenital Zika Syndrome. Congenital Zika Syndrome (Figure 2) is described by the following five features:

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[5] CDPH Weekly Update on Number of Zika Virus InfecÃons in California. (2018, January 5). Retrieved from hÃps://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/TravelAssociatedCasesofZikaVirusinCA.pdf

[6] CDPH Weekly Update on Number of Zika Virus InfecÃons in California. (2018, January 5). Retrieved from hÃps://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/TravelAssociatedCasesofZikaVirusinCA.pdf

[7] Oster, A. M., Brooks, J. T., Stryker, J. E., et al. (2016, February 12). Interim Guidelines for PrevenÃon of Sexual Transmission of Zika Virus — United States, 2016. *MMWR. Morbidity and Mortality Weekly Report, 65*(5), 120–121. dio:10.15585/mmwr.mm6505e1

[8] Shan, C., Muruato, A. E., Jagger, B. W., Richner, J., Nunes, B. T., Medeiros, D. B., Shi, P., et al. (2017). A single-dose live-aÃenuated vaccine prevents Zika virus pregnancy transmission and tesÃs damage. *Nature Communications, 8*(676), 1-9. doi:10.1038/s41467-017-00737-8

[9] California Department of Public Health. (2017, August 2). Updated Guidance for Health Care Providers Caring for Pregnant Women with Possible Zika Virus Exposure. Retrieved from hÃps://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/UpdatedZikaGuidanceforHCPsCaringforPregnantWomen.pdf

[10] Honein MA, Dawson AL, Petersen EE et al. Birth Defects Among Fetuses and Infants of US Women With Evidence of Possible Zika Virus InfecÃon During Pregnancy. *JAMA*. 2017;317(1):59-68. doi:10.1001/jama.2016.19006

[11] Shapiro-Mendoza, C. K., Rice, M. E., Galang, R. R., et al. (2017, June 16). Pregnancy Outcomes AÃer Maternal Zika Virus InfecÃon During Pregnancy —U.S. Territories, January 1, 2016–April 25, 2017. *MMWR. Morbidity and Mortality Weekly Report, 66*(23), 615-621. dio:10.15585/mmwr.mm6623e1

1. Severe microcephaly in which the skull has partially collapsed

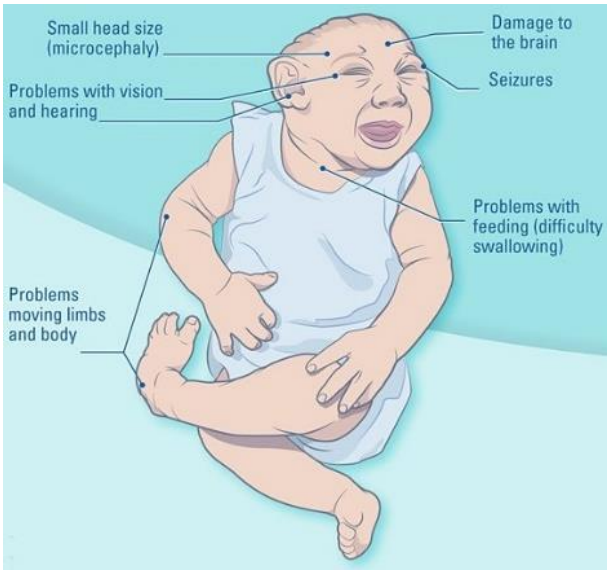
2. Decreased brain tissue with a specific pattern of brain damage, including subcortical calcifications

3. Damage to the back of the eye, including macular scarring and focal pigmentary retinal mottling

4. Congenital contractures, such as clubfoot or arthrogryposis

5. Hypertonia restricting body movement soon after birth

Figure 2: Congenital Zika Abnormalities



Congenital Zika virus infection has also been associated with other abnormalities including, but not limited to, brain atrophy and asymmetry, abnormally formed or absent brain structures, hydrocephalus, and neuronal migration disorders.[12] Other anomalies include excessive and redundant scalp skin. Reported neurologic findings include hyperreflexia, irritability, tremors, seizures, brainstem dysfunction, and dysphagia. Reported eye abnormalities include, but are not limited to, focal pigmentary mottling and chorioretinal atrophy in the macula, optic nerve hypoplasia, cupping, and atrophy, other retinal lesions, iris colobomas, congenital glaucoma, microphthalmia, lens subluxation, cataracts, and intraocular calcifications.[13]

Zika virus infection may also have neurological effects on adults, including Guillain-Barré syndrome,[14] cardiovascular complications,[15] hearing problems,[16] vision problems,[17] and a growing number of other effects as more research develops. This Zika Hospital Toolkit serves as a guide for providers who interact with women during their pregnancy, labor and delivery, and postpartum, and for providers who care for infants of Zika-positive mothers.

[12] CDC. (2017, August 9). Congenital Zika Syndrome & Other Birth Defects. Retrieved from hĀps://www.cdc.gov/zika/hc-providers/infants-children/zika-syndrome-birth-defects.html

[13] CDC. (2017, August 9). Congenital Zika Syndrome & Other Birth Defects. Retrieved from hĀps://www.cdc.gov/zika/hc-providers/infants-children/zika-syndrome-birth-defects.html

[14] Styczynski, A. R., Malta, J. M., Krow-Lucal, E. R., Percio, J., Nóbrega, M. E., Vargas, A., Coelho, G. E., et al. (2017, August 30). Increased rates of Guillain-Barré syndrome associated with Zika virus outbreak in the Salvador metropolitan area, Brazil. *PLOS Neglected Tropical Diseases, 11*(8). doi:10.1371/journal.pntd.0005869

[15] American College of Cardiology. (2017, March 9). Researchers Sound Alarm Over Zika's PotenĀally Harmful Heart Eff cts. Retrieved from hĀp://www.acc.org/about-acc/press-releases/2017/03/09/13/25/researchers-sound-alarm-over-zikas-potenĀally-harmful-heart-eff_cts

[16] Vinhaes, E. S., Santos, L. A., Dias, L., Andrade, N. A., Bezerra, V. H., Carvalho, A. T., Boaventura, V. S., et al. (2017, March 1). Transient Hearing Loss in Adults Associated with Zika Virus InfecĀon. *Clinical Infectious Diseases, 64*(5), 675-677. doi:10.1093/cid/ciw770

[17] KodaĀ, S., Palmore, T. N., Spellman, F. A., Cunningham, D., Weistrop, B., & Sen, H. N. (2017, January 7). Bilateral posterior uveiĀs associated with Zika virus infecĀon. The Lancet, 389(10064), 125-126. doi:10.1016/s0140-6736(16)32518-1

GUIDE FOR OBSTETRIC PROVIDERS

IN THIS SECTION…

OCCUPATIONAL EXPOSURE

The CDC released a report emphasizing the importance of healthcare personnel following standard precautions to prevent the spread of infectious diseases such as Zika when caring for all patients, including pregnant patients in labor and delivery settings (Appendix A). There have been no confirmed reports of Zika spreading from an infected patient to a healthcare provider or other patients. However, healthcare personnel are reminded to use standard precautions[18] when they might come in contact with body fluids (Appendix B). Standard precautions (**Table 1**) for all patients to minimize contact with body fluids are important to reduce the possibility of spreading infectious diseases such as Zika.[19]

Table 1: Occupational Safety for Caring with Zika-Positive Patient

Use standard precautions
Healthcare providers should use soap and water or alcohol-based products (gels, rinses, foams), at a minimum, before and after all patient contacts

Preventing Transmission of Zika Virus in Labor and Delivery Settings Through Implementation of Standard Precautions[20] (Appendix A)

Morbidity and Mortality Weekly Report

Preventing Transmission of Zika Virus in Labor and Delivery Settings Through Implementation of Standard Precautions — United States, 2016

Christine K. Olson, MD[1]; Martha Iwamoto, MD[1]; Kiran M. Perkins, MD[1]; Kara N.D. Polen, MPH[1]; Jeffrey Hageman, MHS[1]; Dana Meaney-Delman, MD[1]; Irogue I. Igbinosa, MD[1]; Sumaiya Khan, MPH[1]; Margaret A. Honein, PhD[1]; Michael Bell, MD[1]; Sonja A. Rasmussen, MD[1]; Denise J. Jamieson, MD[1]

On March 22, 2016, this report was posted as an MMWR *Early Release on the* MMWR *website (http://www.cdc.gov/mmwr).*

Zika virus transmission was detected in the Region of the Americas (Americas) in Brazil in May 2015, and as of March 21, 2016, local mosquito-borne transmission of Zika virus had been reported in 32 countries and territories in the Americas, including Puerto Rico and the U.S. Virgin Islands.* Most persons infected with Zika virus have a mild illness or are asymptomatic. However, increasing evidence supports a link between Zika virus infection during pregnancy and adverse pregnancy and birth outcomes (*1*), and a possible association between recent Zika virus infection and Guillain-Barré syndrome has been reported (*2*). Although Zika virus is primarily transmitted through the bite of *Aedes* species of mosquitoes, sexual transmission also has been documented (*3*). Zika virus RNA has been detected in a number of body fluids, including blood, urine, saliva, and amniotic fluid (*3–5*), and whereas transmission associated with occupational exposure to these body fluids is theoretically possible, it has not been documented. Although there are no reports of transmission of Zika virus from infected patients to health care personnel or other patients, minimizing exposures to body fluids is important to reduce the possibility of such transmission. CDC recommends Standard Precautions in all health care settings to protect both health care personnel and patients from infection with Zika virus as well as from blood-borne pathogens (e.g., human immunodeficiency virus [HIV] and hepatitis C virus [HCV]) (*6*). Because of the potential for exposure to large volumes of body fluids during the labor and delivery process and the sometimes unpredictable and fast-paced nature of obstetrical care, the use of Standard Precautions in these settings is essential to prevent possible transmission of Zika virus from patients to health care personnel.

Use of Standard Precautions in Health Care Settings

Health care personnel should adhere to Standard Precautions in every health care setting. Standard Precautions are designed to protect health care personnel and to prevent them from spreading infections to patients. They are based on the premise that all blood, body fluids, secretions, excretions (except sweat), nonintact skin, and mucous membranes might contain transmissible infectious agents and include 1) hand hygiene, 2) use of personal protective equipment (PPE), 3) respiratory hygiene and cough etiquette, 4) safe injection practices, and 5) safe handling of potentially contaminated equipment or surfaces in the patient environment (*6*). Because patients with Zika virus infection might be asymptomatic, Standard Precautions should be in place at all times, regardless of whether the infection is suspected or confirmed. Health care personnel should assess the potential for exposure to potentially infectious material during health care delivery and protect themselves accordingly, based on the level of clinical interaction with the patient and the physical distance at which care is provided (*6*). In addition, health care providers should use soap and water or alcohol-based products (gels, rinses, foams), at a minimum, before and after a patient contact and after removing PPE, including gloves (*6*).

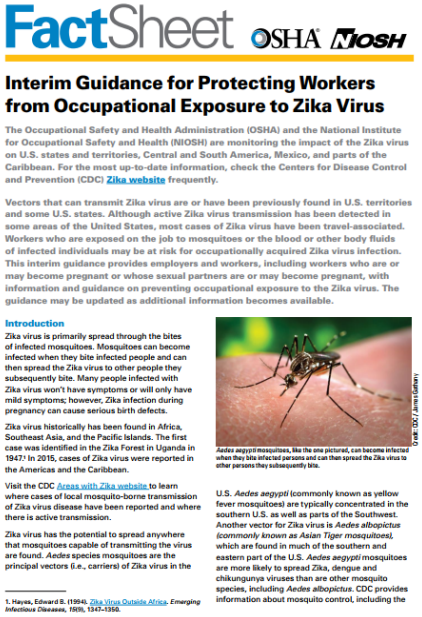
Use of Standard Precautions in Labor and Delivery Settings

Pregnant women lose an average of 500 mL of blood during uncomplicated vaginal deliveries, with higher losses during complicated vaginal deliveries and cesarean deliveries (*7*). Amniotic fluid volume at the time of full-term delivery typically exceeds 500 mL (*8*). Eye protection used during deliveries has been demonstrated to be contaminated with blood and body fluids (*9*), and when double layers of gloves are used for procedures and surgeries, the outer layers often have significant perforations, whereas the inner layers are intact or have many fewer perforations (*10*). Although health care personnel in these settings are at substantial risk for exposure to blood and body fluids, varying levels of adherence to Standard Precautions have been reported in health care settings, including in labor and delivery units (*11*). Numerous barriers to the appropriate use of PPE have been cited, including the perception that PPE is uncomfortable and limits dexterity, fogging of goggles or face masks, the misperception that prescription eyeglasses provide adequate eye protection, lack of available PPE, forgetting to use PPE, lack of time in urgent clinical situations to don appropriate PPE, the perception that the patient poses minimal risk, and concerns about interference with patient care (*11*). Given the theoretic risk for transmission of Zika virus through contact with body fluids in a health care

* http://www.cdc.gov/zika/geo/active-countries.html.

290 MMWR / March 25, 2016 / Vol. 65 / No. 11 US Department of Health and Human Services/Centers for Disease Control and Prevention

Interim Guidance for Protecting Workers from Occupational Exposure to Zika Virus[21] (Appendix B)



FactSheet OSHA NIOSH

Interim Guidance for Protecting Workers from Occupational Exposure to Zika Virus

The Occupational Safety and Health Administration (OSHA) and the National Institute for Occupational Safety and Health (NIOSH) are monitoring the impact of the Zika virus on U.S. states and territories, Central and South America, Mexico, and parts of the Caribbean. For the most up-to-date information, check the Centers for Disease Control and Prevention (CDC) Zika website frequently.

Vectors that can transmit Zika virus are or have been previously found in U.S. territories and some U.S. states. Although active Zika virus transmission has been detected in some areas of the United States, most cases of Zika virus have been travel-associated. Workers who are exposed on the job to mosquitoes or the blood or other body fluids of infected individuals may be at risk for occupationally acquired Zika virus infection. This interim guidance provides employers and workers, including workers who are or may become pregnant or whose sexual partners are or may become pregnant, with information and guidance on preventing occupational exposure to the Zika virus. The guidance may be updated as additional information becomes available.

Introduction

Zika virus is primarily spread through the bites of infected mosquitoes. Mosquitoes can become infected when they bite infected people and can then spread the Zika virus to other people they subsequently bite. Many people infected with Zika virus won't have symptoms or will only have mild symptoms; however, Zika infection during pregnancy can cause serious birth defects.

Zika virus historically has been found in Africa, Southeast Asia, and the Pacific Islands. The first case was identified in the Zika Forest in Uganda in 1947.[1] In 2015, cases of Zika virus were reported in the Americas and the Caribbean.

Visit the CDC Areas with Zika website to learn where cases of local mosquito-borne transmission of Zika virus disease have been reported and where there is active transmission.

Zika virus has the potential to spread anywhere that mosquitoes capable of transmitting the virus are found. *Aedes* species mosquitoes are the principal vectors (i.e., carriers) of Zika virus in the

1. Hayes, Edward B. (1994). Zika Virus Outside Africa. *Emerging Infectious Diseases, 15*(9), 1347–1350.

Aedes aegypti mosquitoes, like the one pictured, can become infected when they bite infected persons and can then spread the Zika virus to other persons they subsequently bite.

U.S. *Aedes aegypti* (commonly known as yellow fever mosquitoes) are typically concentrated in the southern U.S. as well as parts of the Southwest. Another vector for Zika virus is *Aedes albopictus (commonly known as Asian Tiger mosquitoes)*, which are found in much of the southern and eastern part of the U.S. *Aedes aegypti* mosquitoes are more likely to spread Zika, dengue and chikungunya viruses than are other mosquito species, including *Aedes albopictus*. CDC provides information about mosquito control, including the

[18] CDC. (2017, December 12). Healthcare Exposure to Zika and InfecÃon Control. Retrieved from hÃps://www.cdc.gov/zika/hc-providers/infecÃon-control.html

[19] CDC. (2017, September 18). Key Messages Zika Virus Disease. Retrieved from hÃps://www.cdc.gov/zika/pdfs/zika-key-messages.pdf

[20] Olson, C. K., Iwamoto, M., Perkins, K. M., Polen, K. N., Hageman, J., Meaney-Delman, D., Jamieson, D. J., et al. (2016, march 25). PrevenÃng Transmission of Zika Virus in Labor and Delivery SeÃ ngs Through ImplementaÃon of Standard PrecauÃons — United States, 2016. *MMWR. Morbidity and Mortality Weekly Report, 65*(11), 290-292. doi:10.15585/mmwr.mm6511e3er

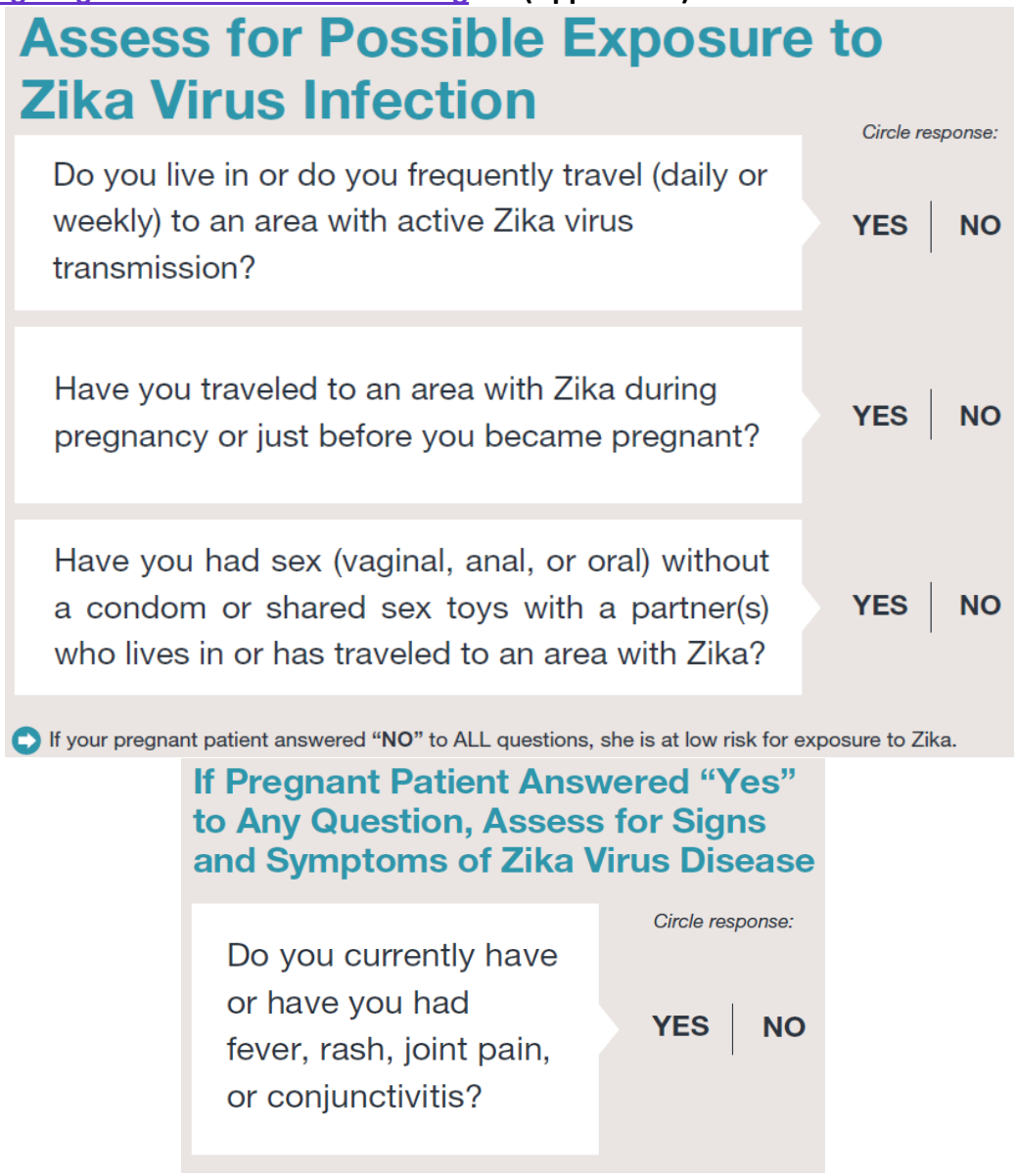
[21] OccupaÃonal Safety and Health AdministraÃon (OSHA), & NaÃonal InsÃtute for OccupaÃonal Safety and Health (NIOSH). (2017, June 1). Interim Guidance for ProtecÃng Workers from OccupaÃonal Exposure to Zika Virus. Retrieved from hÃps://www.osha.gov/PublicaÃons/OSHA3855.pdf

PATIENT SCREENING FOR ZIKA VIRUS

PRENATAL SCREENING QUESTIONS

All pregnant women should be asked about Zika exposure that could have occurred before becoming pregnant or during pregnancy (Appendix C). Every pregnant woman should be assessed for signs and symptoms of Zika virus at every prenatal visit.

Screening Pregnant Women for Zika Testing[22,23] (Appendix C)



[22] CDC. (2016, October 4). Zika Screening Tool For Pregnant Women. Retrieved from hĀp://publichealth.lacounty.gov/mch/ReproducĀveHealth/Zika-MCAH/Forms/ZikaScreeningTool.pdf
[23] CDC. (2017, August 9). Screening Pregnant Women For Zika TesĀng. Retrieved from hĀps://www.cdc.gov/zika/pdfs/zikapreg_screeningtool.pdf

PATIENT SELF-ASSESSMENT

Pregnant women should be encouraged to complete the *Zika Virus Patient Self-Assessment Form* (Appendix D)[24] as early as possible to determine exposure risk. The self-assessment should be discussed and reviewed with providers to determine if testing is needed. The 8-question form can be found on the California Department of Public Health website.

Zika Virus Exposure Patient Self-Assessment Form (Appendix D)

CDPH California Department of Public Health

Zika Virus Exposure
Patient Self-Assessment Form

ZIKA and Pregnancy
Californians, Let's #TalkZIKA

Zika is a virus that spreads to people in many parts of the world through mosquitoes or through sex with an infected partner. Most people with Zika don't get sick, so they may not know they have it. If a woman gets Zika and is pregnant or becomes pregnant, the virus can cause miscarriage, stillbirth or severe birth defects. **The following questions will help identify your risk of Zika virus exposure and determine if follow-up care is needed.** Please answer to the best of your ability.

1. **Have you recently been to…?** *(Select and/or circle all that apply)*

○ **United States and Territories**
Puerto Rico | Brownsville, Texas | U.S. Virgin Islands

○ **Mexico**
○ **Central America**
○ **South America**
○ **Caribbean Islands**
Including: Aruba, The Bahamas, Barbados, British Virgin Islands, Cuba, Dominican Republic, Grenada Haiti, Jamaica, Saint Kitts/Lucia/Martin/Vincent, Trinidad and Tobago, Turks and Caicos, etc.

○ **Oceana/Pacific Islands**
Fiji | Papua New Guinea | Solomon Islands
Marshall Islands | Samoa | Tonga

○ **Africa**

Angola	Congo (Congo-Brazzaville)	Ghana	Senegal
Benin	Cote d'Ivoire	Guinea	Sierra Leone
Burkina-Faso	Democratic Republic of the Congo (Congo-Kinshasa)	Guinea-Bissau	South Sudan
Burundi	Equatorial Guinea	Kenya	Sudan
Cameroon	Gabon	Liberia	Tanzania
Cape Verde	Gambia	Mali	Togo
Central African Republic		Niger	Uganda
Chad		Nigeria	
		Rwanda	

○ **Asia**

Bangladesh	Laos	Singapore
Burma (Myanmar)	Malaysia	Thailand
Cambodia	Maldives	Timor-Leste (East Timor)
India	Pakistan	Vietnam
Indonesia	Philippines	

○ **Other:** _____

○ **NONE OF THE ABOVE** *(Skip to Question 4)*

For a recent list of areas with Zika, visit: http://www.cdc.gov/zika/geo/active-countries.html.

2. **If yes, please list the date you returned from your most recent trip**: _____

If you have been to one of these areas, there is a chance you could be infected with Zika. If you are pregnant or have symptoms, you may need to be tested. Tell your doctor about your possible Zika virus exposure. For a complete doctor's visit checklist, visit: http://www.cdc.gov/zika/pdfs/docvisit-checklist-travelpreg.pdf.

Tell your doctor about your trip and if you were bitten by mosquitoes:
1. How long did you stay?
2. What did you do? Outdoor activities?
3. How often did you use insect repellent?

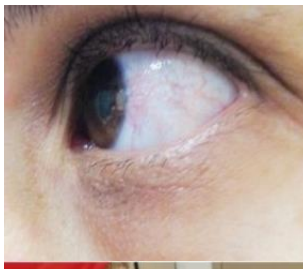
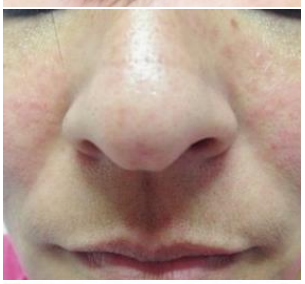
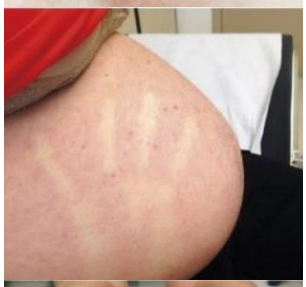
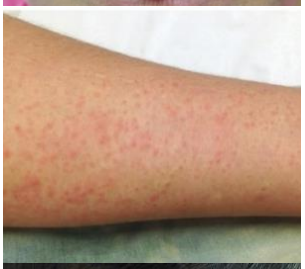
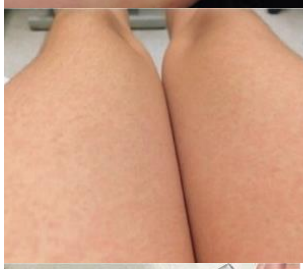
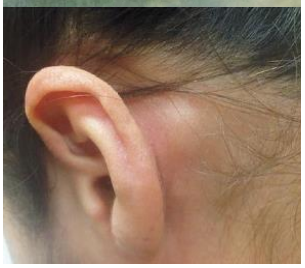
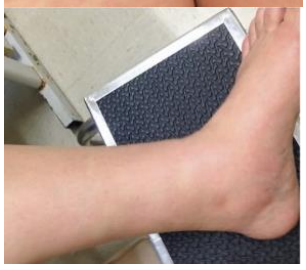
Good questions to ask your doctor are:
1. Should I be tested for Zika virus?
2. How can I prevent sexual transmission of Zika?
3. What should I do if I plan to go to any of these areas?

[24] CDPH (2017, December). Zika Virus PaĀent Self-Assessment Form. Retrieved from hĀps://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/ZikaVirusExposureSelfAssesmentForm.pdf

SIGNS AND SYMPTOMS

Infection with Zika virus is **asymptomatic** in an estimated 80% of cases, and when Zika virus does cause illness, symptoms are generally mild and self-limiting.[25,26] The most common symptom of Zika virus is **exanthema** (skin rash)[27]. Other symptoms of Zika virus include fever, conjunctivitis, headache, joint pain, and muscle pain. Clinical features of Zika virus infection may be found in **Table 2** below (Appendix E). People usually do not get sick enough to go to the hospital, and they very rarely die of Zika.[28]

Table 2: Clinical Features of Zika Virus Infection in Pregnant Women (Appendix E)

	Conjunctival and palpebral erythema		Conjunctival injection with promience of vasculature
	Maculopapular rash on the face		Blanching macular rash on the gravid abdomen
	Rash on inner arm		Rash on legs
	Retroauricular lymphadenopathy		Edema of the foot

[25] Oster, A. M., Brooks, J. T., Stryker, J. E., et al. (2016, February 12). Interim Guidelines for PrevenÃon of Sexual Transmission of Zika Virus — United States, 2016. *MMWR. Morbidity and Mortality Weekly Report, 65*(5), 120–121. doi:10.15585/mmwr.mm6505e1

[26] Zika Virus Response Updates from FDA. (2017, September 28). U.S. Food and Drug AdministraÃon. Emergency Preparedness and Response. Retrieved from hÃps://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMIssues/ucm485199.htm

[27] Pan American Health OrganizaÃon & World Health OrganizaÃons. (2016, March 25). Zika virus infecÃon and Zika fever: Frequently asked quesÃons. Retrieved from hÃp://www2.paho.org/hq/index.php?opÃon=com_content&view=arÃcle&id=9183&Itemid=41711&lang=en

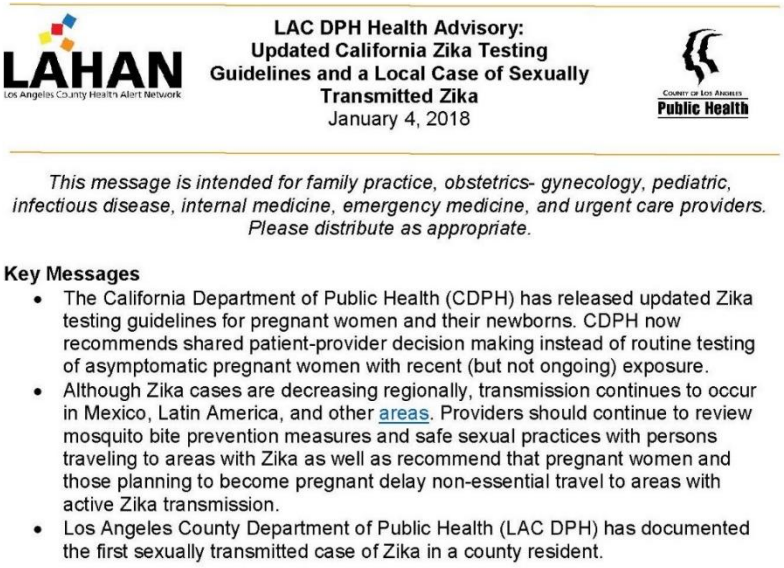
[28] CDC. (2017, September 18). Key Messages Zika Virus Disease. Retrieved from hÃps://www.cdc.gov/zika/pdfs/zika-key-messages.pdf

ZIKA SCREENING AND CONFIRMATORY LAB TESTS

In Los Angeles County, the current recommendation is to evaluate all pregnancy women for possible Zika virus exposure during each prenatal care visit. The most current guidelines for testing pregnant women with possible Zika Virus exposure comes from the latest Los Angeles County Health Alert Network (LAHAN): *Updated California Zika Testing Guidelines and a Local Case of Sexually Transmitted Zika* [29] (Appendix F).

Los Angeles County, the California Department of Public Health,[30] and the CDC[31] recommends a shared decision-making model which includes pretest counseling, individualized risk assessment, clinical judgment, and patient preferences. A patient's risk tolerance and decision-making regarding the pregnancy may be sufficient justification to test for Zika virus infection. [32]

Updated California Zika Testing Guidelines and a Local Case of Sexually Transmitted Zika
(Appendix F)



LAHAN
Los Angeles County Health Alert Network

LAC DPH Health Advisory:
Updated California Zika Testing Guidelines and a Local Case of Sexually Transmitted Zika
January 4, 2018

County of Los Angeles Public Health

This message is intended for family practice, obstetrics- gynecology, pediatric, infectious disease, internal medicine, emergency medicine, and urgent care providers. Please distribute as appropriate.

Key Messages

- The California Department of Public Health (CDPH) has released updated Zika testing guidelines for pregnant women and their newborns. CDPH now recommends shared patient-provider decision making instead of routine testing of asymptomatic pregnant women with recent (but not ongoing) exposure.
- Although Zika cases are decreasing regionally, transmission continues to occur in Mexico, Latin America, and other areas. Providers should continue to review mosquito bite prevention measures and safe sexual practices with persons traveling to areas with Zika as well as recommend that pregnant women and those planning to become pregnant delay non-essential travel to areas with active Zika transmission.
- Los Angeles County Department of Public Health (LAC DPH) has documented the first sexually transmitted case of Zika in a county resident.

[29] Los Angeles County Health Alert Network. (2018, January 4). Updated California Zika TesÃng Guidelines and a Local Case of Sexually TransmiÃed Zika. Retrieved from hÃp://publichealth.lacounty.gov/eprp/Health%20Alerts/LAHAN%20Zika%20Advisory%20with%20CDPH%20Guidance%201.4.18.pdf

[30] California Department of Public Health (2018, January 10). Updated Guidance for Health Care Providers: Assessment and TesÃng for Zika Virus InfecÃon in Pregnant Women and their Newborns. Retrieved from hÃps://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/UpdatedZikaGuidanceforHCPsCaringforPregnantWomen.pdf

[31] CDC. (2018, January 19). TesÃng & Diagnosis. Retrieved from hÃps://www.cdc.gov/pregnancy/zika/tesÃng-follow-up/tesÃng-and-diagnosis.html

[32] California Department of Public Health (2018, January 10). Updated Guidance for Health Care Providers: Assessment and TesÃng for Zika Virus InfecÃon in Pregnant Women and their Newborns. Retrieved from hÃps://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/UpdatedZikaGuidanceforHCPsCaringforPregnantWomen.pdf

There are three types of tests which are used to diagnose Zika virus infection.[33] There are limitations in Zika virus testing because of the cross-sensitivity of antibodies generated in response to flavivirus infections (including Zika, dengue, and yellow fever).[34] For this reason, Zika test results may be positive, presumptive, or negative.

The U.S. Food and Drug Administration has issued Emergency Use Authorization (EUA) for the three diagnostic tools for Zika virus listed below, which are being distributed by CDC to qualified laboratories.[35]

The three diagnostic tools for Zika virus testing are described below.

1. **RT-PCR** (also known as **NAT**) detects Zika virus RNA. This test will henceforth be referred to as **PCR/NAT**. Current CDC guidelines recommend concurrent testing of PCR/NAT and IgM serology.[36,37,38]
   - Collect serum and urine
   - Sensitive ≤ 12 weeks after symptom onset
   - If positive, ***confirms*** current or recent Zika virus infection
   - If negative, ***does not*** exclude Zika virus infection

2. **IgM serology**
   - Collect serum
   - Sensitive within 2 to 12 weeks after symptom onset
   - If positive, ***presumptive*** recent flavivirus infection
   - If negative, ***does not exclude*** Zika virus infection
   - Confirmatory testing by PRNT is needed

KEY NOTES:

If positive symptoms occur, test as soon as possible up to 12 weeks.

Send PCR/NAT (serum and urine) **AND** Zika virus IgM serology (serum) **concurrently**.

3. **PRNT** measures virus-specific neutralizing antibodies
   - This final confirmatory test will identify the source of infection
   - If positive, multiple interpretations
     - ~ ***Confirms*** Zika virus infection
     - ~ ***Confirms*** unspecified flavivirus infection (dengue, chikungunya, Zika)
     - ~ ***Presence*** of vaccination against flavivirus (yellow fever, West Nile virus)
   - If negative, ***no*** Zika virus infection

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[33] State of California Health and Human Services Agency, & California Division of Communicable Disease Control. (2016, August 22). CDPH Zika Virus TesĀng FAQs for Healthcare Providers. Retrieved from hĀps://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/ZikaVirusTesĀngFAQsforHCPs.pdf

[34] Balmaseda, A., SteĀler, K., Medialdea-Carrera, R., Collado, D., Jin, X., Zambrana, J. V., CorĀ, D., et al. (2017, August 1). AnĀbody-based assay discriminates Zika virus infecĀon from other Āaviviruses. *Proceedings of the National Academy of Sciences, 114*(31), 8384-8389. doi:10.1073/pnas.1704984114

[35] CDC. (2017, July 23). DiagnosĀc Tests for Zika Virus. Retrieved from hĀps://www.cdc.gov/zika/hc-providers/types-of-tests.html

[36] CDC. (2017, July 23). Types of Zika Virus Tests. Retrieved from hĀps://www.cdc.gov/zika/laboratories/types-of-tests.html

[37] CDC. (2017). Updated Interim Guidance for Pregnant Women with Possible Zika Virus Exposure. Retrieved from hĀps://www.chicagohan.org/documents/14171/155633/Key takeaways for healthcare providers/3658eb87-32f3-4d5d-a795-8862c5a32985

[38] Oduyebo, T., Polen, K. D., Walke, H. T., et al. (2017, July 28). Update: Interim Guidance for Health Care Providers Caring for Pregnant Women with Possible Zika Virus Exposure — United States (Including U.S. Territories). *MMWR. Morbidity and Mortality Weekly Report, 66*(29), 781-793. doi:10.15585/mmwr.mm6629e1

INDICATIONS FOR ZIKA TESTING

The Los Angeles County Department of Public Health Acute Communicable Disease Control has created the following table to assess Indications for Zika Testing for pregnant women (Appendix G). Please contact the Los Angeles County Public Health Laboratory at 562-658-1330 for the most updated specimen collection recommendations.

Indications for Zika Testing (Appendix G)

Indications for Zika Testing	RT-PCR (serum, urine, or other)	IgM[1] (serum)
Pregnancy-associated		
Symptomatic[2] pregnant woman *with* travel[3] or sexual[4] exposure history	ASAP Serum & Urine < 12 weeks of onset	Concurrent with PCR
Symptomatic pregnant woman *without* travel or sexual exposure history	Not recommended	Not recommended
Pregnant woman with travel or sexual exposure history and ultrasound evidence of fetal microcephaly and/or calcifications OR fetal loss, regardless of symptom status	ASAP Serum & Urine < 12 weeks after possible exposure (amniotic fluid if amniocentesis preformed)	Concurrent with PCR
Pregnant woman with ongoing exposure (lives in or frequently travels to Zika risk area or ongoing unprotected sexual activity with potentially infected partner)	Serum & Urine Test 3 times during pregnancy	Consider concurrent with PCR but not routinely recommended
Asymptomatic pregnant traveler	Not routinely recommended**	Not routinely recommended

INTERPRETATION OF ZIKA SCREENING AND CONFIRMATORY LAB TESTS

The CDC *Interpretation of Results of Nucleic Acid and Antibody Testing for Suspected Zika Virus Infection*[39] (Appendix H) charts the interpretations and recommendations for Zika PCR/NAT, IgM serology, and PRNT test results.

Interpretation of Results of Nucleic Acid and Antibody Testing for Suspected Zika Virus Infection (Appendix H)

Zika NAT (serum)[4]	Zika NAT (urine)[4]	Zika virus IgM[5]	Zika virus PRNT	Dengue virus PRNT	Interpretation and recommendations
Positive	Positive	Any result	Not indicated	Not indicated	**Acute Zika virus infection**
Negative	Positive	Positive	Not indicated	Not indicated	**Acute Zika virus infection**
Negative	Positive	Negative	Not indicated	Not indicated	**Suggests acute Zika virus infection** *Repeat testing on original urine specimen* • *If repeat NAT result is positive, interpret as **evidence of acute Zika virus infection*** • *If repeat NAT result is negative, repeat Zika virus IgM antibody testing on a serum specimen collected ≥2 weeks after symptom onset or possible exposure or specimen collection date* – *If repeat IgM antibody result is positive,[6] interpret as **evidence of acute Zika virus infection*** – *If repeat IgM antibody result is not positive, interpret as no evidence of Zika virus infection*
Positive	Negative or not performed	Positive	Not indicated	Not indicated	**Acute Zika virus infection**
Positive	Negative or not performed	Negative	Not indicated	Not indicated	**Suggests acute Zika virus infection** *Repeat testing on original serum specimen* • *If repeat NAT result is positive, interpret as **evidence of acute Zika virus infection*** • *If repeat NAT result is negative, repeat Zika virus IgM antibody testing on a serum specimen collected ≥2 weeks after symptom onset or possible exposure or specimen collection date* – *If repeat IgM antibody result is positive,[6] interpret as **evidence of acute Zika virus infection*** – *If repeat IgM antibody result is not positive, interpret as no evidence of Zika virus infection*
Negative	Negative or not performed	Any non-negative result[7]	≥10	<10	**Zika virus infection; timing of infection cannot be determined.** • *For persons without prior Zika virus exposure, a positive IgM result represents recent Zika virus infection*
Negative	Negative or not performed	Any non-negative result[7]	≥10	≥10	**Flavivirus infection; specific virus cannot be identified; timing of infection cannot be determined** • *For persons without prior Zika virus exposure, a positive IgM result represents recent unspecified flavivirus infection*
Negative	Negative or not performed	Any non-negative result[7]	<10	Any result	**No evidence of Zika virus infection**
For areas where PRNT is not recommended[3]					
Negative	Negative or not performed	Positive for Zika virus AND negative for dengue virus	Not performed because PRNT is not recommended		**Presumptive Zika virus infection; timing of infection cannot be determined[8]**
Negative	Negative or not performed	Positive for Zika virus AND positive for dengue virus	Not performed because PRNT is not recommended		**Presumptive flavivirus infection; specific virus cannot be identified; timing of infection cannot be determined[8]**
Negative	Negative or not performed	Equivocal (either or both assays)	Not performed because PRNT is not recommended		**Insufficient information for interpretation** • *Consider repeat testing*
Negative	Negative or not performed	Negative on both assays	Not performed because PRNT is not recommended		**No laboratory evidence of Zika virus infection**

Abbreviations: IgM = immunoglobulin M; NAT = nucleic acid test; PRNT = plaque reduction neutralization test.

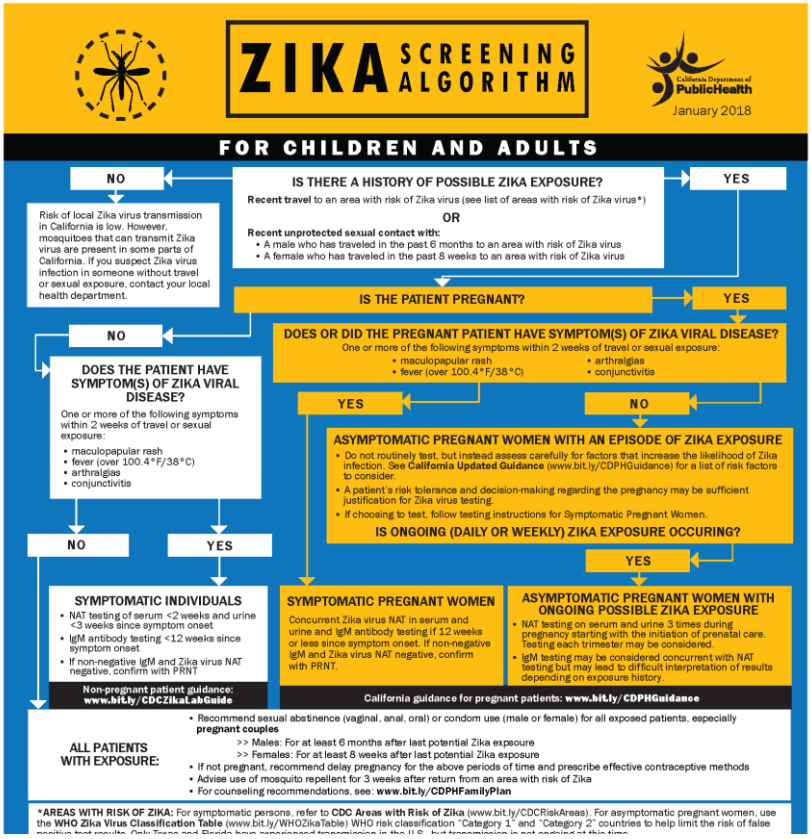
[39] CDC. (2017, July 24). InterpretaĀon of Results of Nucleic Acid and AnĀbody TesĀng for Suspected Zika Virus InfecĀon. Retrieved from hĀps://www.cdc.gov/zika/pdfs/lab-table.pdf

ALGORITHM OF ZIKA SCREENING AND CONFIRMATORY LAB TESTS

The CDPH *Zika Screening Algorithm*[40] (Appendix I) includes a testing algorithm for pregnant women. Los Angeles County is adapting this algorithm in accordance with the latest Los Angeles County Health Alert Network (LAHAN): *Updated California Zika Testing Guidelines and a Local Case of Sexually Transmitted Zika* [41] (Appendix F).

Los Angeles County, the California Department of Public Health,[42] and the CDC[43] recommends a shared decision-making model which includes pretest counseling, individualized risk assessment, clinical judgment, and patient preferences. A patient's risk tolerance and decision-making regarding the pregnancy may be sufficient justification to test for Zika virus infection. [44]

Zika Screening Algorithm (Appendix I)



[40] CDPH. (2018, January). Updated Zika Screening Algorithm. Retrieved from hÃps://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/ZikaAlgorithmPoster.pdf

[41] Los Angeles County Health Alert Network. (2018, January 4). Updated California Zika TesÃng Guidelines and a Local Case of Sexually TransmiÃed Zika. Retrieved from hÃp://publichealth.lacounty.gov/eprp/Health%20Alerts/LAHAN%20Zika%20Advisory%20with%20CDPH%20Guidance%201.4.18.pdf

[42] California Department of Public Health (2018, January 10). Updated Guidance for Health Care Providers: Assessment and TesÃng for Zika Virus InfecÃon in Pregnant Women and their Newborns. Retrieved from hÃps://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/UpdatedZikaGuidanceforHCPsCaringforPregnantWomen.pdf

[43] CDC. (2018, January 19). TesÃng & Diagnosis. Retrieved from hÃps://www.cdc.gov/pregnancy/zika/tesÃng-follow-up/tesÃng-and-diagnosis.html

[44] California Department of Public Health (2018, January 10). Updated Guidance for Health Care Providers: Assessment and TesÃng for Zika Virus InfecÃon in Pregnant Women and their Newborns. Retrieved from hÃps://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/UpdatedZikaGuidanceforHCPsCaringforPregnantWomen.pdf

PATIENT COUNSELING AFTER ZIKA SCREENING AND CONFIRMATORY LAB TESTS

The CDC has created a sample script, *Pretest Counseling Conversation Guide for Healthcare Providers for Pregnant Women with Symptoms of Zika*[45] (Appendix J). This guide includes talking points and recommendations on how to explain what each test result (positive, presumptive, or negative) could mean for a woman's pregnancy.

Pretest Counseling Conversation Guide for Healthcare Providers for Pregnant Women with Symptoms of Zika **(Appendix J)**

This guide describes recommendations for conducting pretesting counseling for symptomatic pregnant women with possible recent exposure (they or their sex partner live in or recently traveled to an area with risk of Zika). Symptoms of Zika include red eyes, fever, joint pain, and rash. CDC recommends testing for pregnant women with symptoms of Zika.This material includes sample scripts to guide discussions with your patients about the complexity of Zika testing and the testing process with patients. Because a lot of content is outlined for discussion, make additional information available to support messaging and ensure that patients understand what they are being told.

Pregnant women coming in for Zika testing may feel worried or anxious. Support them by providing them with clear and easy-to-understand information and expressing empathy by acknowledging their concerns and feelings during pretesting counseling.

Recommendation	Sample Script
Provide the patient with information on why you will be testing them for Zika and a brief overview of what to expect	*Use one of the two following sentences to begin the discussion:* 1. You may be at risk for having Zika since you or your sex partner recently traveled to *(replace "recently traveled to" with "live in" as appropriate)* an area with risk of Zika within the past 12 weeks and you have had *(replace 'have had' with "during your pregnancy you previously had" as appropriate)* symptoms of Zika. OR/AND 2. You may be at risk of having Zika because you recently had sex without a condom with a person who traveled to *(replace "traveled to" with "lives in" as appropriate)* an area with risk of Zika within the past 12 weeks and you have had *(replace 'have had' with "during your pregnancy you previously developed" as appropriate)* symptoms of Zika. Since you may have been exposed to Zika and are experiencing symptoms *(replace "are experiencing" with 'during your pregnancy you previously experienced" as appropriate)*, I think it is best to move forward with testing you for Zika. Before we begin, I would like to tell you what to expect throughout this process.

[45] CDC. (2017, August 25). Pretest Counseling ConversaÃon Guide for Healthcare Providers for Pregnant Women with Symptoms of Zika. Retrieved from hÃps://www.cdc.gov/zika/pdfs/clinician-guide-symptoms.pdf

PRENATAL MANAGEMENT

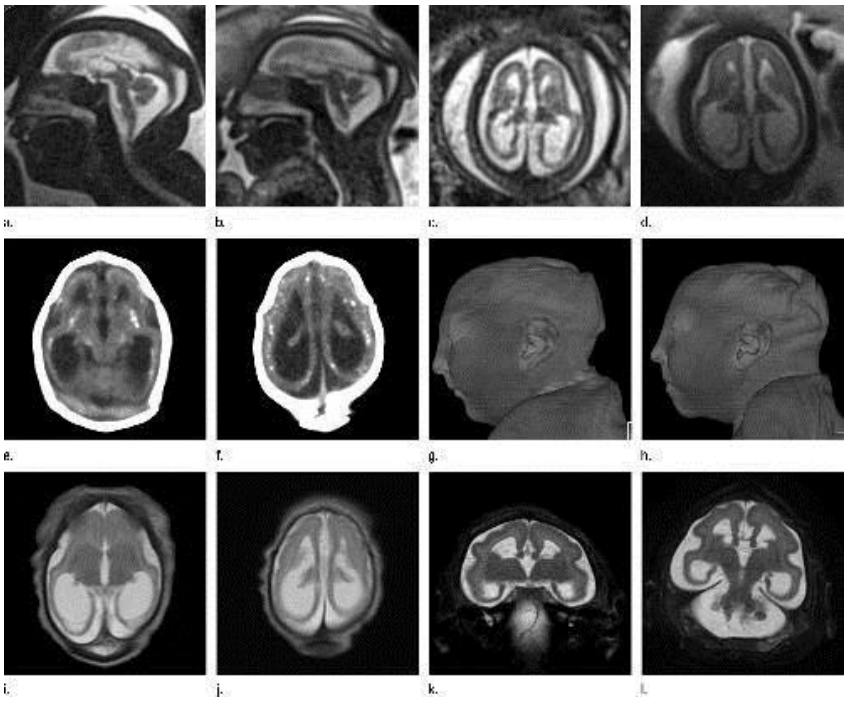
Pregnant women with laboratory evidence of possible Zika virus infection should receive fetal ultrasounds every 3-4 weeks. This is to assess fetal anatomy and to monitor growth. Given the length of time for the detection of prenatal microcephaly, prenatal ultrasounds should carefully evaluate the fetal anatomy, particularly the neuroanatomy, to identify brain or structural abnormalities that might occur before microcephaly.[46]

Infants with abnormal prenatal ultrasound findings (such as microcephaly, hydrocephaly, anencephaly, and intracranial calcification) are susceptible to a high risk delivery. Arrangements should be made for these infants to be born at an equipped facility.

Prenatal care should proceed as usual, addressing complications as they arise during routine care. Once a pregnant woman has tested positive for Zika virus infection, she does **NOT** need to be tested again.

The following images are from a case of a 24-year-old woman pregnant with twins, with characteristic rash at 9 weeks of pregnancy and confirmed Zika virus infection (Figure 3). [47] For each pair of images, the first image is of twin A, and the second image is of twin B.

Figure 3: Abnormalities in twins of woman with confirmed Zika virus infection



[46] Oduyebo, T., Polen, K. D., Walke, H. T., et al. (2017, July 28). Update: Interim Guidance for Health Care Providers Caring for Pregnant Women with Possible Zika Virus Exposure — United States (Including U.S. Territories). *MMWR. Morbidity and Mortality Weekly Report, 66*(29), 781-793. doi:10.15585/mmwr.mm6629e1

[47] Oliveira-Szejnfeld, P. S., Levine, D., Melo, A. S., Amorim, M. M., BaĀsta, A. G., Chimelli, L., et al. (2016). Congenital Brain AbnormaliĀes and Zika Virus: What the Radiologist Can Expect to See Prenatally and Postnatally. *Radiology, 281*(1), 203-218. doi:10.1148/radiol.2016161584

LABOR

ROUTINE CARE

Any pregnant healthcare personnel can care for patients with Zika virus infection.[48] The CDC and OSHA recommend use of standard precautions in all healthcare settings to protect both healthcare personnel and other patients from infection with Zika virus.[49] Because Zika can be asymptomatic in any patient, healthcare personnel should adhere to standard precautions for all patients.[50] Healthcare providers should use soap and water or alcohol-based products (gels, rinses, foams) before and after all patient contact and after removing personal protective equipment.

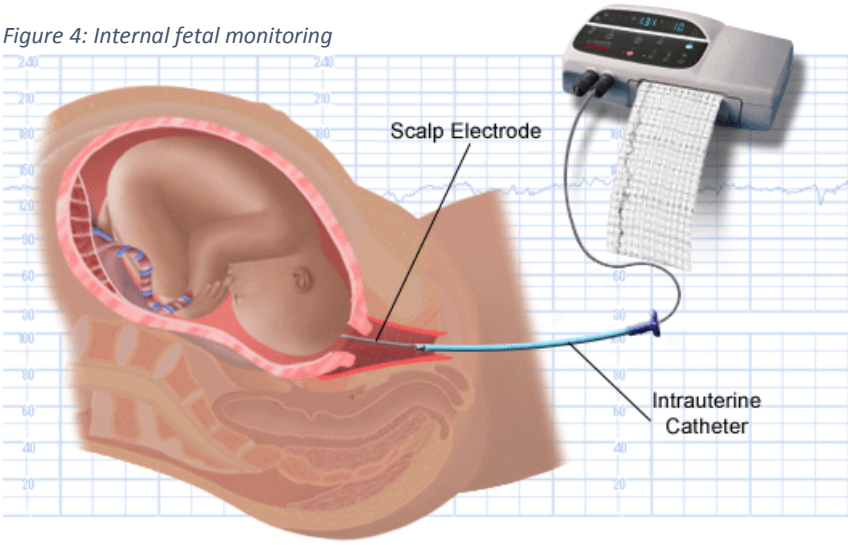
PAIN MANAGEMENT

Pain management (i.e. epidural, IV pain medication) for a laboring woman is routine, regardless of Zika virus status. No other precaution, other than standard precautions, is required.[51]

INTERNAL FETAL MONITORING

Internal fetal monitoring should be implemented as necessary (Figure 4). Standard precautions are recommended in caring for any patient, including those with Zika virus infection. Placement of a fetal scalp electrode require protection of healthcare personnel's skin and clothing using gloves and an impermeable gown.[52]

Figure 4: Internal fetal monitoring



[48] CDC. (2017, December 12). Healthcare Exposure to Zika and InfecĀon Control. Retrieved from hĀps://www.cdc.gov/zika/hc-providers/infecĀon-control.html
[49] Olson, C. K., Iwamoto, M., Perkins, K. M., et al. (2016, March 25). PrevenĀng Transmission of Zika Virus in Labor and Delivery SeĀ ngs Through ImplementaĀon of Standard PrecauĀons. *MMWR. Morbidity and Mortality Weekly Report, 65*(11), 290–292. doi:10.15585/mmwr.mm6511e3
[50] CDC. (2017, August 29). Healthcare Exposure to Zika and InfecĀon Control. hĀps://www.cdc.gov/zika/hc-providers/infecĀon-control.html
[51] Olson, C. K., Iwamoto, M., Perkins, K. M., et al. (2016, March 25). PrevenĀng Transmission of Zika Virus in Labor and Delivery SeĀ ngs Through ImplementaĀon of Standard PrecauĀons. *MMWR. Morbidity and Mortality Weekly Report, 65*(11), 290–292. doi:10.15585/mmwr.mm6511e3
[52] Olson, C. K., Iwamoto, M., Perkins, K. M., et al. (2016, March 25). PrevenĀng Transmission of Zika Virus in Labor and Delivery SeĀ ngs Through ImplementaĀon of Standard PrecauĀons. *MMWR. Morbidity and Mortality Weekly Report, 65*(11), 290–292. doi:10.15585/mmwr.mm6511e3

DELIVERY

Presence of Zika infection does not alter the management of delivery for a vaginal or cesarean delivery. The delivery of a woman with Zika virus infection should proceed routinely. Any complications may be addressed as per hospital protocol. Universal precautions are recommended throughout the delivery.

KEY NOTES:

For women with unknown Zika virus infection status, maternal screening and testing should be performed prior to admission into Labor and Delivery.

Infants born to women with laboratory evidence of confirmed or possible Zika virus infection should be evaluated for congenital Zika virus infection through testing of placental and infant serum and urine in accordance with the Los Angeles County Public Health Laboratory (PHL) guidance. Zika virus testing is recommended for these infants regardless of the presence or absence of phenotypic abnormalities, but the types of specimens to collect vary according to maternal Zika screening and confirmatory lab test results. Testing placental tissue specimens from pregnancies with possible Zika virus infection can be considered for diagnostic purposes in certain scenarios.[53] Please contact the PHL at 562-658-1330 for the most updated placenta collection recommendations.

[53] Oduyebo, T., Polen, K. D., Walke, H. T., et al. (2017, July 28). Update: Interim Guidance for Health Care Providers Caring for Pregnant Women with Possible Zika Virus Exposure. *MMWR. Morbidity and Mortality Weekly Report, 66*(29), 781-793. doi:10.15585/mmwr.mm6629e1

SPECIMEN COLLECTION

For women with known Zika virus infection test results, no maternal blood needs to be drawn on admission.

Infant testing is performed after delivery. Infant testing *may* depend on maternal Zika screening and confirmatory lab test results. Please contact the Los Angeles County Public Health Laboratory at 562-658-1330 for the most updated placenta collection recommendations.

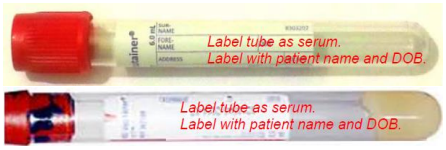
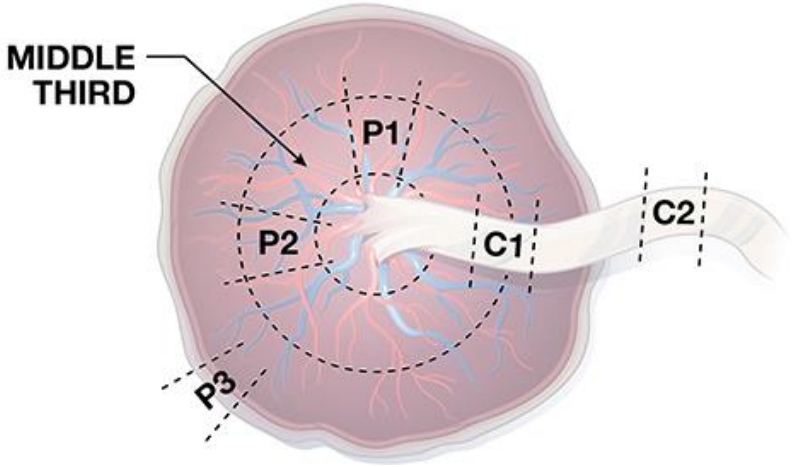
KEY NOTES:

Infant serum and urine specimens are collected at the delivery of every Zika-positive mother.

Collection of placenta and umbilical cord specimens *depends* on maternal Zika screening and confirmatory lab test results. Please contact the Los Angeles County Public Health Laboratory at 562-658-1330 for the most updated placenta collection recommendations.

Table 3 describes what infant specimens and equipment are needed for collection.

Table 3: Infant Specimens Collected

Serum	Red top pediatric microtainer tube	
Urine	Sterile urine container	
Placenta and umbilical cord	10% neutral buffered formalin for fixed tissue samples	

INDICATIONS FOR ZIKA TESTING

The Los Angeles County Department of Public Health Acute Communicable Disease Control has created the following table to assess Indications for Zika Testing for pregnant women and infants (Appendix G). Please contact the Los Angeles County Public Health Laboratory at 562-658-1330 for the most updated specimen collection recommendations.

Indications for Zika Testing (Appendix G)

Indications for Zika Testing	RT-PCR (serum, urine, or other)	IgM[1] (serum)
Pregnancy-associated		
Symptomatic[2] pregnant woman *with* travel[3] or sexual[4] exposure history	ASAP Serum & Urine < 12 weeks of onset	Concurrent with PCR
Symptomatic pregnant woman *without* travel or sexual exposure history	Not recommended	Not recommended
Pregnant woman with travel or sexual exposure history and ultrasound evidence of fetal microcephaly and/or calcifications OR fetal loss, regardless of symptom status	ASAP Serum & Urine < 12 weeks after possible exposure (amniotic fluid if amniocentesis preformed)	Concurrent with PCR
Pregnant woman with ongoing exposure (lives in or frequently travels to Zika risk area or ongoing unprotected sexual activity with potentially infected partner)	Serum & Urine Test 3 times during pregnancy	Consider concurrent with PCR but not routinely recommended
Asymptomatic pregnant traveler	Not routinely recommended**	Not routinely recommended
Infants*		
Infant with microcephaly and/or calcifications, and maternal Zika virus exposure regardless of maternal test results	Serum & Urine (CSF if available***) < 2 DAYS after birth	Concurrent with PCR (CSF if available)
Infant with no apparent defect and evidence of maternal Zika virus infection (IgM), or exposure history and awaiting maternal lab results (PRNT)	Serum & Urine (CSF if available) < 2 DAYS after birth	Concurrent with PCR (CSF if available)
Infant with no apparent defect, and no evidence of maternal Zika virus infection or exposure history	Not Recommended	Not Recommended

* Cord blood is not recommended for testing

The CDC *Interim Guidance for Zika Virus Testing of Formalin-Fixed Paraffin-Embedded Placenta, Fetal, or Infant Autopsy Tissues*[54] (Appendix K) also provides instructions for determining when placenta and umbilical cord specimen collection is recommended. Please contact the Los Angeles County Public Health Laboratory (PHL) at 562-658-1330 for the most updated placenta collection recommendations.

[54] CDC. (2017, August 15). Interim Guidance for Zika Virus TesĀng of Formalin-Fixed ParaĀ n-Embedded Placenta, Fetal, or Infant Autopsy Tissues. Retrieved from hĀps://www.cdc.gov/zika/pdfs/specimen-zika-virus-tesĀng-fact-sheet.pdf

INSTRUCTIONS FOR INFANT ZIKA SPECIMEN COLLECTION

The *Instructions for Infant Zika Specimen Collection*[55] (Appendix L) are pictured below as per the Los Angeles County Public Health Laboratory (PHL). Placenta and umbilical cord cutting and storage, if collected, should be performed by a laboratory pathologist. Please contact the PHL at 562-658-1330 for the most updated placenta collection recommendations.

Instructions for Infant Zika Specimen Collection **(Appendix L)**

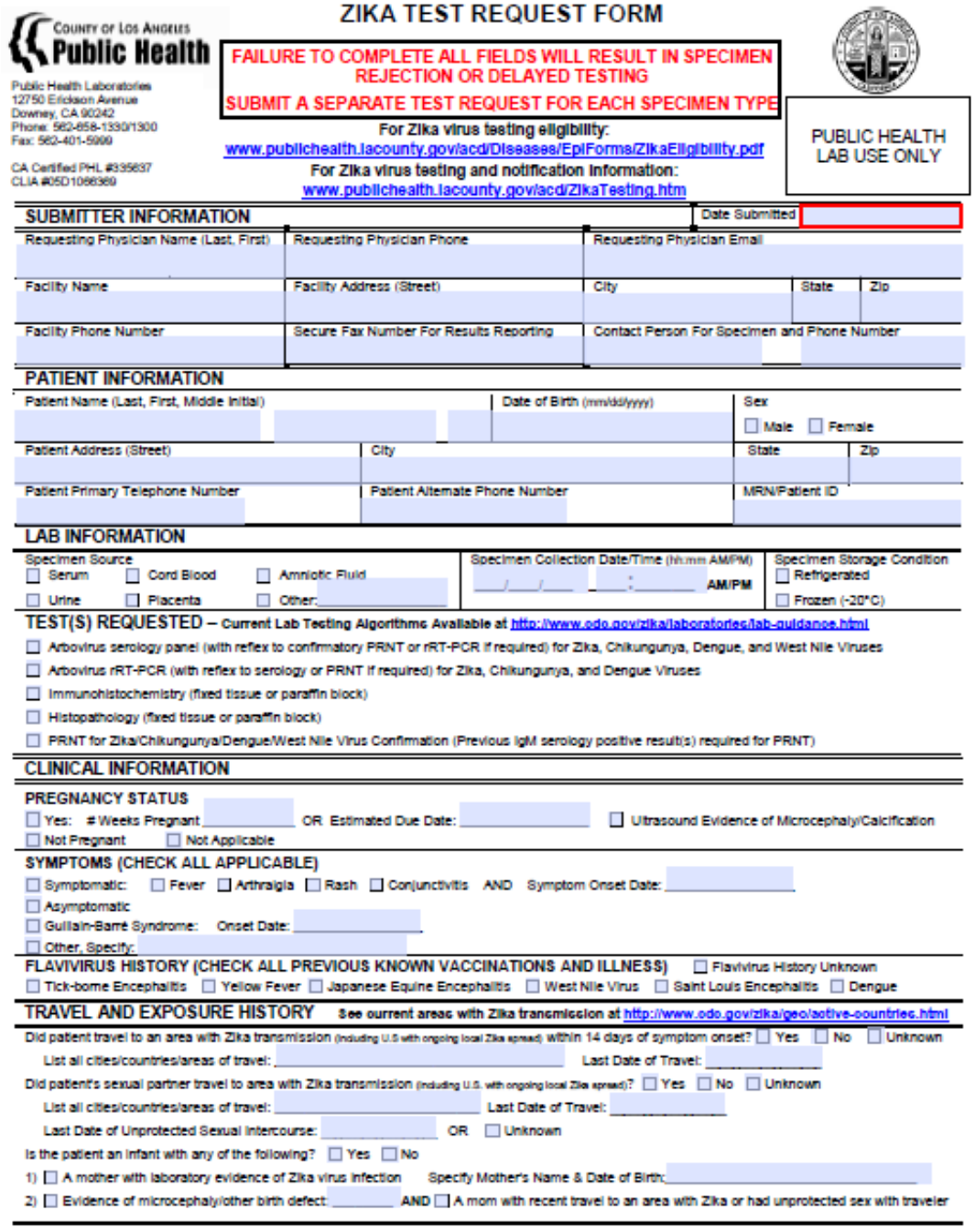
SPECIMEN	GENERAL INSTRUCTIONS	NOTES	STORAGE
Placenta and fetal membranes (fixed)	Several full thickness pieces including **at least 3** full thickness pieces (0.5–1 cm x 3–4 cm in depth) from middle third of placental disk and **at least 1** from the placental disk margin 5 x 12 cm strip of fetal membranes Please include sections of the placental disk, fetal membranes, and pathologic lesions when possible.	Please include information about placenta weight and sample both maternal and fetal side of the placenta Label all specimens to identify location of sample Fix specimens in formalin Volume of formalin used should be about 10x mass of tissue. Place in 10% neutral buffered formalin for a minimum of 3 days. **Order histopathology**	**Storage and transport at room temperature for fixed specimens**
Umbilical cord	2.5 cm segments of cord **At least 4** specimens Umbilical cord segments should be obtained proximal, middle, and distal to umbilical cord insertion site on the placenta	Label all specimens to identify location of sample. Fix specimens in formalin Volume of formalin used should be about 10x mass of tissue. Place in 10% neutral buffered formalin for a minimum of 3 days **Order histopathology**	**Storage and transport at room temperature for fixed specimens**
Infant urine	1-5 mL in sterile container (bagged urine transferred to sterile container)	Collection recommended within first 2 days after birth. Specimens collected up to 12 weeks will be tested. **Order PCR**	**Store in fridge** **Transport on cold pack**
Infant serum	**At least 1mL collected in red top pediatric microtainer tube**	**Collection recommended within first 2 days after birth. Specimens collected up to 12 weeks will be tested.** Order PCR and serology	**Store in fridge** **Transport on cold pack**

[55] Los Angeles County Public Health Laboratories (2017, April 18). InstrucĀons for Zika (pregnant mother at Āme of birth). Retrieved from hĀp://publichealth.lacounty.gov/mch/ReproducĀveHealth/Zika-MCAH/Forms/InstrucĀonsForSpecimenCollecĀon(4-18-17).pdf

PUBLIC HEALTH LABORATORY ZIKA TEST RQEUEST FORM

A *Zika Test Request Form*[56] (Appendix M) must be included with **each** specimen collected at the time of delivery. If maternal screening tests are performed prior to admission into Labor and Delivery, a separate *Zika Test Request Form* must be completed for maternal tests.

Zika Test Request Form (Appendix M)



ZIKA TEST REQUEST FORM

COUNTY OF LOS ANGELES Public Health

Public Health Laboratories
12750 Erickson Avenue
Downey, CA 90242
Phone: 562-658-1330/1300
Fax: 562-401-5999

CA Certified PHL #335637
CLIA #05D1066360

FAILURE TO COMPLETE ALL FIELDS WILL RESULT IN SPECIMEN REJECTION OR DELAYED TESTING
SUBMIT A SEPARATE TEST REQUEST FOR EACH SPECIMEN TYPE

For Zika virus testing eligibility:
www.publichealth.lacounty.gov/acd/Diseases/EpiForms/ZikaEligibility.pdf
For Zika virus testing and notification information:
www.publichealth.lacounty.gov/acd/ZikaTesting.htm

PUBLIC HEALTH LAB USE ONLY

SUBMITTER INFORMATION — Date Submitted
Requesting Physician Name (Last, First) | Requesting Physician Phone | Requesting Physician Email
Facility Name | Facility Address (Street) | City | State | Zip
Facility Phone Number | Secure Fax Number For Results Reporting | Contact Person For Specimen and Phone Number

PATIENT INFORMATION
Patient Name (Last, First, Middle Initial) | Date of Birth (mm/dd/yyyy) | Sex ☐ Male ☐ Female
Patient Address (Street) | City | State | Zip
Patient Primary Telephone Number | Patient Alternate Phone Number | MRN/Patient ID

LAB INFORMATION
Specimen Source: ☐ Serum ☐ Cord Blood ☐ Amniotic Fluid ☐ Urine ☐ Placenta ☐ Other:
Specimen Collection Date/Time (hh:mm AM/PM) AM/PM
Specimen Storage Condition: ☐ Refrigerated ☐ Frozen (-20°C)

TEST(S) REQUESTED – Current Lab Testing Algorithms Available at http://www.cdc.gov/zika/laboratories/lab-guidance.html
☐ Arbovirus serology panel (with reflex to confirmatory PRNT or rRT-PCR if required) for Zika, Chikungunya, Dengue, and West Nile Viruses
☐ Arbovirus rRT-PCR (with reflex to serology or PRNT if required) for Zika, Chikungunya, and Dengue Viruses
☐ Immunohistochemistry (fixed tissue or paraffin block)
☐ Histopathology (fixed tissue or paraffin block)
☐ PRNT for Zika/Chikungunya/Dengue/West Nile Virus Confirmation (Previous IgM serology positive result(s) required for PRNT)

CLINICAL INFORMATION
PREGNANCY STATUS
☐ Yes: # Weeks Pregnant ____ OR Estimated Due Date: ____ ☐ Ultrasound Evidence of Microcephaly/Calcification
☐ Not Pregnant ☐ Not Applicable

SYMPTOMS (CHECK ALL APPLICABLE)
☐ Symptomatic: ☐ Fever ☐ Arthralgia ☐ Rash ☐ Conjunctivitis AND Symptom Onset Date: ____
☐ Asymptomatic
☐ Guillain-Barré Syndrome: Onset Date: ____
☐ Other, Specify: ____

FLAVIVIRUS HISTORY (CHECK ALL PREVIOUS KNOWN VACCINATIONS AND ILLNESS) ☐ Flavivirus History Unknown
☐ Tick-borne Encephalitis ☐ Yellow Fever ☐ Japanese Equine Encephalitis ☐ West Nile Virus ☐ Saint Louis Encephalitis ☐ Dengue

TRAVEL AND EXPOSURE HISTORY See current areas with Zika transmission at http://www.cdc.gov/zika/geo/active-countries.html
Did patient travel to an area with Zika transmission (including U.S with ongoing local Zika spread) within 14 days of symptom onset? ☐ Yes ☐ No ☐ Unknown
List all cities/countries/areas of travel: ____ Last Date of Travel: ____
Did patient's sexual partner travel to area with Zika transmission (including U.S. with ongoing local Zika spread)? ☐ Yes ☐ No ☐ Unknown
List all cities/countries/areas of travel: ____ Last Date of Travel: ____
Last Date of Unprotected Sexual Intercourse: ____ OR ☐ Unknown
Is the patient an infant with any of the following? ☐ Yes ☐ No
1) ☐ A mother with laboratory evidence of Zika virus infection Specify Mother's Name & Date of Birth: ____
2) ☐ Evidence of microcephaly/other birth defect: ____ AND ☐ A mom with recent travel to an area with Zika or had unprotected sex with traveler

[56] County of Los Angeles Public Health Laboratories. (2016, December 6). Zika Test Request Form Retrieved from hĀp://publichealth.lacounty.gov/acd/Diseases/EpiForms/ZikaInfoTestReq.pdf

CONTACTS FOR ASSISTANCE AND COURIER SERVICES

The Los Angeles County Public Health Laboratory is the point of contact for all Zika screening testing (blood or serum) and Zika specimen collection (infant specimens). Hospitals may arrange for Public Health Laboratory courier services to retrieve Zika specimens after they have been collected, cut, and stored properly.

Any questions regarding Zika specimen collection should be made to the Public Health Laboratory at the number listed on the *Laboratory Contact Information for Zika* (Appendix N) sheet below. Arrangements for courier services may also be made at the number below.

Laboratory Contact Information for Zika (Appendix N)

Los Angeles County Public Health Department
Laboratory Contact Information for Zika

Please notify the Los Angeles County Department of Public Health when a pregnant woman positive for ZIKA arrives at your hospital. Call 213-240-7941.

For questions regarding **ZIKA specimen collection**, please contact the Los Angeles County Public Health Laboratories:

Business hours, **562-658-1330**
After hours, **213-974-1234** (press # 8)

Remember:

- A separate **ZIKA Test Request Form** must accompany each specimen
- Mother must give consent in advance if the provider wants to collect placental specimens

To arrange courier service and pick up of ZIKA specimens, contact the Public Health Laboratory:

Business hours, **562-658-1460**
After hours, **213-974-1234** (press # 8)

For questions regarding the **Neonate Form**, call **626-569-6508**

ZIKA LABOR AND DELIVERY ALGORITHMS

The following three figures show the management of care of women who present on Labor and Delivery (Figures 5, 6, and 7).

Figure 5: Pregnant Woman Discharged Home Undelivered

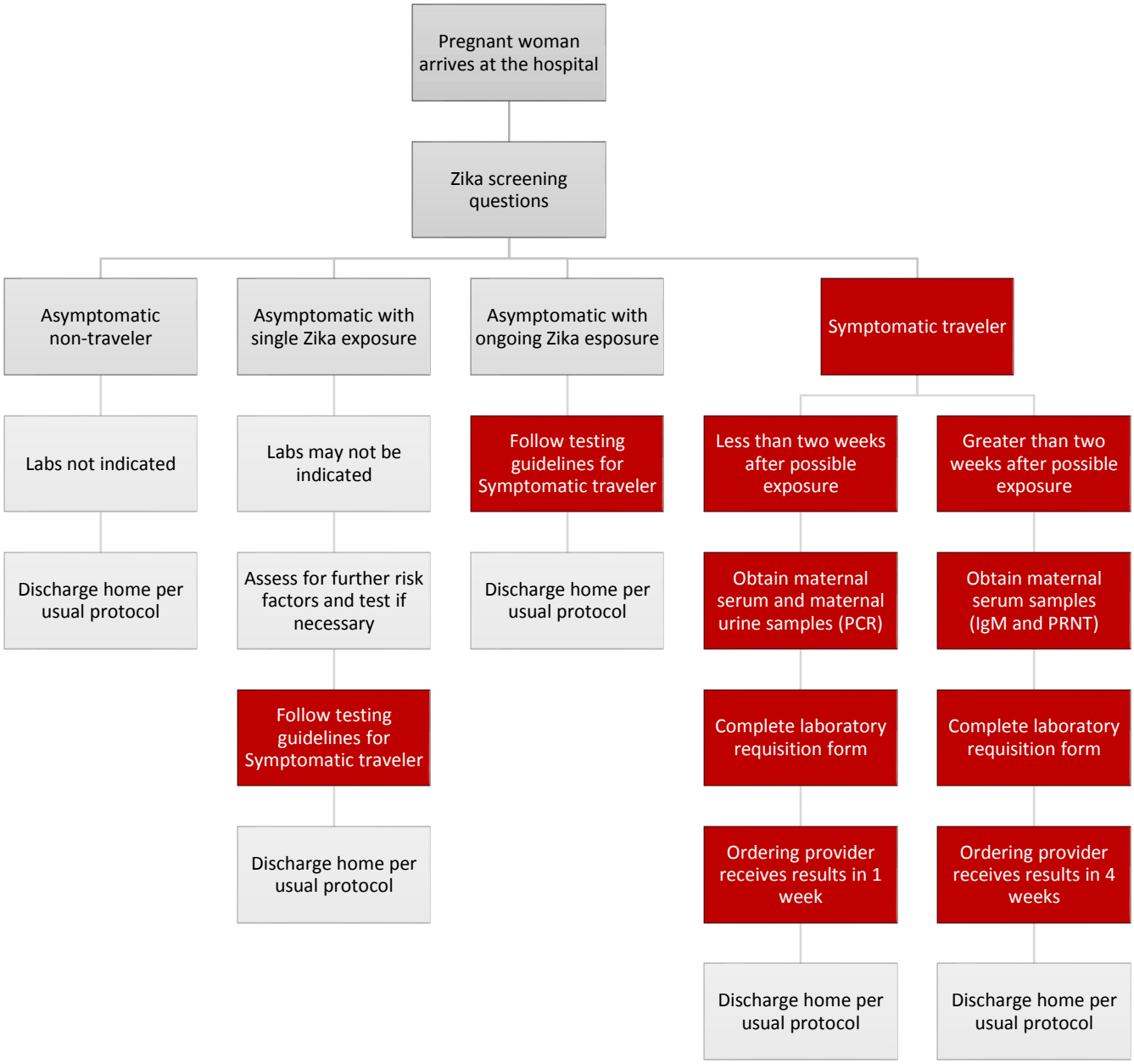


Figure 6: Pregnant Woman Arrives in Labor and Delivery

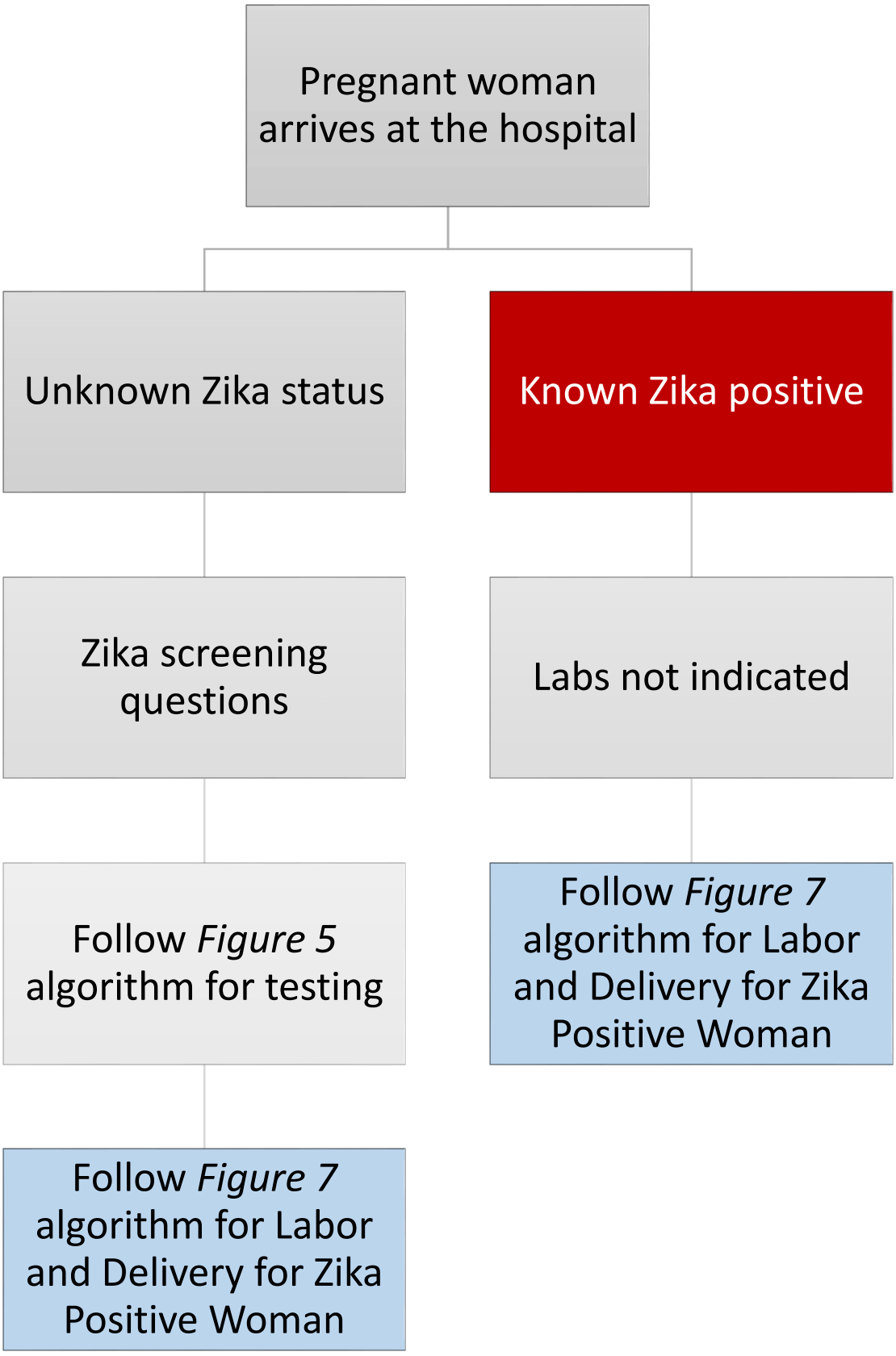
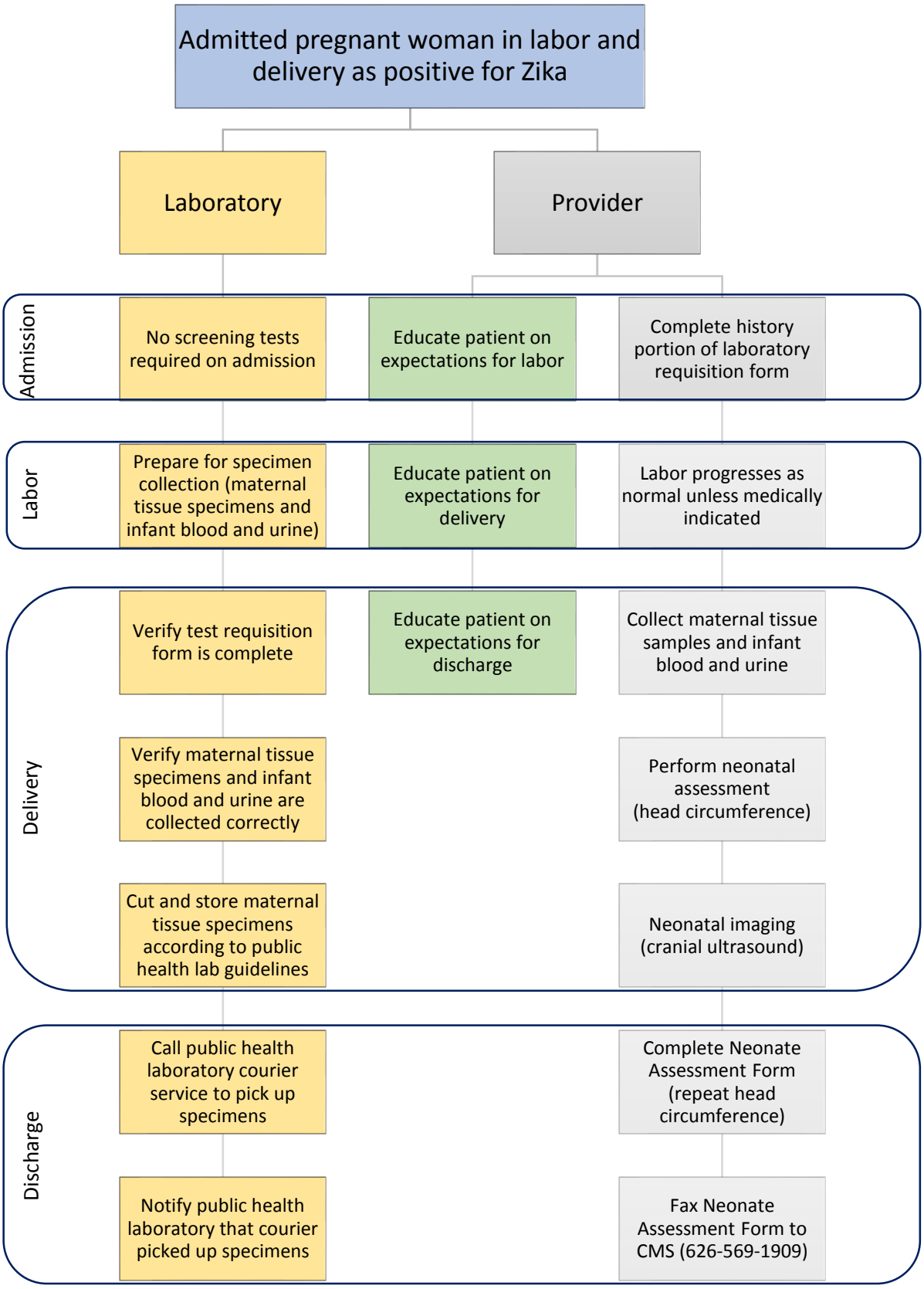


Figure 7: Labor and Delivery for Zika Positive Woman



POSTPARTUM

Standard postpartum care should be provided to Zika positive women regardless of vaginal or cesarean delivery.

COUPLET CARE

Newborns of Zika-positive mothers who are born without any observable malformations and with no other medical anomalies may receive standard evaluations at the time of birth.[57] Routine care can be provided in the newborn nursery or in couplet care *without* being transferred to the neonatal intensive care unit (NICU), unless otherwise medically necessary. NICU admission is not necessary for routine care of Zika specimen collection work-up. Couplet care helps with breastfeeding and bonding (Figure 8).

Figure 8: Woman breastfeeding

BREASTFEEDING

Transmission of Zika virus infection through breastfeeding has not been documented, but theoretical transmission is possible. Although Zika virus has been detected in breast milk, no cases of Zika virus infection associated with breastfeeding have been reported, and current evidence suggests that the benefits of breastfeeding outweigh the theoretical risk of Zika virus transmission.[58] Breastfeeding should be encouraged for nutrition and bonding.

The CDC and the World Health Organization recommend that infants born to women with suspected, probable, or confirmed Zika virus infection, or who live in or have traveled to areas with risk of Zika, should be fed according to established infant feeding guidelines:[59]

- These infants should start breastfeeding within one hour of birth, be exclusively breastfed for 6 months, and have introduction of adequate, safe, and properly fed complementary foods, while continuing breastfeeding up to 2 years old or beyond

- All mothers who decide to breastfeed should receive skilled support to initiate and sustain breastfeeding

[57] Adebanjo, T., Godfred-Cato, S., Viens, L., et al. (2017, October 20). Update: Interim Guidance for the Diagnosis, EvaluaÃon, and Management of Infants with Possible Congenital Zika Virus InfecÃon *MMWR. Morbidity and Mortality Weekly Report, 66*(41), 1089–1099. doi:10.15585/mmwr.mm6641a1

[58] Russell, K., Oliver, S. E., Lewis, L., BarÃeld, W. D., Cragan, J., Meaney-Delman, D., et al. (2016, August 26). Update: Interim Guidance for the EvaluaÃon and Management of Infants with Possible Congenital Zika Virus InfecÃon. *MMWR. Morbidity and Mortality Weekly Report, 65*(33), 870-878. doi:10.15585/mmwr.mm6533e2

[59] CDC. (2017, September 18). Key Messages Zika Virus Disease. Retrieved from hÃps://www.cdc.gov/zika/pdfs/zika-key-messages.pdf

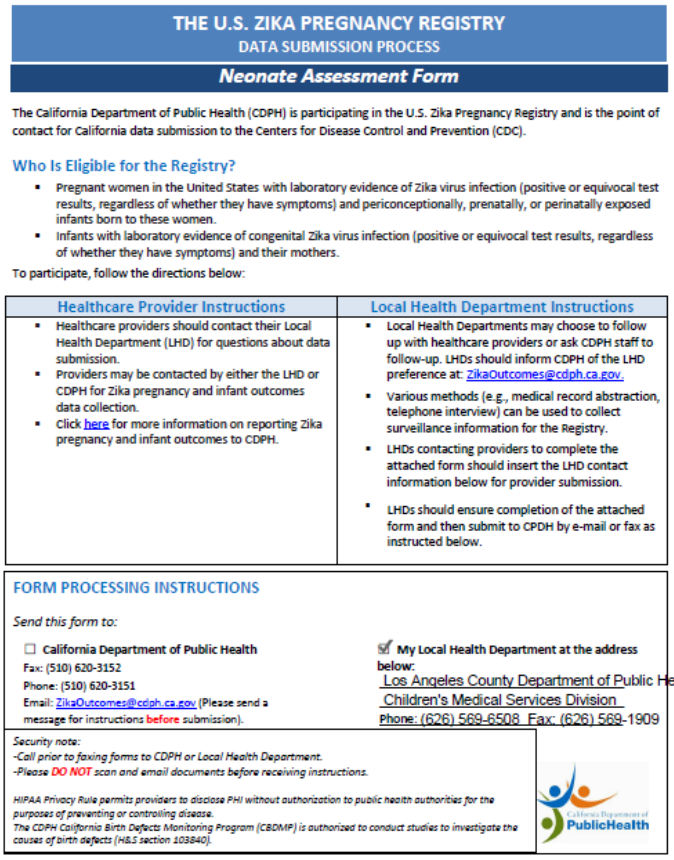
- Mothers and families of infants born with congenital anomalies, such as microcephaly, or those presenting with feeding difficulties, should receive skilled feeding support from health professionals

- Multidisciplinary teams may be necessary for infants who need specialist support in infant feeding, which may be the case in particular for infants born with congenital anomalies, including microcephaly; and long-term management may be necessary

NEONATE ASSESSMENT FORM

The *Neonate Assessment Form*[60] (Appendix O) collects preliminary data on an infant's status at the time of delivery, including a physical assessment, neonate imaging, postnatal infection testing, and any suspected or diagnosed birth defects. This form is to be completed by the pediatrician prior to discharge. The completed Neonate Assessment Form will be faxed to Children's Medical Services for further follow up. After discharge, Children's Medical Services may follow up with these infants for up to 2 years.[61] The Los Angeles County Department of Public Health Children's Medical Services Division may be reached at 626-569-6508.

Neonate Assessment Form (Appendix O)



THE U.S. ZIKA PREGNANCY REGISTRY
DATA SUBMISSION PROCESS

Neonate Assessment Form

The California Department of Public Health (CDPH) is participating in the U.S. Zika Pregnancy Registry and is the point of contact for California data submission to the Centers for Disease Control and Prevention (CDC).

Who Is Eligible for the Registry?

- Pregnant women in the United States with laboratory evidence of Zika virus infection (positive or equivocal test results, regardless of whether they have symptoms) and periconceptionally, prenatally, or perinatally exposed infants born to these women.
- Infants with laboratory evidence of congenital Zika virus infection (positive or equivocal test results, regardless of whether they have symptoms) and their mothers.

To participate, follow the directions below:

Healthcare Provider Instructions	Local Health Department Instructions
▪ Healthcare providers should contact their Local Health Department (LHD) for questions about data submission. ▪ Providers may be contacted by either the LHD or CDPH for Zika pregnancy and infant outcomes data collection. ▪ Click here for more information on reporting Zika pregnancy and infant outcomes to CDPH.	▪ Local Health Departments may choose to follow up with healthcare providers or ask CDPH staff to follow-up. LHDs should inform CDPH of the LHD preference at: ZikaOutcomes@cdph.ca.gov. ▪ Various methods (e.g., medical record abstraction, telephone interview) can be used to collect surveillance information for the Registry. ▪ LHDs contacting providers to complete the attached form should insert the LHD contact information below for provider submission. ▪ LHDs should ensure completion of the attached form and then submit to CPDH by e-mail or fax as instructed below.

FORM PROCESSING INSTRUCTIONS

Send this form to:

☐ **California Department of Public Health**
Fax: (510) 620-3152
Phone: (510) 620-3151
Email: ZikaOutcomes@cdph.ca.gov (Please send a message for instructions before submission).

☑ **My Local Health Department at the address below:**
Los Angeles County Department of Public Health
Children's Medical Services Division
Phone: (626) 569-6508 Fax: (626) 569-1909

Security note:
-Call prior to faxing forms to CDPH or Local Health Department.
-Please DO NOT scan and email documents before receiving instructions.

HIPAA Privacy Rule permits providers to disclose PHI without authorization to public health authorities for the purposes of preventing or controlling disease.
The CDPH California Birth Defects Monitoring Program (CBDMP) is authorized to conduct studies to investigate the causes of birth defects (H&S section 103840).

California Department of PublicHealth

KEY NOTE:

Neonate Assessment Form must be completed by the pediatrician **prior** to hospital discharge.

[60] California Department of Public Health & CDC. (2016, October 14). Neonate Assessment Form. Retrieved from hĀp://publichealth.lacounty.gov/mch/ReproducĀveHealth/Zika-MCAH/Forms/NeonateAssessmentFormLAC_CMS.pdf

[61] CDC. (2018, January 23). US Zika Pregnancy and Infant Registry. Retrieved from hĀps://www.cdc.gov/pregnancy/zika/research/registry.html

ZIKA PREGNANCY REGISTRY

The CDC established the United States Zika Pregnancy Registry (USZPR) to facilitate data collection to update recommendations for clinical care, to plan for services for pregnant women and families affected by Zika virus, and to improve prevention of Zika virus infection during pregnancy.

The USZPR tracks Zika virus infections that occur in pregnant women and their infants.[62] It collects date from both asymptomatic and symptomatic pregnant women with laboratory evidence of possible Zika virus infection and their infants up to 1 year of age (regardless of infant test results). All collected data is de-identified and participation is optional and voluntary.[63]

Provider influence is shown to be critical in getting patients to participate in the registry. The data collected through the Zika pregnancy and infant registries will provide more comprehensive information to complement notifiable disease case reporting, to update recommendations for clinical care, to plan for services for pregnant women and families affected by Zika virus, to improve prevention of Zika virus infection during pregnancy, and to learn more about the effects of Zika virus on the baby's development.[64]

The figure below (Appendix P) is an example of an informational brochure on the USZPR created by the Los Angeles County Department of Public Health MCAH.

United States Zika Pregnancy Registry Brochures in English and Spanish (Appendix P)

KEY NOTE:

The Zika Pregnancy Registry is optional. Pediatricians should encourage new moms to participate in the Zika Pregnancy Registry.

[62] American Congress of Obstetrics and Gynecologists. (2017). US Zika Pregnancy Registry. Retrieved from hĀps://www.acog.org/About-ACOG/ACOG-Departments/Zika-Virus/US-Zika-Pregnancy-Registry

[63] California Department of Public Health. (2017, June 20). US Zika Pregnancy Registry. Retrieved from hĀps://www.cdph.ca.gov/Programs/CID/DCDC/Pages/USZikaPregnancyRegistry.aspx

[64] CDC. (2017, September 18). Key Messages Zika Virus Disease. Retrieved from hĀps://www.cdc.gov/zika/pdfs/zika-key-messages.pdf

DISCHARGE FROM HOSPITAL

Zika-positive women with no complications during hospitalization may be discharged as per usual hospital procedure. Hospitalization does not need to be extended for Zika-positive women. All maternal exposure history and testing results should be shared with all providers caring for the newborn after delivery, including outpatient providers.

FOLLOW UP

Infants should be followed by an established medical home to facilitate coordination of care and receive preventive care, including immunizations, assessment of development and feeding, and monitoring of growth parameters (head circumference, weight, and length). Coordination of care for follow-up appointments with specialists and services recommended during hospital evaluation should be arranged prior to discharge. Hospital medical records, including all Zika testing and evaluation results for both mother and infant, should be shared with the pediatric provider caring for the infant after discharge.

Birth hospitals and primary care providers may consider using Zika Care Connect[65], a national online database with a geographical network of healthcare specialists who care for patients affected by Zika.

If mother and infant enroll in the USZPR, the infant will be followed by case managers at CMS for up to 2 years.[66] This ensures that any signs of Zika Congenital Syndrome are diagnosed at an early age and the appropriate referrals are made. If mother and infant do not enroll in the Zika Pregnancy Registry, the mother will be responsible for ensuring appropriate infant visits with the pediatrician.

In LA County, Children's Medical Services (CMS) coordinates Zika exams with infant's regular pediatric visits at 2, 6, 12, 18, and 24 months of age. The CMS case manager will coordinate the completion of *Infant Follow-Up Forms*[67] with the pediatrician at the appropriate times. CMS may be reached at 626-569-6508.

The CDC has provided multiple resources to guide parents and providers through the first 12 months of an infant's life, with or without apparent Zika-associated birth defects (Appendix Q and Appendix R). The CDC's *Evaluation for Infants with Possible Congenital Zika Virus Infection*[68] (Appendix S) algorithm lists evaluations and tests for an infant prior to discharge, and standard evaluations recommended at birth and during each will-child visit for all infants with possible congenital Zika virus exposure during pregnancy.

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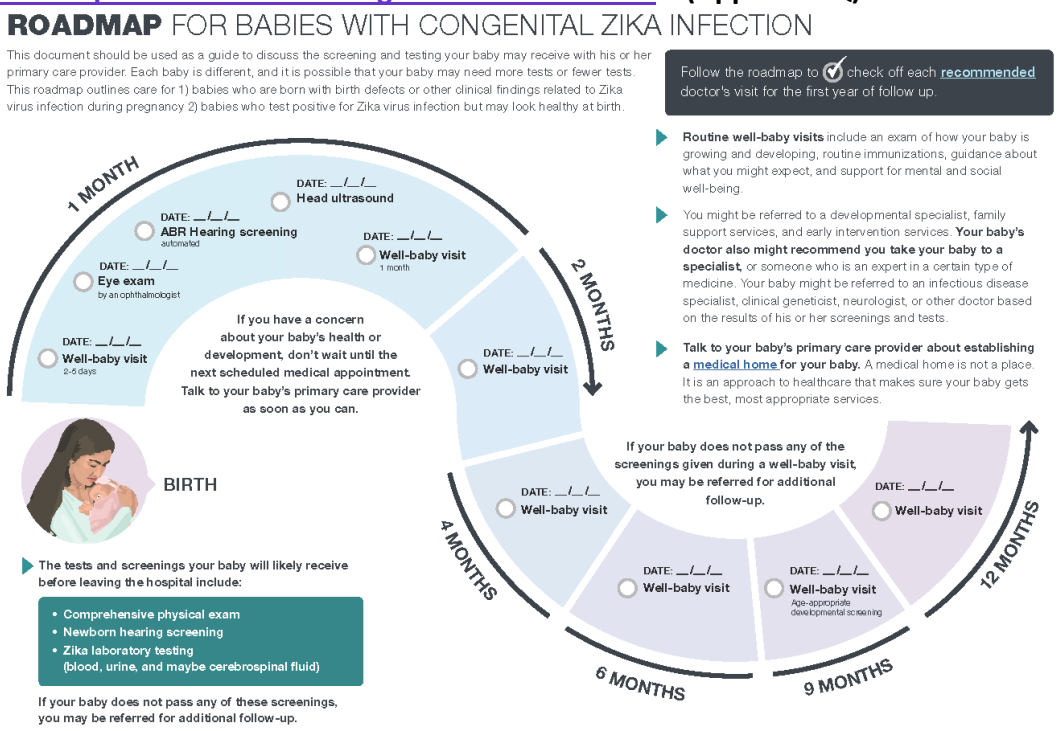
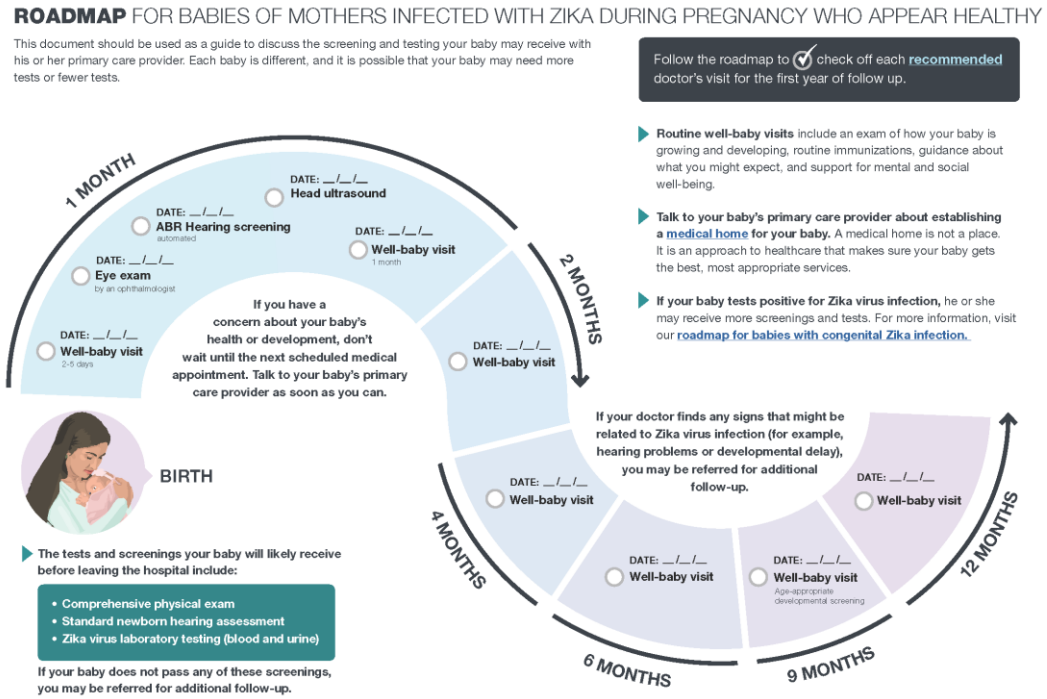
[65] Zika Care Connect & March of Dimes (2017). Retrieved from hĀps://www.zikacareconnect.org/
[66] CDC. (2018, January 23). US Zika Pregnancy and Infant Registry. Retrieved from hĀps://www.cdc.gov/pregnancy/zika/research/registry.html
[67] California Department of Public Health & CDC. (2016, October 14). Infant Follow-Up Form. Retrieved from hĀp://publichealth.lacounty.gov/mch/ReproducĀveHealth/Zika-MCAH/Forms/InfantFollowUpForm_revised10_14_16.pdf
[68] CDC. (2017, November 17). EvaluaĀon for Infants with Possible Congenital Zika Virus InfecĀon. Retrieved from hĀps://www.cdc.gov/zika/pdfs/pediatric-evaluaĀon-follow-up-tool.pdf

CDC Roadmap for Babies with Congenital Zika Infection[69] (Appendix Q)



CDC Roadmap for Babies of Mothers Infected with Zika During Pregnancy Who Appear Healthy[70] (Appendix R)



[69] CDC. (2017, June 5). Roadmap for Babies with Congenital Zika InfecĀon. Retrieved from hĀps://www.cdc.gov/zika/pdfs/roadmap-for-parents.pdf

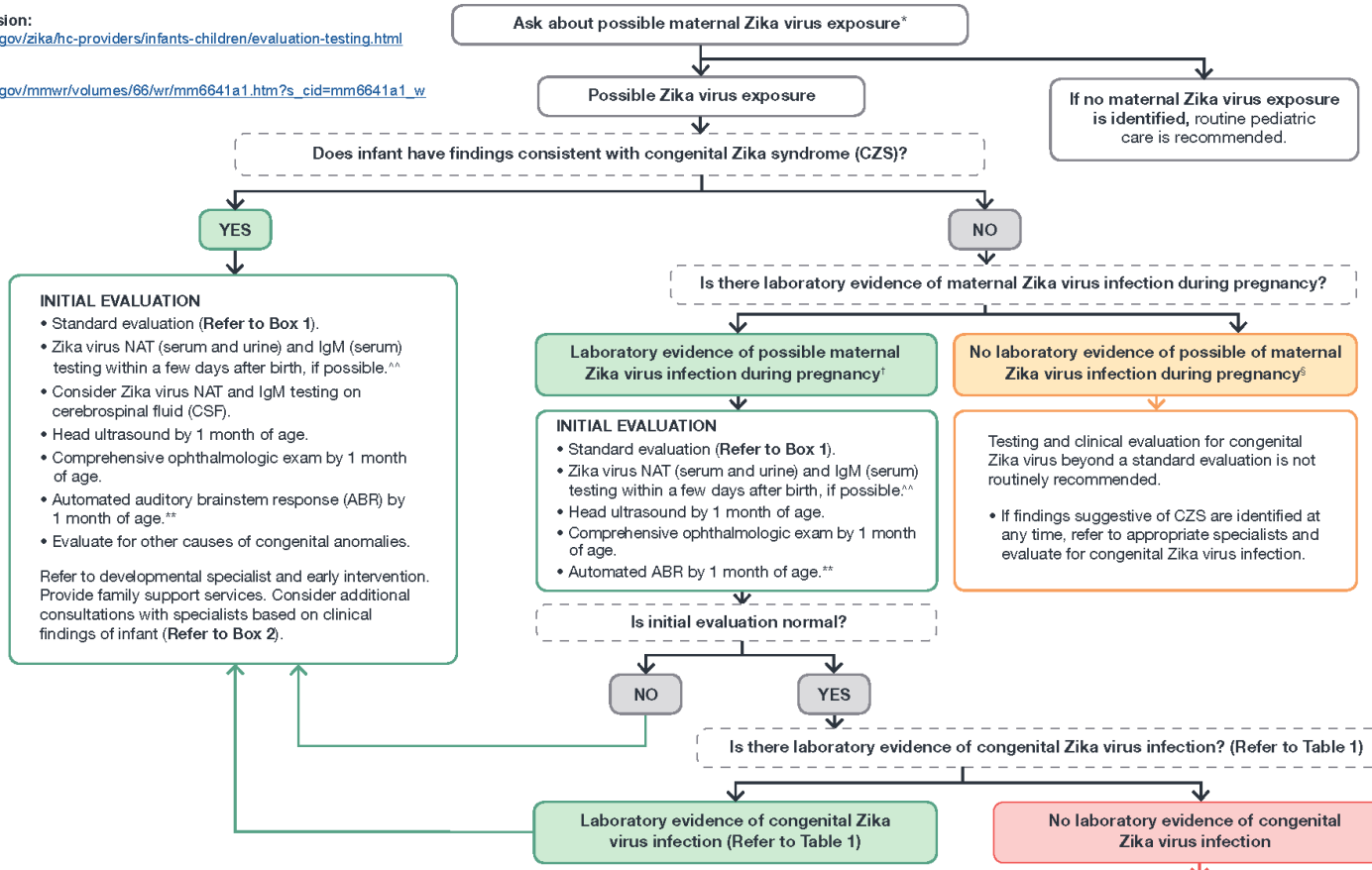
[70] CDC. (2017, June 5). Roadmap for Babies of Mothers Infected with Zika During Pregnancy Who Appear Healthy. Retrieved from hĀps://www.cdc.gov/zika/pdfs/roadmap-for-parents-babies-infected-before-birth.pdf

Evaluation for Infants with Possible Congenital Zika Virus Infection (Appendix S)

EVALUATION FOR INFANTS WITH POSSIBLE CONGENITAL ZIKA VIRUS INFECTION

Accessible Version:
https://www.cdc.gov/zika/hc-providers/infants-children/evaluation-testing.html

MMWR:
https://www.cdc.gov/mmwr/volumes/66/wr/mm6641a1.htm?s_cid=mm6641a1_w



* Possible Zika virus exposure includes travel to, or residence in an area with mosquito-borne Zika virus transmission or sex without the use of condoms with a partner who has traveled to or resides in an area with mosquito-borne Zika virus transmission

† Laboratory evidence of possible Zika virus infection during pregnancy is defined as 1) Zika virus infection detected by a Zika virus RNA NAT on any maternal, placental, or fetal specimen (referred to as NAT-confirmed), or 2) diagnosis of Zika virus infection, timing of infection cannot be determined or unspecified flavivirus infection, timing of infection cannot be determined by serologic tests on a maternal specimen (i.e., positive/equivocal Zika virus IgM and Zika virus PRNT titer ≥10, regardless of dengue virus PRNT value; or negative Zika virus IgM, and positive or equivocal dengue virus IgM, and Zika virus PRNT titer ≥10, regardless of dengue virus PRNT titer). The use of PRNT for confirmation of Zika virus infection, including in pregnant women, is not routinely recommended in Puerto Rico (https://www.cdc.gov/zika/laboratories/lab-guidance.html).

§ This group includes women who were never tested during pregnancy as well as those whose test result was negative because of issues related to timing or sensitivity and specificity of the test. Because the latter issues are not easily discerned, all mothers with possible exposure to Zika virus during pregnancy who do not have laboratory evidence of possible Zika virus infection, including those who tested negative with currently available technology, should be considered in this group.

** Automated ABR by 1 month of age if newborn hearing screen passed but performed with otoacoustic emission (OAE) methodology

^^ If CSF is obtained for other purposes, Zika virus NAT and IgM antibody testing should be performed on CSF.

CS284288 October 19, 2017

Evaluation for Infants with Possible Congenital Zika Virus Infection (Appendix S)

TABLE 1

Interpretation of results of laboratory testing of infant's blood, urine, and/or cerebrospinal fluid for evidence of congenital Zika virus infection		
Infant test results*		
NAT	**IgM**	**Interpretation**
Positive	Any result	Confirmed congenital Zika virus infection†
Negative	Nonnegative§	Probable congenital Zika virus infection¶,**
Negative	Negative	Congenital virus infection unlikely¶,††

Abbreviations: NAT = nucleic acid test; IgM = immunoglobulin M

*Infant serum, urine, or cerebrospinal fluid.
† Distinguishing between congenital and postnatal infection is difficult in infants who live in areas where there is ongoing transmission of Zika virus and who are not tested soon after birth. If the timing of infection cannot be determined, infants should be evaluated as if they had congenital Zika virus infection.
§ Nonnegative serology terminology varies by assay and might include "positive," "equivocal," "presumptive positive," or "possible positive." For explanation of a specific interpretation, refer to the instructions for use for the specific assay performed.
¶ Laboratory results should be interpreted in the context of timing of infection during pregnancy, maternal serology results, clinical findings consistent with congenital Zika syndrome, and any confirmatory testing with plaque reduction neutralization testing.
** A negative Zika virus plaque reduction neutralization test suggests that the infant's Zika virus IgM test is a false positive.
†† Congenital Zika virus infection is unlikely if specimens are collected within the first few days after birth and the clinical evaluation is normal; however, health care providers should remain alert for any new findings of congenital Zika virus infection.

BOX 1. Standard evaluation recommended at birth and during each well visit for all infants with possible congenital Zika virus exposure during pregnancy

- Comprehensive physical exam, including growth parameters
- Developmental monitoring and screening using validated screening tools recommended by the American Academy of Pediatrics (https://www.aap.org/en-us/advocacy-and-policy/aap-health-initiatives/Screening/Pages/Screening-Tools.aspx)
- Vision screening as recommended by the American Academy of Pediatrics Policy Statement "Visual System Assessment in Infants, Children, and Young Adults by Pediatricians" (www.pediatrics.org/cgi/doi/10.1542/peds.2015-3596)
- Newborn hearing screen at birth, preferably with automated auditory brainstem response

BOX 2. Consultations for infants with clinical findings consistent with congenital Zika syndrome

- **Consider consultation with the following specialists:**
  - Infectious disease specialist for evaluation for other congenital infections (e.g., toxoplasmosis, syphilis, rubella, cytomegalovirus, or herpes simplex virus) and assistance with Zika virus diagnosis, testing, and counseling
  - Neurologist by age 1 month for comprehensive neurologic examination and consideration for other evaluations such as advanced neuroimaging and EEG
  - Ophthalmologist for comprehensive eye exam by age 1 month
  - Clinical geneticist for confirmation of the clinical phenotype and evaluation for other causes of microcephaly or congenital anomalies
  - Early intervention and developmental specialists
  - Family and supportive services
- **Additional possible consultations, based on clinical findings of the infant:**
  - Endocrinologist for evaluation of hypothalamic or pituitary dysfunction and consideration for thyroid testing
  - Lactation specialist, nutritionist, gastroenterologist or speech or occupational therapist for evaluation for dysphagia and management of feeding issues
  - Orthopedist, physiatrist, or physical therapist for the management of hypertonia, clubfoot or arthrogrypotic-like conditions
  - Pulmonologist or otolaryngologist for concerns about aspiration

BEST PRACTICES

The following best practices were used by hospitals to improve the coordination and care of Zika-affected women in Labor and Delivery.

ZIKA RESOURCE BINDER

Creation of several Zika resource binders to keep with the charge nurse in labor and delivery and NICU units. This Zika resource binder included the following information:

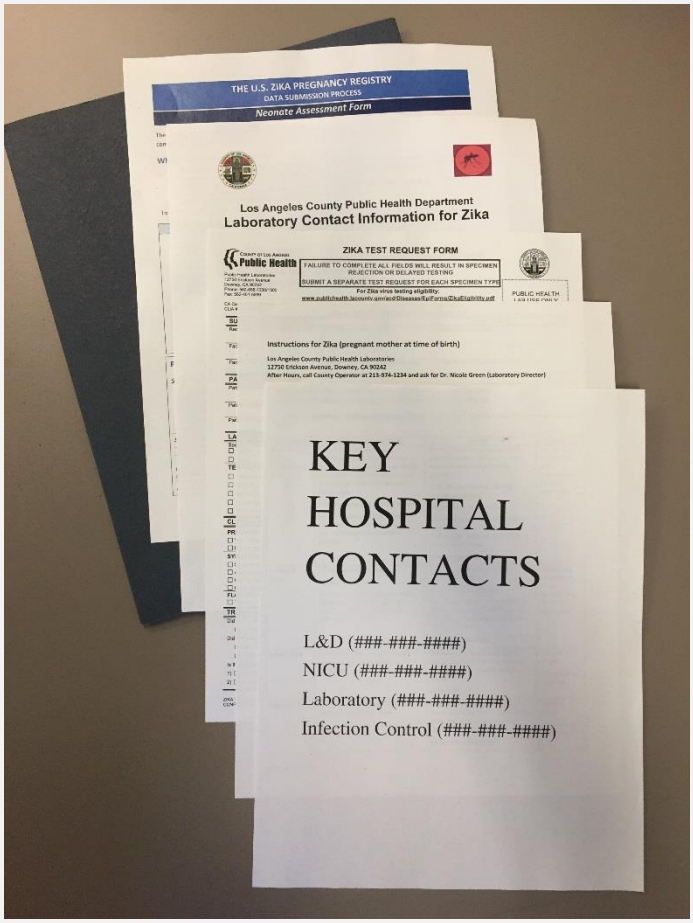
1. Key hospital contacts, including direct numbers to the nurse manager in labor and delivery, nurse manager in NICU, laboratory director, and a key Zika leader (if applicable).

2. *Instructions for Infant Zika Specimen Collection* (Appendix L): This form was produced by the Los Angeles County Public Health Laboratory to provide clear instructions on how to collect, cut, store, and ship specimens for Zika testing at the time of delivery.

3. *Zika Test Request Form* (Appendix M): This requisition form is to be completed for **each** specimen collected.

4. *Laboratory Contact Information for Zika* (Appendix N): This form may be posted in staff lounges, physician call rooms, and inside bathroom stalls for frequent access.

5. *Neonate Assessment Form* (Appendix O): The neonate assessment form is to be completed by the attending pediatrician at the delivery hospital prior to discharge of the mother and infant.



STAFF MEETINGS

Cross collaboration between infection control, labor and delivery, and NICU during departmental meetings or pass-on rounds increased communication, facilitated delegation of roles and responsibilities, and provided team support. Active participation in these meetings included sharing newly acquired education to expand knowledge and address unknowns. One example of this was when an infection control preventionist shared knowledge of using standard precautions to caring for a Zika-affected woman. This knowledge alleviated the fear of transmission expressed by labor and delivery nurses.

LABOR AND DELIVERY NAME ALERT

Hospitals that flagged Zika-affected patients prior to their admission were able to detect these patients upon admission. This information was useful for nurses, who immediately were aware of their patients' conditions and could provide the appropriate education and care.

GUIDE FOR NICU AND PEDIATRIC PROVIDERS

IN THIS SECTION

INFANT SPECIMEN COLLECTION AT TIME OF DELIVERY

Please contact the Los Angeles County Public Health Laboratory (PHL) at 562-658-1330 for the most updated placenta collection recommendations.

Testing placental tissue from pregnancies with possible Zika virus exposure that result in live births can be considered for diagnostic purposes in certain scenarios including: [71]

- Symptomatic pregnant women with possible Zika virus exposure who have no prior testing for Zika virus
- Symptomatic or asymptomatic pregnant women with prior laboratory diagnosis of probable positive Zika and/or Flavivirus infection by IgM antibody testing and PRNT results are still pending – submitting facilities should fix and store the placenta until the PRNT are resulted
- Women with abnormal fetal ultrasound findings during pregnancy with consultation and prior approval by the Los Angeles County Acute Communicable Disease Control Program (213) 240-7941
- Observable abnormalities/birth defect consistent with congenital Zika syndrome

KEY NOTES:

For women with unknown Zika virus infection status, maternal screening and testing should be performed prior to admission into Labor and Delivery.

Please contact the Los Angeles County Public Health Laboratory at 562-658-1330 for the most updated placenta collection recommendations.

Testing of placental tissue for Zika virus infection is not routinely recommended for asymptomatic pregnant women who have recent possible Zika virus exposure (but no ongoing exposure) and who have a live born infant without evidence of possible Zika virus–associated birth defects.[72]

Testing of placental and fetal tissues may be considered in pregnancies resulting in a miscarriage or fetal loss to provide insight into the potential etiology of the fetal loss or infant death. This could help inform a woman's future pregnancy planning.[73]

[71] CDC. (2017, September 1). CollecÃon and Submission of Specimens for Zika Virus TesÃng at Time of Birth. Retrieved from hÃps://www.cdc.gov/zika/pdfs/collecÃon-submission-specimens-zika-tesÃng-at-birth.pdf

[72] Oduyebo, T., Polen, K. D., Walke, H. T., et al. (2017, July 28). Update: Interim Guidance for Health Care Providers Caring for Pregnant Women with Possible Zika Virus Exposure — United States (Including U.S. Territories). *MMWR. Morbidity and Mortality Weekly Report, 66*(29), 781-793. doi:10.15585/mmwr.mm6629e1

[73] Oduyebo, T., Polen, K. D., Walke, H. T., et al. (2017, July 28). Update: Interim Guidance for Health Care Providers Caring for Pregnant Women with Possible Zika Virus Exposure — United States (Including U.S. Territories). *MMWR. Morbidity and Mortality Weekly Report, 66*(29), 781-793. doi:10.15585/mmwr.mm6629e1

INFANT SPECIMEN COLLECTION

Infant testing is performed after delivery. The California Department of Public Health guidelines includes recommendations for Zika Virus Testing for newborn infants.[74] Please contact the Los Angeles County Public Health Laboratory at 562-658-1330 for the most updated placenta collection recommendations.

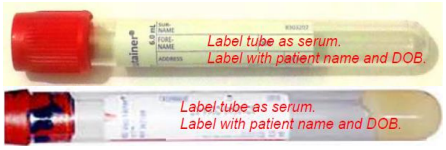
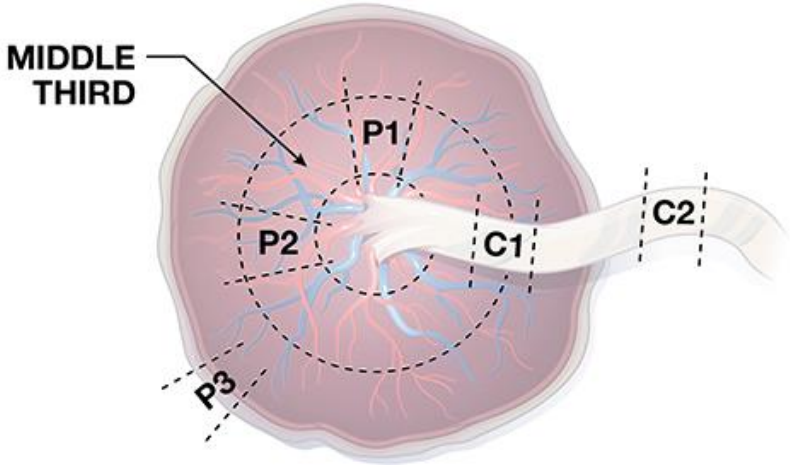
KEY NOTES:

Infant serum and urine specimens are collected at the delivery of every Zika-positive mother.

Collection of placenta and umbilical cord specimens *depends* on maternal Zika screening and confirmatory lab test results. Please contact the Los Angeles County Public Health Laboratory at 562-658-1330 for the most updated placenta collection recommendations.

Table 3 describes what infant specimens and equipment are needed for collection.

Table 3: Infant Specimens Collected

Serum	Red top pediatric microtainer tube	
Urine	Sterile urine container	
Placenta and umbilical cord	10% neutral buffered formalin for fixed tissue samples	

[74] California Department of Public Health (2018, January 10). Updated Guidance for Health Care Providers: Assessment and TesĀng for Zika Virus InfecĀon in Pregnant Women and their Newborns. Retrieved from hĀps://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/UpdatedZikaGuidanceforHCPsCaringforPregnantWomen.pdf

INDICATIONS FOR ZIKA TESTING

The Los Angeles County Department of Public Health Acute Communicable Disease Control has created the following table to assess Indications for Zika Testing for infants (Appendix G). Please contact the Los Angeles County Public Health Laboratory at 562-658-1330 for the most updated specimen collection recommendations.

Indications for Zika Testing (Appendix G)

Indications for Zika Testing	RT-PCR (serum, urine, or other)	IgM[1] (serum)
Infants*		
Infant with microcephaly and/or calcifications, and maternal Zika virus exposure regardless of maternal test results	Serum & Urine (CSF if available***) < 2 DAYS after birth	Concurrent with PCR (CSF if available)
Infant with no apparent defect and evidence of maternal Zika virus infection (IgM), or exposure history and awaiting maternal lab results (PRNT)	Serum & Urine (CSF if available) < 2 DAYS after birth	Concurrent with PCR (CSF if available)
Infant with no apparent defect, and no evidence of maternal Zika virus infection or exposure history	Not Recommended	Not Recommended

* Cord blood is not recommended for testing

The CDC *Interim Guidance for Zika Virus Testing of Formalin-Fixed Paraffin-Embedded Placenta, Fetal, or Infant Autopsy Tissues*[75] (Appendix K) also provides instructions for determining when placenta and umbilical cord specimen collection is recommended. Please contact the Los Angeles County Public Health Laboratory (PHL) at 562-658-1330 for the most updated placenta collection recommendations.

[75] CDC. (2017, August 15). Interim Guidance for Zika Virus TesĀng of Formalin-Fixed ParaĀ n-Embedded Placenta, Fetal, or Infant Autopsy Tissues. Retrieved from hĀps://www.cdc.gov/zika/pdfs/specimen-zika-virus-tesĀng-fact-sheet.pdf

INSTRUCTIONS FOR INFANT ZIKA SPECIMEN COLLECTION

The *Instructions for Infant Zika Specimen Collection*[76] (Appendix L) are pictured below as per the Los Angeles County Public Health Laboratory (PHL). Placenta and umbilical cord cutting and storage, if collected, should be performed by a laboratory pathologist. Please contact the PHL at 562-658-1330 for the most updated placenta collection recommendations.

Instructions for Infant Zika Specimen Collection (Appendix L)

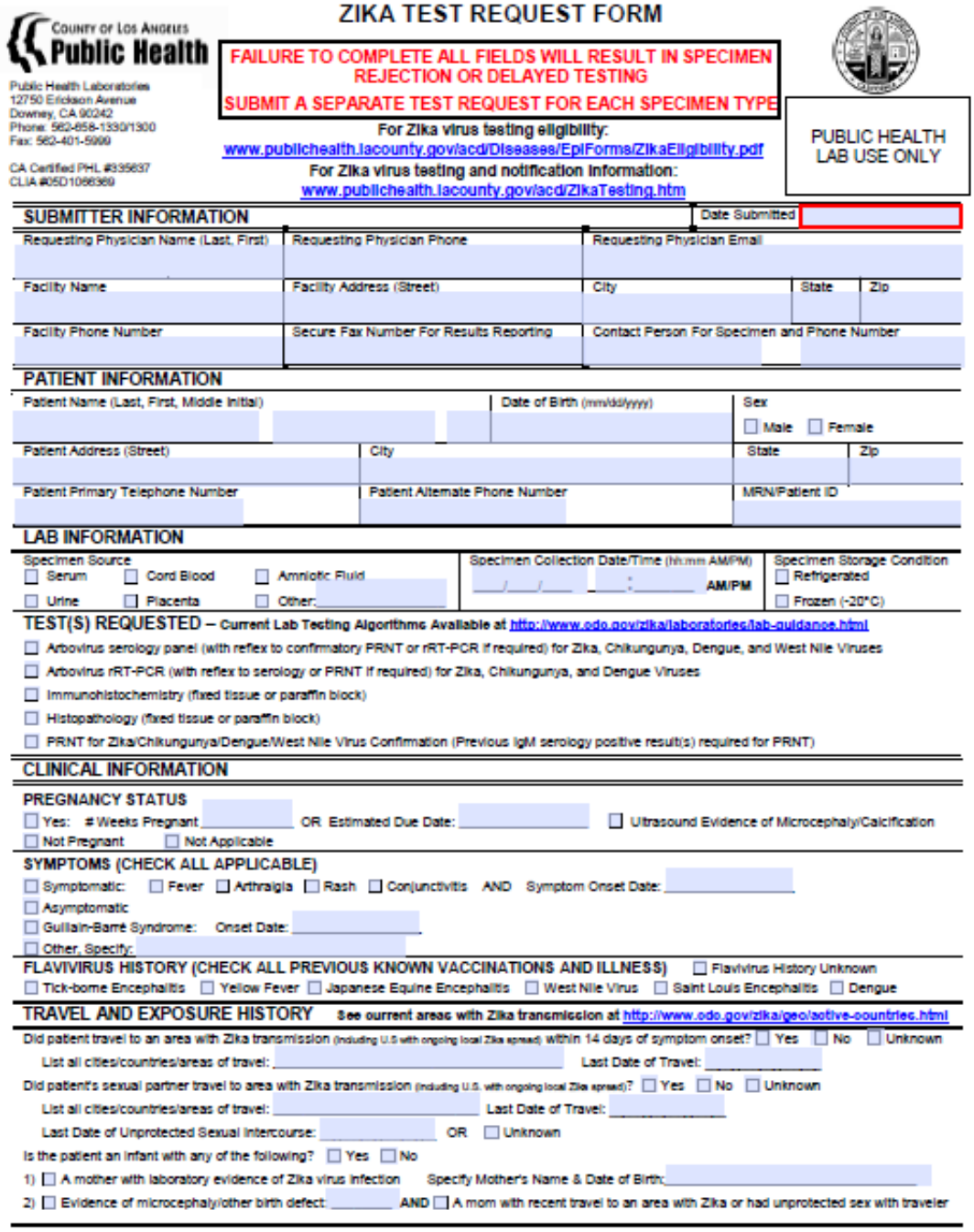
SPECIMEN	GENERAL INSTRUCTIONS	NOTES	STORAGE
Placenta and fetal membranes (fixed)	Several full thickness pieces including **at least 3** full thickness pieces (0.5–1 cm x 3–4 cm in depth) from middle third of placental disk and **at least 1** from the placental disk margin 5 x 12 cm strip of fetal membranes Please include sections of the placental disk, fetal membranes, and pathologic lesions when possible.	Please include information about placenta weight and sample both maternal and fetal side of the placenta Label all specimens to identify location of sample Fix specimens in formalin Volume of formalin used should be about 10x mass of tissue. Place in 10% neutral buffered formalin for a minimum of 3 days. **Order histopathology**	**Storage and transport at room temperature for fixed specimens**
Umbilical cord	2.5 cm segments of cord **At least 4** specimens Umbilical cord segments should be obtained proximal, middle, and distal to umbilical cord insertion site on the placenta	Label all specimens to identify location of sample. Fix specimens in formalin Volume of formalin used should be about 10x mass of tissue. Place in 10% neutral buffered formalin for a minimum of 3 days **Order histopathology**	**Storage and transport at room temperature for fixed specimens**
Infant urine	1-5 mL in sterile container (bagged urine transferred to sterile container)	Collection recommended within first 2 days after birth. Specimens collected up to 12 weeks will be tested. **Order PCR**	**Store in fridge** **Transport on cold pack**
Infant serum	**At least 1mL collected in red top pediatric microtainer tube**	**Collection recommended within first 2 days after birth. Specimens collected up to 12 weeks will be tested.** Order PCR and serology	**Store in fridge** **Transport on cold pack**

[76] Los Angeles County Public Health Laboratories (2017, April 18). InstrucĀons for Zika (pregnant mother at Āme of birth). Retrieved from hĀp://publichealth.lacounty.gov/mch/ReproducĀveHealth/Zika-MCAH/Forms/InstrucĀonsForSpecimenCollecĀon(4-18-17).pdf

PUBLIC HEALTH LABORATORY ZIKA TEST REQUEST FORM

A *Zika Test Request Form*[77] (Appendix M) must be included with **each** specimen collected at the time of delivery. If maternal screening tests are performed prior to admission into Labor and Delivery, a separate *Zika Test Request Form* must be completed for maternal tests.

Zika Test Request Form (Appendix M)



ZIKA TEST REQUEST FORM

County of Los Angeles Public Health

Public Health Laboratories
12750 Erickson Avenue
Downey, CA 90242
Phone: 562-658-1330/1300
Fax: 562-401-5999

CA Certified PHL #335637
CLIA #05D1068360

FAILURE TO COMPLETE ALL FIELDS WILL RESULT IN SPECIMEN REJECTION OR DELAYED TESTING
SUBMIT A SEPARATE TEST REQUEST FOR EACH SPECIMEN TYPE

For Zika virus testing eligibility:
www.publichealth.lacounty.gov/acd/Diseases/EpiForms/ZikaEligibility.pdf
For Zika virus testing and notification information:
www.publichealth.lacounty.gov/acd/ZikaTesting.htm

PUBLIC HEALTH LAB USE ONLY

SUBMITTER INFORMATION — Date Submitted
Requesting Physician Name (Last, First) | Requesting Physician Phone | Requesting Physician Email
Facility Name | Facility Address (Street) | City | State | Zip
Facility Phone Number | Secure Fax Number For Results Reporting | Contact Person For Specimen and Phone Number

PATIENT INFORMATION
Patient Name (Last, First, Middle Initial) | Date of Birth (mm/dd/yyyy) | Sex ☐ Male ☐ Female
Patient Address (Street) | City | State | Zip
Patient Primary Telephone Number | Patient Alternate Phone Number | MRN/Patient ID

LAB INFORMATION
Specimen Source: ☐ Serum ☐ Cord Blood ☐ Amniotic Fluid ☐ Urine ☐ Placenta ☐ Other:
Specimen Collection Date/Time (hh:mm AM/PM) AM/PM
Specimen Storage Condition: ☐ Refrigerated ☐ Frozen (-20°C)

TEST(S) REQUESTED – Current Lab Testing Algorithms Available at http://www.cdc.gov/zika/laboratories/lab-guidance.html
☐ Arbovirus serology panel (with reflex to confirmatory PRNT or rRT-PCR if required) for Zika, Chikungunya, Dengue, and West Nile Viruses
☐ Arbovirus rRT-PCR (with reflex to serology or PRNT if required) for Zika, Chikungunya, and Dengue Viruses
☐ Immunohistochemistry (fixed tissue or paraffin block)
☐ Histopathology (fixed tissue or paraffin block)
☐ PRNT for Zika/Chikungunya/Dengue/West Nile Virus Confirmation (Previous IgM serology positive result(s) required for PRNT)

CLINICAL INFORMATION

PREGNANCY STATUS
☐ Yes: # Weeks Pregnant ____ OR Estimated Due Date: ____ ☐ Ultrasound Evidence of Microcephaly/Calcification
☐ Not Pregnant ☐ Not Applicable

SYMPTOMS (CHECK ALL APPLICABLE)
☐ Symptomatic: ☐ Fever ☐ Arthralgia ☐ Rash ☐ Conjunctivitis AND Symptom Onset Date: ____
☐ Asymptomatic
☐ Guillain-Barré Syndrome: Onset Date: ____
☐ Other, Specify:

FLAVIVIRUS HISTORY (CHECK ALL PREVIOUS KNOWN VACCINATIONS AND ILLNESS) ☐ Flavivirus History Unknown
☐ Tick-borne Encephalitis ☐ Yellow Fever ☐ Japanese Equine Encephalitis ☐ West Nile Virus ☐ Saint Louis Encephalitis ☐ Dengue

TRAVEL AND EXPOSURE HISTORY See current areas with Zika transmission at http://www.cdc.gov/zika/geo/active-countries.html
Did patient travel to an area with Zika transmission (including U.S with ongoing local Zika spread) within 14 days of symptom onset? ☐ Yes ☐ No ☐ Unknown
List all cities/countries/areas of travel: ____ Last Date of Travel: ____
Did patient's sexual partner travel to area with Zika transmission (including U.S. with ongoing local Zika spread)? ☐ Yes ☐ No ☐ Unknown
List all cities/countries/areas of travel: ____ Last Date of Travel: ____
Last Date of Unprotected Sexual Intercourse: ____ OR ☐ Unknown
Is the patient an infant with any of the following? ☐ Yes ☐ No
1) ☐ A mother with laboratory evidence of Zika virus infection Specify Mother's Name & Date of Birth: ____
2) ☐ Evidence of microcephaly/other birth defect: ____ AND ☐ A mom with recent travel to an area with Zika or had unprotected sex with traveler

[77] County of Los Angeles Public Health Laboratories. (2016, December 6). Zika Test Request Form Retrieved from hĀp://publichealth.lacounty.gov/acd/Diseases/EpiForms/ZikaInfoTestReq.pdf

CONTACTS FOR ASSISTANCE AND COURIER SERVICES

The Los Angeles County Public Health Laboratory (PHL) is the point of contact for all Zika screening testing (blood or serum) and Zika specimen collection (infant specimens). Hospitals may arrange for Public Health Laboratory courier services to retrieve Zika specimens after they have been collected, cut, and stored properly.

Any questions regarding Zika specimen collection should be made to the Public Health Laboratory at the number listed on the *Laboratory Contact Information for Zika* (Appendix N) sheet below. Arrangements for courier services may also be made at the number below.

Laboratory Contact Information for Zika (Appendix N)

Los Angeles County Public Health Department
Laboratory Contact Information for Zika

Please notify the Los Angeles County Department of Public Health when a pregnant woman positive for ZIKA arrives at your hospital. Call 213-240-7941.

For questions regarding **ZIKA specimen collection**, please contact the Los Angeles County Public Health Laboratories:

Business hours, **562-658-1330**
After hours, **213-974-1234** (press # 8)

Remember:

- A separate **ZIKA Test Request Form** must accompany each specimen
- Mother must give consent in advance if the provider wants to collect placental specimens

To arrange courier service and pick up of ZIKA specimens, contact the Public Health Laboratory:

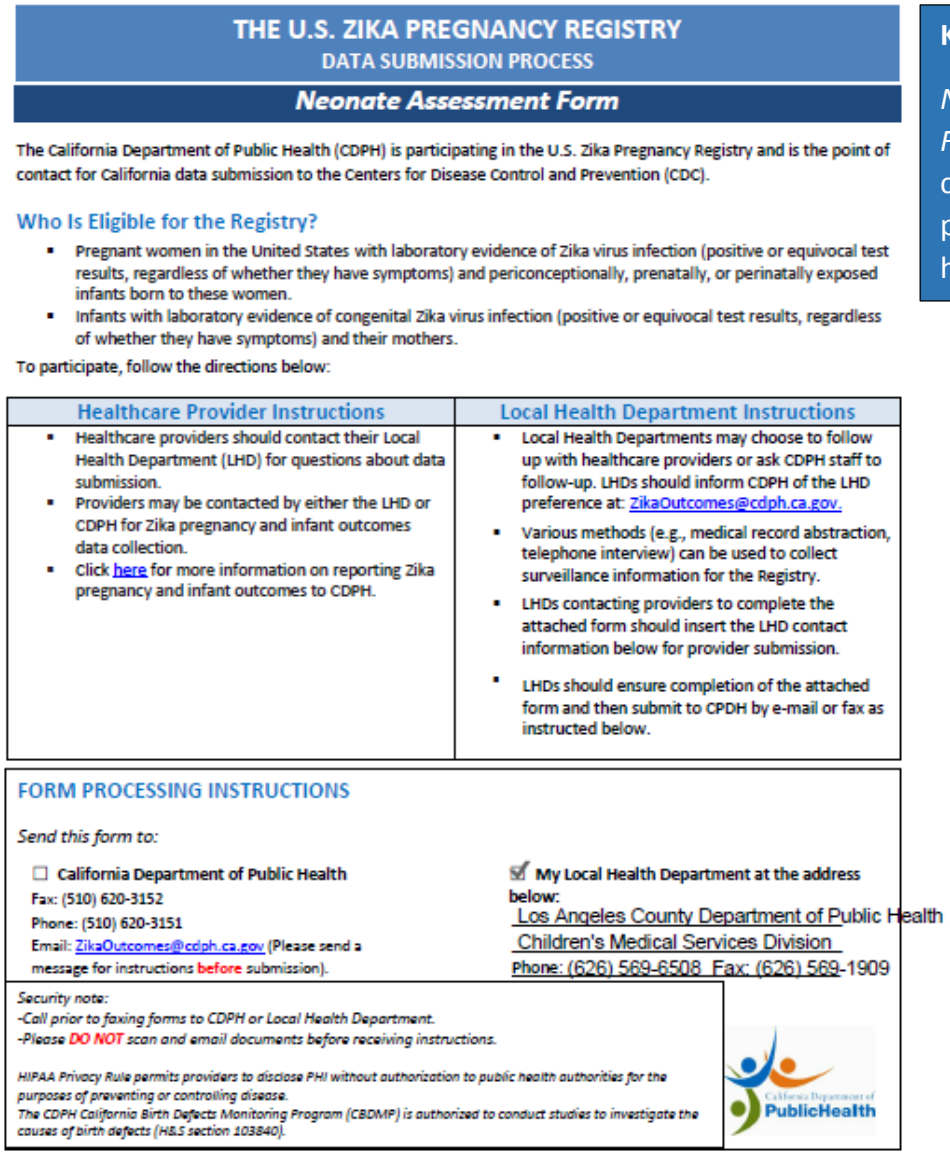
Business hours, **562-658-1460**
After hours, **213-974-1234** (press # 8)

For questions regarding the **Neonate Form**, call **626-569-6508**

NEONATE ASSESSMENT FORM

The *Neonate Assessment Form*[78] (Appendix O) collects preliminary data on an infant's status at the time of delivery, including a physical assessment, neonate imaging, postnatal infection testing, and any suspected or diagnosed birth defects. This form is to be completed by the pediatrician prior to discharge. The completed Neonate Assessment Form will be faxed to Children's Medical Services for further follow up. The Los Angeles County Department of Public Health Children's Medical Services Division may be reached at 626-569-6508. The following section details the physical assessment portion, which will be documented on the Neonate Assessment Form.

Neonate Assessment Form (Appendix O)



THE U.S. ZIKA PREGNANCY REGISTRY
DATA SUBMISSION PROCESS

Neonate Assessment Form

The California Department of Public Health (CDPH) is participating in the U.S. Zika Pregnancy Registry and is the point of contact for California data submission to the Centers for Disease Control and Prevention (CDC).

Who Is Eligible for the Registry?

- Pregnant women in the United States with laboratory evidence of Zika virus infection (positive or equivocal test results, regardless of whether they have symptoms) and periconceptionally, prenatally, or perinatally exposed infants born to these women.
- Infants with laboratory evidence of congenital Zika virus infection (positive or equivocal test results, regardless of whether they have symptoms) and their mothers.

To participate, follow the directions below:

Healthcare Provider Instructions	Local Health Department Instructions
▪ Healthcare providers should contact their Local Health Department (LHD) for questions about data submission. ▪ Providers may be contacted by either the LHD or CDPH for Zika pregnancy and infant outcomes data collection. ▪ Click here for more information on reporting Zika pregnancy and infant outcomes to CDPH.	▪ Local Health Departments may choose to follow up with healthcare providers or ask CDPH staff to follow-up. LHDs should inform CDPH of the LHD preference at: ZikaOutcomes@cdph.ca.gov. ▪ Various methods (e.g., medical record abstraction, telephone interview) can be used to collect surveillance information for the Registry. ▪ LHDs contacting providers to complete the attached form should insert the LHD contact information below for provider submission. ▪ LHDs should ensure completion of the attached form and then submit to CPDH by e-mail or fax as instructed below.

FORM PROCESSING INSTRUCTIONS

Send this form to:

☐ **California Department of Public Health**
Fax: (510) 620-3152
Phone: (510) 620-3151
Email: ZikaOutcomes@cdph.ca.gov (Please send a message for instructions before submission).

☑ **My Local Health Department at the address below:**
Los Angeles County Department of Public Health
Children's Medical Services Division
Phone: (626) 569-6508 Fax: (626) 569-1909

Security note:
-Call prior to faxing forms to CDPH or Local Health Department.
-Please DO NOT scan and email documents before receiving instructions.

HIPAA Privacy Rule permits providers to disclose PHI without authorization to public health authorities for the purposes of preventing or controlling disease.
The CDPH California Birth Defects Monitoring Program (CBDMP) is authorized to conduct studies to investigate the causes of birth defects (H&S section 103840).

California Department of PublicHealth

KEY NOTE:

Neonate Assessment Form must be completed by the pediatrician **prior** to hospital discharge.

[78] California Department of Public Health & CDC. (2016, October 14). Neonate Assessment Form. Retrieved from hĀp://publichealth.lacounty.gov/mch/ReproducĀveHealth/Zika-MCAH/Forms/NeonateAssessmentFormLAC_CMS.pdf

INFANT PHYSICAL ASSESSMENT AT TIME OF DELIVERY

All infants born to mothers with laboratory evidence of Zika virus infection during pregnancy should receive the following assessments, even if no abnormalities are apparent at birth:[79]

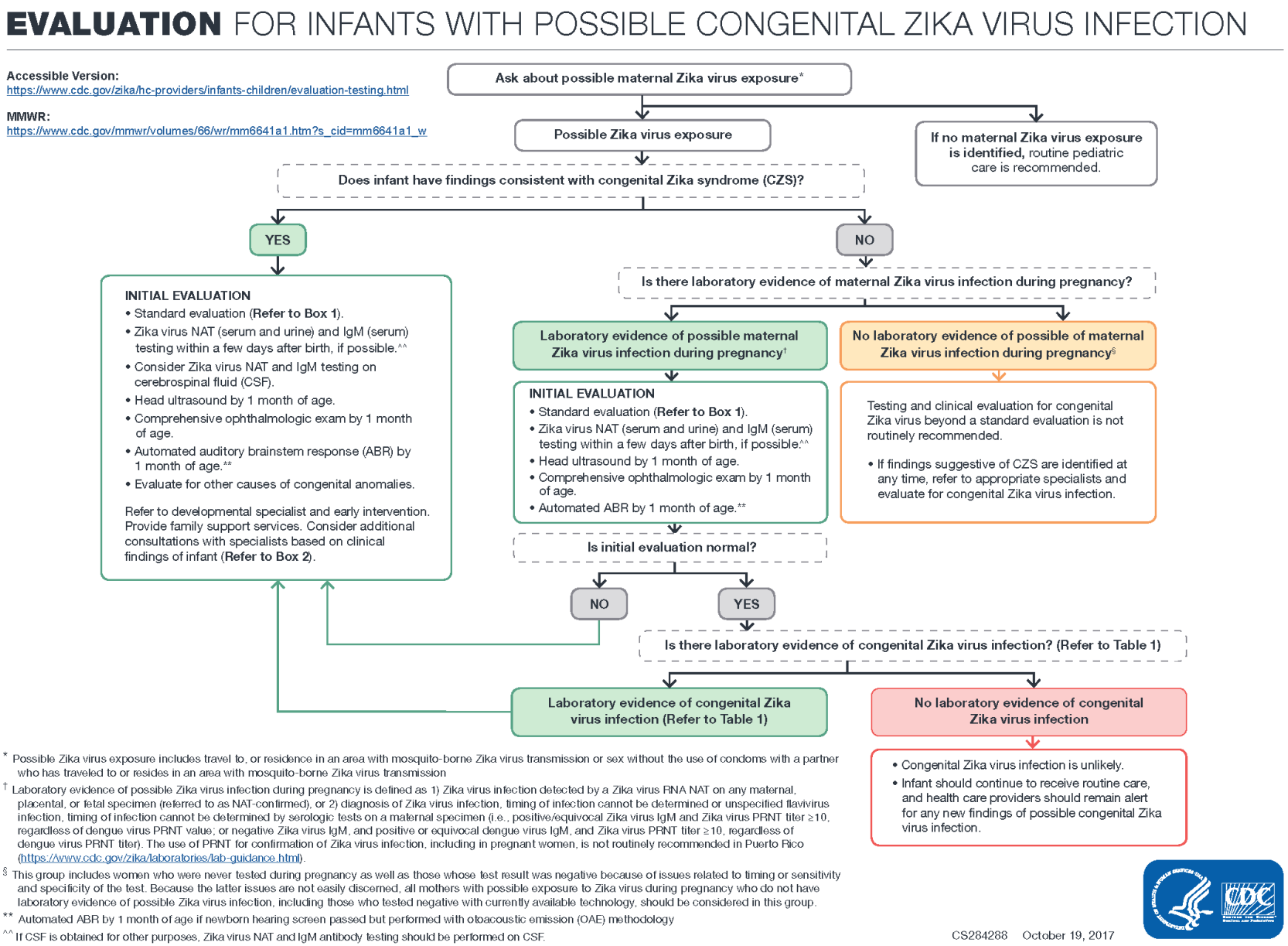
- Comprehensive physical exam, including neuro exam
- Standard newborn hearing screen
- Head ultrasound
- Infant specimen collection to test for Zika virus

If a mother has an unknown Zika virus status, further evaluation and infant testing can be deferred until maternal test results are available (as long as the infant appears clinically well). The provider may consider whether testing of the newborn for possible congenital Zika virus infection is warranted, depending on the possibility of the mother's Zika virus exposure.[80] In all cases, infants or fetuses with possible Zika virus–associated birth defects should be evaluated for other etiologies of congenital anomalies.[81]

Depending on the initial evaluation of the infant at the time of birth, the infant may receive more or less testing and careful management as he or she develops. The CDC's *Evaluation for Infants with Possible Congenital Zika Virus Infection*[82] (Appendix S) algorithm lists evaluations and tests for an infant prior to discharge, and standard evaluations recommended at birth and during each will-child visit for all infants with possible congenital Zika virus exposure during pregnancy.

[79] CDC. (2017, September 18). Key Messages Zika Virus Disease. Retrieved from hĀps://www.cdc.gov/zika/pdfs/zika-key-messages.pdf
[80] CDC. (2017, September 18). Key Messages Zika Virus Disease. Retrieved from hĀps://www.cdc.gov/zika/pdfs/zika-key-messages.pdf
[81] CDC. (2017, September 1). CollecĀon and Submission of Specimens for Zika Virus TesĀng at Time of Birth. Retrieved from hĀps://www.cdc.gov/zika/pdfs/collecĀon-submission-specimens-zika-tesĀng-at-birth.pdf
[82] CDC. (2017, November 17). EvaluaĀon for Infants with Possible Congenital Zika Virus InfecĀon. Retrieved from hĀps://www.cdc.gov/zika/pdfs/pediatric-evaluaĀon-follow-up-tool.pdf

Evaluation for Infants with Possible Congenital Zika Virus Infection (Appendix S)



Evaluation for Infants with Possible Congenital Zika Virus Infection (Appendix S)

TABLE 1

Interpretation of results of laboratory testing of infant's blood, urine, and/or cerebrospinal fluid for evidence of congenital Zika virus infection		
Infant test results*		
NAT	**IgM**	**Interpretation**
Positive	Any result	Confirmed congenital Zika virus infection†
Negative	Nonnegative§	Probable congenital Zika virus infection¶,**
Negative	Negative	Congenital virus infection unlikely¶,††

Abbreviations: NAT = nucleic acid test; IgM = immunoglobulin M

*Infant serum, urine, or cerebrospinal fluid.

† Distinguishing between congenital and postnatal infection is difficult in infants who live in areas where there is ongoing transmission of Zika virus and who are not tested soon after birth. If the timing of infection cannot be determined, infants should be evaluated as if they had congenital Zika virus infection.

§ Nonnegative serology terminology varies by assay and might include "positive," "equivocal," "presumptive positive," or "possible positive." For explanation of a specific interpretation, refer to the instructions for use for the specific assay performed.

¶ Laboratory results should be interpreted in the context of timing of infection during pregnancy, maternal serology results, clinical findings consistent with congenital Zika syndrome, and any confirmatory testing with plaque reduction neutralization testing.

** A negative Zika virus plaque reduction neutralization test suggests that the infant's Zika virus IgM test is a false positive.

†† Congenital Zika virus infection is unlikely if specimens are collected within the first few days after birth and the clinical evaluation is normal; however, health care providers should remain alert for any new findings of congenital Zika virus infection.

BOX 1. Standard evaluation recommended at birth and during each well visit for all infants with possible congenital Zika virus exposure during pregnancy

- Comprehensive physical exam, including growth parameters
- Developmental monitoring and screening using validated screening tools recommended by the American Academy of Pediatrics (https://www.aap.org/en-us/advocacy-and-policy/aap-health-initiatives/Screening/Pages/Screening-Tools.aspx)
- Vision screening as recommended by the American Academy of Pediatrics Policy Statement "Visual System Assessment in Infants, Children, and Young Adults by Pediatricians" (www.pediatrics.org/cgi/doi/10.1542/peds.2015-3596)
- Newborn hearing screen at birth, preferably with automated auditory brainstem response

BOX 2. Consultations for infants with clinical findings consistent with congenital Zika syndrome

- **Consider consultation with the following specialists:**
  - Infectious disease specialist for evaluation for other congenital infections (e.g., toxoplasmosis, syphilis, rubella, cytomegalovirus, or herpes simplex virus) and assistance with Zika virus diagnosis, testing, and counseling
  - Neurologist by age 1 month for comprehensive neurologic examination and consideration for other evaluations such as advanced neuroimaging and EEG
  - Ophthalmologist for comprehensive eye exam by age 1 month
  - Clinical geneticist for confirmation of the clinical phenotype and evaluation for other causes of microcephaly or congenital anomalies
  - Early intervention and developmental specialists
  - Family and supportive services
- **Additional possible consultations, based on clinical findings of the infant:**
  - Endocrinologist for evaluation of hypothalamic or pituitary dysfunction and consideration for thyroid testing
  - Lactation specialist, nutritionist, gastroenterologist or speech or occupational therapist for evaluation for dysphagia and management of feeding issues
  - Orthopedist, physiatrist, or physical therapist for the management of hypertonia, clubfoot or arthrogrypotic-like conditions
  - Pulmonologist or otolaryngologist for concerns about aspiration

MEASURING HEAD CIRCUMFERENCE

Head circumference should be measured and documented on the *Neonate Assessment Form* (Appendix O) at the time of delivery and **repeated** prior to discharge. Step-by-step instructions for measuring head circumference are provided by the CDC *Measuring Head Circumference*[83] (Appendix T) below.

Measuring Head Circumference (Appendix T)

- Use a measuring tape that cannot be stretched
- Securely wrap the tape around the widest possible circumference of the head
  - » Broadest part of the forehead above eyebrow
  - » Above the ears
  - » Most prominent part of the back of the head
- Take the measurement three times and select the largest measurement to the nearest 0.1 cm
- Head circumference measurements should be taken on the first day of life because commonly-used birth head circumference reference charts by age and sex are based on measurements taken before 24 hours of age

[83] CDC. (2016, September 8). Measuring Head Circumference. Retrieved from hĀps://www.cdc.gov/zika/pdfs/microcephaly_measuring.pdf

ASSESSMENT OF INFANT HEARING

All infants born to mothers with possible Zika virus exposure during pregnancy should receive a standard evaluation at birth and at each subsequent well-child visit including a comprehensive physical examination, age-appropriate vision screening and developmental monitoring and screening using validated tools, and newborn hearing screen at birth, preferably using auditory brainstem response (ABR) methodology.[84] If the newborn hearing screening was passed only using only otoacoustic emissions methodology, infants born to mothers with possible Zika virus exposure should be referred for automated ABR by age 1 month.[85] If findings consistent with congenital Zika syndrome (e.g., impaired visual acuity/function, hearing problems, developmental delay, or delay in head growth) are identified at any time, referrals to the appropriate specialists should be made and further evaluation should follow recommendations for infants with clinical findings consistent with congenital Zika syndrome.

[84] Adebanjo, T., Godfred-Cato, S., Viens, L., et al. (2017, October 20). Update: Interim Guidance for the Diagnosis, EvaluaĀon, and Management of Infants with Possible Congenital Zika Virus InfecĀon *MMWR. Morbidity and Mortality Weekly Report, 66*(41), 1089–1099. doi:10.15585/mmwr.mm6641a1

[85] Adebanjo, T., Godfred-Cato, S., Viens, L., et al. (2017, October 20). Update: Interim Guidance for the Diagnosis, EvaluaĀon, and Management of Infants with Possible Congenital Zika Virus InfecĀon *MMWR. Morbidity and Mortality Weekly Report, 66*(41), 1089–1099. doi:10.15585/mmwr.mm6641a1

PEDIATRIC FOLLOW UP AFTER DISCHARGE

Infants should be followed by an established medical home to facilitate coordination of care and receive preventive care, including immunizations, assessment of development and feeding, and monitoring of growth parameters (head circumference, weight, and length). Coordination of care for follow-up appointments with specialists and services recommended during hospital evaluation should be arranged prior to discharge. Hospital medical records, including all Zika testing and evaluation results for both mother and infant, should be shared with the pediatric provider caring for the infant after discharge.

It is critical that pediatricians ask about potential maternal and congenital Zika exposure for every newborn. The American Academy of Pediatrics (AAP) and the American College of Obstetrics and Gynecology (ACOG) will work closely together to assess the need for additional guidance for infants and children in terms of diagnostics and developmental assessments.[86]

The CDC has provided multiple resources to guide parents and providers through the first 12 months of an infant's life, with or without apparent Zika-associated birth defects. The following resources are explained and provided below:

Appendix	Resource Title
P	*United States Zika Pregnancy Registry Brochures in English and Spanish*
Q	*CDC Roadmap for Parents of Babies with Congenital Zika Syndrome*
R	*CDC Roadmap for Parents of Babies Infected with Zika Before Birth Who Appear Healthy*

Birth hospitals and primary care providers may consider using Zika Care Connect,[87] a national online database with a geographical network of healthcare specialists who care for patients affected by Zika.

[86] CDC. (2017, September 18). Key Messages Zika Virus Disease. Retrieved from hĀps://www.cdc.gov/zika/pdfs/zika-key-messages.pdf
[87] Zika Care Connect & March of Dimes (2017). Retrieved from hĀps://www.zikacareconnect.org/

ZIKA PREGNANCY REGISTRY

The CDC established the United States Zika Pregnancy Registry (USZPR) to facilitate data collection to update recommendations for clinical care, to plan for services for pregnant women and families affected by Zika virus, and to improve prevention of Zika virus infection during pregnancy.

The USZPR tracks Zika virus infections that occur in pregnant women and their infants.[88] It collects date from both asymptomatic and symptomatic pregnant women with laboratory evidence of possible Zika virus infection and their infants up to 2 years of age (regardless of infant test results). [89] All collected data is de-identified and participation is optional and voluntary.[90]

Provider influence is shown to be critical in getting patients to participate in the registry. The data collected through the Zika pregnancy and infant registries will provide more comprehensive information to complement notifiable disease case reporting, to update recommendations for clinical care, to plan for services for pregnant women and families affected by Zika virus, to improve prevention of Zika virus infection during pregnancy, and to learn more about the effects of Zika virus on the baby's development.[91]

The figure below (Appendix P) is an example of an informational brochure on the USZPR created by the Los Angeles County Department of Public Health MCAH.

United States Zika Pregnancy Registry Brochures in English and Spanish (Appendix P)

KEY NOTE: The Zika Pregnancy Registry is optional. Pediatricians should encourage new moms to participate in the Zika Pregnancy Registry.

[88] American Congress of Obstetrics and Gynecologists. (2017). US Zika Pregnancy Registry. Retrieved from hĀps://www.acog.org/About-ACOG/ACOG-Departments/Zika-Virus/US-Zika-Pregnancy-Registry
[89] CDC. (2018, January 23). US Zika Pregnancy and Infant Registry. Retrieved from hĀps://www.cdc.gov/pregnancy/zika/research/registry.html
[90] California Department of Public Health. (2017, June 20). US Zika Pregnancy Registry. Retrieved from hĀps://www.cdph.ca.gov/Programs/CID/DCDC/Pages/USZikaPregnancyRegistry.aspx
[91] CDC. (2017, September 18). Key Messages Zika Virus Disease. Retrieved from hĀps://www.cdc.gov/zika/pdfs/zika-key-messages.pdf

CHILDREN'S MEDICAL SERVICES FOLLOW-UP

In LA County, Children's Medical Services (CMS) coordinates Zika exams with infant's regular pediatric visits at 2, 6, 12, 18, and 24 months of age. The CMS case manager will coordinate the completion of *Infant Follow-Up Forms*[92] with the pediatrician at the appropriate times.

If mother and infant enroll in the USZPR, the infant will be followed by case managers at CMS for up to 2 years. [93] This ensures that any signs of Zika Congenital Syndrome are diagnosed at an early age and the appropriate referrals are made. If mother and infant do not enroll in the Zika Pregnancy Registry, the mother will be responsible for ensuring appropriate infant visits with the pediatrician.

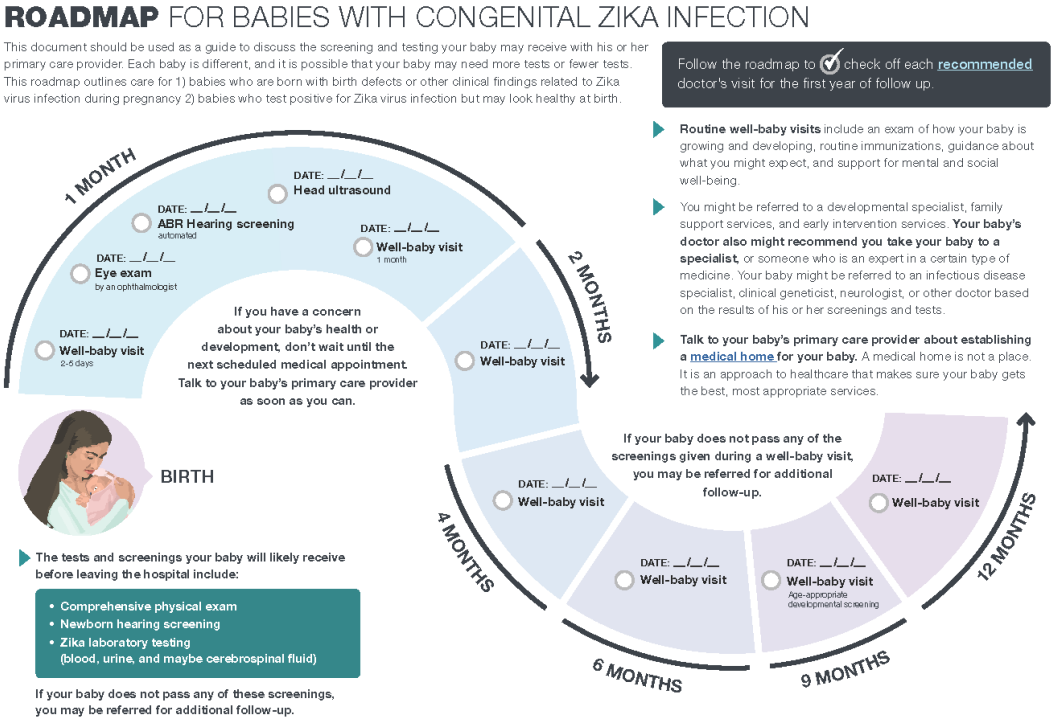
FIRST 12 MONTHS

The CDC has created two roadmaps; *Roadmap for Babies with Congenital Zika Infection*[94] (Appendix Q), and *Roadmap for Babies of Mothers Infected with Zika During Pregnancy Who Appear Healthy*[95] (Appendix R). The following section includes these two CDC roadmaps.

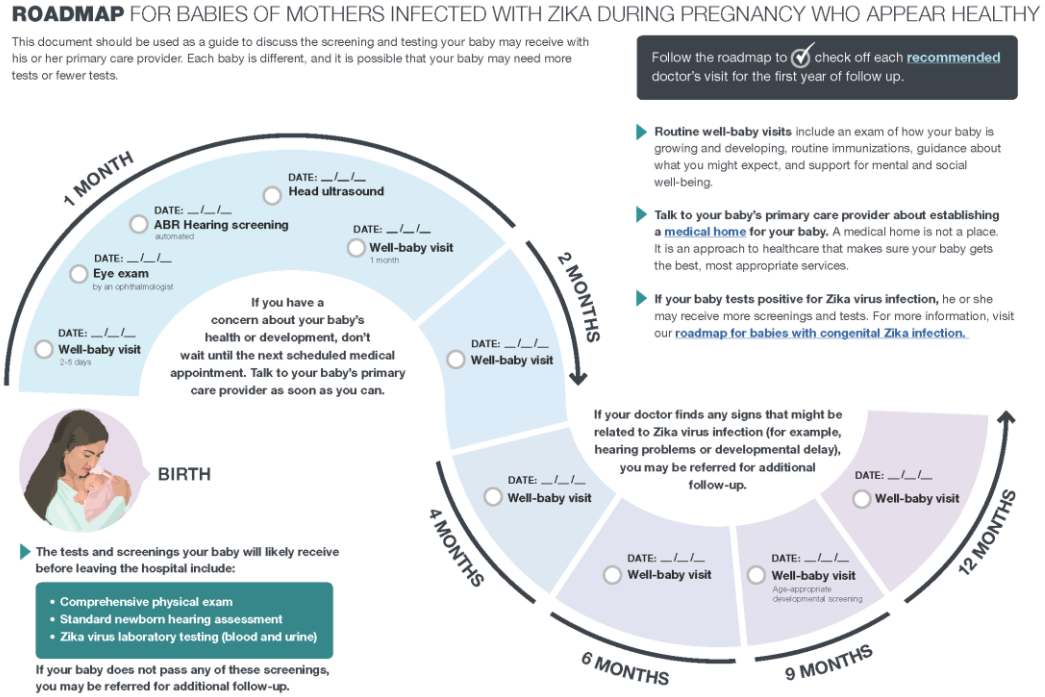
Depending on the initial evaluation of the infant at the time of birth, the infant may receive more or less testing and careful management as he or she develops. The CDC's *Evaluation for Infants with Possible Congenital Zika Virus Infection*[96] (Appendix S) algorithm lists standard evaluations recommended at birth and during each will-child visit for all infants with possible congenital Zika virus exposure during pregnancy.

[92] California Department of Public Health & CDC. (2016, October 14). Infant Follow-Up Form. Retrieved from hĀp://publichealth.lacounty.gov/mch/ReproducĀveHealth/Zika-MCAH/Forms/InfantFollowUpForm_revised10_14_16.pdf
[93] CDC. (2018, January 23). US Zika Pregnancy and Infant Registry. Retrieved from hĀps://www.cdc.gov/pregnancy/zika/research/registry.html
[94] CDC. (2017, November 17). Roadmap for Babies with Congenital Zika InfecĀon. Retrieved from hĀps://www.cdc.gov/zika/pdfs/roadmap-for-parents.pdf
[95] CDC. (2017, November 17). Roadmap for Babies of Mothers Infected with Zika During Pregnancy Who Appear Healthy. Retrieved from hĀps://www.cdc.gov/zika/pdfs/roadmap-for-parents-babies-infected-before-birth.pdf
[96] CDC. (2017, November 17). EvaluaĀon for Infants with Possible Congenital Zika Virus InfecĀon. Retrieved from hĀps://www.cdc.gov/zika/pdfs/pediatric-evaluaĀon-follow-up-tool.pdf

CDC Roadmap for Babies with Congenital Zika Infection[97] (Appendix Q)



CDC Roadmap for Babies of Mothers Infected with Zika During Pregnancy Who Appear Healthy[98] (Appendix R)



[97] CDC. (2017, June 5). Roadmap for Babies with Congenital Zika InfecĀon. Retrieved from hĀps://www.cdc.gov/zika/pdfs/roadmap-for-parents.pdf

[98] CDC. (2017, June 5). Roadmap for Babies of Mothers Infected with Zika During Pregnancy Who Appear Healthy. Retrieved from hĀps://www.cdc.gov/zika/pdfs/roadmap-for-parents-babies-infected-before-birth.pdf

BEST PRACTICES

The following best practices were used by hospitals to improve the coordination and care of Zika-affected women in the NICU.

NEWBORN CHECKLIST

Create a checklist highlighting required care. Some recommendations for the checklist include:

- ✓ Collect infant serum and urine specimen
- ✓ Complete LA County *Zika Test Request Form* (Appendix M) for each serum and urine specimen
- ✓ Complete LA County *Neonate Assessment Form* (Appendix O)
- ✓ Perform cranial ultrasound; update LA County *Neonate Assessment Form*
- ✓ Perform hearing screening examination; update LA County *Neonate Assessment Form*
- ✓ Repeat head circumference; update LA County *Neonate Assessment Form*
- ✓ Fax completed LA County *Neonate Assessment Form* to Children's Medical Services
- ✓ Schedule follow up appointment for infant

NEWBORN ASSESSMENT AT BEDSIDE

All newborn assessments may be performed at the bedside, when no other medical anomalies are noted, providing more mother and baby bonding time.

Newborns of Zika-positive mothers who are born without any observable malformations and with no other medical anomalies may receive standard evaluations at the time of birth.[99] NICU admission is not necessary for routine care of Zika specimen collection work-up. Routine care can be provided newborn nursery or in couplet care **without** being transferred to the NICU, unless otherwise medically necessary.

[99] Adebanjo, T., Godfred-Cato, S., Viens, L., et al. (2017, October 20). Update: Interim Guidance for the Diagnosis, EvaluaĀon, and Management of Infants with Possible Congenital Zika Virus InfecĀon *MMWR. Morbidity and Mortality Weekly Report, 66*(41), 1089–1099. doi:10.15585/mmwr.mm6641a1

LABORATORY GUIDANCE

IN THIS SECTION

All pregnant women should be asked about Zika exposure that could have occurred before becoming pregnant or during pregnancy. Women who are at high risk for exposure to Zika are those who answer affirmatively to the screening questions[100,101] (Appendix C). Women with high risk for exposure to Zika should be tested to diagnose Zika virus infection. Ideally, maternal Zika lab testing should be performed **prior** to admission into the Labor and Delivery unit.

Infants born to women with laboratory evidence of confirmed or possible Zika virus infection should be evaluated for congenital Zika virus infection through testing of placental and infant serum and urine in accordance with the Los Angeles County Public Health Laboratory (PHL) guidance. Zika virus testing is recommended for these infants regardless of the presence or absence of phenotypic abnormalities, but the types of specimens to collect vary according to maternal Zika screening and confirmatory lab test results. Testing placental tissue specimens from pregnancies with possible Zika virus infection can be considered for diagnostic purposes in certain scenarios.[102] Please contact the PHL at 562-658-1330 for the most updated placenta collection recommendations.

MATERNAL ZIKA LAB TEST COLLECTION

ZIKA SCREENING AND CONFIRMATORY LAB TESTS

In Los Angeles County, the current recommendation is to evaluate all pregnancy women for possible Zika virus exposure during each prenatal care visit. The most current guidelines for testing pregnant women with possible Zika Virus exposure comes from the latest Los Angeles County Health Alert Network (LAHAN): *Updated California Zika Testing Guidelines and a Local Case of Sexually Transmitted Zika* [103] (Appendix F).

Los Angeles County, the California Department of Public Health,[104] and the CDC[105] recommends a shared decision-making model which includes pretest counseling, individualized risk assessment, clinical judgment, and patient preferences. A patient's risk tolerance and decision-making regarding the pregnancy may be sufficient justification to test for Zika virus infection. [106]

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[100] CDC. (2016, October 4). Zika Screening Tool For Pregnant Women. Retrieved from hĀp://publichealth.lacounty.gov/mch/ReproducĀveHealth/Zika-MCAH/Forms/ZikaScreeningTool.pdf

[101] CDC. (2017, August 9). Screening Pregnant Women For Zika TesĀng. Retrieved from hĀps://www.cdc.gov/zika/pdfs/zikapreg_screeningtool.pdf

[102] Oduyebo, T., Polen, K. D., Walke, H. T., et al. (2017, July 28). Update: Interim Guidance for Health Care Providers Caring for Pregnant Women with Possible Zika Virus Exposure. *MMWR. Morbidity and Mortality Weekly Report, 66*(29), 781-793. doi:10.15585/mmwr.mm6629e1

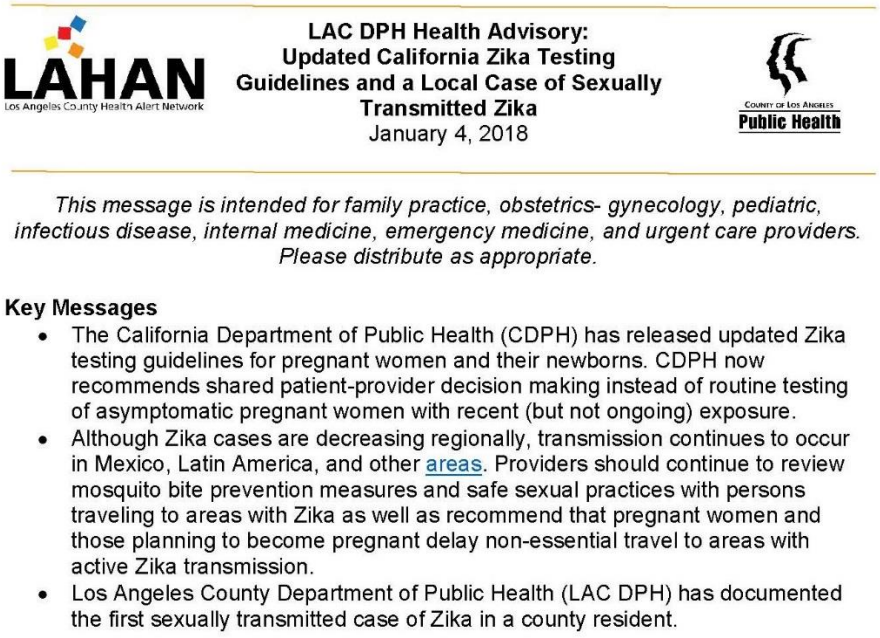
[103] Los Angeles County Health Alert Network. (2018, January 4). Updated California Zika TesĀng Guidelines and a Local Case of Sexually TransmiĀed Zika. Retrieved from hĀp://publichealth.lacounty.gov/eprp/Health%20Alerts/LAHAN%20Zika%20Advisory%20with%20CDPH%20Guidance%201.4.18.pdf

[104] California Department of Public Health (2018, January 10). Updated Guidance for Health Care Providers: Assessment and TesĀng for Zika Virus InfecĀon in Pregnant Women and their Newborns. Retrieved from hĀps://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/UpdatedZikaGuidanceforHCPsCaringforPregnantWomen.pdf

[105] CDC. (2018, January 19). TesĀng & Diagnosis. Retrieved from hĀps://www.cdc.gov/pregnancy/zika/tesĀng-follow-up/tesĀng-and-diagnosis.html

[106] California Department of Public Health (2018, January 10). Updated Guidance for Health Care Providers: Assessment and TesĀng for Zika Virus InfecĀon in Pregnant Women and their Newborns. Retrieved from hĀps://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/UpdatedZikaGuidanceforHCPsCaringforPregnantWomen.pdf

Updated California Zika Testing Guidelines and a Local Case of Sexually Transmitted Zika
(Appendix F)



LAHAN
Los Angeles County Health Alert Network

LAC DPH Health Advisory:
Updated California Zika Testing Guidelines and a Local Case of Sexually Transmitted Zika
January 4, 2018

County of Los Angeles Public Health

This message is intended for family practice, obstetrics- gynecology, pediatric, infectious disease, internal medicine, emergency medicine, and urgent care providers. Please distribute as appropriate.

Key Messages

- The California Department of Public Health (CDPH) has released updated Zika testing guidelines for pregnant women and their newborns. CDPH now recommends shared patient-provider decision making instead of routine testing of asymptomatic pregnant women with recent (but not ongoing) exposure.
- Although Zika cases are decreasing regionally, transmission continues to occur in Mexico, Latin America, and other areas. Providers should continue to review mosquito bite prevention measures and safe sexual practices with persons traveling to areas with Zika as well as recommend that pregnant women and those planning to become pregnant delay non-essential travel to areas with active Zika transmission.
- Los Angeles County Department of Public Health (LAC DPH) has documented the first sexually transmitted case of Zika in a county resident.

There are three types of tests which are used to diagnose Zika virus infection. [107] There are limitations in Zika virus testing because of the cross-sensitivity of antibodies generated in response to flavivirus infections (including Zika, dengue, and yellow fever).[108] For this reason, Zika test results may be positive, presumptive, or negative.

The U.S. Food and Drug Administration has issued Emergency Use Authorization (EUA) for the three diagnostic tools for Zika virus listed on the following page, which are being distributed by CDC to qualified laboratories.[109]

[107] State of California Health and Human Services Agency, & California Division of Communicable Disease Control. (2016, August 22). CDPH Zika Virus TesĀng FAQs for Healthcare Providers. Retrieved from hĀps://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/ZikaVirusTesĀngFAQsforHCPs.pdf

[108] Balmaseda, A., SteĀler, K., Medialdea-Carrera, R., Collado, D., Jin, X., Zambrana, J. V., CorĀ, D., et al. (2017, August 1). AnĀbody-based assay discriminates Zika virus infecĀon from other Āaviviruses. *Proceedings of the National Academy of Sciences, 114*(31), 8384-8389. doi:10.1073/pnas.1704984114

[109]CDC. (2017, July 23). DiagnosĀc Tests for Zika Virus. Retrieved from hĀps://www.cdc.gov/zika/hc-providers/types-of-tests.html

The three diagnostic tools for Zika virus testing are described below.

1. **RT-PCR** (also known as **NAT**) detects Zika virus RNA. This test will henceforth be referred to as **PCR/NAT**. Current CDC guidelines recommend concurrent testing of PCR/NAT and IgM serology.[110,111,112]
   - Collect serum and urine
   - Sensitive ≤ 12 weeks after symptom onset
   - If positive, ***confirms*** current or recent Zika virus infection
   - If negative, ***does not*** exclude Zika virus infection

2. **IgM serology**
   - Collect serum
   - Sensitive within 2 to 12 weeks after symptom onset
   - If positive, ***presumptive*** recent flavivirus infection
   - If negative, ***does not exclude*** Zika virus infection
   - Confirmatory testing by PRNT is needed

KEY NOTES:

If positive symptoms occur, test as soon as possible up to 12 weeks.

Send PCR/NAT (serum and urine) **AND** Zika virus IgM serology (serum) **concurrently**.

3. **PRNT** measures virus-specific neutralizing antibodies
   - This final confirmatory test will identify the source of infection
   - If positive, multiple interpretations
     - ~ ***Confirms*** Zika virus infection
     - ~ ***Confirms*** unspecified flavivirus infection (dengue, chikungunya, Zika)
     - ~ ***Presence*** of vaccination against flavivirus (yellow fever, West Nile virus)
   - If negative, ***no*** Zika virus infection

[110] CDC. (2017, July 23). Types of Zika Virus Tests. Retrieved from hĀps://www.cdc.gov/zika/laboratories/types-of-tests.html
[111] CDC. (2017). Updated Interim Guidance for Pregnant Women with Possible Zika Virus Exposure. Retrieved from hĀps://www.chicagohan.org/documents/14171/155633/Key takeaways for healthcare providers/3658eb87-32f3-4d5d-a795-8862c5a32985
[112] Oduyebo, T., Polen, K. D., Walke, H. T., et al. (2017, July 28). Update: Interim Guidance for Health Care Providers Caring for Pregnant Women with Possible Zika Virus Exposure — United States (Including U.S. Territories). *MMWR. Morbidity and Mortality Weekly Report, 66*(29), 781-793. doi:10.15585/mmwr.mm6629e1

INDICATIONS FOR ZIKA TESTING

The Los Angeles County Department of Public Health Acute Communicable Disease Control has created the following table to assess Indications for Zika Testing for pregnant women (Appendix G). Please contact the Los Angeles County Public Health Laboratory at 562-658-1330 for the most updated specimen collection recommendations.

Indications for Zika Testing (Appendix G)

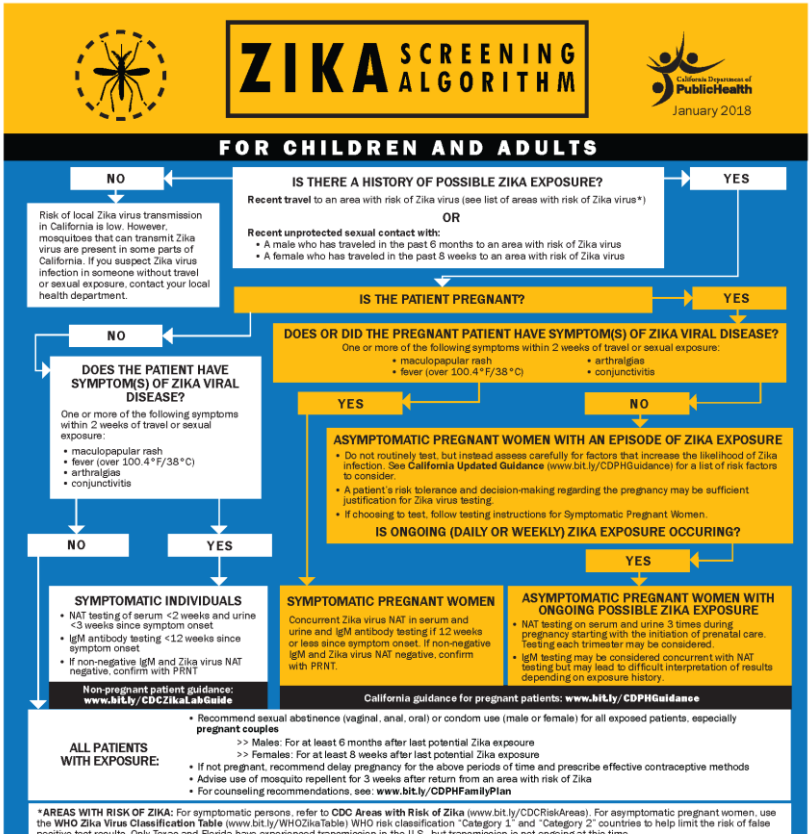
Indications for Zika Testing	RT-PCR (serum, urine, or other)	IgM[1] (serum)
Pregnancy-associated		
Symptomatic[2] pregnant woman *with* travel[3] or sexual[4] exposure history	ASAP Serum & Urine < 12 weeks of onset	Concurrent with PCR
Symptomatic pregnant woman *without* travel or sexual exposure history	Not recommended	Not recommended
Pregnant woman with travel or sexual exposure history and ultrasound evidence of fetal microcephaly and/or calcifications OR fetal loss, regardless of symptom status	ASAP Serum & Urine < 12 weeks after possible exposure (amniotic fluid if amniocentesis preformed)	Concurrent with PCR
Pregnant woman with ongoing exposure (lives in or frequently travels to Zika risk area or ongoing unprotected sexual activity with potentially infected partner)	Serum & Urine Test 3 times during pregnancy	Consider concurrent with PCR but not routinely recommended
Asymptomatic pregnant traveler	Not routinely recommended**	Not routinely recommended

ALORITHM OF ZIKA SCREENING AND CONFIRMATORY LAB TESTS

The CDPH *Zika Screening Algorithm*[113] (Appendix I) includes a testing algorithm for pregnant women. Los Angeles County is adapting this algorithm in accordance with the latest Los Angeles County Health Alert Network (LAHAN): *Updated California Zika Testing Guidelines and a Local Case of Sexually Transmitted Zika* [114] (Appendix F).

Los Angeles County, the California Department of Public Health,[115] and the CDC[116] recommends a shared decision-making model which includes pretest counseling, individualized risk assessment, clinical judgment, and patient preferences. A patient's risk tolerance and decision-making regarding the pregnancy may be sufficient justification to test for Zika virus infection. [117]

Zika Screening Algorithm (Appendix I)



[113] CDPH. (2018, January). Updated Zika Screening Algorithm. Retrieved from hĀps://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/ZikaAlgorithmPoster.pdf

[114] Los Angeles County Health Alert Network. (2018, January 4). Updated California Zika TesĀng Guidelines and a Local Case of Sexually TransmiĀed Zika. Retrieved from hĀp://publichealth.lacounty.gov/eprp/Health%20Alerts/LAHAN%20Zika%20Advisory%20with%20CDPH%20Guidance%201.4.18.pdf

[115] California Department of Public Health (2018, January 10). Updated Guidance for Health Care Providers: Assessment and TesĀng for Zika Virus InfecĀon in Pregnant Women and their Newborns. Retrieved from hĀps://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/UpdatedZikaGuidanceforHCPsCaringforPregnantWomen.pdf

[116] CDC. (2018, January 19). TesĀng & Diagnosis. Retrieved from hĀps://www.cdc.gov/pregnancy/zika/tesĀng-follow-up/tesĀng-and-diagnosis.html

[117] California Department of Public Health (2018, January 10). Updated Guidance for Health Care Providers: Assessment and TesĀng for Zika Virus InfecĀon in Pregnant Women and their Newborns. Retrieved from hĀps://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/UpdatedZikaGuidanceforHCPsCaringforPregnantWomen.pdf

INFANT ZIKA SPECIMEN COLLECTION

For women with known Zika virus infection test results, no maternal blood needs to be drawn on admission. Maternal screening and testing (PCR/NAT, IgM, and PRNT) is described in detail under *Screening and Confirmatory Lab Tests*.

Please contact the Los Angeles County Public Health Laboratory (PHL) at 562-658-1330 for the most updated placenta collection recommendations.

KEY NOTES:

For women with unknown Zika virus infection status, maternal screening and testing should be performed prior to admission into Labor and Delivery.

INFANT SPECIMEN COLLECTION

Infant testing is performed after delivery. Infant testing may include the collection of any combination of the following four types of specimen. The California Department of Public Health guidelines includes recommendations for Zika Virus Testing for newborn infants.[118]

Please contact the Los Angeles County Public Health Laboratory at 562-658-1330 for the most updated placenta collection recommendations.

KEY NOTES:

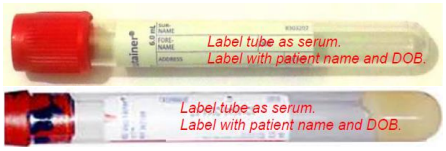
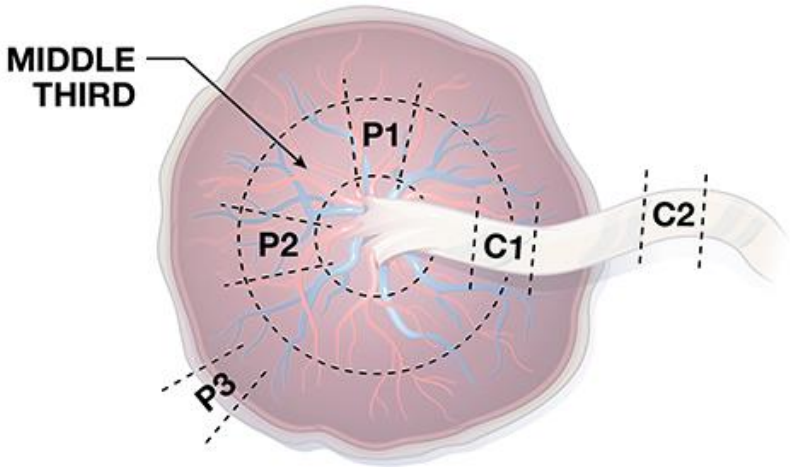
Infant serum and urine specimens are collected at the delivery of every Zika-positive mother.

Collection of placenta and umbilical cord specimens *depends* on maternal Zika screening and confirmatory lab test results. Please contact the Los Angeles County Public Health Laboratory at 562-658-1330 for the most updated placenta collection recommendations.

Table 3 describes what infant specimens and equipment are needed for collection.

[118] California Department of Public Health (2018, January 10). Updated Guidance for Health Care Providers: Assessment and TesĀng for Zika Virus InfecĀon in Pregnant Women and their Newborns. Retrieved from hĀps://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/UpdatedZikaGuidanceforHCPsCaringforPregnantWomen.pdf

Table 3: Infant Specimens Collected

Serum	Red top pediatric microtainer tube	
Urine	Sterile urine container	
Placenta and umbilical cord	10% neutral buffered formalin for fixed tissue samples	

INDICATIONS FOR ZIKA TESTING

The Los Angeles County Department of Public Health Acute Communicable Disease Control has created the following table to assess Indications for Zika Testing for infants (Appendix G). Please contact the Los Angeles County Public Health Laboratory at 562-658-1330 for the most updated specimen collection recommendations.

Indications for Zika Testing (Appendix G)

Indications for Zika Testing	RT-PCR (serum, urine, or other)	IgM[1] (serum)
Infants*		
Infant with microcephaly and/or calcifications, and maternal Zika virus exposure regardless of maternal test results	Serum & Urine (CSF if available***) < 2 DAYS after birth	Concurrent with PCR (CSF if available)
Infant with no apparent defect and evidence of maternal Zika virus infection (IgM), or exposure history and awaiting maternal lab results (PRNT)	Serum & Urine (CSF if available) < 2 DAYS after birth	Concurrent with PCR (CSF if available)
Infant with no apparent defect, and no evidence of maternal Zika virus infection or exposure history	Not Recommended	Not Recommended

* Cord blood is not recommended for testing

The CDC *Interim Guidance for Zika Virus Testing of Formalin-Fixed Paraffin-Embedded Placenta, Fetal, or Infant Autopsy Tissues*[119] (Appendix K) also provides instructions for determining when placenta and umbilical cord specimen collection is recommended. Please contact the Los Angeles County Public Health Laboratory (PHL) at 562-658-1330 for the most updated placenta collection recommendations.

[119] CDC. (2017, August 15). Interim Guidance for Zika Virus TesĀng of Formalin-Fixed ParaĀ n-Embedded Placenta, Fetal, or Infant Autopsy Tissues. Retrieved from hĀps://www.cdc.gov/zika/pdfs/specimen-zika-virus-tesĀng-fact-sheet.pdf

INSTRUCTIONS FOR INFANT ZIKA SPECIMEN COLLECTION

The *Instructions for Infant Zika Specimen Collection*[120] (Appendix L) are pictured below as per the Los Angeles County Public Health Laboratory (PHL). Placenta and umbilical cord cutting and storage, if collected, should be performed by a laboratory pathologist. Please contact the PHL at 562-658-1330 for the most updated placenta collection recommendations.

Instructions for Infant Zika Specimen Collection (Appendix L)

SPECIMEN	GENERAL INSTRUCTIONS	NOTES	STORAGE
Placenta and fetal membranes (fixed)	Several full thickness pieces including **at least 3** full thickness pieces (0.5–1 cm x 3–4 cm in depth) from middle third of placental disk and **at least 1** from the placental disk margin 5 x 12 cm strip of fetal membranes Please include sections of the placental disk, fetal membranes, and pathologic lesions when possible.	Please include information about placenta weight and sample both maternal and fetal side of the placenta Label all specimens to identify location of sample Fix specimens in formalin Volume of formalin used should be about 10x mass of tissue. Place in 10% neutral buffered formalin for a minimum of 3 days. **Order histopathology**	**Storage and transport at room temperature for fixed specimens**
Umbilical cord	2.5 cm segments of cord **At least 4** specimens Umbilical cord segments should be obtained proximal, middle, and distal to umbilical cord insertion site on the placenta	Label all specimens to identify location of sample. Fix specimens in formalin Volume of formalin used should be about 10x mass of tissue. Place in 10% neutral buffered formalin for a minimum of 3 days **Order histopathology**	**Storage and transport at room temperature for fixed specimens**
Infant urine	1-5 mL in sterile container (bagged urine transferred to sterile container)	Collection recommended within first 2 days after birth. Specimens collected up to 12 weeks will be tested. **Order PCR**	**Store in fridge** **Transport on cold pack**
Infant serum	**At least 1mL collected in red top pediatric microtainer tube**	**Collection recommended within first 2 days after birth. Specimens collected up to 12 weeks will be tested.** Order PCR and serology	**Store in fridge** **Transport on cold pack**

[120] Los Angeles County Public Health Laboratories (2017, April 18). InstrucĀons for Zika (pregnant mother at Āme of birth). Retrieved from hĀp://publichealth.lacounty.gov/mch/ReproducĀveHealth/Zika-MCAH/Forms/InstrucĀonsForSpecimenCollecĀon(4-18-17).pdf

CONTACTS FOR ASSISTANCE AND COURIER SERVICES

The Los Angeles County Public Health Laboratory is the point of contact for all Zika screening testing (blood or serum) and Zika specimen collection (infant specimens). Hospitals may arrange for Public Health Laboratory courier services to retrieve Zika specimens after they have been collected, cut, and stored properly.

Any questions regarding Zika specimen collection should be made to the Public Health Laboratory at the number listed on the *Laboratory Contact Information for Zika* (Appendix N) sheet below. Arrangements for courier services may also be made at the number below.

Laboratory Contact Information for Zika (Appendix N)

Los Angeles County Public Health Department
Laboratory Contact Information for Zika

Please notify the Los Angeles County Department of Public Health when a pregnant woman positive for ZIKA arrives at your hospital. Call 213-240-7941.

For questions regarding **ZIKA specimen collection**, please contact the Los Angeles County Public Health Laboratories:

Business hours, **562-658-1330**
After hours, **213-974-1234** (press # 8)

Remember:

- A separate **ZIKA Test Request Form** must accompany each specimen
- Mother must give consent in advance if the provider wants to collect placental specimens

To arrange courier service and pick up of ZIKA specimens, contact the Public Health Laboratory:

Business hours, **562-658-1460**
After hours, **213-974-1234** (press # 8)

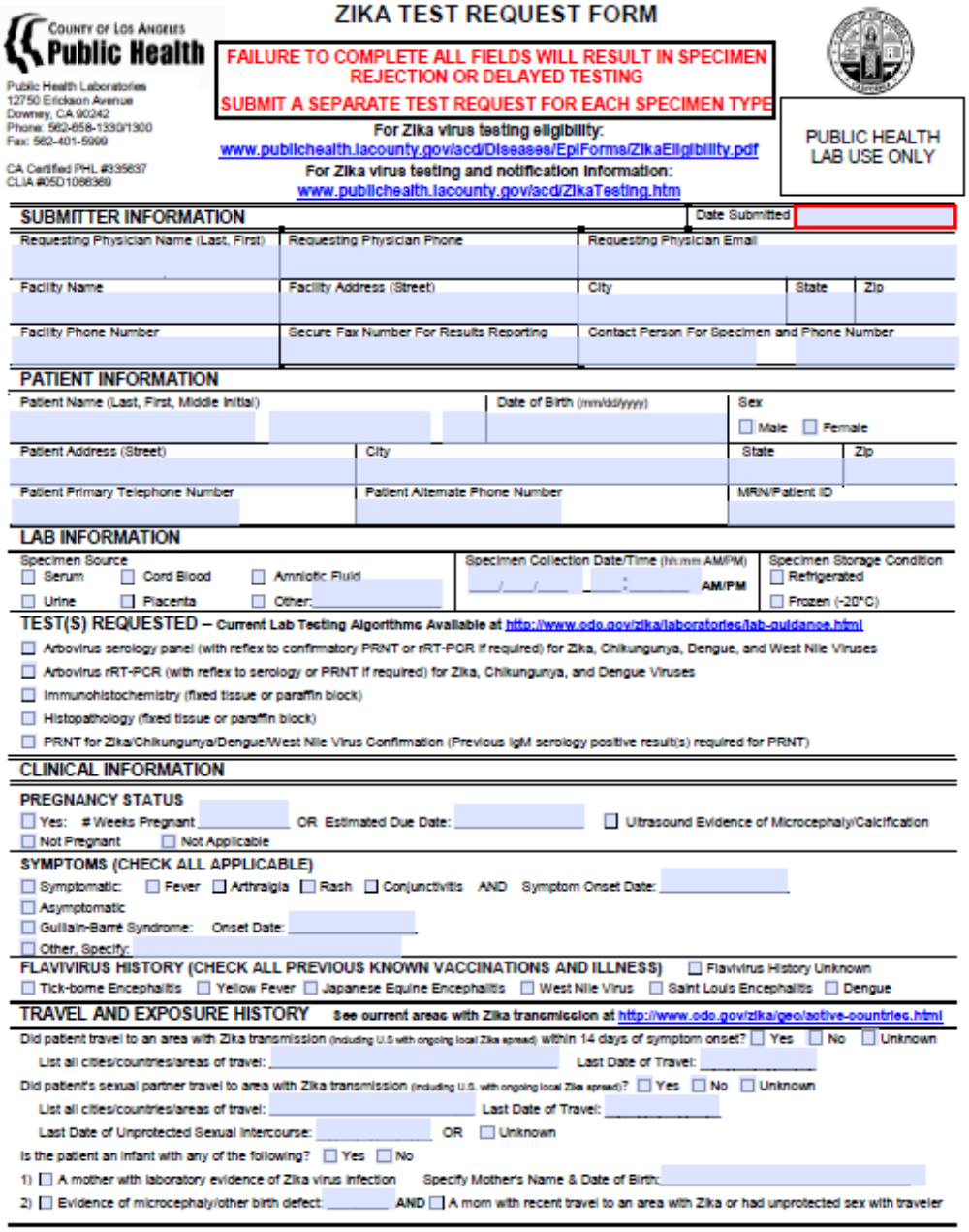
For questions regarding the **Neonate Form**, call **626-569-6508**

SUBMISSION OF ZIKA TESTS

PUBLIC HEALTH LABORATORY ZIKA TEST REQUEST FORM

A *Zika Test Request Form*[121] (Appendix M) must be included with **each** specimen collected at the time of delivery. Separate *Zika Test Request Forms* must be completed for maternal tests and/or infant specimens.

Zika Test Request Form (Appendix M)



ZIKA TEST REQUEST FORM

COUNTY OF LOS ANGELES Public Health

Public Health Laboratories
12750 Erickson Avenue
Downey, CA 90242
Phone: 562-658-1330/1300
Fax: 562-401-5999

CA Certified PHL #335837
CLIA #05D1068389

FAILURE TO COMPLETE ALL FIELDS WILL RESULT IN SPECIMEN REJECTION OR DELAYED TESTING
SUBMIT A SEPARATE TEST REQUEST FOR EACH SPECIMEN TYPE

For Zika virus testing eligibility:
www.publichealth.lacounty.gov/acd/Diseases/EpiForms/ZikaEligibility.pdf
For Zika virus testing and notification information:
www.publichealth.lacounty.gov/acd/ZikaTesting.htm

PUBLIC HEALTH LAB USE ONLY

SUBMITTER INFORMATION — Date Submitted
Requesting Physician Name (Last, First) | Requesting Physician Phone | Requesting Physician Email
Facility Name | Facility Address (Street) | City | State | Zip
Facility Phone Number | Secure Fax Number For Results Reporting | Contact Person For Specimen and Phone Number

PATIENT INFORMATION
Patient Name (Last, First, Middle Initial) | Date of Birth (mm/dd/yyyy) | Sex ☐ Male ☐ Female
Patient Address (Street) | City | State | Zip
Patient Primary Telephone Number | Patient Alternate Phone Number | MRN/Patient ID

LAB INFORMATION
Specimen Source: ☐ Serum ☐ Cord Blood ☐ Amniotic Fluid ☐ Urine ☐ Placenta ☐ Other:
Specimen Collection Date/Time (hh:mm AM/PM) AM/PM
Specimen Storage Condition: ☐ Refrigerated ☐ Frozen (-20°C)

TEST(S) REQUESTED – Current Lab Testing Algorithms Available at http://www.cdc.gov/zika/laboratories/lab-guidance.html
☐ Arbovirus serology panel (with reflex to confirmatory PRNT or rRT-PCR if required) for Zika, Chikungunya, Dengue, and West Nile Viruses
☐ Arbovirus rRT-PCR (with reflex to serology or PRNT if required) for Zika, Chikungunya, and Dengue Viruses
☐ Immunohistochemistry (fixed tissue or paraffin block)
☐ Histopathology (fixed tissue or paraffin block)
☐ PRNT for Zika/Chikungunya/Dengue/West Nile Virus Confirmation (Previous IgM serology positive result(s) required for PRNT)

CLINICAL INFORMATION
PREGNANCY STATUS
☐ Yes: # Weeks Pregnant OR Estimated Due Date: ☐ Ultrasound Evidence of Microcephaly/Calcification
☐ Not Pregnant ☐ Not Applicable

SYMPTOMS (CHECK ALL APPLICABLE)
☐ Symptomatic: ☐ Fever ☐ Arthralgia ☐ Rash ☐ Conjunctivitis AND Symptom Onset Date:
☐ Asymptomatic
☐ Guillain-Barré Syndrome: Onset Date:
☐ Other, Specify:

FLAVIVIRUS HISTORY (CHECK ALL PREVIOUS KNOWN VACCINATIONS AND ILLNESS) ☐ Flavivirus History Unknown
☐ Tick-borne Encephalitis ☐ Yellow Fever ☐ Japanese Equine Encephalitis ☐ West Nile Virus ☐ Saint Louis Encephalitis ☐ Dengue

TRAVEL AND EXPOSURE HISTORY See current areas with Zika transmission at http://www.cdc.gov/zika/geo/active-countries.html
Did patient travel to an area with Zika transmission (including U.S with ongoing local Zika spread) within 14 days of symptom onset? ☐ Yes ☐ No ☐ Unknown
List all cities/countries/areas of travel: Last Date of Travel:
Did patient's sexual partner travel to area with Zika transmission (including U.S. with ongoing local Zika spread)? ☐ Yes ☐ No ☐ Unknown
List all cities/countries/areas of travel: Last Date of Travel:
Last Date of Unprotected Sexual Intercourse: OR ☐ Unknown
Is the patient an infant with any of the following? ☐ Yes ☐ No
1) ☐ A mother with laboratory evidence of Zika virus infection Specify Mother's Name & Date of Birth:
2) ☐ Evidence of microcephaly/other birth defect: AND ☐ A mom with recent travel to an area with Zika or had unprotected sex with traveler

[121] County of Los Angeles Public Health Laboratories. (2016, December 6). Zika Test Request Form Retrieved from hĀp://publichealth.lacounty.gov/acd/Diseases/EpiForms/ZikaInfoTestReq.pdf

INTERPRETATION OF LABORATORY RESULTS

INTERPRETATION OF MATERNAL LABORATORY RESULTS

The CDC *Interpretation of Results of Nucleic Acid and Antibody Testing for Suspected Zika Virus Infection*[122] (Appendix H) charts the interpretations and recommendations for Zika PCR/NAT, IgM serology, and PRNT test results.

Interpretation of Results of Nucleic Acid and Antibody Testing for Suspected Zika Virus Infection (Appendix H)

Zika NAT (serum)[4]	Zika NAT (urine)[4]	Zika virus IgM[5]	Zika virus PRNT	Dengue virus PRNT	Interpretation and recommendations
Positive	Positive	Any result	Not indicated	Not indicated	**Acute Zika virus infection**
Negative	Positive	Positive	Not indicated	Not indicated	**Acute Zika virus infection**
Negative	Positive	Negative	Not indicated	Not indicated	**Suggests acute Zika virus infection** *Repeat testing on original urine specimen* • *If repeat NAT result is positive, interpret as **evidence of acute Zika virus infection*** • *If repeat NAT result is negative, repeat Zika virus IgM antibody testing on a serum specimen collected ≥2 weeks after symptom onset or possible exposure or specimen collection date* – *If repeat IgM antibody result is positive,[6] interpret as **evidence of acute Zika virus infection*** – *If repeat IgM antibody result is not positive, interpret as no evidence of Zika virus infection*
Positive	Negative or not performed	Positive	Not indicated	Not indicated	**Acute Zika virus infection**
Positive	Negative or not performed	Negative	Not indicated	Not indicated	**Suggests acute Zika virus infection** *Repeat testing on original serum specimen* • *If repeat NAT result is positive, interpret as **evidence of acute Zika virus infection*** • *If repeat NAT result is negative, repeat Zika virus IgM antibody testing on a serum specimen collected ≥2 weeks after symptom onset or possible exposure or specimen collection date* – *If repeat IgM antibody result is positive,[6] interpret as **evidence of acute Zika virus infection*** – *If repeat IgM antibody result is not positive, interpret as no evidence of Zika virus infection*
Negative	Negative or not performed	Any non-negative result[7]	≥10	<10	**Zika virus infection; timing of infection cannot be determined.** • *For persons without prior Zika virus exposure, a positive IgM result represents recent Zika virus infection*
Negative	Negative or not performed	Any non-negative result[7]	≥10	≥10	**Flavivirus infection; specific virus cannot be identified; timing of infection cannot be determined** • *For persons without prior Zika virus exposure, a positive IgM result represents recent unspecified flavivirus infection*
Negative	Negative or not performed	Any non-negative result[7]	<10	Any result	**No evidence of Zika virus infection**
For areas where PRNT is not recommended[3]					
Negative	Negative or not performed	Positive for Zika virus AND negative for dengue virus	Not performed because PRNT is not recommended		**Presumptive Zika virus infection; timing of infection cannot be determined[8]**
Negative	Negative or not performed	Positive for Zika virus AND positive for dengue virus	Not performed because PRNT is not recommended		**Presumptive flavivirus infection; specific virus cannot be identified; timing of infection cannot be determined[8]**
Negative	Negative or not performed	Equivocal (either or both assays)	Not performed because PRNT is not recommended		**Insufficient information for interpretation** • *Consider repeat testing*
Negative	Negative or not performed	Negative on both assays	Not performed because PRNT is not recommended		**No laboratory evidence of Zika virus infection**

Abbreviations: IgM = immunoglobulin M; NAT = nucleic acid test; PRNT = plaque reduction neutralization test.

[122] CDC. (2017, July 24). InterpretaĀon of Results of Nucleic Acid and AnĀbody TesĀng for Suspected Zika Virus InfecĀon. Retrieved from hĀps://www.cdc.gov/zika/pdfs/lab-table.pdf

INTERPRETATION OF INFANT LABORATORY RESULTS

The CDC *Evaluation for Infants with Possible Congenital Zika Virus Infection*[123] (Appendix S) charts the interpretations of results of laboratory testing of infant's blood, urine, and/or cerebrospinal fluid for evidence of congenital Zika virus infection.

Evaluation for Infants with Possible Congenital Zika Virus Infection (Appendix S)

TABLE 1

Interpretation of results of laboratory testing of infant's blood, urine, and/or cerebrospinal fluid for evidence of congenital Zika virus infection		
Infant test results*		
NAT	**IgM**	**Interpretation**
Positive	Any result	Confirmed congenital Zika virus infection†
Negative	Nonnegative§	Probable congenital Zika virus infection¶,**
Negative	Negative	Congenital virus infection unlikely¶,††

Abbreviations: NAT = nucleic acid test; IgM = immunoglobulin M

*Infant serum, urine, or cerebrospinal fluid.

† Distinguishing between congenital and postnatal infection is difficult in infants who live in areas where there is ongoing transmission of Zika virus and who are not tested soon after birth. If the timing of infection cannot be determined, infants should be evaluated as if they had congenital Zika virus infection.

§ Nonnegative serology terminology varies by assay and might include "positive," "equivocal," "presumptive positive," or "possible positive." For explanation of a specific interpretation, refer to the instructions for use for the specific assay performed.

¶ Laboratory results should be interpreted in the context of timing of infection during pregnancy, maternal serology results, clinical findings consistent with congenital Zika syndrome, and any confirmatory testing with plaque reduction neutralization testing.

** A negative Zika virus plaque reduction neutralization test suggests that the infant's Zika virus IgM test is a false positive.

†† Congenital Zika virus infection is unlikely if specimens are collected within the first few days after birth and the clinical evaluation is normal; however, health care providers should remain alert for any new findings of congenital Zika virus infection.

BOX 1. Standard evaluation recommended at birth and during each well visit for all infants with possible congenital Zika virus exposure during pregnancy

- Comprehensive physical exam, including growth parameters
- Developmental monitoring and screening using validated screening tools recommended by the American Academy of Pediatrics (https://www.aap.org/en-us/advocacy-and-policy/aap-health-initiatives/Screening/Pages/Screening-Tools.aspx)
- Vision screening as recommended by the American Academy of Pediatrics Policy Statement "Visual System Assessment in Infants, Children, and Young Adults by Pediatricians" (www.pediatrics.org/cgi/doi/10.1542/peds.2015-3596)
- Newborn hearing screen at birth, preferably with automated auditory brainstem response

BOX 2. Consultations for infants with clinical findings consistent with congenital Zika syndrome

- **Consider consultation with the following specialists:**
  - Infectious disease specialist for evaluation for other congenital infections (e.g., toxoplasmosis, syphilis, rubella, cytomegalovirus, or herpes simplex virus) and assistance with Zika virus diagnosis, testing, and counseling
  - Neurologist by age 1 month for comprehensive neurologic examination and consideration for other evaluations such as advanced neuroimaging and EEG
  - Ophthalmologist for comprehensive eye exam by age 1 month
  - Clinical geneticist for confirmation of the clinical phenotype and evaluation for other causes of microcephaly or congenital anomalies
  - Early intervention and developmental specialists
  - Family and supportive services
- **Additional possible consultations, based on clinical findings of the infant:**
  - Endocrinologist for evaluation of hypothalamic or pituitary dysfunction and consideration for thyroid testing
  - Lactation specialist, nutritionist, gastroenterologist or speech or occupational therapist for evaluation for dysphagia and management of feeding issues
  - Orthopedist, physiatrist, or physical therapist for the management of hypertonia, clubfoot or arthrogrypotic-like conditions
  - Pulmonologist or otolaryngologist for concerns about aspiration

[123] CDC. (2017, November 17). EvaluaÃon for Infants with Possible Congenital Zika Virus InfecÃon. Retrieved from hÃps://www.cdc.gov/zika/pdfs/pediatric-evaluaÃon-follow-up-tool.pdf

BEST PRACTICES

The following best practices are recommended to improve the coordination of Zika specimens.

COORDINATION OF ROLES AND RESPONSIBILITIES

Prior to admission and delivery of a Zika-positive women, coordination of roles and responsibilities within the L&D, NICU, and laboratory should be performed. Sample of key personnel roles and responsibilities are listed below.

- ✓ Labor and delivery nurse: Manage care of mother and newborn
- ✓ Pediatrician: Manage the care and assessment of newborn
- ✓ Pathologist: Manage the collection, storage, and transportation of placenta and umbilical cord specimens (if necessary)
- ✓ Laboratory: Manage the collection and transportation of infant specimens (serum and urine)
- ✓ Zika coordinator: Manage communication between all departments and with LAC Department of Public Health (i.e. Infection Control personnel)

If necessary, the laboratory pathologist may be present at the time of delivery to collect the placenta and umbilical cord appropriately. Alternatively, a labor and delivery nurse may also hand-deliver the placenta and umbilical cord specimens to the laboratory to ensure accurate retrieval of specimens. These roles may be assigned as per the jurisdiction of each hospital.

CONTACT INFORMATION

Contact information for the key personnel should be easily assessable by laboratory personnel. The Laboratory Contact Information for Zika (Appendix M) flyer may be shared with L&D and posted in staff lounges in the laboratory units where they can be easily accessed when needed.

APPENDICES

Morbidity and Mortality Weekly Report

Preventing Transmission of Zika Virus in Labor and Delivery Settings Through Implementation of Standard Precautions — United States, 2016

Christine K. Olson, MD[1]; Martha Iwamoto, MD[2]; Kiran M. Perkins, MD[3]; Kara N.D. Polen, MPH[4]; Jeffrey Hageman, MHS[3]; Dana Meaney-Delman, MD[5]; Irogue I. Igbinosa, MD[6]; Sumaiya Khan, MPH[7]; Margaret A. Honein, PhD[4]; Michael Bell, MD[3]; Sonja A. Rasmussen, MD[8]; Denise J. Jamieson, MD[1]

On March 22, 2016, this report was posted as an MMWR *Early Release on the* MMWR *website (http://www.cdc.gov/mmwr).*

Zika virus transmission was detected in the Region of the Americas (Americas) in Brazil in May 2015, and as of March 21, 2016, local mosquito-borne transmission of Zika virus had been reported in 32 countries and territories in the Americas, including Puerto Rico and the U.S. Virgin Islands.* Most persons infected with Zika virus have a mild illness or are asymptomatic. However, increasing evidence supports a link between Zika virus infection during pregnancy and adverse pregnancy and birth outcomes (*1*), and a possible association between recent Zika virus infection and Guillain-Barré syndrome has been reported (*2*). Although Zika virus is primarily transmitted through the bite of *Aedes* species of mosquitoes, sexual transmission also has been documented (*3*). Zika virus RNA has been detected in a number of body fluids, including blood, urine, saliva, and amniotic fluid (*3*–*5*), and whereas transmission associated with occupational exposure to these body fluids is theoretically possible, it has not been documented. Although there are no reports of transmission of Zika virus from infected patients to health care personnel or other patients, minimizing exposures to body fluids is important to reduce the possibility of such transmission. CDC recommends Standard Precautions in all health care settings to protect both health care personnel and patients from infection with Zika virus as well as from blood-borne pathogens (e.g., human immunodeficiency virus [HIV] and hepatitis C virus [HCV]) (*6*). Because of the potential for exposure to large volumes of body fluids during the labor and delivery process and the sometimes unpredictable and fast-paced nature of obstetrical care, the use of Standard Precautions in these settings is essential to prevent possible transmission of Zika virus from patients to health care personnel.

Use of Standard Precautions in Health Care Settings

Health care personnel should adhere to Standard Precautions in every health care setting. Standard Precautions are designed to protect health care personnel and to prevent them from spreading infections to patients. They are based on the premise that all blood, body fluids, secretions, excretions (except sweat), nonintact skin, and mucous membranes might contain transmissible infectious agents and include 1) hand hygiene, 2) use of personal protective equipment (PPE), 3) respiratory hygiene and cough etiquette, 4) safe injection practices, and 5) safe handling of potentially contaminated equipment or surfaces in the patient environment (*6*). Because patients with Zika virus infection might be asymptomatic, Standard Precautions should be in place at all times, regardless of whether the infection is suspected or confirmed. Health care personnel should assess the potential for exposure to potentially infectious material during health care delivery and protect themselves accordingly, based on the level of clinical interaction with the patient and the physical distance at which care is provided (*6*). In addition, health care providers should use soap and water or alcohol-based products (gels, rinses, foams), at a minimum, before and after a patient contact and after removing PPE, including gloves (*6*).

Use of Standard Precautions in Labor and Delivery Settings

Pregnant women lose an average of 500 mL of blood during uncomplicated vaginal deliveries, with higher losses during complicated vaginal deliveries and cesarean deliveries (*7*). Amniotic fluid volume at the time of full-term delivery typically exceeds 500 mL (*8*). Eye protection used during deliveries has been demonstrated to be contaminated with blood and body fluids (*9*), and when double layers of gloves are used for procedures and surgeries, the outer layers often have significant perforations, whereas the inner layers are intact or have many fewer perforations (*10*). Although health care personnel in these settings are at substantial risk for exposure to blood and body fluids, varying levels of adherence to Standard Precautions have been reported in health care settings, including in labor and delivery units (*11*). Numerous barriers to the appropriate use of PPE have been cited, including the perception that PPE is uncomfortable and limits dexterity, fogging of goggles or face masks, the misperception that prescription eyeglasses provide adequate eye protection, lack of available PPE, forgetting to use PPE, lack of time in urgent clinical situations to don appropriate PPE, the perception that the patient poses minimal risk, and concerns about interference with patient care (*11*). Given the theoretic risk for transmission of Zika virus through contact with body fluids in a health care

* http://www.cdc.gov/zika/geo/active-countries.html.

setting in which female health care personnel might be pregnant, or male or female health care personnel might be trying to conceive a pregnancy, the outbreak of Zika virus disease provides an opportunity to emphasize the importance of maintaining appropriate infection control.

The goals of Standard Precautions include 1) preventing contact between a patient's body fluids and health care personnel's mucous membranes (including conjunctivae), skin, and clothing; 2) preventing health care personnel from carrying potentially infectious material from one patient to another; and 3) avoiding unnecessary exposure to contaminated sharp implements. Health care personnel must assess the likelihood of body fluid exposure, based on the type of contact and the nature of the procedure or activity, and use appropriate PPE. For example, because the risk for splashes to areas of the body other than the hands is small when performing vaginal examinations of pregnant women with minimal cervical dilation and intact membranes, only gloves are required. Placement of a fetal scalp electrode when membranes have already been ruptured or handling newborns before blood and amniotic fluid have been removed from the newborn's skin require protection of health care personnel's skin and clothing using gloves and an impermeable gown. In contrast, when performing procedures where exposure to body fluids is anticipated, such as an amniotomy or placement of an intrauterine pressure catheter, protection of mucous membranes, skin, and clothing are recommended, with a mask and eye protection, in addition to gloves and an impermeable gown.

Anesthesia providers in the labor and delivery setting should adhere to Standard Precautions and wear sterile gloves and a surgical mask when placing a catheter or administering intrathecal injections; additional PPE should be worn based on anticipated exposure to body fluids (*6*). Double gloves might minimize the risk for percutaneous injury when sharps are handled. Patient body fluids also should not come into direct contact with health care personnel clothing or footwear. When performing procedures including vaginal deliveries, manual placenta removal, bimanual uterine massage, and repair of vaginal lacerations, PPE should include (in addition to mucous membrane and skin protection) impermeable gowns and knee-high impermeable shoe covers. Clothing, skin, and mucous membrane protections should be maintained for procedures performed in operating room settings.

Health care personnel should assess their risk for exposure and select PPE appropriate for the situation, and all personnel on a team involved in the same procedures should use the same level of PPE. All health care personnel should be trained in the correct use and disposal of PPE and be able to demonstrate the ability to don PPE quickly in urgent situations and remove it safely. Non–health care personnel in attendance should be positioned away from areas of exposure risk or adequately protected. Any occupational exposures, including mucous membrane exposure following splash of body fluids, sustained by health care personnel should be reported as soon as possible to the facility's occupational health clinic to ensure appropriate assessment of health care personnel, and so that any systemic safety risks can be addressed.

In addition to use of PPE by health care personnel, placement of disposable absorbent material on the floor around the procedure and delivery area to absorb fluid can reduce the risk for splash exposure to body fluids. Infection control supplies should be available and accessible in all patient care areas where they will be needed. Standard cleaning and disinfection procedures for environmental surfaces, using Environmental Protection Agency-registered hospital disinfectants, should be followed.

Importance of Ongoing Education and Training

Standard Precautions represent the minimum infection prevention expectations for safe care across all health care settings. Ongoing education and training of all health care personnel in a facility, including those employed by outside entities, on the principles and rationale for use of Standard Precautions and use of specific PPE help ensure that infection control policies and procedures are understood and followed (*6*). These educational efforts should emphasize that infection prevention strategies enhance the quality of patient care and do not alter the relationship between provider and patient. Barriers (e.g., cost and lack of standardized protocols in facilities) to implementation of Standard Precautions and use of PPE should be addressed as soon as they are recognized. Facility, nursing, and obstetric leadership is critical for instituting infection prevention policies and promoting routine use of and adherence to Standard Precautions (*6*). Infectious disease outbreaks, such as the current Zika virus disease outbreak, provide an opportunity to emphasize the importance of adherence to published infection prevention strategies to prevent transmission of infectious diseases in all health care settings, including labor and delivery units.

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FactSheet OSHA NIOSH

Interim Guidance for Protecting Workers from Occupational Exposure to Zika Virus

The Occupational Safety and Health Administration (OSHA) and the National Institute for Occupational Safety and Health (NIOSH) are monitoring the Zika virus outbreak spreading through Central and South America, Mexico, and parts of the Caribbean, including U.S. territories. For the most up-to-date information, check the Centers for Disease Control and Prevention (CDC) Zika website frequently. Some U.S. states have mosquitoes that can become infected with and spread Zika virus, and travel-associated Zika virus infections in U.S. states may result in local spread of the virus. Visit the CDC Areas with Zika website to learn where there is current transmission. Workers who are exposed on the job to mosquitoes or the blood or other body fluids of infected individuals may be at risk for occupationally acquired Zika virus infection. This interim guidance provides employers and workers with information and guidance on preventing occupational exposure to the Zika virus. The guidance may be updated as additional information becomes available.

Introduction

Zika virus is primarily spread through the bites of infected mosquitoes. Mosquitoes can become infected when they bite infected persons and can then spread the Zika virus to other persons they subsequently bite.

Zika virus historically has been found in Africa, Southeast Asia, and the Pacific Islands. The first case was identified in the Zika Forest in Uganda in 1947.[1] In 2015, cases of Zika virus infection emerged in the Americas and the Caribbean.

Zika virus has the potential to spread anywhere that mosquitoes capable of spreading this virus are found. *Aedes* species mosquitoes are a principal vector (i.e., carrier) of Zika virus in the U.S. *Aedes aegypti* (commonly known as yellow fever mosquitoes) are typically concentrated in the southern U.S. as well as parts of the Southwest. Another vector for Zika virus is *Aedes albopictus* (commonly known as Asian Tiger mosquitoes), which are found in much of the southern and eastern part of the U.S. *Aedes* mosquitoes can also carry other arboviruses, including dengue, yellow fever, chikungunya, Japanese encephalitis, and West Nile. CDC provides information about surveillance of *Aedes* mosquitoes in the U.S.

Credit: CDC / James Gathany

Aedes aegypti mosquitoes, like the one pictured, can become infected when they bite infected persons and can then spread the Zika virus to other persons they subsequently bite.

Zika Virus Infection in Humans

Current science-based evidence suggests that approximately one out of five infected people develops symptoms of Zika virus, usually beginning 2-7 days after the bite of an infected mosquito. Symptoms are usually mild and can last 2–7 days. The most common symptoms of

1. *Hayes, Edward B. "Zika Virus Outside Africa," Emerging Infectious Diseases, 15, 9, 1347–1350 (2009).*

Zika virus infection are fever, rash, joint pain and red or pink eyes. Other symptoms include myalgia (muscle pain) and headache. These symptoms are similar to those of dengue fever or chikungunya. Neurological and autoimmune complications are infrequent but have been described in outbreaks in Polynesia and, more recently, Brazil.

During the first week of infection, Zika virus can be detected in the blood and is capable of being spread from an infected person to a mosquito that feeds on that person. Infected mosquitoes can then spread the virus to other people through bites. In some instances, having direct contact with infectious blood or other body fluids (such as semen through sexual transmission) of an infected person may result in transmission of the virus.

Zika virus can be spread from a pregnant woman to her fetus and has been linked to a serious birth defect of the brain called microcephaly in babies of mothers who had Zika virus while pregnant. Other problems have been detected among fetuses and infants infected with Zika virus before birth, such as absent or poorly developed brain structures, defects of the eye, hearing deficits, and impaired growth. CDC recommends special precautions for women who are or may become pregnant.

Control and Prevention

In areas affected by Zika virus transmission, protect yourself and others from possible exposure to Zika virus by always taking steps to prevent mosquito bites. There is no vaccine to prevent Zika virus and there is no specific treatment for individuals who become infected.

Although Zika virus is generally spread by the bites of infected mosquitoes, exposure to an infected person's blood or other body fluids (such as semen through sexual transmission) may also result in transmission. Employers should train workers about their risks of exposure to Zika virus through mosquito bites and direct contact with infectious blood and other body fluids and how to protect themselves. Employers should also provide information about Zika virus infection, including modes of transmission and possible links to birth defects, to workers who are pregnant or may become pregnant or whose sexual partners are or may become pregnant.

Outdoor workers may be at the greatest risk of exposure to Zika virus. Some workers, including those working with insecticides to control mosquitoes and healthcare workers who may be exposed to contaminated blood or other potentially infectious materials from individuals infected with Zika virus, may require additional protections (e.g., certain types of personal protective equipment, PPE). Employers must comply with universal precautions for potential bloodborne pathogens (BBP) exposures, as described in OSHA's BBP standard (29 CFR 1910.1030), and any applicable requirements in OSHA's PPE standards (29 CFR 1910 Subpart I), among other OSHA requirements.

Consult the CDC Zika website for the most up-to-date information to help employers implement effective worker protections.

Outdoor workers

Recommended employer actions:

- Inform workers about their risks of exposure to Zika virus through mosquito bites and train them how to protect themselves. Check the CDC Zika website to find Zika-affected areas.
- Provide insect repellents and encourage their use according to the guidance below.
- Provide workers with, and encourage them to wear, clothing that covers their hands, arms, legs, and other exposed skin. Consider providing workers with hats with mosquito netting to protect the face and neck.
- In warm weather, encourage workers to wear lightweight, loose-fitting clothing. This type of clothing protects workers against the sun's harmful rays and provides a barrier to mosquitoes. Always provide workers with adequate water, rest and shade, and monitor workers for signs and symptoms of heat illness.
- Get rid of sources of standing water (e.g., tires, buckets, cans, bottles, barrels) whenever possible to reduce or eliminate mosquito breeding areas. Train workers about the importance of eliminating areas where mosquitos can breed at the worksite.
- If requested by a worker, consider reassigning anyone who indicates she is or may become pregnant, or who is male and has a sexual partner who is or may become pregnant, to indoor tasks to reduce their risk of mosquito bites.

Recommended worker actions:

- Use insect repellents according to the guidance below.
- Wear clothing that covers hands, arms, legs, and other exposed skin. Wear hats with mosquito netting to protect the face and neck. Wear socks that cover the ankles and lower legs.
- In warm weather, wear lightweight, loose-fitting clothing. This type of clothing protects workers against the sun's harmful rays and provides a barrier to mosquitoes. Drink plenty of water, take rest breaks in shaded areas, and watch for signs and symptoms of heat illness, including in coworkers.
- Get rid of sources of standing water (e.g., tires, buckets, cans, bottles, barrels) whenever possible to reduce or eliminate mosquito breeding areas.
- Talk to your supervisor(s) about any outdoor work assignment(s) if you are or may become pregnant, or, for males, if your sexual partner is or may become pregnant. Such workers should be familiar with CDC information on Zika virus and pregnancy.
- If symptoms develop, seek medical attention promptly. Discuss any possible exposure to mosquitoes or infections spread by mosquitoes with a healthcare provider.

Guidance on use of insect repellents for employers and workers:

- Always follow label precautions when using insect repellent.
- Use insect repellent containing an EPA-registered active ingredient. All of the EPA-registered active ingredients have demonstrated repellency, but some provide longer-lasting protection than others. Research suggests that repellents containing DEET (N,N-diethyl-m-toluamide) or picaridin (KBR 3023) typically provide longer-lasting protection than the other products, and oil of lemon eucalyptus (p-menthane-3,8-diol) provides longer-lasting protection than other plant-based repellents. Permethrin is another long-lasting repellent that is intended for application to clothing and gear, but not directly to skin.
- Choose a repellent that provides protection for the amount of time that you will be outdoors. In general, the more active ingredient (higher concentration) a repellent contains, the longer it will protect against mosquito bites. For example, the more DEET a repellent contains, the longer time it can protect you from mosquito bites, with protection times ranging from 1 hour (4.75% DEET) to 5 hours (23.8% DEET). Studies suggest that concentrations of DEET above approximately 50% do not offer a marked increase in protection time against mosquitoes; DEET efficacy tends to plateau at a concentration of approximately 50%.
- To avoid reaction to DEET or other ingredients in insect repellents, read and follow the directions on all insect repellents before use. Spray insect repellent (permethrin) on the outside of clothing, as it is possible for mosquitoes to bite through thin clothing.
- Do NOT spray insect repellent on skin that is under clothing.
- Do NOT apply insect repellent to skin that is already irritated, or to cuts/lacerations.
- Do NOT spray aerosol or pump products in enclosed areas. Do NOT spray a pump or aerosol product directly on the face. First spray it on hands and then carefully spread it on the face (do not allow insect repellent to contact eyes or mouth).
- After returning indoors and before eating, use soap and water to wash skin that has been treated with insect repellent. Reapply repellent when returning outdoors or after eating.
- Outdoor workers may need to use sunscreen in conjunction with insect repellent. Repellents that are applied according to label instructions may be used with sunscreen with no reduction in repellent activity. However, limited data show a one-third decrease in the sun protection factor (SPF) of sunscreens when DEET-containing insect repellents are used after a sunscreen is applied. Products that combine sunscreen and repellent are not recommended, because sunscreen may need to be reapplied more often and in larger amounts than needed for the repellent component to provide protection from biting insects. The best option is to use separate products, applying sunscreen first and then applying the repellent. Due to the decrease in SPF when using a DEET-containing insect repellent after applying sunscreen, users may need to reapply the sunscreen more frequently.[2]

2. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, "CDC Health Information for International Travel, 2016 (Yellow Book)."

- Stop using insect repellent and/or sunscreen if a rash or other adverse symptoms develop. Wash skin with soap and water. Consult a healthcare provider or poison control center for further guidance. Be sure to inform the healthcare provider or poison control center about the insect repellent used (e.g., type, when and where applied). Take other actions, as described in this guidance, to avoid mosquito bites if insect repellent cannot be used.

Healthcare and laboratory workers

Employers and workers in healthcare settings and laboratories should follow good infection control and biosafety practices (including universal precautions) as appropriate, to prevent or minimize the risk of transmission of infectious agents (e.g., Zika virus). Always follow universal precautions for potential BBP exposures, as described in OSHA's BBP standard (29 CFR 1910.1030). In healthcare, standard precautions can be used to expand the universal precautions required by the BBP standard by adding several protections (including expanded PPE) not covered by the BBP standard. Standard precautions include, but are not limited to, hand hygiene and the use of PPE to avoid direct contact with blood and other potentially infectious materials, including laboratory specimens/samples. PPE may include gloves, gowns, masks and eye protection.

Hand hygiene consists of washing with soap and water or using alcohol-based hand rubs containing at least 60 percent alcohol.[3] Soap and water are best for hands that are visibly soiled. Perform hand hygiene before and after any contact with a patient, after any contact with potentially infectious material, and before putting on and upon removing PPE, including gloves.

Laboratories should ensure that their facilities and practices meet the appropriate Biosafety Level (BSL) for the type of work being conducted (including the specific biological agents – in this case, Zika virus) in the laboratory. CDC has specific Biosafety Guidance for the Transportation of Specimens and for Work with Zika virus in the Laboratory. The Biosafety in Microbiological and Biomedical Laboratories (BMBL), 5th Edition also provides detailed guidance on biosafety when working with arboviruses, including Zika, in Section VIII – F: Arboviruses and Related Zoonotic Viruses. Laboratories should handle Zika virus at BSL-2, including limiting access to laboratories and other work areas when work is occurring and conducting certain procedures in biosafety cabinets or other containment equipment. Some procedures may require BSL-3 precautions, including additional respiratory protection, based on the risk assessment of the proposed work.[4] The BMBL guidance also describes BSLs in Section IV - Laboratory Biosafety Level Criteria (PDF).

Employers must comply with applicable requirements in the BBP (29 CFR 1910.1030), PPE (29 CFR 1910.132), and Respiratory Protection (29 CFR 1910.134) standards, among other OSHA requirements.

Additionally, employers should ensure that workers:

- Follow workplace standard operating procedures (e.g., workplace exposure control plans) and use the engineering controls and work practices available in the workplace to prevent exposure to blood or other potentially infectious materials. See 29 CFR 1910.1030.
- Do NOT bend, recap, or remove contaminated needles or other contaminated sharps. Properly dispose of these items in closable, puncture-resistant, leakproof, and labeled or color-coded containers. See 29 CFR 1910.1030.
- Use sharps with engineered sharps injury protection (SESIP) to avoid sharps-related injuries.
- Report all needlesticks, lacerations, and other exposure incidents to supervisors as soon as possible.

Employers should consider enhanced precautions in situations where workers are at increased risk of exposure to Zika virus or other hazards. CDC recommends healthcare workers use standard precautions during patient care regardless of suspected or confirmed Zika infection status.[5] While there is no evidence of Zika transmission through aerosol exposure, minimizing the

3. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, "Show Me the Science – When to Use Hand Sanitizer."

4. U.S. Department of Health and Human Services, "Biosafety in Microbiological and Biomedical Laboratories (BMBL), 5th ed."

5. Healthcare Infection Control Practices Advisory Committee, "2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings," Centers for Disease Control and Prevention (CDC), U.S. Department of Health and Human Services (HHS).

aerosolization of blood or body fluids as much as possible during patient care or laboratory tasks may help prevent workers from being exposed to other pathogens. Additional protections, including engineering controls to ensure containment of pathogens or enhanced PPE to prevent or reduce exposure, may be necessary during any aerosol-generating procedures or other such tasks.

Mosquito control workers

When working outdoors, follow the same precautions recommended above for general outdoor workers for protection against mosquito bites. Workers performing tasks related to mosquito control may need additional protection, depending on their job tasks.

Workers entering or working around areas with dense mosquito populations, such as ponds and other locations with standing water, may need enhanced skin protection to prevent mosquito bites. Employers should assess such workers' risks of mosquito bites, and consider providing any additional protective clothing to fully cover workers' exposed skin.

Workers who mix, load, apply, or perform other tasks involving wide-area (or area) insecticides may need additional protection to prevent or reduce exposure to hazardous chemicals.

The EPA regulates pesticide safety use through the Agricultural Worker Protection Standard (WPS). Although the WPS is a regulation for agricultural pesticides aimed at reducing the risk of pesticide poisonings and injuries among agricultural workers and pesticide handlers, its requirements may provide a model for protecting workers using insecticides in mosquito control operations. The EPA WPS page provides information on pesticide safety training, notification of pesticide applications, use of PPE, restricted-entry intervals after pesticide application, decontamination supplies, and emergency medical assistance.

Workers conducting mosquito control operations with insecticides may require respirators, which must be used in accordance with the respirator selection, medical clearance, fit-testing, and other requirements of OSHA's Respiratory Protection standard (29 CFR 1910.134). Employers should monitor use of respirators by any worker who must drive vehicles (e.g., trucks used for insecticide application) to ensure that respirator use does not restrict the worker's ability to operate the vehicle safely. OSHA's Safety and Health Topics page on Respiratory Protection provides general information on respirator use and OSHA standards that may apply to the use of other chemicals.

Employers also must comply with any applicable requirements in OSHA's PPE standards (29 CFR 1910 Subpart I), among other OSHA requirements.

General Guidance for Employers of Workers with Suspected or Confirmed Zika

CDC advises individuals, including workers, infected with Zika virus to[6]:

- Get plenty of rest.
- Drink fluids to prevent dehydration.
- Take medicine such as acetaminophen to reduce fever and pain.
- Avoid taking aspirin, ibuprofen, naproxen, or other non-steroidal anti-inflammatory drugs because of rare cases of bleeding occurring with flaviviruses and these medications.
- Talk to a healthcare provider before taking any medications, including prescriptions, for other medical conditions.
- To help prevent others from getting sick, avoid mosquito bites during the first week of infection. Wearing clothing that covers skin and using insect repellents can help prevent mosquito bites.
- To help prevent transmission to partners via sexual contact, abstain from sexual activity or use condoms during sexual activity during and following infection. For specific recommendations to prevent sexual transmission, please visit the CDC Zika and Sexual Transmission website.

Employers should:

- Ensure that supervisors and all potentially exposed workers are aware of the symptoms of Zika.
- Train workers to seek medical evaluation if they develop symptoms of Zika.
- Assure that workers receive prompt and appropriate medical evaluation and follow-up after a suspected exposure to Zika virus. If the exposure falls under OSHA's BBP

6. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, "Zika Virus – Symptoms, Diagnosis, & Treatment."

standard (29 CFR 1910.1030), employers must comply with medical evaluation and follow-up requirements in the standard. See 29 CFR 1910.1030(f).
- Consider options for granting sick leave during the infectious period. CDC describes steps employers and employees can take to protect others (PDF) during the first week of Zika virus illness.

Paragraph 11(c) of the OSH Act, 29 USC 660(c), prohibits employers from retaliating against workers for raising concerns about safety and health conditions. OSHA encourages workers who suffer such discrimination to submit a complaint to OSHA. Workers have 30 days from an alleged reprisal to file their complaints.

Travel to Zika-affected Areas

When traveling to or through Zika-affected areas, follow the precautions described above for specific work activities. CDC guidance for travel to Zika-affected areas may also help employers and workers in travel-related operations, such as airlines, airline crew members, and cruise line workers take appropriate protective actions.

Employers should consider allowing flexibility in required travel for workers who are concerned about Zika virus exposure. Flexible travel and leave policies may help control the spread of Zika virus, including to workers who are concerned about reproductive effects potentially associated with Zika virus infection.

Consider delaying travel to Zika-affected areas, especially for workers who are or may become pregnant or whose sexual partners may become pregnant. CDC recommends that pregnant women in any trimester not travel to an area with active Zika virus transmission. CDC has published Zika Travel Information by region, which may assist workers and employers in making travel-related decisions or implementing precautions when traveling. Pregnant women, women who may become pregnant, and men with sexual partners who are or may become pregnant should consult with their healthcare providers about risks associated with Zika virus infection during pregnancy. More information can also be found on the CDC Zika and Pregnancy website.

Even if they do not feel sick, travelers returning to the United States from an area with Zika should take steps to prevent mosquito bites for three weeks so they do not pass Zika to mosquitoes that could spread the virus to other people. CDC provides information on mosquito bite prevention for travelers (PDF).

Additional Resources

- Zika Virus. Centers for Disease Control and Prevention (CDC), U.S. Department of Health and Human Services (HHS).
- Zika Travel Information. Centers for Disease Control and Prevention (CDC), U.S. Department of Health and Human Services (HHS).
- Mosquito-Borne Diseases. National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control and Prevention (CDC), U.S. Department of Health and Human Services.
- Zika Virus Fact Sheet. World Health Organization (WHO).
- Zika virus infection and Zika fever: Frequently asked questions. Pan American Health Organization (PAHO).
- Mosquito Bite Prevention for Travelers (PDF). Centers for Disease Control and Prevention (CDC), U.S. Department of Health and Human Services (HHS).
- Zika information repository. Center for Infectious Disease Research and Policy (CIDRAP), University of Minnesota.
- Rodents, Snakes and Insects QuickCard. Occupational Safety and Health Administration (OSHA), U.S. Department of Labor (DOL).
- 2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings (PDF). Healthcare Infection Control Practices Advisory Committee (HICPAC), Centers for Disease Control and Prevention (CDC), U.S. Department of Health and Human Services (HHS).
- Safety and Health Information Bulletin: Workplace Precautions Against West Nile Virus. Occupational Safety and Health Administration (OSHA), U.S. Department of Labor (DOL). Provides related guidance for workers and employers that is also generally applicable to Zika virus and other mosquito-borne diseases.

- West Nile Virus Fact Sheet (PDF*). Occupational Safety and Health Administration (OSHA), U.S. Department of Labor (DOL). Provides related guidance for workers and employers that is also generally applicable to Zika virus and other mosquito-borne diseases.
- West Nile Virus QuickCard. Occupational Safety and Health Administration (OSHA), U.S. Department of Labor (DOL). Provides related guidance for outdoor workers that is also generally applicable to Zika virus and other mosquito-borne diseases.
- Surveillance and Control of *Aedes aegypti* and *Aedes albopictus* in the United States. Centers for Disease Control and Prevention (CDC), U.S. Department of Health and Human Services (HHS).
- Bloodborne Pathogens and Needlestick Prevention Safety and Health Topics. Occupational Safety and Health Administration (OSHA), U.S. Department of Labor (DOL).
- West Nile Virus Prevention. National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control and Prevention (CDC), U.S. Department of Health and Human Services (HHS). Provides related guidance for workers and employers that is also generally applicable to Zika virus and other mosquito-borne diseases.
- Fast Facts: Protecting Yourself from Ticks and Mosquitoes (PDF). National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control and Prevention (CDC), U.S. Department of Health and Human Services (HHS).
- Heat Stress Topic Page. National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control and Prevention (CDC), U.S. Department of Health and Human Services (HHS).
- Fast Facts: Protecting Yourself from Heat Stress (PDF). National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control and Prevention (CDC), U.S. Department of Health and Human Services (HHS).
- Respirator Topic Page. National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control and Prevention (CDC), U.S. Department of Health and Human Services (HHS).
- Preventing Transmission of Zika Virus in Labor and Delivery Settings Through Implementation of Standard Precautions – United States, 2016. Centers for Disease Control and Prevention (CDC), U.S. Department of Health and Human Services (HHS).
- Questions and Answers for Healthcare Providers Caring for Pregnant Women and Women of Reproductive Age with Possible Zika Virus Exposure. Centers for Disease Control and Prevention (CDC), U.S. Department of Health and Human Services (HHS).

***Accessibility Assistance**: Contact OSHA's Directorate of Technical Support and Emergency Management at (202) 693-2300 for assistance accessing PDF materials.

U.S. Department of Labor

OSHA Occupational Safety and Health Administration

CDC Workplace Safety and Health

NIOSH National Institute for Occupational Safety and Health

CDC's Response to **Zika**

ZIKA SCREENING TOOL FOR PREGNANT WOMEN

APPENDIX C

(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 to Zika Virus Infection

Circle response:

Do you live in or do you frequently travel (daily or weekly) to an area with active Zika virus transmission?	**YES** | **NO**
Have you traveled to an area with Zika during pregnancy or just before you became pregnant?	**YES** | **NO**
Have you had sex (vaginal, anal, or oral) without a condom or shared sex toys with a partner(s) who lives in or has traveled to an area with Zika?	**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 fever, rash, joint pain, or conjunctivitis?	**YES** | **NO**

➡ If your pregnant patient answered **"YES"** to having any of these signs or symptoms, she might have symptomatic Zika virus infection.

➡ If your pregnant patient answered **"NO"** to having any signs or symptoms, she has been exposed and might have an asymptomatic Zika virus infection.

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.
2. Visit CDC's website to see areas with active Zika transmission: http://www.cdc.gov/zika/geo/index.html
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)

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

CS270355A October 4, 2016

Zika Virus Exposure
Patient Self-Assessment Form

Zika and Pregnancy
Californians, Let's #TalkZIKA

Zika is a virus that spreads to people in many parts of the world through mosquitoes or through sex with an infected partner. Most people with Zika don't get sick, so they may not know they have it. If a woman gets Zika and is pregnant or becomes pregnant, the virus can cause miscarriage, stillbirth or severe birth defects. **The following questions will help identify your risk of Zika virus exposure and determine if follow-up care is needed.** Please answer to the best of your ability.

1. Have you recently been to…? *(Select and/or circle all that apply)*

◯ **United States and Territories**

Puerto Rico | Brownsville, Texas | U.S. Virgin Islands

◯ **Mexico**

◯ **Central America**

◯ **South America**

◯ **Caribbean Islands**

Including: Aruba, The Bahamas, Barbados, British Virgin Islands, Cuba, Dominican Republic, Grenada Haiti, Jamaica, Saint Kitts/Lucia/Martin/Vincent, Trinidad and Tobago, Turks and Caicos, etc.

◯ **Oceana/Pacific Islands**

Fiji	Papua New Guinea	Solomon Islands
Marshall Islands	Samoa	Tonga

◯ **Africa**

Angola	Congo (Congo-Brazzaville)	Ghana	Senegal
Benin	Cote d'Ivoire	Guinea	Sierra Leone
Burkina-Faso	Democratic Republic of the Congo (Congo-Kinshasa)	Guinea-Bissau	South Sudan
Burundi	Equatorial Guinea	Kenya	Sudan
Cameroon	Gabon	Liberia	Tanzania
Cape Verde	Gambia	Mali	Togo
Central African Republic		Niger	Uganda
Chad		Nigeria	
		Rwanda	

◯ **Asia**

Bangladesh	Laos	Singapore
Burma (Myanmar)	Malaysia	Thailand
Cambodia	Maldives	Timor-Leste (East Timor)
India	Pakistan	Vietnam
Indonesia	Philippines	

◯ **Other:** _____

◯ **NONE OF THE ABOVE** *(Skip to Question 4)*

For a recent list of areas with Zika, visit: http://www.cdc.gov/zika/geo/active-countries.html.

2. If yes, please list the date you returned from your most recent trip: _____

If you have been to one of these areas, there is a chance you could be infected with Zika. If you are pregnant or have symptoms, you may need to be tested. Tell your doctor about your possible Zika virus exposure. For a complete doctor's visit checklist, visit: http://www.cdc.gov/zika/pdfs/docvisit-checklist-travelpreg.pdf.

Tell your doctor about your trip and if you were bitten by mosquitoes:

1. How long did you stay?
2. What did you do? Outdoor activities?
3. How often did you use insect repellent?

Good questions to ask your doctor are:

1. Should I be tested for Zika virus?
2. How can I prevent sexual transmission of Zika?
3. What should I do if I plan to go to any of these areas?

3. Did you have any of these symptoms while traveling or within 2 weeks after you returned?

◯ Fever
◯ Joint Pain
◯ Headache
◯ No symptoms
◯ Rash
◯ Pink/red eyes
◯ Muscle Pain

Zika Symptoms?
If you have any of these symptoms, ask your doctor about testing for Zika virus.

4. In the past 6 months, have you had unprotected sex with someone who lives in or has been to any of the countries listed in Question 1?

◯ Yes ◯ No

Did You Know?
Zika virus can be spread through sex. Ask your doctor about ways to prevent spreading Zika virus if you or your partner have been exposed.

5. Are you currently pregnant?

◯ Yes *(Skip Question 6)*
◯ No

Ask Your Doctor:
If you are pregnant and answered "Yes" to questions 1 or 4, you may have been exposed to Zika while pregnant or within the 8 weeks before conception. Ask your doctor about testing.

6. Would you like to become pregnant in the next 12 months?

◯ Yes ◯ No

Planning for Pregnancy:
Talk to your doctor about your risk of Zika and what you can do to prepare for pregnancy. This is a concept called "preconception health." Visit www.everywomancalifornia.org to learn more.

7. Do you use condoms (male or female) or other barriers like dental dams every time, from start to finish, during vaginal, anal or oral sex?

◯ Yes, all the time
◯ Sometimes
◯ No

Protect Yourself:
If you are pregnant and answered yes to questions 1 or 4, either don't have sex or practice safer sex by using condoms (male or female) and dental dams during all types of sex (vaginal, anal and oral).

8. Are you currently using any birth control methods?
(Select all that apply)

◯ Sterilization (you/partner)
◯ IUD
◯ Implant
◯ Injection
◯ Ring
◯ Patch
◯ Pill
◯ Sponge
◯ Condoms (male or female)
◯ Cervical Cap
◯ Natural/Fertility Awareness
◯ None

Avoiding Pregnancy:
Ask your doctor about birth control methods that might be right for you. Visit www.bedsider.org to learn about available methods.

Please return this form to your healthcare provider. If you have questions about Zika virus, please ask during your visit. Learn about Zika at www.cdph.ca.gov/Zika.

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Zika Virus Infection in Pregnant Women in Rio de Janeiro

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ABSTRACT

BACKGROUND

Zika virus (ZIKV) has been linked to central nervous system malformations in fetuses. To characterize the spectrum of ZIKV disease in pregnant women and infants, we followed patients in Rio de Janeiro to describe clinical manifestations in mothers and repercussions of acute ZIKV infection in infants.

METHODS

We enrolled pregnant women in whom a rash had developed within the previous 5 days and tested blood and urine specimens for ZIKV by reverse-transcriptase–polymerase-chain-reaction assays. We followed women prospectively to obtain data on pregnancy and infant outcomes.

RESULTS

A total of 345 women were enrolled from September 2015 through May 2016; of these, 182 women (53%) tested positive for ZIKV in blood, urine, or both. The timing of acute ZIKV infection ranged from 6 to 39 weeks of gestation. Predominant maternal clinical features included a pruritic descending macular or maculopapular rash, arthralgias, conjunctival injection, and headache; 27% had fever (short-term and low-grade). By July 2016, a total of 134 ZIKV-affected pregnancies and 73 ZIKV-unaffected pregnancies had reached completion, with outcomes known for 125 ZIKV-affected and 61 ZIKV-unaffected pregnancies. Infection with chikungunya virus was identified in 42% of women without ZIKV infection versus 3% of women with ZIKV infection ($P<0.001$). Rates of fetal death were 7% in both groups; overall adverse outcomes were 46% among offspring of ZIKV-positive women versus 11.5% among offspring of ZIKV-negative women ($P<0.001$). Among 117 live infants born to 116 ZIKV-positive women, 42% were found to have grossly abnormal clinical or brain imaging findings or both, including 4 infants with microcephaly. Adverse outcomes were noted regardless of the trimester during which the women were infected with ZIKV (55% of pregnancies had adverse outcomes after maternal infection in the first trimester, 52% after infection in the second trimester, and 29% after infection in the third trimester).

CONCLUSIONS

Despite mild clinical symptoms in the mother, ZIKV infection during pregnancy is deleterious to the fetus and is associated with fetal death, fetal growth restriction, and a spectrum of central nervous system abnormalities. (Funded by Ministério da Saúde do Brasil and others.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Brasil at Laboratorio de Doenças Febris Agudas, INI, Fiocruz, 4365 Av Brasil, Rio de Janeiro-RJ 21040-900, or at patricia.brasil33@gmail.com, or to Dr. Nielsen-Saines at the Division of Pediatric Infectious Diseases, David Geffen School of Medicine at UCLA, MDCC 22-442, 10833 LeConte Ave., Los Angeles, CA 90095, or at knielsen@mednet.ucla.edu.

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A Quick Take is available at NEJM.org

We have been conducting active surveillance for dengue infection in the general population of Rio de Janeiro since 2007. In 2012, we established a prospective cohort for dengue surveillance in mother–infant pairs within the Manguinhos Rio de Janeiro area. In 2015, we noted an increase in cases of a dengue-like illness that was characterized by a descending rash, generally without fever; this increase coincided with a surge in the number of cases of illness characterized by a pruriginous rash in northeastern Brazil.[1] In early 2015, most cases were originally reported to surveillance systems as dengue; however, Zika virus (ZIKV) was eventually identified.[2-8] To identify ZIKV cases in our population, we modified our pregnancy cohort study and enrolled women who presented with a rash at any week of gestation. This report is a follow-up to a previously published preliminary report, available with the full text of this article at NEJM.org.

Methods

Study Population

In this cohort study, pregnant women at any week of gestation who presented to the acute febrile illness clinic at the Oswaldo Cruz Foundation with a rash that had developed within the previous 5 days were offered enrollment and were included in the study after they had provided written informed consent. After the women were enrolled, detailed demographic, medical, and prenatal history information, as well as clinical findings, were entered into case-report forms. Laboratory data on rubella, cytomegalovirus, and Venereal Disease Research Laboratory (VDRL) serologic testing were abstracted from prenatal medical records and entered in case-report forms. Serum and urine specimens were obtained at study entry. Weekly follow-up was conducted by telephone, and a second visit was scheduled within 30 days after enrollment for clinical and laboratory follow-up. Women were referred for fetal ultrasonography before 20 weeks of gestation, between 20 and 30 weeks of gestation, and after 30 weeks of gestation. No women had had a diagnosis of fetal malformations in the current pregnancy before enrollment. The study population was generally healthy; women reported no coexisting conditions or medication use. Infants born to ZIKV-positive mothers are being followed prospectively.

Study Oversight

The study protocol was approved by the institutional review boards at Fundação Oswaldo Cruz (Fiocruz) and the University of California, Los Angeles. The authors vouch for the accuracy and completeness of the data and the analyses and for the fidelity of the study to the protocol.

Laboratory Testing

Real-time reverse-transcriptase–polymerase-chain-reaction (RT-PCR) assays for ZIKV were performed with the QuantiTect Probe RT-PCR kit (Qiagen), as described previously,[9] with the same primers and cycle times, at the Fiocruz Flavivirus Laboratory; assays were performed on blood specimens, urine specimens, or both that were obtained at the entry visit. The Fiocruz Flavivirus Laboratory is a reference laboratory for flavivirus infections in the region. Serologic testing for IgG antibodies to dengue (Abcam) and IgM antibodies to chikungunya (Euroimmun) were performed on serum specimens obtained at the entry visit. Patient specimens were also tested by RT-PCR for dengue[10] and chikungunya.[9] Patients were tested for parvovirus B19 and cytomegalovirus by PCR (TaqMan RT PCR, Applied Biosystems) and by serologic testing during regular prenatal care. PCR assays for human immunodeficiency virus (HIV) DNA (Abbott RT HIV Viral Load) were performed on all patient specimens. Screening tests for syphilis were performed during prenatal care with the use of VDRL assays, with treponemal assays (Alere Determine Syphilis) used as confirmatory tests.

Fetal Ultrasonography

All abdominal scanning was performed with a 4-to-8-mHz probe (Voluson 730 Expert/Voluson E6, GE) by perinatologists who were certified by the Brazilian College of Radiology and the Brazilian Federation of Societies of Gynecology and Obstetrics (Febrasgo). The variables that were measured are listed in the Supplementary Appendix, available at NEJM.org. For Doppler studies, the pulsatility index of the umbilical artery and of the middle cerebral artery were used.[11] Abnormalities such as cerebral calcifications and microcephaly were noted. Measured fetal ultrasono-

graphic variables were plotted by gestational age according to the nomograms published on www.perinatology.com. Fetal growth restriction was defined as fetal weight estimated according to the Hadlock formula that was below the 10th percentile.[12] Microcephaly in fetal imaging was defined as fetal head measurements (e.g., head circumference) that were two standard deviations below the mean expected at a particular gestational age or below the 3rd percentile.[13]

INFANT CLINICAL ASSESSMENTS

Anthropometric measures at birth (weight, length, and head circumference) were obtained in all live-born infants. History taking and physical examinations were performed for all infants by pediatric specialists. ZIKV-exposed infants were evaluated by a multidisciplinary team that included neonatologists, neurologists, infectious disease specialists, geneticists, ophthalmologists, and physical therapists. All abnormal diagnoses were reviewed by a panel of specialists for confirmation. Microcephaly was defined as a head-circumference z score of less than −2 (moderate) or less than −3 (severe). Small-for-gestational-age infants were defined as infants with body-weight z scores of less than −1.28 at birth.[14]

INFANT IMAGING STUDIES

Brain imaging studies were offered for infants born to mothers who had positive PCR results for ZIKV. Transfontanel ultrasonography, computed tomography (CT) of the head with and without contrast, and magnetic resonance imaging (MRI; AERA Siemens, 1.5 tesla) with or without contrast were performed according to the standard of care. If abnormalities were suspected on transfontanel ultrasonography, patients were referred for CT or MRI brain imaging. All infant assessments were conducted with knowledge of ZIKV infection status.

STATISTICAL ANALYSIS

We compared the demographic and clinical variables of pregnant women who were positive for ZIKV on PCR with those who were negative for ZIKV on PCR, using Fisher's exact test (two-sided); P values of 0.05 or less were considered to indicate statistical significance. We performed similar analyses comparing pregnancy and infant outcomes in ZIKV-infected and ZIKV-uninfected mother–infant pairs. For comparison of medians, an independent-samples median test was used. Comparisons of negative pregnancy outcomes according to maternal trimester of infection between ZIKV-infected and ZIKV-uninfected mother–infant pairs were compared with the use of McNemar's test.

RESULTS

CHARACTERISTICS OF THE PARTICIPANTS

During the period from September 2015 through May 2016, we enrolled 345 pregnant women and tested blood specimens, urine specimens, or both for ZIKV by qualitative RT-PCR. Of these 345 women, 182 (53%) had positive results for ZIKV on PCR in blood, urine, or both. The current report focuses on 134 ZIKV-positive women and 73 ZIKV-negative women who were expected to deliver by July 31, 2016 (Fig. 1). Among the 134 ZIKV-positive women, quantitative ZIKV PCR results were available for 130 (4 PCR assays were performed at outside facilities). Among women with quantitative PCR results, 85 had positive PCR results in serum specimens, 76 had positive PCR results in urine, and 31 had positive PCR results in both specimens; 45 women had positive results in urine only and 54 had positive results in blood specimens only (median number of PCR cycles for serum specimens, 32.0; interquartile range, 30.0 to 34.0; range, 24.2 to 37.0; and median number of PCR cycles for urine specimens, 30.0; interquartile range, 27.0 to 33.0; range, 22.0 to 37.0). Demographic and clinical characteristics are described in Table 1. Among ZIKV-positive women, 38% reported similar illnesses in other family members, and only 14% reported that their partner had been ill. ZIKV infection was present in women of all socioeconomic strata. More than half the women presented with acute infection in the second trimester of pregnancy. ZIKV-negative women were more likely to have used insect repellent than ZIKV-positive women (83% vs. 60%, P=0.006), but otherwise there were no significant differences in demographic characteristics or medical history between the two groups. ZIKV-positive women resided across multiple neighborhoods and municipalities within the larger metropolitan Rio de Janeiro area (Fig. S1 in the Supplementary Appendix).

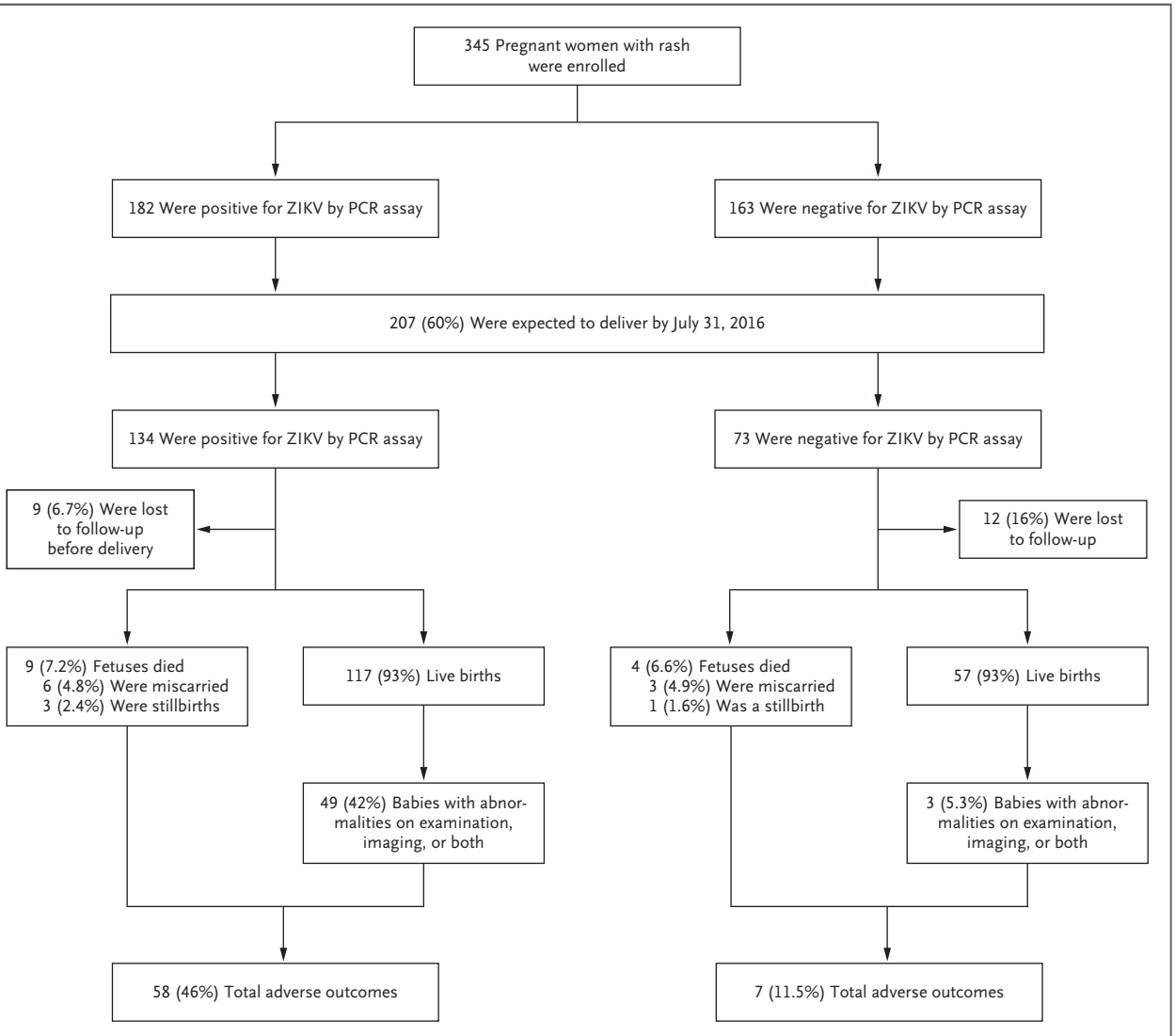

Figure 1. Prospective Maternal Cohort and Pregnancy Outcomes.

Among 134 ZIKV-positive women, 9 were lost to follow-up before delivery and 125 had outcomes that could be evaluated; 116 of these pregnancies resulted in 117 live-born babies (there was one set of twins); 9 pregnancies ended in fetal death. One ZIKV-positive mother who had a miscarriage was coinfected with chikungunya virus; two ZIKV-negative mothers whose pregnancies ended in fetal death were infected with chikungunya virus. Three infants of ZIKV-negative mothers were small for gestational age at birth (listed as "abnormalities on examination"); one was born to a mother with confirmed chikungunya virus infection.

CLINICAL PRESENTATION OF THE MOTHERS

All pregnant women had rash as part of their clinical presentation, since rash was an inclusion criterion. A descending macular or maculopapular rash was the most common type of exanthem noted in ZIKV-positive women (Fig. S5 in the Supplementary Appendix). The maculopapular rash was seen far more frequently in ZIKV-positive women than in ZIKV-negative women (P=0.02). The other prevalent finding was pruritus, which was seen in 90% of ZIKV-positive women in our study. The next most common finding was arthralgia, which was reported in 62% of ZIKV-positive women and in 70% of ZIKV-negative women (P=0.29). Conjunctival injection was present in 58% of ZIKV-positive women and in a smaller percentage (40%) of ZIKV-negative women (P=0.03). Fatigue or malaise was described in 52% of ZIKV-positive women versus 75% of ZIKV-negative women (P=0.002), and myalgia was

described in 41% versus 62% (P=0.005); the higher rates among ZIKV-negative women were probably due to the diagnosis of underlying chikungunya virus in some ZIKV-negative women. Lymphadenopathy (isolated or generalized) was present in both groups (in 38% of ZIKV-positive women and 27% of ZIKV-negative women, P=0.12). Fever was not a highly prominent finding, occurring in less than a third of the women with acute ZIKV infection but in 58% of ZIKV-negative women (P<0.001). When fever was present, it was generally short-term and low grade (37.5 to 38.0°C). Nausea or vomiting was reported in 31% of ZIKV-positive women and was more common (occurring in 44%) among ZIKV-negative women (P=0.07).

OUTCOMES OF PREGNANCIES

Among 134 women who had positive results for ZIKV on PCR testing, information on confirmed outcomes of pregnancy was available for 125, with 117 live births in 116 pregnancies (one set of twins) between January 1 and July 31, 2016. There were 9 cases of fetal death (Fig. 1 and Table 2, and Table S2 in the Supplementary Appendix): 5 miscarriages in the first trimester of pregnancy, 2 miscarriages in the second trimester, and 2 stillbirths in the third trimester. Among 73 ZIKV-negative women, 61 had known outcomes, including 4 cases of fetal death and 57 live births. In the ZIKV-positive group, 93% of the women remained in the study, whereas retention in the ZIKV-negative group was 84% (P=0.03).

Three of seven negative pregnancy outcomes in the ZIKV-negative group — two of the four fetal losses and one small-for-gestational-age infant — occurred in women with chikungunya virus. One of the first-trimester miscarriages in the ZIKV-positive cohort occurred in a woman who was coinfected with ZIKV and chikungunya virus. Three ZIKV-infected patients (2.8%) were coinfected with chikungunya virus; however, chikungunya infection was more prevalent in the ZIKV-negative group (42%, P<0.001) (Table 2). No patients in either group were found to have active dengue infection on PCR; however, prior dengue infection was very common, with 88% in the ZIKV-positive group and 86% in the ZIKV-negative group having IgG antibodies to dengue. One woman in each group had a positive treponemal syphilis test; those pregnancies did not have adverse outcomes. No women had evidence of active cytomegalovirus infection by either PCR or IgM detection. Among ZIKV-negative women, 29 other infections were identified, including 23 cases of chikungunya, 4 cases of parvovirus B19, and 1 case of syphilis. None of the women were found to have HIV by RT-PCR testing.

Among 125 pregnancies in ZIKV-positive women, 58 adverse pregnancy outcomes were noted (46.4%); in contrast, 7 of the 61 pregnancies (11.5%) in the ZIKV-negative cohort resulted in adverse outcomes (P<0.001). Despite the high rate of adverse outcomes in our control group of pregnant women with other infectious illnesses, the findings in the ZIKV-positive group were far more striking. Adverse pregnancy outcomes by the timing of maternal ZIKV infection are shown in Figure 2. The timing of maternal ZIKV infection ranged from 6 to 39 weeks of gestation. Adverse outcomes after ZIKV infection occurred regardless of the timing of maternal infection; adverse outcomes occurred in 55% of pregnancies in which the mother was infected in the first trimester (11 of 20 ZIKV-infected pregnancies), in 52% of those in which the mother was infected in the second trimester (37 of 71 ZIKV-infected pregnancies), and in 29% of those in which the mother was infected in the last trimester of pregnancy (10 of 34 ZIKV-infected pregnancies). Among ZIKV-infected pregnancies, there were 5 miscarriages (25% of the 20 pregnancies with first-trimester infection), 2 fetal losses (3% of the 71 pregnancies with second-trimester infection); and 2 stillbirths (6% of the 34 pregnancies with third-trimester infection). Among 117 live births in the ZIKV-positive cohort, 49 infants (42%) were found to have abnormalities on clinical examination, imaging, or both; in contrast, among 57 live births in the ZIKV-negative cohort, 3 infants (5%) had such abnormalities (P<0.001).

Three infants with abnormalities who were born to ZIKV-negative women were small for gestational age; one was born to a woman who was found to have chikungunya virus infection. Because of the large number of chikungunya infections in the control group, adverse pregnancy outcomes were also frequent in this group. There was no significant difference in the rate of fetal loss between ZIKV-positive mothers and ZIKV-negative mothers (7.2% and 6.6%, respectively; P=1.0). Obstetrical complications were very high in both groups: 39% in ZIKV-positive women

Table 1. Baseline Demographic and Clinical Characteristics of Women in the Pregnancy Cohort.*

Variable	ZIKV-Positive Women (N=134)	ZIKV-Negative Women (N=73)	P Value†
Demographics			
Age — yr			0.57‡
Median (IQR)	31 (26–34)	29 (25.5–34)	
Range	16–46	17–41	
Other family members ill — no./total no. (%)	44/115 (38.3)	15/60 (25.0)	0.09
Partner ill — no./total no. (%)	14/103 (13.6)	4/53 (7.5)	0.30
Use of repellent — no./total no. (%)	48/80 (60.0)	52/63 (82.5)	0.006
History of dengue — no./total no. (%)	33/127 (26.0)	20/69 (29.0)	0.74
Socioeconomic status — no./total no. (%)§			
Income ≤2× minimum wage	48/108 (44.4)	28/63 (44.4)	1.0
Income >2 to ≤5× minimum wage	38/108 (35.2)	21/63 (33.3)	0.87
Income >5× minimum wage	22/108 (20.4)	14/63 (22.2)	0.85
Week of gestation at time of infection			
Median (IQR)	24.5 (18–31)	27 (23–31)	0.23‡
Range	5–39	7–36	
Distribution — no. (%)			
0 to ≤13 wk	26 (19.4)	4 (5.5)	0.15
14 to ≤28 wk	72 (53.7)	41 (56.2)	1.0
≥29 wk	36 (26.9)	28 (38.4)	0.45
Symptoms — no./total no. (%)			
Rash¶			
Any	134/134 (100)	73/73 (100)	0.24‡
Median duration (IQR)	5 (4–7)	4 (3–6.5)	
Range	1–16	1–12	
Macular	57/134 (42.5)	37/73 (50.7)	0.31
Maculopapular	57/134 (42.5)	19/73 (26.0)	0.02
Other	20/134 (14.9)	17/73 (23.3)	0.18
Pruritus	116/129 (89.9)	64/73 (87.7)	0.64
Arthralgia or arthritis	81/130 (62.3)	51/73 (69.9)	0.29
Conjunctival injection	73/127 (57.5)	29/72 (40.3)	0.03
Headache	69/127 (54.3)	47/73 (64.4)	0.18
Fatigue or malaise	66/127 (52.0)	55/73 (75.3)	0.002
Retro-orbital pain	53/131 (40.5)	29/73 (39.7)	1.0
Myalgia	53/130 (40.8)	43/69 (62.3)	0.005
Lymphadenopathy	48/125 (38.4)	19/70 (27.1)	0.12
Localized	22/39 (56.4)	5/10 (50.0)	0.74
Generalized	17/39 (43.6)	5/10 (50.0)	0.74
Paresthesia	36/100 (36.0)	26/67 (38.8)	0.75
Edema	54/99 (54.5)	37/73 (50.7)	0.64
Fever, body temperature ≥37.5°C	34/124 (27.4)	42/72 (58.3)	<0.001
Duration <24 hr	10/20 (50.0)	12/23 (52.2)	1.0
Duration ≥24 to <72 hr	10/20 (50.0)	11/23(47.8)	1.0

Table 1. (Continued.)

Variable	ZIKV-Positive Women (N=134)	ZIKV-Negative Women (N=73)	P Value†
Fever, body temperature ≥38°C	3/12 (25.0)	26/38 (68.4)	0.02
Photophobia	44/131 (33.6)	31/73 (42.5)	0.29
Anorexia	37/131 (28.2)	32/73 (43.8)	0.03
Diarrhea	37/130 (28.5)	23/73 (31.5)	0.75
Nausea or vomiting	41/131 (31.3)	32/72 (44.4)	0.07
Bleeding, petechia, or enanthema	12/131 (9.2)	5/73 (6.8)	0.79
Abdominal pain	25/131 (19.1)	21/72 (29.2)	0.12
Dizziness or lightheadedness	28/131 (21.4)	13/67 (19.4)	0.85
Respiratory symptoms: coryza, cough, or sore throat	21/123 (17.1)	26/69 (37.7)	0.003
Dysuria	3/119 (2.5)	8/70 (11.4)	0.02

* Differences in denominators across variables are due to missing data. Details on duration of fever or whether lymphadenopathy was generalized or localized were not available for all patients with those findings. IQR denotes interquartile range, and ZIKV Zika virus.
† P values were calculated with Fisher's exact test (two-sided), except as otherwise noted.
‡ The P value was calculated with the use of an independent-samples median test.
§ The Brazilian minimum monthly wage is R$880 Brazilian reals (approximately $260 U.S.).
¶ Rash was an inclusion criterion.

and 35% in ZIKV-negative women (P=0.62). ZIKV-positive women, however, were nearly 10 times as likely as ZIKV-negative women to have emergency cesarean sections performed owing to fetal distress (23.5% vs. 2.5%, P=0.003) (Table 2). Infants born to ZIKV-positive mothers were also nearly 4 times as likely to need critical care assistance immediately after birth (a finding that is reflective of fetal distress) as infants who had not been exposed to ZIKV (21% vs. 6%, P=0.01).

A total of 153 ultrasound studies were performed in 59 women who were found to be positive for ZIKV during pregnancy; the remaining 75 ZIKV-positive women declined imaging studies either because the obstetrical facility was too far away or because of fear of possible fetal abnormalities related to ZIKV infection. Detailed ultrasonographic findings are described in Table S1 in the Supplementary Appendix. ZIKV-negative women underwent fetal ultrasonography as part of regular prenatal care. All the women in the cohort received prenatal care. Nine women with ZIKV infection (6.7%) were lost to follow-up (i.e., did not seek prenatal care at our obstetrical facility and were unable to be reached for further evaluation despite multiple attempts; pregnancy outcomes are unknown). Included among these 9 women was 1 woman whose fetus had severe abnormalities on fetal ultrasonography. In the ZIKV-negative cohort, 12 women (16%) were lost to follow-up, mainly because of a change in their contact information. ZIKV-negative women did not deliver at our obstetrical facility. In addition, women were less likely to continue follow-up in the study if ZIKV infection was ruled out.

INFANT OUTCOMES

Infants who were small for gestational age, as a potential consequence of fetal growth restriction or poor placental perfusion, constituted 9% of ZIKV-exposed babies and 5.3% of babies in the control group (P=0.06). Four infants in the ZIKV-positive group (3.4%) were noted to have microcephaly at birth; two were small-for-gestational-age infants with proportionate microcephaly (i.e., the head size is small but is proportional to the weight and length of the infant), and two had disproportionate microcephaly (i.e., the head size is small relative to the weight and length of the infant). None of the infants in the control group had microcephaly. Fetal growth variables for fetuses of ZIKV-positive women who had ultrasonography performed during pregnancy are shown in Figure 3, and anthropometric measurements, including birth weight and head circumference, of live-born infants in both groups are shown in Figure 4 and Table 3.

Table 2. Pregnancy Outcomes According to ZIKV Exposure.

Variable	ZIKV-Positive Women (N=134)	ZIKV-Negative Women (N=73)	P Value
	no. of women/total no. (%)		
Lost to follow-up before birth of infant	9/134 (6.7)	12/73 (16.4)	0.003
Known pregnancy outcomes	125/134 (93.3)	61/73 (83.6)	0.03
Live births, including one set of twins	116/125 (92.8)	57/61 (93.4)	1.00
Adverse pregnancy outcomes*	58/125 (46.4)	7/ 61 (11.5)	<0.001
Fetal loss	9/125 (7.2)	4/61 (6.6)	1.00
During first trimester	5/125 (4.0)	3/61 (4.9)	0.72
Rate per total no. of first-trimester maternal infections	5/20 (25)	3/4 (75)	0.72
During second trimester	2/125 (1.6)	0/61	1.00
Rate per total no. of second-trimester maternal infections	2/71 (2.8)	0/35	1.00
During third trimester	2/125 (1.6)	1/61 (1.6)	1.00
Rate per total no. of third-trimester maternal infections	2/34 (5.9)	1/22 (4.5)	1.00
Adverse pregnancy outcomes including fetal loss			
First trimester	11/20 (55.0)	3/4 (75.0)	<0.001
Second trimester	37/72 (51.4)†	2/35 (5.7)	<0.001
Third trimester	10/34 (29.4)	2/22 (9.1)	<0.001
Obstetrical complications‡	42/107 (39.3)	20/57 (35.1)	0.62
Vaginal deliveries	20/108 (18.5)	13/57 (22.8)	0.54
Cesarean section deliveries	89/108 (82.4)	44/57 (77.2)	0.54
Emergency cesarean section deliveries§	19/81 (23.5)	1/40 (2.5)	0.003
Positive dengue results			
IgG testing	107/121 (88.4)	60/70 (85.7)	0.13
PCR assay	0/134	0/73	
Positive chikungunya IgM or PCR results	3/106 (2.8)	25/60 (41.7)	<0.001

* The first trimester was 0 to 13 weeks of gestation, the second trimester 14 to 28 weeks of gestation, and the third trimester 29 weeks or more of gestation.
† Included is one set of twins (71 pregnancy outcomes for 72 infants).
‡ Obstetrical complications included arterial hypertension, eclampsia or preeclampsia, gestational diabetes, acute fetal distress, umbilical prolapse, and abruptio placentae.
§ Information regarding elective versus emergency cesarean sections was not available for 8 of the 89 cesarean deliveries.

A total of 49 of the 117 live-born infants (42%) who had been exposed to ZIKV in utero had abnormal findings in the first month of life (Table S2 in the Supplementary Appendix). Almost all the abnormalities affected the central nervous system (CNS). Microcephaly was observed in infants whose mothers were infected in weeks 8, 12, 30, and 38 of gestation. Disproportionate microcephaly was seen only in infants infected in the first trimester of pregnancy; 2 infants infected in later trimesters had proportionate microcephaly and were small for gestational age. One of the infants with disproportionate microcephaly was also small for gestational age. Cerebral calcifications, cerebral atrophy, ventricular enlargement, and hypoplasia of cerebral structures were seen in multiple infants, with cerebral calcifications seen in infants infected as late as 34 weeks of gestation. Parenchymal brain hemorrhages were seen in

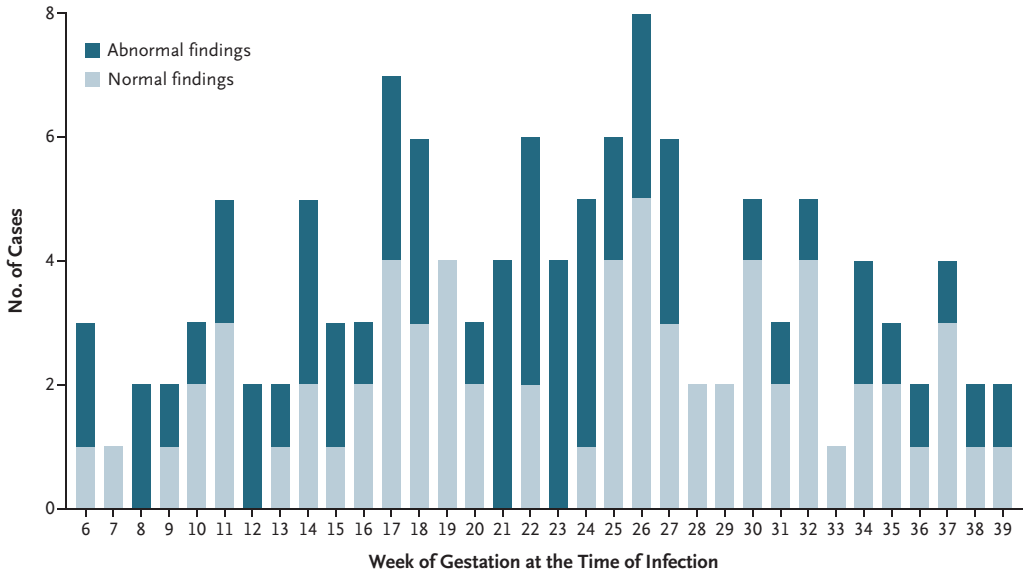

Figure 2. Pregnancy and Infant Outcomes According to the Week of Gestation at the Time of ZIKV Infection.
Adverse outcomes included 9 cases of fetal death in 125 pregnancies (7.2%) and 49 abnormal clinical findings, imaging findings, or both during the newborn period in 117 infants (42%) born from 116 pregnancies. Adverse outcomes occurred in women who were infected during the period from 6 to 39 weeks of gestation. Abnormalities are detailed in Table S2 in the Supplementary Appendix.

some infants, including one whose mother was infected shortly before delivery at 39 weeks of gestation. A total of 31 of the 49 infants (63%) had grossly abnormal results on neurologic examinations; hypertonicity, clonus, hyperreflexia, abnormal movements, spasticity, contractures, and seizures were identified. Abnormal funduscopic examinations and abnormal hearing assessments were also noted.

Other features that were identified included persistence of the cortical thumb sign, with maintained clenched fists beyond 3 months of age, which reflects CNS disease; foveas in the knees or elbows due to limb contractures in utero; and redundant scalp skin in infants with normal head circumference. MRIs have not been performed in all infants to date. Conversely, a number of infants with normal clinical assessments in early infancy had abnormal nonspecific MRI findings; a common description was "excessive hypersignaling in T_2 in the white matter, diffuse in the peritrigonal posterior areas and less evident in the frontal parietal white matter with hyposignaling in the diffusion sequence." These findings are abnormal and may reflect cortical tract dysfunction; nevertheless, close follow-up will be needed to ascertain the degree of CNS involvement.

Two infants were born large for gestational age owing to maternal gestational diabetes; one of these infants, born to a mother who had been infected at 15 weeks of pregnancy, was found to have congenital heart disease, which probably was associated with maternal gestational diabetes, although we cannot exclude the possibility of a potential association with ZIKV infection. Follow-up of ZIKV-exposed infants is ongoing.

DISCUSSION

ZIKV is a flavivirus that was recently introduced into Brazil. Its rapid expansion into a population that is probably fully susceptible is due to the effectiveness of its vector, the *Aedes aegypti* mosquito. Diagnosis of ZIKV infection in Brazil has been complicated by the cross-reactivity among flavivirus antibodies and by the fact that dengue has been endemic in Brazil for more than 30 years. Serosurveillance studies have found evidence of dengue antibodies in more than 90% of the population of Recife.[15] In our cohort, dengue IgG antibodies were present in 88% of the

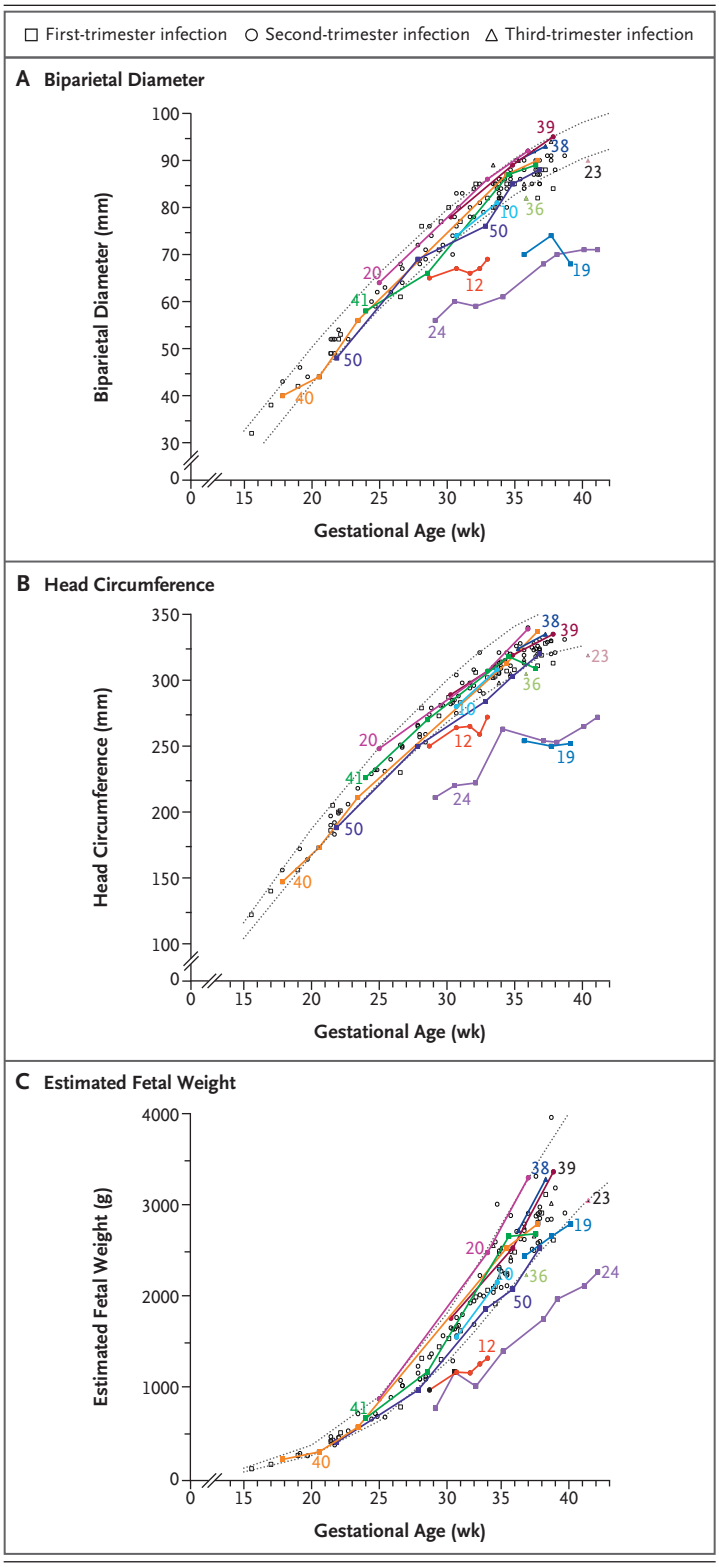

Figure 3. Fetal Biometric Variables as Measured on Ultrasonography.

Fetal measurements of biparietal diameter (Panel A), head circumference (Panel B), and estimated fetal weight (Panel C), plotted according to gestational age, are shown for each fetus of ZIKV-positive women who had ultrasonography performed during pregnancy. Dotted lines show the 10th and 90th percentiles for gestational age, based on established nomograms from www.perinatology.com. Fetal weight curves are based on the Hadlock formula, in which a measurement of less than the 10th percentile is considered to indicate fetal growth restriction. Microcephaly was defined as a head circumference of more than 2 standard deviations below the mean expected for gestational age. Symbols denote the trimester of PCR-documented infection (first trimester, <14 weeks; second trimester, 14 to 28 weeks; third trimester, ≥29 weeks). Repeat measurements for the same fetus are connected with a solid line to show growth trajectory. Results for fetuses with abnormal findings are denoted in color and labeled with maternal patient number. Not all measurements were obtained for every fetus at each ultrasound examination.

women, but no patients were found to have acute dengue infection. The diagnosis of ZIKV infection in Brazil relies on identification of the virus through RT-PCR during the acute period of infection. The virus is detectable in blood during the period of acute viremia and initial symptoms and subsequently is shed in the urine, generally for 3 to 14 days.[16] Because RT-PCR assays for ZIKV are generally not available, most cases of ZIKV infection in Brazil are diagnosed clinically, without laboratory confirmation. In our study, 134 women who were positive for ZIKV had acute infection with virus that was detected in blood, urine, or both.

Nevertheless, the starting point in our cohort study was an illness with rash in a pregnant woman who presented to our clinic. As more women presented with a similar illness, we dichotomized the illnesses into two groups on the basis of the results of PCR testing for Zika virus infection. However, a number of clinical categories relating to the illnesses clearly indicate that the illnesses in the Zika-negative women differed from those in the Zika-positive women. Zika-negative women were more likely to have nausea, vomiting or anorexia, fatigue or malaise, myalgia, respiratory symptoms, and fever than were Zika-

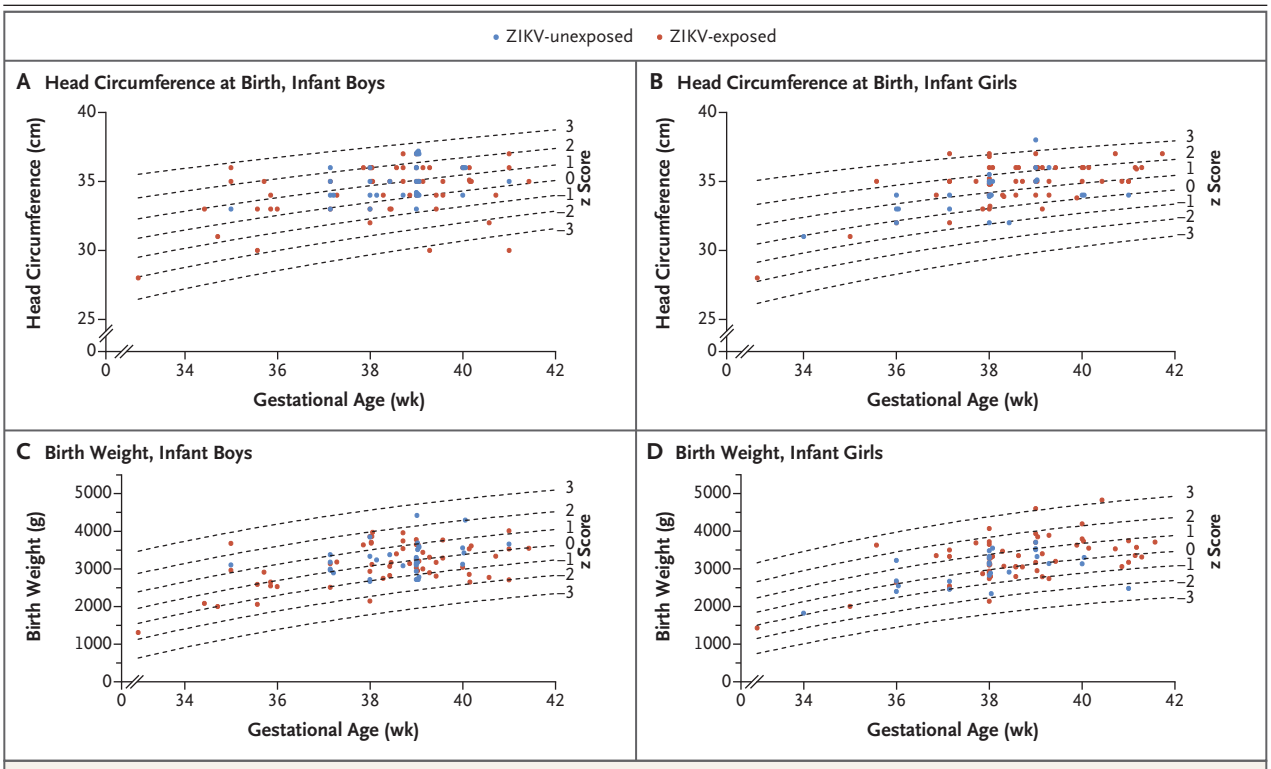

Figure 4. Infant Anthropometric Measures at Birth.

Shown are measurements of head circumference at birth in infant boys (Panel A) and girls (Panel B) and estimated birth weight in infant boys (Panel C) and girls (Panel D), according to gestational age at birth. A total of 117 live infants were born to women in our cohort who had positive results for ZIKV on polymerase-chain-reaction (PCR) assays, and 57 were born to women who had negative PCR results for ZIKV. Small for gestational age was defined as a z score for birth weight of less than –1.28. Microcephaly was defined as a z score of less than –2 (moderate) and less than –3 (severe).

positive subjects. Also the exanthems generally differed between the two groups. As compared with women who tested negative for acute ZIKV infection, women who tested positive for the virus had distinctive clinical features that included conjunctival injection and a maculopapular pruritic rash. The presence of these clinical features should raise suspicion for ZIKV infection. Low-grade fever was observed in 27% of the women; therefore a case definition that is based on the presence of fever would miss more than 70% of cases.[17]

The potential cause of illness in the ZIKV-uninfected women is known in some of the cases. Rio de Janeiro saw a rise in the number of chikungunya virus cases as of April–May 2016, coinciding with a decline in ZIKV cases. No patients were identified with ZIKV in our cohort after May 2016. Chikungunya virus was responsible for 42% of the infections in our control group and coinfected three ZIKV-positive women. Additional infections identified were parvovirus B19 in four ZIKV-negative women and two cases of syphilis, but no adverse pregnancy or infant outcomes were noted in these six patients.

Whether sexual transmission of ZIKV played a role in transmission to pregnant women in our cohort is difficult to assess, since couples usually cohabitate and would presumably have the same type of vector exposure. ZIKV-positive women more frequently had a history of affected family members than ZIKV-negative women.

Links between the current ZIKV epidemic in Brazil and the rise in the number of observed cases of neonatal microcephaly have generated considerable debate about whether the observed

Table 3. Infant Outcomes According to ZIKV Exposure.

Variable	ZIKV-Exposed Live-Born Infants (N = 117)*	ZIKV-Unexposed Live-Born Infants (N = 57)	P Value
Male sex — no. (%)	59 (50.4)	32 (56.1)	0.52
Birth weight — g			0.79
Median (IQR)	3192.5 (2872.5– 3673.5)	3165.0 (2890.5– 3452.5)	
Range	1310–4825	1825–4424	
Birth length — cm			0.01
Median (IQR)	49 (47–50)	48 (47–49)	
Range	35–57	36–52	
Head circumference — cm			0.45
Median (IQR)	35 (34–36)	34 (34–36)	
Range	28–37	31–38	
Apgar score			
At 1 min			0.14
Median	9	9	
Range	1–10	6–10	
At 5 min			0.59
Median	9	9	
Range	5–10	9–10	
Admitted to the NICU immediately after birth — no./total no. (%)	22/107 (20.6)	3/55 (5.5)	0.01
Duration of NICU stay — days			1.0
Median (IQR)	5 (2–10)	5†	
Range	2–30	2–8	
Premature — no. (%)			
Birth at <37 wk of gestation	17 (14.5)	6 (10.5)	0.63
Birth at <35 wk of gestation	5 (4.3)	1 (1.8)	0.66
Small for gestational age — no./total no. (%)	10/116 (8.6)	3/57 (5.3)	0.06
Microcephaly — no. (%)‡	4 (3.4)	0	0.31
Proportionate microcephaly	2 (1.7)	0	1.00
Disproportionate microcephaly	2 (1.7)	0	1.00
Total number of adverse infant outcomes — no. (%)	49 (41.9)	3 (5.3)	<0.001

* Included is one set of twins.
† The IQR was not calculated (NC) since only 3 non–ZIKV-exposed infants were admitted to the NICU.
‡ Proportionate microcephaly is defined as a condition in which the head size is small but is proportional to the weight and length of the infant; disproportionate microcephaly is a condition in which the head size is small relative to the weight and length of the infant.

phenomenon is real and, if so, whether microcephaly is a direct effect of ZIKV or whether it could be due to potential environmental exposure of pregnant women to teratogenic agents.[18] There is now a growing body of evidence that suggests a causality link between ZIKV and neonatal structural malformations.[19-21] Both prenatal and postnatal imaging studies in our cohort showed serious and frequent problems in CNS development in utero, as well as in fetal develop-

ment overall, with such problems affecting 46% of 125 pregnancies and 42% of 117 live-born infants. Though the clinical illness in women has similarities to rubella,[22] the effects in the unborn infants differ. With rubella, the time window for adverse outcomes in utero occurs in the first 16 weeks of pregnancy.[23-25] In contrast, with ZIKV, the time window appears to be throughout pregnancy. ZIKV pathogenicity was evident in our cohort even in the presence of a "control" group that was affected by chikungunya virus, which is also linked to adverse pregnancy outcomes, particularly fetal loss.[26]

Fetuses infected in the first trimester had findings suggestive of pathologic change during embryogenesis, but CNS abnormalities were seen in fetuses infected as late as 39 weeks of gestation, which underscores the CNS viral tropism. Potential findings suggestive of placental insufficiency were identified in infants who were born small for gestational age or who were born after signs of fetal distress. Microcephaly as detected by ultrasonography and confirmed at birth was noted in four cases (3.4%), but in only one case was it an isolated finding that was not present in conjunction with fetal growth restriction. Nevertheless, two cases of microcephaly were found to be disproportionate. Although microcephaly has been widely discussed in relation to ZIKV infection, it is important to note that other findings such as cerebral calcifications and fetal growth restriction were present more frequently. Many of the clinical and radiographic abnormalities identified in our cohort have been described in prior case series.[27,28] We have observed a variety of neurologic findings, including visual and hearing deficits, seizure activity, hypertonicity, spasticity, hyperreflexia, contractures, dysphagia, and feeding difficulties. A troubling aspect of our study is that children were assessed in early infancy, when some subtle neurologic manifestations of disease are difficult to identify. On further follow-up, we suspect that additional clinical manifestations of neurologic disease may be identified in infants who were not previously found to have abnormalities.

Our results should be interpreted with caution since they reflect individual neurologic assessments and imaging performed in early infancy and with knowledge of in utero ZIKV infection status. All infants are still being monitored and will be periodically reevaluated with neurodevelopmental assessments. It is important to note that the potential effect of asymptomatic ZIKV infection during pregnancy was not assessed in this cohort.

In summary, our data show that the risk of severe adverse pregnancy and infant outcomes after maternal ZIKV infection was substantial.

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Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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APPENDIX

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Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Brasil P, Pereira JP Jr, Moreira ME, et al. Zika virus infection in pregnant women in Rio de Janeiro. N Engl J Med 2016;375:2321-34. DOI: 10.1056/NEJMoa1602412

Table of Contents for Supplement Materials:

Supplemental Table 1: Ultrasound findings of 59 ZIKV-positive subjects with outcomes.

Mother No.	US exam No.	GA at Infection (w)	TM Infection	GA at US (w+d)	US Anatomy Result	Umb art	MCA	Biometry	Final result	Abnormalities	HC%	EFW %	FGR (<10%)	Outcome	Notes
1	1	18	2	21+5	Normal	Normal	Normal	20+6	Normal		6.7		No		
1	2	18	2	32+5	Abnormal	Normal	Normal	32+2	Abnormal	Polyhydramnios	5.5	41.3	No	Live birth	
1	3	18	2	36+5	Normal	Normal	Normal	36+3	Normal		11.5	43.9	No		
2	1	30	3	34+0	Normal	Normal	Normal	34+4	Normal		38.2	67.3	No	Live birth	
3	1	31	3	33+6	Normal	Normal	Normal	33+5	Normal		5.5	36.1	No	Live birth	Outcome #50. Abnormal neurologic exam, polydactyly left foot.
4	1	14	2	17+6	Normal	Normal	Normal	17+5	Normal		75.8		No	Live birth	
5	1	13	1	19+0	Normal	Normal	Normal	19+1	Normal		21.2	52.2	No		
5	2	13	1	31+0	Normal	Normal	Normal	30+3	Normal		15.9	39.4	No	Live birth	
5	3	13	1	35+0	Normal	Normal	Normal	34+3	Normal		8.1	37.8	No		
5	4	13	1	37+0	Normal	Normal	Normal	36+3	Normal		8.1	39.5	No		
6	1	21	2	28+0	Normal	Normal	Normal	27+2	Normal		24.2	47.1	No	Live birth	Outcome #41. Abnormal neurologic and funduscopic exam, abnormal EEG
6	2	21	2	32+0	Normal	Normal	Normal	32+0	Normal		75.8	55.6	No		
7	1	9	1	15+4	Normal	Normal	Normal	15+5	Normal		65.2	41.9	No		
7	2	9	1	26+4	Abnormal	Normal	Normal	25+2	Abnormal	HC<2.5%	**1.4**	18.3	No	Live birth	
7	3	9	1	33+4	Normal	Normal	Normal	31+5	Normal		15.9	14.7	No		
7	4	9	1	37+6	Abnormal	Normal	Normal	35+0	Abnormal	HC<2.5%	0.6	10.6	No		

8	1	14	2	19+5	Normal	Normal	Normal	19+1	Normal		18.4		No		
8	2	14	2	31+5	Normal	Normal	High	32+0	Normal		46.0	51.7	No	Live birth	Outcome #12. Cortical thumb, elbow fovea, redundant scalp, TFUS/MRI findings
8	3	14	2	34+5	Normal	Normal	Normal	35+2	Normal		4.5	82.4	No		
8	4	14	2	37+5	Normal	Normal		39+0	Normal		24.2	99.9	No		
9	1	14	2	19+1	Normal	Normal	Normal	19+3	Normal		72.6	63.3	No		
9	2	14	2	31+1	Normal	Normal	Normal	31+6	Normal		65.2	62.2	No	Live birth	
9	3	14	2	35+1	Abnormal	Normal		36+0	Abnormal	Unilateral pelviectasis	61.8	57.8	No		
10	1	25	2	30+5	Normal	Normal	Normal	30+0	Normal		13.6	38	No	Stillbirth	Outcome #42. Stillbirth
10	2	25	2	33+5	Normal	Normal	High	33+2	Normal		30.9	32.9	No		
10	3	25	3	36+0	Abnormal				Abnormal	Fetal demise					
11	1	16	2	22+0	Normal	Normal	Normal	22+0	Normal		42.1	46.2	No	Live birth	
12	1	22	2	28+5	Abnormal	Normal	Normal	26+4	Abnormal	Microcephaly, FGR	1.1	8.7	Yes		
12	2	22	2	30+5	Abnormal	Normal	Normal	28+3	Abnormal	Same as above	0.4	2.9	Yes		
12	3	22	2	31+5	Abnormal	Abnormal	Low	27+5	Abnormal	Microcephaly, FGR, cerebral calcifications, abnormal UA and MCA dopplers	<0.1	0.5	Yes	Live birth	Outcome #31. Small for GA, HC proportional to body size, macular lesions, abnormal neurologic exam
12	4	22	2	32+3	Abnormal	Abnormal	Low	28+6	Abnormal	Microcephaly, FGR, cerebral calcifications, abnormal UA and MCA dopplers, oligohydramnios	<0.1	0.5	Yes		
12	5	22	2	33+0	Abnormal	Abnormal	Low	29+3	Abnormal	Same as above	<0.1	0.7	Yes		
13	1	10	1	17+0	Normal	Abnormal		17+1	Abnormal	Abnormal UA doppler	57.9		No		
13	2	10	1	22+0	Normal	Abnormal	Normal	21+6	Abnormal	Abnormal UA doppler	46.0		No	Live birth	Outcome #7. MRI findings.
13	3	10	1	33+0	Normal	Normal	Normal	32+5	Normal		27.4	41.7	No		
13	4	10	1	37+2	Normal	Normal	Normal	37+3	Normal		24.2	53.8	No		
14	1	20	2	27+6	Normal	Normal	Low	27+3	Abnormal	Abnormal MCA doppler	54.0	66.1	No		
14	2	20	2	33+6	Normal	Normal	Normal	33+5	Normal		75.8	45.3	No	Live birth	
14	3	20	2	36+6	Normal	Normal	Normal	35+0	Normal		15.9	17.4	No		
15	1	23	2	28+5	Normal	Normal	Normal	29+3	Normal		54.0	69.7	No	Live birth	Outcome #33. Knee fovea, redundant scalp,

															hyper-reflexia
16	1	25	2	30+5	Normal	Normal	Normal	32+2	Normal		90.3	71.6	No	Live birth	
16	2	25	2	35+5	Normal	Normal	Normal	35+3	Normal		24.2	45.8	No		
17	1	22	2	26+4	Normal	Normal	Low	27+2	Abnormal	Abnormal MCA doppler	46.0	86.9	No	Live birth	Outcome #30. TFUS/MRI findings
17	2	22	2	33+4	Normal	Normal	Normal	35+0	Normal		38.2	83.6	No		
17	3	22	2	36+4	Normal	Normal	Normal	37+0	Normal		24.2	81.5	No		
18	1	22	2	27+6	Normal	Normal	Normal	28+2	Normal		50.0	79.9	No	Live birth	Outcome #34. Abnormal neurologic and funduscopic exams
18	2	22	2	33+6	Normal	Normal	Normal	34+3	Normal		18.4	64.4	No		
18	3	22	2	36+6	Normal	Normal	Normal	36+0	Normal		18.4	42.9	No		
19	1	8	1	35+5	Abnormal	Normal	Normal	37+0	Abnormal	Microcephaly	<0.1	21.0	No	Live birth	Outcome #3: Microcephaly, cerebral calcifications on CT, global cerebral atrophy, macular lesions
19	2	8	1	37+5	Abnormal	Normal	High	37+5	Abnormal	Microcephaly, cerebral calcifications, ventriculomegaly, abnormal MCA doppler	<0.1	13.3	No		
19	3	8	1	39+1	Abnormal	Normal	Normal	38+4	Abnormal	Microcephaly, cerebral calcifications, lagging growth	<0.1	10.3	No		
20	1	18	2	25+0	Normal	Normal	Normal	26+2	Normal		90.3	80.0	No	Live birth	Outcome # 24. TFUS/MRI findings
20	2	18	2	33+0	Abnormal	Normal	Normal	34+3	Abnormal		46.0	86.9	No		
20	3	18	2	36+0	Normal	Normal	Normal	37+3	Normal		86.4	87.8	No		
21	1	16	2	21+3	Normal	Normal		21+6	Normal		34.5	79.3	No	Live birth	
21	2	16	2	23+3	Normal	Normal	Normal	24+4	Normal		50.0.0	92.7	No		
21	3	16	2	32+3	Normal	Normal	Normal	33+6	Normal		95.5	77.8	No		
22	1	19	2	25+6	Normal	Normal	Normal	26+1	Normal		30.9	64.2	No	Live birth	
22	2	19	2	33+6	Normal	Normal	Normal	34+2	Normal		21.2	67.7	No		
22	3	19	2	36+6	Normal	Normal	Normal	35+5	Normal		11.5	36.9	No		
23	1	35	3	40+3	Abnormal	Normal	Normal	37+1	Abnormal	HC< 2.5%, Oligohydramnios	0.2	16.2	No	Live birth	Outcome #54: Hypoactivity, hypotonia, altered primitive reflexes, abnormal EEG, dysphagia

24	1	12	1	29+1	Abnormal	Normal	Normal	24+5	Abnormal	Microcephaly, cerebral calcifications, ventriculomegaly, arthrogryposis, club foot, FGR	<0.1	0.3	Yes		
24	2	12	1	30+4	Abnormal	Normal	Normal	26+3	Abnormal	Same as above	<0.1	3.5	Yes		
24	3	12	1	32+1	Abnormal	Normal	Normal	26+6	Abnormal	Microcephaly, cerebral calcifications, ventriculomegaly, Blake's pouch cyst, cerebellar agenesis, arthrogryposis, liver heterogeneity, mega cisterna magna, club foot, FGR	<0.1	2.9	Yes		
24	4	12	1	34+1	Abnormal	Normal	High	29+1	Abnormal	Same as above	<0.1	0.2	Yes	Live birth	Outcome #9. Microcephaly, small for GA, TFUS/ MRI findings, macular atrophy and hypoplastic ocular nerve, abnormal neurologic exam, abnormal EEG.
24	5	12	1	37+1	Abnormal	Normal	Normal	31+0	Abnormal	Same as above	<0.1	0.1	Yes		
24	6	12	1	38+1	Abnormal	Normal	Normal	32+1	Abnormal	Same as above	<0.1	0.3	Yes		
24	7	12	1	40+1	Abnormal	Normal	Normal	31+5	Abnormal	Same as above	<0.1	0.1	Yes		
24	8	12	1	41+1	Abnormal	Normal	Normal	32+2	Abnormal	Microcephaly, cerebral calcifications, ventriculomegaly, Blake's pouch cyst, cerebellar agenesis, arthrogryposis, liver heterogeneity, mega cisterna magna, club foot, FGR, oligohydramnios	<0.1	0.4	Yes		

26	1	16	2	22+5	Normal	Normal	Normal	22+5	Normal		34.5	44.1	No	Live birth	Outcome #17. Large for GA, cortical thumb
26	2	16	2	31+5	Normal	Normal	Normal	32+0	Normal		30.9	61.9	No		
26	3	16	2	35+5	Normal	Normal	Normal	35+4	Normal		38.2	53.0	No		
27	1	16	2	24+6	Normal	Normal	Normal	24+2	Normal		42.1	24.6	No	Live birth	Outcome #18. Clenched fists, abnormal neurologic exam
27	2	16	2	30+6	Normal	Normal	Normal	31+3	Normal		34.5	53.6	No		
27	3	16	2	36+6	Normal	Normal	Normal	36+5	Normal		42.1	48.2	No		
29	1	23	2	30+5	Normal	Normal	Normal	30+4	Normal		30.9	56.9	No	Live birth	
29	2	23	2	34+5	Normal	Normal	Normal	34+2	Normal		50.0	34.2	No		
29	3	23	2	37+5	Normal	Normal	Normal	36+0	Normal		50.0	24.6	No		
30	1	26	3	33+3	Normal	Normal	Normal	33+4	Normal		15.9	83.7	No	Live birth	
31	1	14	2	21+5	Normal	Abnormal	Normal	21+5	Abnormal	Abnormal UA Ddoppler	27.4		No	Live birth	Outcome #15. Large for GA (gestational diabetes); Congenital heart disease, hypoactive, TFUS/MRI findings
31	2	14	2	26+5	Normal	Abnormal	Normal	27+0	Abnormal	Abnormal UA doppler	34.5	72.3	No		
31	3	14	2	29+5	Normal	Abnormal		29+6	Abnormal	Abnormal UA doppler	46.0	75.1	No		
31	4	14	2	33+5	Abnormal	Normal	Abnormal	35+2	Abnormal	Macrosomia, polyhydramnios, abnormal MCA doppler	46.0	98.1	No		
32	1	18	2	24+3	Normal	Normal	Normal	24+3	Normal		50.0	22.3	No	Live birth	Outcome #39. MRI findings
32	2	18	2	33+3	Normal	Normal	Normal	33+4	Normal		42.1	28.1	No		
34	1	23	2	32+0	Normal	Normal	Normal	32+0	Normal		30.9	21.6	No	Live birth	Outcome #36. Small for GA, abnormal neurologic exam, abnormal hearing
35	1	25	2	35+3	Normal	Normal	Normal	35+1	Normal		61.8	43.2	No	Live birth	
36	1	26	3	35+6	Abnormal	Abnormal	Normal	34+3	Abnormal	HC<2.5%, abnormal UA dopplers, FGR	1.4	8.3	Yes	Live birth	Outcome #45. Small for GA, HC proportional to body size
38	1	26	3	35+2	Abnormal	Normal	Normal	35+2	Abnormal	Cerebral calcifications, ventriculomegaly 13mm, brachicephaly	50	56.0	No	Live birth	Outcome #47. TFUS: cerebral calcifications

38	2	26	3	37+2	Abnormal	Normal	High	38+2	Abnormal	Cerebral calcifications, ventriculomegaly, abnormal MCA dopplers	50	68.4	No		
39	1	21	2	30+2	Abnormal	Normal	Normal	31+3	Abnormal	Cerebral calcifications	57.9	83.3	No		
39	2	21	2	34+6	Abnormal	Normal	Normal	35+3	Abnormal	Cerebral calcifications, periventricular calcifications, mega cisterna magna	42.1	45.5	No	Live birth	Outcome #28. Hypertonic upper extremities, head lag
39	3	21	2	37+6	Abnormal	Normal	Normal	38+2	Abnormal	Cerebral calcifications, periventricular calcifications,	38.2	66.7	No		
40	1	8	1	17+6	Abnormal			18+1	Abnormal	Choroid plexus cyst	42.1	68.6	No		
40	2	8	1	20+4	Abnormal	Normal	Normal	20+4	Abnormal	Choroid plexus cyst, small transverse cerebellar diameter	13.6	16.1	No	Live birth	Outcome #4. Periventricular lesions on CT, global cerebral atrophy, macular lesions
40	3	8	1	23+3	Abnormal	Normal	Normal	23+1	Abnormal	Choroid plexus cyst	24.2	41.4	No		
40	4	8	1	34+3	Normal	Normal	Normal	35+0	Normal		30.9	56.8	No		
40	5	8	1	36+5	Normal	Normal	Normal	36+0	Normal		69.2	34.0	No		
41	1	12	1	24+0	Abnormal	Normal		24+1	Abnormal	Mega cisterna magna	57.6	50.1	No		
41	2	12	1	28+4	Abnormal	Normal	Normal	28+1	Abnormal	Mega cisterna magna	46	42.7	No	LTF	
41	3	12	1	34+4	Abnormal	Normal	Normal	35+2	Abnormal	Mega cisterna magna	46	66.0	No		
41	4	12	1	36+4	Normal	Normal	Normal	35+4	Normal	HC<2.5%	1.4	27.2	No		
42	1	17	2	30+2	Normal	Normal	Abnormal	30+6	Abnormal	Abnormal MCA doppler	30.9	69.3	No	Live birth	
42	2	17	2	34+2	Normal	Normal	Normal	34+1	Normal		42.1	30.2	No		
48	1	18	2	28+6		Normal	Normal	29+5			69.2	71.2	No	Live birth	
48	2	18	2	33+6	Normal	Normal	Normal	34+4	Normal		46	47.8	No		
49	1	15	2	24+5	Normal	Normal	Normal	24+6	Normal		50	35.3	No		
49	2	15	2	30+5	Normal	Normal	Normal	30+4	Normal		5.5	40.0	No	Live birth	
49	3	15	2	35+5	Normal	Normal	Normal	35+2	Normal		9.7	36.4	No		
49	4	15	2	38+0	Normal	Normal	Normal	36+6	Normal		4.5	49.2	No		
50	1	13	1	21+6	Normal	Normal	Normal	21+1	Normal		11.5	28.2	No	LTF	
50	2	13	1	27+6	Abnormal	Normal	Normal	27+0	Abnormal	Mega cisterna magna	6.7	25.8	No		

50	3	13	1	32+6	Abnormal	Normal	Abnormal	31+2	Abnormal	HC <2.5%, abnormal MCA dopplers	1.1	21.9	No		
50	4	13	1	34+6	Abnormal	Normal	Normal	33+4	Abnormal	FGR	3.6	9.6	Yes		
50	5	13	1	36+6	Normal	Normal	Normal	35+1	Normal		9.7	13.7	No		
51	1	26	3	35+5	Normal	Normal	Normal	35+3	Normal		15.9	49.9	No	Live birth	Outcome #43. Redundant scalp, abnormal neurologic exam, MRI findings
52	1	11	1	21+3	Normal	Normal	Normal	21+2	Normal		21.2	50.1	No		
52	2	11	1	29+3	Normal	Normal	Normal	30+0	Normal		27.4	64.7	No	Live birth	
52	3	11	1	33+3	Normal	Normal	Normal	33+3	Normal		15.9	32.6	No		
52	4	11	1	36+5	Abnormal	Normal	Abnormal	36+1	Abnormal	HC<2.5%	1.8	35.1	No		
53	1	24	2	34+0	Normal	Normal	Normal	33+4	Normal		46.0	21.7	No	Live birth	
55	1	18	2	28+3	Normal	Normal	Normal	27+4	Normal		4.5	31.4	No	Live birth	
55	2	18	2	34+3	Normal	Normal	Normal	33+5	Normal		30.9	26.5	No		
57	1	27	3	36+3	Normal	Normal	Normal	36+1	Normal		46.0	27.5	No	Live birth	
59	1	22	2	30+4	Normal	Normal	Normal	30+6	Normal		34.5	47.4	No	Live birth	Outcome #35. Dysmorphic features, hypertonicity, MRI findings
59	2	22	2	36+4	Normal	Normal	Normal	36+0	Normal		9.7	44.3	No		
63	1	17	2	26+5	Normal	Normal	Normal	27+3	Normal		38.2	72.8	No	Live birth	
63	2	17	2	34+5	Normal	Normal	Normal	35+0	Normal		18.4	45.0	No		
64	1	12	1	21+4	Normal	Normal	Normal	21+6	Normal		81.6		No		
64	2	12	1	29+4	Normal	Normal	Low	28+3	Normal		50.0	33.6	No	Live birth	
64	3	12	1	33+4	Normal	Normal	Normal	32+4	Normal		38.2	31.7	No		
65	1	20	2	28+0	Normal	Normal	Normal	27+6	Normal		18.4	47.6	No	Live birth	Outcome #27. Hypertonicity, TFUS/MRI findings
65	2	20	2	34+0	Normal	Normal	Normal	33+6	Normal		27.4	39.2	No		
65	3	20	2	36+2	Normal	Normal	Normal	35+3	Normal		30.9	18.8	No		
66	1	18	2	25+3	Normal	Normal	Normal	24+5	Normal		18.4	15.0	No	LTF	
68	1	18	2	21+3	Normal	Normal		21+5	Normal		61.8	57.7	No	Live birth	
68	2	18	2	28+3	Normal	Normal	Normal	28+3	Normal		13.6	36.3	No		

68	3	18	2	32+3	Normal	Normal	Normal	33+0	Normal		11.5	51.5	No		
70	1	21	2	30+3	Normal	Normal	Normal	29+4	Normal		30.9	12.0	No		
70	2	21	2	34+3	Abnormal	Normal	Abnormal	34+1	Abnormal	Mega cisterna magna	61.8	14.6	No	Live birth	Outcome #29. Seizures, TFUS/ MRI findings, abnormal EEG
70	3	21	2	36+5	Normal	Normal	Normal	35+6	Normal		27.4	18.1	No		
70	4	21	2	38+5	Normal	Normal	Normal	37+0	Normal		15.9	19.2	No		
71	1	10	1	22+1	Normal	Normal	Normal	22+5	Normal		42.1	49.4	No		
71	2	10	1	28+1	Abnormal	Abnormal	Normal	28+5	Abnormal	Abnormal UA doppler	88.5	84.8	No		
71	3	10	1	30+1	Abnormal	Abnormal	Normal	30+1	Abnormal	Abnormal UA doppler	54.0	55.3	No	Live birth	
71	4	10	1	32+1	Normal	Normal	Normal	32+6	Normal		65.2	57.2	No		
71	5	10	1	34+3	Normal	Normal	Normal	32+6	Normal		13.6	26.9	No		
72	1	27	3	34+5	Normal	Normal	Normal	34+3	Normal		6.7	38.7	No	Live birth	
72	2	27	3	37+5	Normal	Normal	Normal	37+2	Normal		24.2	38.6	No		
81	1	23	2	36+3	Normal	Normal	Normal	34+4	Normal		24.2	16.3	No	Live birth	Outcome #37. Small for GA, abnormal neurologic exam, TFUS findings
83	1	19	2	36+0	Normal	Normal	Normal	35+1	Normal		88.5	58.1	No	Live birth	Outcome # 23. TFUS/MRI findings
85	1	17	2	30+3	Normal	Normal	Normal	30+5	Normal		38.2	61.8	No	Live birth	
90	1	19	2	37+3	Normal	Normal	Normal	36+6	Normal		27.4	27.6	No	Live birth	

Supplemental Table 2: Abnormal outcomes and/ or Abnormal Findings at Birth.*

Order No.	Week of Gestation at Infection	Week of Gestation at Ultrasound Examination	Abnormal Prenatal Findings	Week of Gestation at Birth**	Abnormal Findings at Birth
1	6	Not done	Fetal demise in the first trimester of pregnancy	NA	Fetal loss
2	6	Not done	Fetal demise in the first trimester of pregnancy	NA	Fetal loss
3	8	35	Microcephaly, cerebral calcifications, abnormal middle cerebral artery, intrauterine growth restriction	38 weeks 2 days	Microcephaly, cerebral calcifications on CT, global cerebral atrophy, macular lesions
4	8	20	Choroid plexus cyst, cerebellar atrophy (transverse diameter <5th percentile)	39 weeks 2 days	Periventricular lesions on TF exam/ congenital dislocation of hip
5	9	Not done	Fetal demise in the first trimester of pregnancy (13 weeks)	NA	Fetal loss
6	10	Not done	Fetal demise in the first trimester of pregnancy	NA	Fetal loss
7	11	17, 21, 32, 37	None	38 weeks 6 days	MRI findings: Excessive hypersignaling in T2 in the white matter, peritrigonal and tempo-parietal regions. Hyposignaling in the diffusion sequence.
8	11	Not done	Fetal demise in the first trimester of pregnancy (11 weeks)	NA	Fetal loss
9	12	29	Microcephaly, cerebral calcification, Blake's cyst, agenesis vermis, club foot, intrauterine growth restriction	40 weeks 6 days	Microcephaly, small for gestational age; TF Us/ MRI Findings: Cerebral calcifications in thalamus and periventricular areas, supratentorial dilatations, reduction of cerebral parenchyma on both cerebral hemispheres, atrophy of corpus callosum, reduction in thalamic white matter Macular atrophy and hypoplastic optical nerve Abnormal neurologic exam Abnormal EEG
10	12	Not done		34 weeks 3 days	TF Us/ MRI Findings: Excessive hypersignaling in T2 in the white matter, peritrigonal and tempo-parietal regions. Hyposignaling in the diffusion sequence.
11	13	Not done		37 weeks 6 days	Redundant scalp, knee fovea, dysmorphic features, dysphagia, irritability, no tracking TF US: Hypoxic, ischemic parenchymal lesions
12	14	19, 32, 35, 39	None	38 weeks 4 days	Cortical thumb, elbow fovea, redundant scalp TF Us/ MRI Findings: Excessive hypersignaling in T2 in the white matter, diffuse

					in the peritrigonal posterior areas and less evident in the frontal parietal white matter. Hyposignaling in the diffusion sequence. bilaterally
13	14	Not Done		38 weeks	TF Us/ MRI Findings: Excessive hypersignaling in T2 in the white matter, diffuse in the peritrigonal posterior areas and less evident in the frontal parietal white matter. Hyposignaling in the diffusion sequence.
14	14	Not Done		39 weeks 3 days	Cortical thumb and hyperreflexia TF Us/ MRI Findings: Excessive hypersignaling in T2 in the white matter, diffuse in the peritrigonal posterior areas and less evident in the frontal parietal white matter. Hyposignaling in the diffusion sequence
15	15	21, 27, 29, 35	Fetal macrosomia (maternal gestational diabetes)	35 weeks 4 days	Large for gestational age; Congenital heart disease, hypoactive TF Us/ MRI Findings: Excessive hypersignaling in T2 in the white matter, diffuse in the peritrigonal posterior areas and less evident in the frontal parietal white matter. Hyposignaling in the diffusion sequence Hypoplasia of the inferior portion of the vermix
16	15	Not Done		37 weeks	Small for gestational age
17	16	22, 32, 35	Fetal macrosomia (maternal gestational diabetes)	38 weeks	Large for gestational age; Cortical thumb
18	17	24, 31, 36	None	39 weeks 2 days	Clenched fists, abnormal posturing, abnormal movements
19	17	27, 31, 34	None (Twin gestation)	35 weeks 6 days	TF US: Intracranial hemorrhage Grade I
20	17	Not done	Fetal demise in the second trimester of pregnancy (21 weeks)	NA	Fetal Loss
21	18	Not Done		40 weeks	Altered motor reflexes; Hemiparesis

22	18	24, 29, 34, 37, 38	None	38 weeks 4 days	TF Us/ MRI Findings: Excessive hypersignaling in T2 in the white matter, diffuse in the peritrigonal posterior areas and less evident in the frontal parietal white matter. Hyposignaling in the diffusion sequence
23	18	35	None	37 weeks	TF Us/ MRI Findings: Excessive hypersignaling in T2 in the white matter, diffuse in the peritrigonal posterior areas and less evident in the frontal parietal white matter. Hyposignaling in the diffusion sequence
24	20	25, 33, 36 weeks	Ventriculomegaly noted at 33 weeks.	39 weeks	TF Us/ MRI Findings: Excessive hypersignaling in T2 in the white matter, diffuse in the peritrigonal posterior areas and less evident in the frontal parietal white matter. Hyposignaling in the diffusion sequence
25	21	Not Done		38 weeks 5 days	Dysmorphic features; difficulty swallowing, choking episodes, unable to gain weight Abnormal funduscopic exam; rarefaction of retinal pigmented epithelium
26	21	Not Done		41 weeks 1 day	TF US: Intracranial hemorrhage
27	21	27, 33, 35	None	39 weeks	Hypertonicity TF US/ MRI Findings: Excessive hypersignaling in T2 in the white matter, diffuse in the peritrigonal posterior areas and less evident in the frontal parietal white matter. Hyposignaling in the diffusion sequence
28	21	30, 34, 37 weeks	Cerebellar and cerebral right periventricular - calcifications, mega cisterna magna	39 weeks 4 days	Hypertonic upper extremities; head lag
29	22	29, 34, 35, 37	None	40 weeks 1 day	Seizures, abnormal EEG TF Us/ MRI Findings: Excessive hypersignaling in T2 in the white matter, diffuse in the peritrigonal posterior areas and less evident in the frontal parietal white matter. Hyposignaling in the diffusion sequence. Elongated image along posterior portion of dura consistent with small hematoma/ bleed
30	22	26, 33, 36	Middle cerebral artery flow <5th percentile at 26 weeks, normal on subsequent ultrasounds	40 weeks	TF Us/ MRI Findings: Excessive hypersignaling in T2 in the white matter, diffuse in the peritrigonal posterior areas and less evident in the frontal parietal white matter. Hyposignaling in the diffusion sequence

31	22	28, 30, 31, 32, 33	Microcephaly,cerebral calcifications, placental insufficiency as assessed by Doppler study, oligohydramnios, intrauterine growth restriction	33 weeks	Small for gestational age, head circumference proportional to body size, macular lesions, abnormal neurologic exam
32	22	Not done	Fetal demise in the second trimester	NA	Fetal loss
33	23	29	None	39 weeks 1 day	Knee fovea, redundant scalp, hyperreflexia
34	23	28, 34, 36	None	38 weeks	Hyperreflexia, clonus of upper and lower extremities, posturing, head lag; abnormal funduscopic exam
35	23	30, 36	None	38 weeks 4 days	Dysmorphic features, hypertonicity MRI Findings: Excessive hypersignaling in T2 in the white matter, diffuse in the peritrigonal posterior areas and less evident in the frontal parietal white matter. Hyposignaling in the diffusion sequence
36	23	32	None	40 weeks 1 day	Small for gestational age, failure to thrive, abnormal neurologic exam, abnormal hearing
37	24	36	None	37 weeks 6 days	Small for gestational age, spasms and hypertonicity on neurologic exam; TF US: Hyperechoic oval image in thalamus
38	24	Not done		39 weeks	MRI Findings: Excessive hypersignaling in T2 in the white matter, diffuse in the peritrigonal posterior areas and less evident in the frontal parietal white matter. Hyposignaling in the diffusion sequence
39	24	24, 33	None	37 weeks 1 day	MRI Findings: Excessive hypersignaling in T2 in the white matter, diffuse in the peritrigonal posterior areas and the white matter in the frontal and bilateral parietal areas. Hyposignaling in the diffusion sequence. Small hypertintense foci in T1 and hypointense in other sequences in the posterior fossa, close to the dura, posterior to the cerebellar vermix, possible hemorrhage.
40	24	Not done		40 weeks 1 day	MRI Findings: Excessive hypersignaling in T2 in the white matter, diffuse in the peritrigonal posterior areas and less evident in the frontal parietal white matter. Hyposignaling in the diffusion sequence
41	25	28, 32		38 weeks	Abnormal funduscopic exam with pale optic nerve;

					Abnormal neurologic exam (clonus, hyperreflexia, posturing), abnormal EEG
42	25	30, 33, 36	Normal first two ultrasounds, fetal death detected at 36 weeks on repeat ultrasonogram	NA	Stillbirth
43	26	35	None	38 weeks	Redundant scalp, abnormal neurologic exam (abnormal primitive reflexes, hypertonicity and irritability, hyperexcitability); MRI Findings: Hypointense small foci in the subcortical white matter suggesting small hemorrhage
44	26	Not done		35 weeks	Abnormal neurologic exam (hyperextension of extremities, posturing) abnormal hearing assessment, failure to thrive
45	26	35	Microcephaly, abnormal umbilical artery flow (>95th percentile on the pulsatile index), intrauterine growth restriction	35 weeks 4 days	Small for gestational age, head circumference proportional to body size
46	27	Not done		35 weeks	Abnormal neurologic exam (hyperreflexia, hypertonicity), redundant scalp; TF US, CT and MRI Findings: Left periventricular cerebritis, calcifications in the basal ganglia, periventricular bleed
47	27	35, 37	Cerebral calcifications, ventriculomegaly, brachycephaly	39 weeks 1 day	TF US: Cerebral calcifications
48	27	Not done		38 weeks	Knee fovea, abnormal neurologic exam (hypertonicity, abnormal primitive reflexes, posturing)
49	30	Not done		33 weeks	Microcephaly***, Small for gestational age, brachycephaly, dysphagia, irritability
50	31	33	None	37 weeks 6 days	Abnormal neurologic exam (altered palmar and plantar grasp, hypertonicity, irritability, hyperexcitability), polydactyly left foot
51	32	38	Fetal death	NA	Stillbirth
52	34	Not done		37 weeks 4 days	Excessive skin on dorsum; TF US: Echogenic areas on right thalamus; CT: Calcifications right thalamus
53	34	Not done		38 weeks	Redundant scalp, knee and elbow foveas, sacral dimple; Abnormal neurologic exam (hypertonicity, hyperreflexia, spasticity, clonus) Retinal hemorrhage
54	35	40	Anhydramnios, intrauterine growth restriction	40 weeks 4 days	Hypoactivity, hypotonia, altered primitive reflexes,

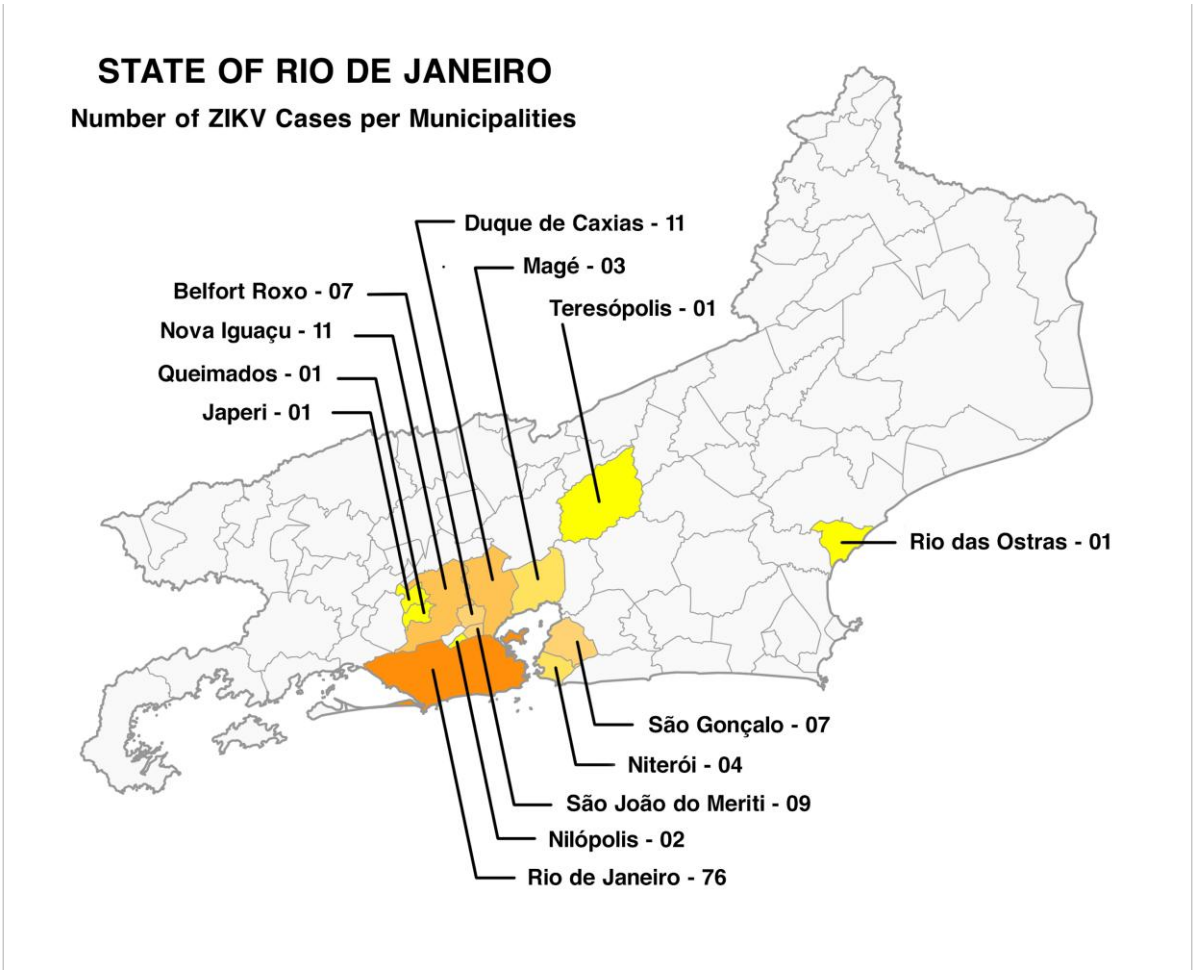
					abnormal EEG, dysphagia
55	36	Not done		39 weeks 1 day	Abnormal neurologic and ophthalmologic exam (hyperexcitability, irritability, converging strabismus)
56	37	Not done		38 weeks	Small for gestational age, abnormal neurologic exam (hyperreflexia, hypertonicity, dysphagia, irritability, altered movements), abnormal hearing assessment.
57	38	Not done		40 weeks 3 days	Microcephaly***, Small for gestational age, abnormal neurologic exam (hyperreflexia, hypertonicity, clonus of upper extremities)
58	39	Not done		39 weeks	TF US: Parenchymal hemorrhages

*Applicable to live births only

**NA denotes not applicable, EEG electroencephalogram, CT computed tomography, MRI magnetic resonance imaging, TF US transfontanel ultrasound

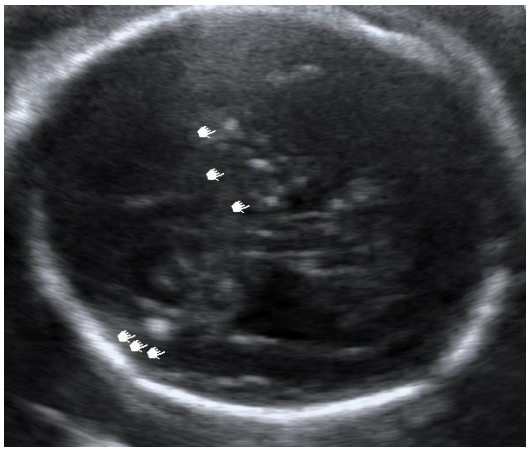
*** Infants with microcephaly and small for gestational age had proportional microcephaly, they were globally small due to in utero growth restriction.

Supplemental Figure 1



Supplemental Figure 2: Fetal ultrasound

A



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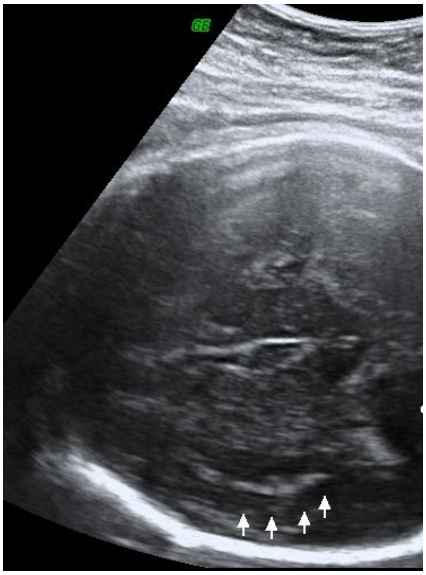

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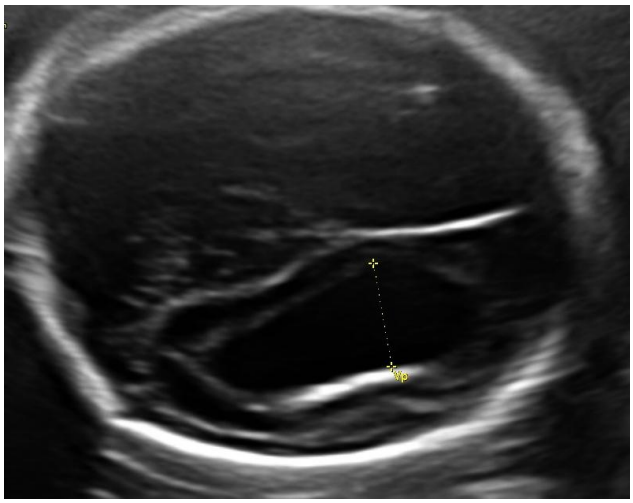
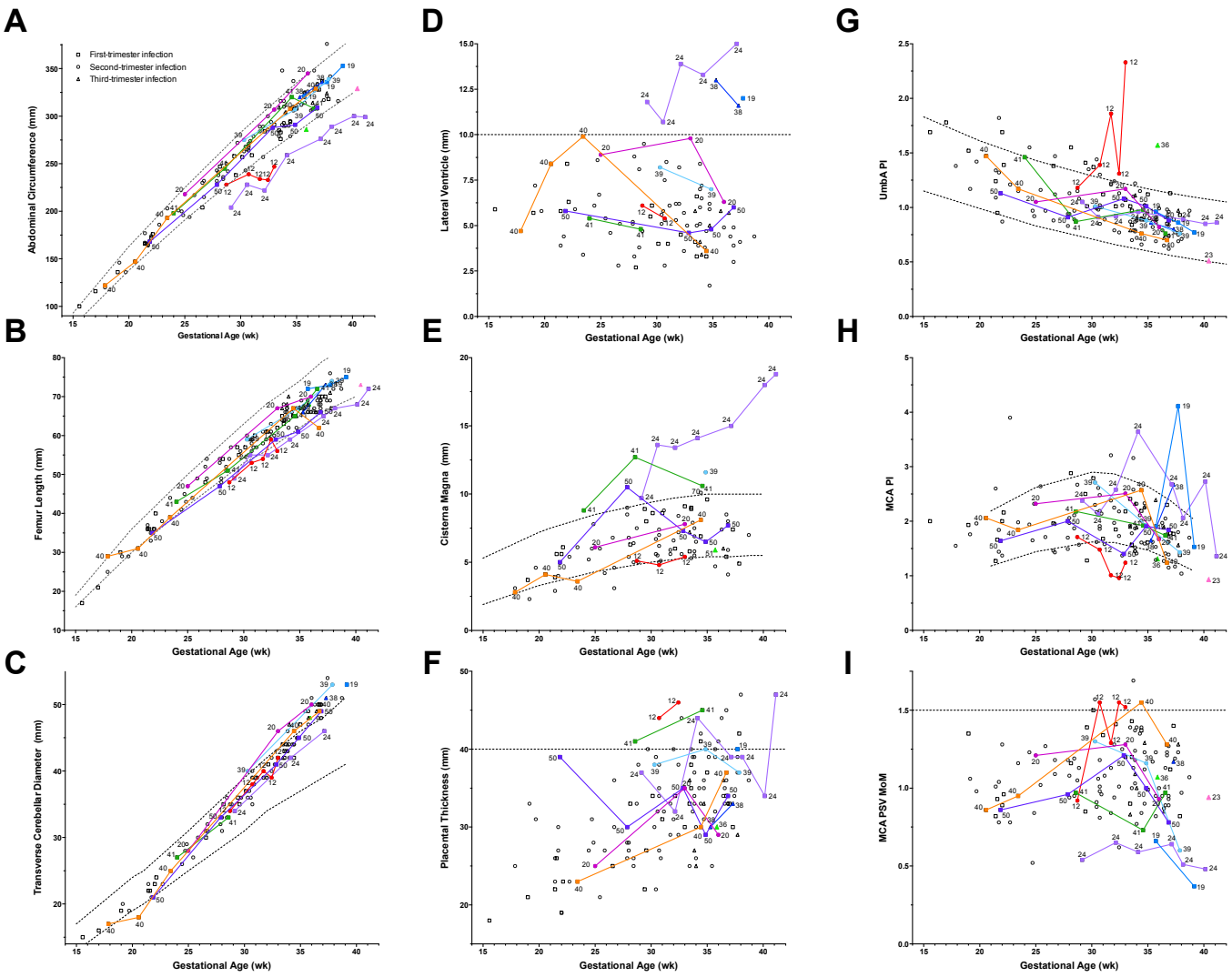
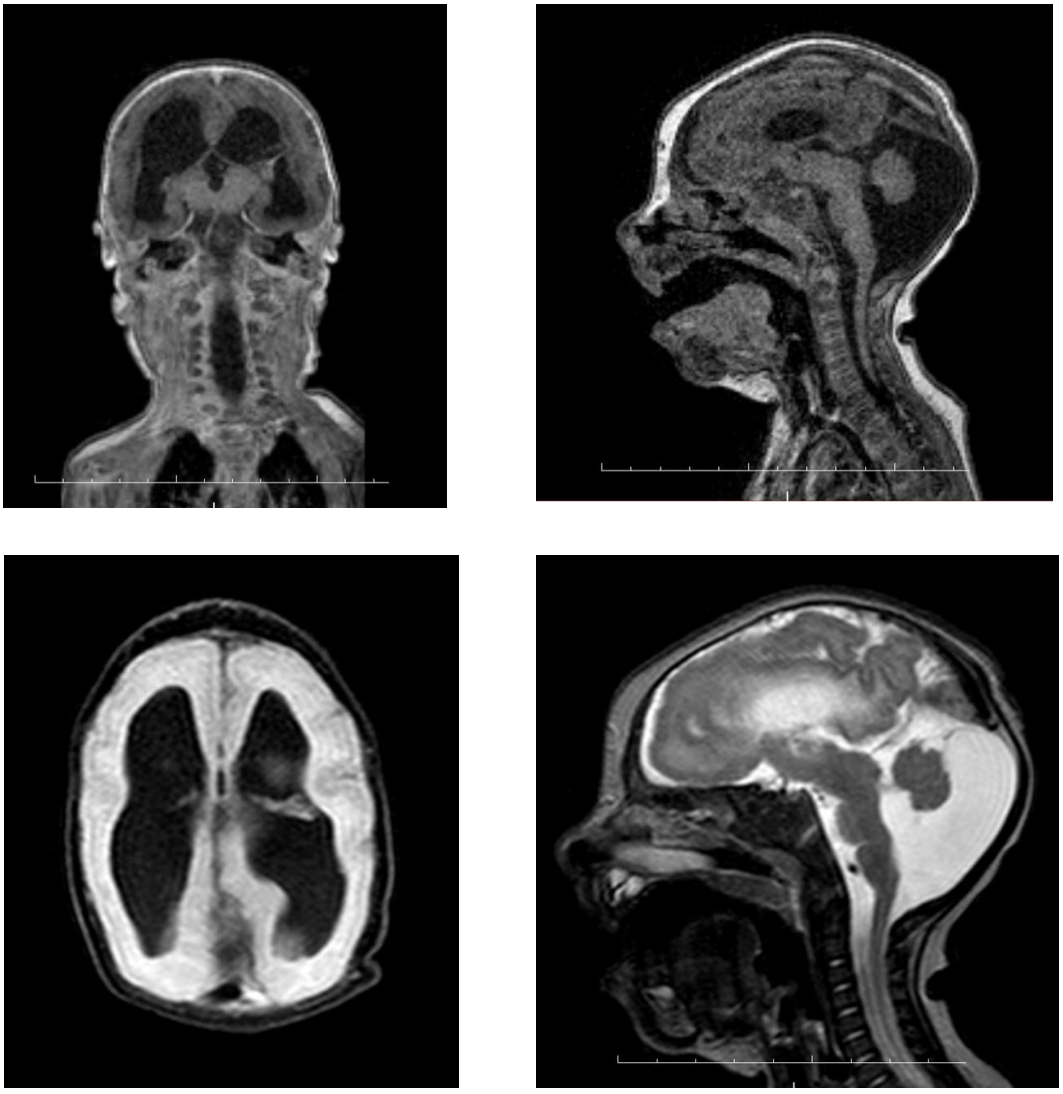


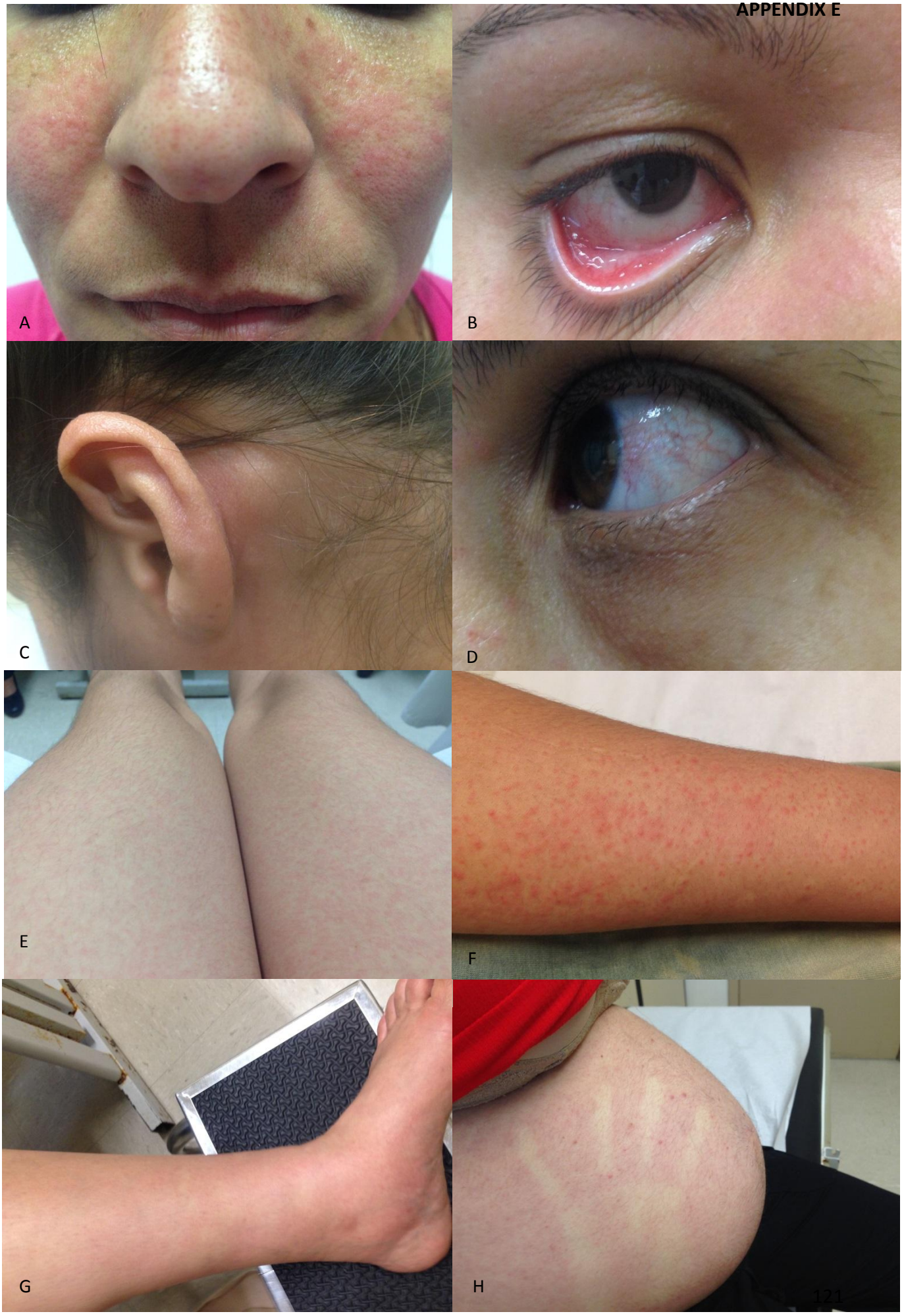
Supplemental Figure 3: Fetal ultrasound measurements



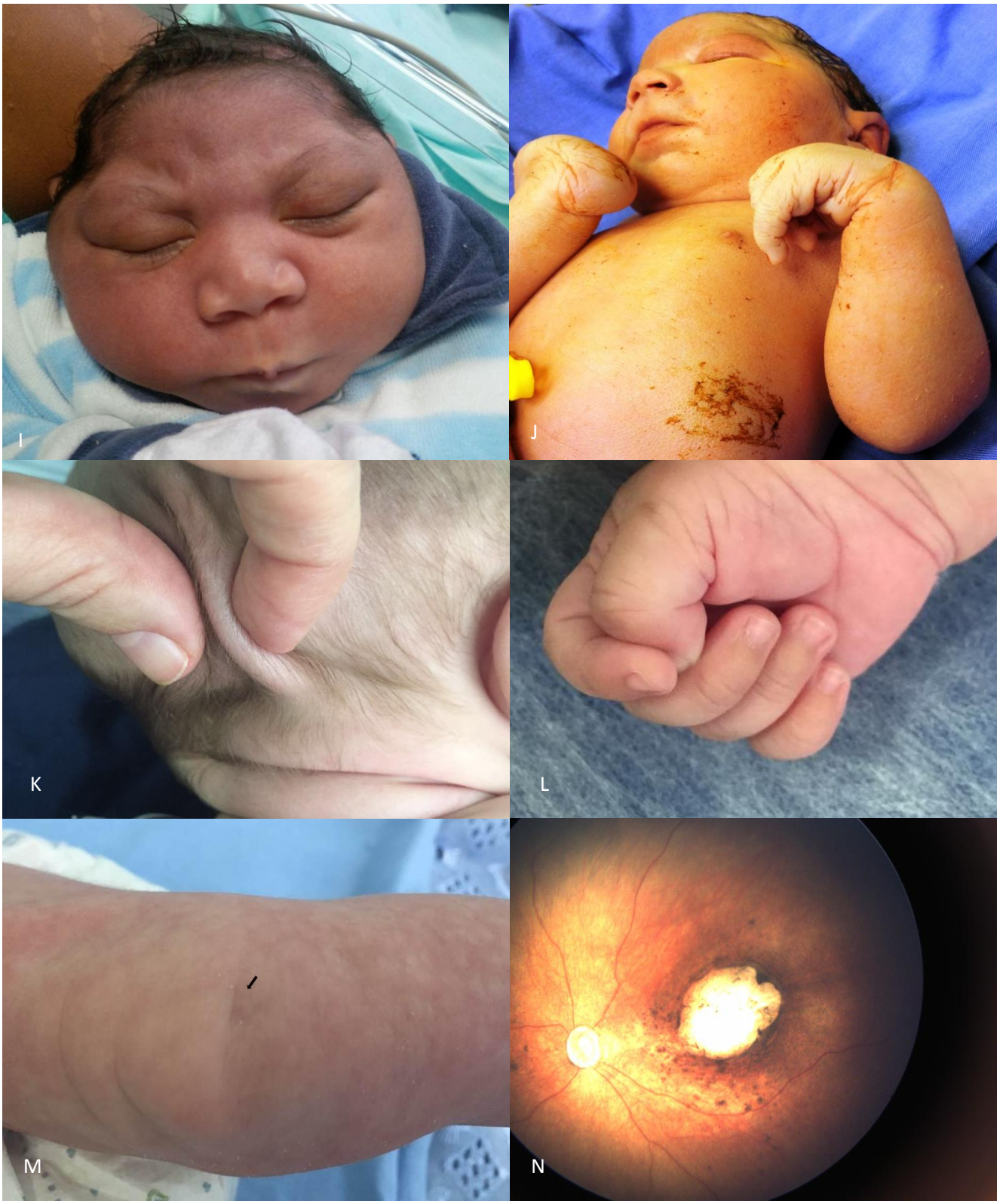
Supplemental Figure 4: MRI images of microcephaly.



Supplemental Figure 5:



Supplemental Figure 5:



Legend for Figures:

SUPPLEMENTAL MATERIALS:

Supplemental Figure 1:

Geographic distribution of 72 ZIKV+ pregnant women in Rio de Janeiro and adjacent municipalities.

Supplemental Figure 2:

A. Cerebral calcifications in fetal US at 29 weeks of subject infected at 12 weeks gestation B. Periventricular calcifications in fetal US at 35 weeks of subject infected at 27 weeks gestation. C. Ventriculomegaly

Supplemental Figure 3:

A-C. Fetal measurements for each patient are plotted by gestational age (GA) for the following parameters: abdominal circumference (A), femur length (B), transverse cerebellar diameter (C), lateral ventricles (D), cisterna magna (E), and placental thickness (F). Measurements are in millimeters. Curved dotted lines show the 10th and 90th percentiles for GA based on established nomograms from perinatology.com (A and B), except for transverse cerebellar diameter (C) and cisterna magna (E), where the dotted lines show the 5th and 95th percentiles for GA based on the nomograms established by Snijders and Nicolaides.[1] The horizontal dotted lines show the cutoffs to diagnose ventriculomegaly (D, 10 mm) and placentomegaly (F, 40 mm).

G-I. Doppler measurements for each patient are plotted by GA for umbilical artery PI (UmbA PI, G), middle cerebral artery pulsatility index (MCA PI, H), and MCA peak systolic velocities (PSV) converted to multiples of the median (MCA PSV MoM, I).

Curved dotted lines show the 5th and 95th percentiles for PI measurements (G and H).[2,3] Elevated UmbA PI indicates increased placental resistance, whereas decreased MCA PI suggests brain-sparing from fetal stress. Measurements for MCA peak systolic velocities (PSV) were converted to multiples of the median (MOM) based on nomograms from www.perinatology.com. The horizontal dotted line shows the established cutoff of 1.5 MOMs predictive of fetal anemia (I).

Symbols denote the trimester of PCR-documented infection (□, first trimester, <14 weeks; ○, second trimester, 14-25 weeks; △, third trimester, ≥26 weeks). Repeat measurements on the same patient are connected with a solid line to show growth trajectory. Abnormal cases are denoted in color and labeled with patient number. Not all measurements were obtained for each patient at each ultrasound.

Abbreviations: GA, gestational age; TM, trimester; UmbA, umbilical artery; PI, pulsatility index; MCA, middle cerebral artery; PSV, peak systolic velocity; MoM, multiples of the median.

[1]Snijders RJ, Nicolaides KH. Fetal biometry at 14-40 weeks' gestation. Ultrasound Obstet Gynecol. 1994 Jan 1;4(1):34-48.

[2]Acharya G et al. Reference ranges for serial measurements of umbilical artery Doppler indices in the second half of pregnancy. Am J Obstet Gynecol. 2005;192:937-44

[3]Ebbing C, Rasmussen S, Kiserud T. Middle cerebral artery blood flow velocities and pulsatility index and the cerebroplacental pulsatility ratio: longitudinal reference ranges and terms for serial measurements. Ultrasound Obstet Gynecol. 2007 Sep;30(3):287-96.

Supplemental Figure 4:

MRI images of cranial facial disproportion with microcephaly. Diffuse reduction in white matter thickness with corpus callosum not identified. Diffuse pachygyria, more evident in the right parietal lobe. Supratentorial ventricular dilatation. Atrophy of the cerebellar vermix with ample communication of the fourth ventricle with the cisterna magna. Widening of the perivascular spaces of the cerebellar hemispheres, with surrounding gliosis.

Supplemental Figure 5: Clinical Features of ZIKV Infection in Pregnant Women and their Infants

Panel A shows a maculopapular rash on the face; Panel B, conjunctival and palpebral erythema; Panel C, retro-auricular lymphadenopathy; Panel D, conjunctival injection with prominence of vasculature; Panel E, a rash on the legs, with a lacy reticular pattern; Panel F, a maculopapular rash on the inner arm; Panel G, edema of the foot, which the patient reported was painful; Panel H, a blanching macular rash on the gravid abdomen; Panel I, disproportionate microcephaly; Panel J, arthrogryposis at birth; Panel K, redundant scalp; Panel L shows a cortical thumb; Panel M, knee fovea; and Panel N, shows the left infant retina demonstrating optic disc hypoplasia, peripapillary atrophy; macular chorioretinal atrophy with a colobomatous- like aspect with hyperpigmented halo and pigmentary mottling.

LAHAN
Los Angeles County Health Alert Network

LAC DPH Health Advisory:
Updated California Zika Testing Guidelines and a Local Case of Sexually Transmitted Zika
January 4, 2018

County of Los Angeles
Public Health

This message is intended for family practice, obstetrics- gynecology, pediatric, infectious disease, internal medicine, emergency medicine, and urgent care providers. Please distribute as appropriate.

Key Messages

- The California Department of Public Health (CDPH) has released updated Zika testing guidelines for pregnant women and their newborns. CDPH now recommends shared patient-provider decision making instead of routine testing of asymptomatic pregnant women with recent (but not ongoing) exposure.
- Although Zika cases are decreasing regionally, transmission continues to occur in Mexico, Latin America, and other areas. Providers should continue to review mosquito bite prevention measures and safe sexual practices with persons traveling to areas with Zika as well as recommend that pregnant women and those planning to become pregnant delay non-essential travel to areas with active Zika transmission.
- Los Angeles County Department of Public Health (LAC DPH) has documented the first sexually transmitted case of Zika in a county resident.

Situation

CDPH released the Updated Guidance for Health Care Providers: Assessment and Testing for Zika Virus Infection in Pregnant Women and their Newborns on December 21, 2017. These revisions were based on a review of regional data and now align with the current CDC interim guidance. LAC DPH concurs with the CDPH revisions and highlights key recommendations in the Actions Requested of Providers section below. The full CDPH document (included below and available online) features the rationale for these changes as well as more detailed clinical recommendations.

In addition, LAC DPH has documented the first sexually transmitted Zika case in a LA County resident. A male developed symptomatic disease in early November while traveling to Mexico. His female partner, who did not travel, subsequently developed symptomatic disease after his return to LA County. Both have confirmed positive for Zika infection. Vector control agencies have found no evidence of mosquito transmission in the area around their local residence. Sexual transmission of Zika is well documented but less common than vector-borne transmission. In California to date, there have been only eight other documented sexually transmitted cases of Zika, accounting for 1% of the total documented cases since 2015. All other cases have been acquired by mosquito transmission during travel to areas with Zika.

Actions Requested of Providers

All patients

- Test for Zika in symptomatic patients with possible recent exposure to the virus.
- Educate about mosquito bite prevention and safe sexual practices during travel to areas with ongoing Zika and on return to the United States.

Pregnant women

- Recommend delaying non-essential travel to areas with active Zika transmission.
- Evaluate for Zika exposure at each prenatal visit.
- If symptomatic with recent possible Zika exposure: test as soon as possible.
- If asymptomatic with ongoing Zika exposure (i.e. currently living in, or frequently traveling to, an area with Zika risk or having ongoing unprotected sexual exposure to a potentially infected partner): offer testing three times in pregnancy using a nucleic acid amplification test (NAAT).
- If asymptomatic with recent but *without ongoing* Zika exposure: consider testing based on risk assessment and shared patient-provider decision making. Routine testing is no longer recommended**. This is a new recommendation**-for further details refer to the updated CDPH testing guidelines.

Preventing Sexual Transmission of Zika

Zika can be sexually transmitted from a person who has Zika to his or her sex partners, even while they are not symptomatic. It is important to counsel patients about reducing the risk of sexual transmission, particularly to pregnant women and to those trying to conceive. The CDC recommendations regarding reducing sexual transmission to pregnant women or those trying to conceive are summarized below. All other guidance regarding reducing sexual transmission can be found in in the CDC document, Clinical Guidance for Healthcare Providers for Prevention of Sexual Transmission of Zika Virus.

Pregnant couples

- If a pregnant woman or her partner travel to a Zika-affected area, the couple should either consistently use condoms, or not have sex, for the entire pregnancy, even if the traveler is asymptomatic.

Non-pregnant couples

- If only the male partner travels: couples should consider using condoms or not have sex, for at least 6 months from male partner's return, start of symptoms or Zika diagnosis, whichever is longest. The 6 months is based on the duration of time that Zika may be identified in the semen.
- If only the female partner travels: the couple should consider using condoms or not have sex for at least 2 months from female partner's return, start of symptoms or Zika diagnosis, whichever is longest.

For Zika Consultation and/or Reporting:

Contact the LAC DPH Acute Communicable Disease Control Program (ACDC):

- Weekdays 8:30 am-5:00 pm call 213-240-7941

- Non-business hours (evenings, weekends and holidays) call 213-974-1234. Ask for the physician on call.

Long Beach Health and Human Services:

- Week days 8-5PM call 562-570-4302
- After hours call 562-435-6711. Ask for Communicable Disease Lead.

Pasadena Public Health Department:

- Weekdays 8am to 5pm (closed every other Friday): Communicable Disease Control Program 626-744-6089
- After hours: 626-744-6043.

Additional Resources on Zika

LAC DPH

- Zika homepage: http://publichealth.lacounty.gov/acd/VectorZika.htm
- Clinician resources: http://publichealth.lacounty.gov/acd/Zika/Provider.htm
- Patient information: http://publichealth.lacounty.gov/acd/Zika/Materials.htm

CDC

- Zika homepage: http://www.cdc.gov/zika
- Clinical Guidance for Healthcare Providers for Prevention of Sexual Transmission of Zika Virus: https://www.cdc.gov/zika/hc-providers/clinical-guidance/sexualtransmission.html
- Update: Interim Guidance for Health Care Providers Caring for Pregnant Women with Possible Zika Virus Exposure — United States (Including U.S. Territories), July 2017: https://www.cdc.gov/mmwr/volumes/66/wr/mm6629e1.htm?s_cid=mm6629e1_w
- World Map of Areas with Risk of Zika: https://wwwnc.cdc.gov/travel/page/world-map-areas-with-zika

This Health Advisory was sent by Dr. Sharon Balter, Director, Acute Communicable Disease Control Program, Los Angeles County Department of Public Health.

To view this and other communications or to sign-up to receive LAHANs, please visit http://publichealth.lacounty.gov/lahan

State of California—Health and Human Services Agency
California Department of Public Health

KAREN L. SMITH, MD, MPH
Director and State Public Health Officer

EDMUND G. BROWN JR.
Governor

Date: December 21, 2017

To: California Health Care Providers

From: California Department of Public Health

Updated Guidance for Health Care Providers: Assessment and Testing for Zika Virus Infection in Pregnant Women and their Newborns

I. **Background:** The impact of Zika virus infection in pregnancy remains a great concern. Pregnant women should have access to Zika virus testing, including testing of asymptomatic pregnant women when appropriate.

Nearly half of all California Zika cases to date have reported travel to Mexico and many others have reported travel to other Central and South American countries. In 2017, Mexico has reported declining numbers of cases and the incidence of new Zika infections in California has substantially declined. These factors together lead to a lower pre-test probability of infection when considering testing pregnant women and their newborns. As of November 24, 2017, 162 pregnant women with travel-associated Zika infection have been reported in California since 2015. Of these, 136 women have had completed pregnancies and 9 infants have been born with microcephaly and other Zika-associated anomalies. More than half of the infants born in California with Zika-associated birth defects were born to Zika-exposed mothers who were asymptomatic for Zika infection.

Based on the changing epidemiology of Zika virus infections in California since 2015, together with input from specialty organizations, CDPH is updating recommendations for the assessment and testing of pregnant women and their newborns for Zika virus infection. These updates align CDPH recommendations with current CDC interim guidance[a,b]. See the CDPH Zika webpage for tools and resources to implement this guidance in California.

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 traditional commercial laboratory resources. Please submit your specimens to commercial laboratories for processing using your regular clinical testing protocol. Local public health laboratories and CDPH conduct confirmatory Zika virus testing as necessary to accurately diagnose and monitor the incidence of Zika virus disease in California.

For questions regarding the application of this updated interim CDPH Zika Guidance in your area, please contact your local health department. CDPH is available to your local health department for consultation as needed.

II. **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[1] of signs and symptoms of Zika virus disease, a travel history to an area with risk of Zika virus transmission[2], and a woman's sexual partner's potential exposure.

A. **Symptomatic Pregnant Women** with possible Zika virus exposure[2] and symptoms (acute onset of fever, rash, arthralgia, or conjunctivitis) of Zika virus disease should be tested for Zika virus as soon as possible:

i. Concurrent Zika virus NAT in serum and urine and IgM antibody testing if 12 weeks or less since symptom onset. If non-negative IgM and Zika virus NAT negative, confirm with plaque reduction neutralization test (PRNT).

B. **Asymptomatic Pregnant Women** *with ongoing*[3] possible Zika virus exposure[2] should be offered:

i. NAT testing on serum and urine three times during pregnancy starting with the initiation of prenatal care and coinciding with prenatal visits. Testing each trimester may be considered.

ii. IgM antibody testing during the first and second trimester may be considered for those with an appropriate exposure history (e.g., exposure limited to current pregnancy), but is not routinely recommended. Prolonged IgM persistence may make it challenging to determine whether the infection occurred during the current pregnancy or prior to the current pregnancy.

iii. Testing should be performed unless woman has prior evidence of laboratory-confirmed Zika virus infection.

C. **Asymptomatic Pregnant Women** with recent *but without ongoing* exposure are not routinely tested but instead should be assessed carefully for factors that increase the likelihood of Zika infection. A patient's risk tolerance and decision-making regarding the pregnancy may be sufficient justification to test for Zika virus infection.

i. 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 a Zika-risk area and unprotected (e.g., without use of male or female condom or dental dam) sexual exposure

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[1] *Screening Pregnant Women for ZIka Testing*, https://www.cdc.gov/zika/pdfs/ZikaPreg_ScreeningTool.pdf

[2] For symptomatic pregnant women/persons, refer to the CDC Areas with Risk of Zika (https://wwwnc.cdc.gov/travel/page/zika-information)

For asymptomatic pregnant women, use the WHO Zika Virus Classification Table (http://www.who.int/emergencies/zika-virus/classification-tables/en/) WHO risk classification "Category 1" countries to help limit the risk of false positive test results.

[3] "Ongoing risk of Zika virus exposure" is defined as follows: Currently living in or frequently (daily or weekly) traveling to an area with Zika virus transmission or having ongoing unprotected exposure to a potentially infected sexual partner.

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 an area 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

ii. When indicated, testing high risk asymptomatic pregnant patients without ongoing exposure should include:

a) Concurrent Zika virus NAT and IgM antibody testing if 12 weeks or less since exposure. If non-negative IgM and Zika NAT negative, confirm with PRNT. Prolonged IgM persistence may make it challenging to determine whether the infection occurred during the current pregnancy or prior to the current pregnancy.

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

i. If amniocentesis is being performed as part of clinical care, NAT testing of amniocentesis specimens should also be performed.

E. **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 infection, as appropriate.**

i. 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.

III. Zika Virus Testing for Pregnant Women at Antenatal and Delivery Hospitalizations

A. **Pregnant women with an exposure history who meet the criteria in II. above and have not yet been tested since last exposure should be evaluated for testing for Zika virus as described.**

IV. Zika Virus Testing for Newborn Infants

A. **Laboratory testing for congenital Zika virus infection is recommended for the following infants:**

   i. Infants born to mothers with laboratory evidence of possible Zika virus infection during pregnancy.

   ii. Infants with clinical findings suggestive of congenital Zika syndrome and possible maternal Zika virus exposure during pregnancy, regardless of maternal testing results.

B. **Newborn specimen collection** should occur *ideally* within the first two days of life.

   i. 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 virus NAT, confirm with PRNT.

   Note: Birth hospitals may consider collecting infant specimens for concurrent Zika virus testing if maternal testing is being done.

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

   iii. 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.

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[a] Adebanjo T, Godfred-Cato S, Viens L, et al. Update: Interim Guidance for the Diagnosis, Evaluation, and Management of Infants with Possible Congenital Zika Virus Infection — United States, October 2017. MMWR Morb Mortal Wkly Rep 2017;66:1089–1099. DOI: http://dx.doi.org/10.15585/mmwr.mm6641a1

[b] Oduyebo T, Polen KD, Walke HT, et al. Update: Interim Guidance for Health Care Providers Caring for Pregnant Women with Possible Zika Virus Exposure—United States (including U.S. territories), July 2017. MMWR Morb Mortal Wkly Rep 2017;66:781–93 DOI: http://dx.doi.org/10.15585/mmwr.mm6629e1

Indications for Zika Testing	RT-PCR (serum, urine, or other)	IgM[1] (serum)
Pregnancy-associated		
Symptomatic[2] pregnant woman *with* travel[3] or sexual[4] exposure history	ASAP Serum & Urine < 12 weeks of onset	Concurrent with PCR
Symptomatic pregnant woman *without* travel or sexual exposure history	Not recommended	Not recommended
Pregnant woman with travel or sexual exposure history and ultrasound evidence of fetal microcephaly and/or calcifications OR fetal loss, regardless of symptom status	ASAP Serum & Urine < 12 weeks after possible exposure (amniotic fluid if amniocentesis preformed)	Concurrent with PCR
Pregnant woman with ongoing exposure (lives in or frequently travels to Zika risk area or ongoing unprotected sexual activity with potentially infected partner)	Serum & Urine Test 3 times during pregnancy	Consider concurrent with PCR but not routinely recommended
Asymptomatic pregnant traveler	Not routinely recommended**	Not routinely recommended
Non–Pregnant Individuals		
Symptomatic individual *with* travel or sexual exposure history	Serum < 2 weeks of onset Urine < 3 weeks of onset	< 12 weeks of onset
Asymptomatic individual *with* travel or sexual exposure history	Not recommended	Not recommended
Asymptomatic traveler with pregnant partner	Not routinely recommended	Not routinely recommended
Traveler with Guillain-Barre Syndrome diagnosis	Not recommended	2-12 weeks after possible exposure
Asymptomatic *without* travel or sexual exposure	Not Recommended	Not Recommended
Infants*		
Infant with microcephaly and/or calcifications, and maternal Zika virus exposure regardless of maternal test results	Serum & Urine (CSF if available***) < 2 DAYS after birth	Concurrent with PCR (CSF if available)
Infant with no apparent defect and evidence of maternal Zika virus infection (IgM), or exposure history and awaiting maternal lab results (PRNT)	Serum & Urine (CSF if available) < 2 DAYS after birth	Concurrent with PCR (CSF if available)
Infant with no apparent defect, and no evidence of maternal Zika virus infection or exposure history	Not Recommended	Not Recommended

* Cord blood is not recommended for testing

[1] With PRNT confirmation specimen sent to State Lab (VRDL)

[2] Two or more of fever, maculopapular rash, arthralgia, non-purulent conjunctivitis

[3] Travel to a Zika risk area within the past 12 weeks

[4] Unprotected sexual contact with a partner who has recently travelled (within 6 months) to a Zika risk area

** Consider based on shared patient-provider decision making and patient preferences after individual risk assessment and pre-test counselling

*** For infants with clinical findings consistent with congenital Zika syndrome, CSF for PCR and IgM should be considered especially if serum & urine are negative and other etiology has not been identified

TABLE 1. Interpretation of results[1] of nucleic acid and antibody[2,3] testing for suspected Zika virus infection — United States (including US territories), 2017

Zika NAT (serum)[4]	Zika NAT (urine)[4]	Zika virus IgM[5]	Zika virus PRNT	Dengue virus PRNT	Interpretation and recommendations
Positive	Positive	Any result	Not indicated	Not indicated	**Acute Zika virus infection**
Negative	Positive	Positive	Not indicated	Not indicated	**Acute Zika virus infection**
Negative	Positive	Negative	Not indicated	Not indicated	**Suggests acute Zika virus infection** *Repeat testing on original urine specimen* • *If repeat NAT result is positive, interpret as **evidence of acute Zika virus infection*** • *If repeat NAT result is negative, repeat Zika virus IgM antibody testing on a serum specimen collected ≥2 weeks after symptom onset or possible exposure or specimen collection date* – *If repeat IgM antibody result is positive,[6] interpret as **evidence of acute Zika virus infection*** – *If repeat IgM antibody result is not positive, interpret as no evidence of Zika virus infection*
Positive	Negative or not performed	Positive	Not indicated	Not indicated	**Acute Zika virus infection**
Positive	Negative or not performed	Negative	Not indicated	Not indicated	**Suggests acute Zika virus infection** *Repeat testing on original serum specimen* • *If repeat NAT result is positive, interpret as **evidence of acute Zika virus infection*** • *If repeat NAT result is negative, repeat Zika virus IgM antibody testing on a serum specimen collected ≥2 weeks after symptom onset or possible exposure or specimen collection date* – *If repeat IgM antibody result is positive,[6] interpret as **evidence of acute Zika virus infection*** – *If repeat IgM antibody result is not positive, interpret as no evidence of Zika virus infection*
Negative	Negative or not performed	Any non-negative result[7]	≥10	<10	**Zika virus infection; timing of infection cannot be determined.** • *For persons without prior Zika virus exposure, a positive IgM result represents recent Zika virus infection*
Negative	Negative or not performed	Any non-negative result[7]	≥10	≥10	**Flavivirus infection; specific virus cannot be identified; timing of infection cannot be determined** • *For persons without prior Zika virus exposure, a positive IgM result represents recent unspecified flavivirus infection*
Negative	Negative or not performed	Any non-negative result[7]	<10	Any result	**No evidence of Zika virus infection**
For areas where PRNT is not recommended[3]					
Negative	Negative or not performed	Positive for Zika virus AND negative for dengue virus	Not performed because PRNT is not recommended		**Presumptive Zika virus infection; timing of infection cannot be determined[8]**
Negative	Negative or not performed	Positive for Zika virus AND positive for dengue virus	Not performed because PRNT is not recommended		**Presumptive flavivirus infection; specific virus cannot be identified; timing of infection cannot be determined[8]**
Negative	Negative or not performed	Equivocal (either or both assays)	Not performed because PRNT is not recommended		**Insufficient information for interpretation** • *Consider repeat testing*
Negative	Negative or not performed	Negative on both assays	Not performed because PRNT is not recommended		**No laboratory evidence of Zika virus infection**

Abbreviations: IgM = immunoglobulin M; NAT = nucleic acid test; PRNT = plaque reduction neutralization test.

1 **Final interpretations of results of Zika virus tests should be performed after all testing is complete.**

2 **Serology test results that indicate flavivirus infection should be interpreted in the context of circulating flaviviruses.**

3 **Currently, PRNT confirmation is not routinely recommended for persons living in Puerto Rico.**

4 **Serum must be submitted for all persons tested for Zika virus infection; a urine specimen for Zika virus NAT testing should always be submitted concurrently with a serum specimen.**

5 **Dengue virus IgM antibody testing is recommended for symptomatic pregnant women, as well as for asymptomatic pregnant women residing in areas where PRNT confirmation is not recommended. For laboratory interpretation in the presence of dengue virus IgM results, refer to https://www.cdc.gov/dengue/clinicallab/laboratory.html.**

6 **Positive results include "positive," "presumptive Zika virus positive," or "possible Zika virus positive." These are examples of assay interpretations that might accompany test results; positive serology terminology varies by assay. For explanation of a specific interpretation, refer to the instructions for use for the specific assay performed. Information on each assay can be found at https://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm#zika under the "Labeling" for the specific assay.**

7 **Non-negative results include "positive," "equivocal," "presumptive positive," or "possible positive." These are examples of assay interpretations that might accompany test results; nonnegative serology terminology varies by assay. For explanation of a specific interpretation, refer to the instructions for use for the specific assay performed. Information on each assay can be found at https://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm#zika under "Labeling" for the specific assay.**

8 **Zika virus IgM positive result is reported as "presumptive positive or flavivirus infection" to denote the need to perform confirmatory PRNT titers against Zika virus, dengue virus, and other flaviviruses to which the person might have been exposed to resolve potential false-positive results that might have been caused by cross-reactivity or nonspecific reactivity. In addition, ambiguous test results (e.g., inconclusive, equivocal, and indeterminate) that are not resolved by retesting also should have PRNT titers performed to rule out a false-positive result. However, PRNT confirmation is currently not routinely recommended for persons living in Puerto Rico.**

ZIKA SCREENING ALGORITHM

APPENDIX I

California Department of PublicHealth

January 2018

FOR CHILDREN AND ADULTS

IS THERE A HISTORY OF POSSIBLE ZIKA EXPOSURE?

Recent travel to an area with risk of Zika virus (see list of areas with risk of Zika virus*)

OR

Recent unprotected sexual contact with:
- A male who has traveled in the past 6 months to an area with risk of Zika virus
- A female who has traveled in the past 8 weeks to an area with risk of Zika virus

NO

Risk of local Zika virus transmission in California is low. However, mosquitoes that can transmit Zika virus are present in some parts of California. If you suspect Zika virus infection in someone without travel or sexual exposure, contact your local health department.

YES

IS THE PATIENT PREGNANT?

YES

DOES OR DID THE PREGNANT PATIENT HAVE SYMPTOM(S) OF ZIKA VIRAL DISEASE?

One or more of the following symptoms within 2 weeks of travel or sexual exposure:
- maculopapular rash
- fever (over 100.4°F/38°C)
- arthralgias
- conjunctivitis

YES

SYMPTOMATIC PREGNANT WOMEN

Concurrent Zika virus NAT in serum and urine and IgM antibody testing if 12 weeks or less since symptom onset. If non-negative IgM and Zika virus NAT negative, confirm with PRNT.

NO

ASYMPTOMATIC PREGNANT WOMEN WITH AN EPISODE OF ZIKA EXPOSURE

- Do not routinely test, but instead assess carefully for factors that increase the likelihood of Zika infection. See **California Updated Guidance** (www.bit.ly/CDPHGuidance) for a list of risk factors to consider.
- A patient's risk tolerance and decision-making regarding the pregnancy may be sufficient justification for Zika virus testing.
- If choosing to test, follow testing instructions for Symptomatic Pregnant Women.

IS ONGOING (DAILY OR WEEKLY) ZIKA EXPOSURE OCCURING?

YES

ASYMPTOMATIC PREGNANT WOMEN WITH ONGOING POSSIBLE ZIKA EXPOSURE

- NAT testing on serum and urine 3 times during pregnancy starting with the initiation of prenatal care. Testing each trimester may be considered.
- IgM testing may be considered concurrent with NAT testing but may lead to difficult interpretation of results depending on exposure history.

California guidance for pregnant patients: www.bit.ly/CDPHGuidance

NO

DOES THE PATIENT HAVE SYMPTOM(S) OF ZIKA VIRAL DISEASE?

One or more of the following symptoms within 2 weeks of travel or sexual exposure:
- maculopapular rash
- fever (over 100.4°F/38°C)
- arthralgias
- conjunctivitis

NO

YES

SYMPTOMATIC INDIVIDUALS

- NAT testing of serum <2 weeks and urine <3 weeks since symptom onset
- IgM antibody testing <12 weeks since symptom onset
- If non-negative IgM and Zika virus NAT negative, confirm with PRNT

Non-pregnant patient guidance: www.bit.ly/CDCZikaLabGuide

ALL PATIENTS WITH EXPOSURE:

- Recommend sexual abstinence (vaginal, anal, oral) or condom use (male or female) for all exposed patients, especially **pregnant couples**
  - >> Males: For at least 6 months after last potential Zika expsoure
  - >> Females: For at least 8 weeks after last potential Zika exposure
- If not pregnant, recommend delay pregnancy for the above periods of time and prescribe effective contraceptive methods
- Advise use of mosquito repellent for 3 weeks after return from an area with risk of Zika
- For counseling recommendations, see: **www.bit.ly/CDPHFamilyPlan**

***AREAS WITH RISK OF ZIKA:** For symptomatic persons, refer to **CDC Areas with Risk of Zika** (www.bit.ly/CDCRiskAreas). For asymptomatic pregnant women, use the **WHO Zika Virus Classification Table** (www.bit.ly/WHOZikaTable) WHO risk classification "Category 1" and "Category 2" countries to help limit the risk of false positive test results. Only Texas and Florida have experienced transmission in the U.S., but transmission is not ongoing at this time.

FOR INFANTS

INFANT ZIKA VIRUS TESTING FOR SUSPECTED CONGENITAL ZIKA VIRUS INFECTION

Indications for testing include maternal exposure history plus any of the following:
- **Maternal laboratory evidence of Zika virus infection**
- **Infant findings consistent with congenital Zika syndrome regardless of maternal test results**

Newborn specimen collection:
- **Zika virus NAT testing on infant serum and urine and Zika virus IgM antibody testing on infant serum. If non-negative IgM and negative Zika virus NAT, confirm with PRNT.**
- **If CSF is collected for other purposes, NAT and IgM antibody testing should be performed on CSF.**
- **For infants with findings consistent with congenital Zika syndrome with unknown etiology, consider CSF for Zika virus NAT and IgM antibodies.**

Birthing hospitals may consider collecting infant specimens for concurrent Zika virus testing if maternal testing is being done: www.bit.ly/CABirthingHospitals

See CDPH guidance for lab testing: **www.bit.ly/VRDLZikaGuidance**
For more Zika information for health professionals, see: **www.bit.ly/CDPHZikaHCPs**
For questions about Zika virus testing or test results, contact your local health department: **www.bit.ly/LHDContactInfo**

www.bit.ly/AlgorithmCDPH
(All links are case sensitive)

PRETEST COUNSELING CONVERSATION GUIDE FOR HEALTHCARE PROVIDERS
FOR PREGNANT WOMEN WITH SYMPTOMS OF ZIKA

This guide describes recommendations for conducting pretesting counseling for symptomatic pregnant women with possible recent exposure (they or their sex partner live in or recently traveled to an area with risk of Zika). Symptoms of Zika include red eyes, fever, joint pain, and rash. CDC recommends testing for pregnant women with symptoms of Zika.This material includes sample scripts to guide discussions with your patients about the complexity of Zika testing and the testing process with patients. Because a lot of content is outlined for discussion, make additional information available to support messaging and ensure that patients understand what they are being told.

Pregnant women coming in for Zika testing may feel worried or anxious. Support them by providing them with clear and easy-to-understand information and expressing empathy by acknowledging their concerns and feelings during pretesting counseling.

Recommendation	Sample Script
Provide the patient with information on why you will be testing them for Zika and a brief overview of what to expect	*Use one of the two following sentences to begin the discussion:* 1. You may be at risk for having Zika since you or your sex partner recently traveled to *(replace "recently traveled to" with "live in" as appropriate)* an area with risk of Zika within the past 12 weeks and you have had *(replace 'have had' with "during your pregnancy you previously had" as appropriate)* symptoms of Zika. OR/AND 2. You may be at risk of having Zika because you recently had sex without a condom with a person who traveled to *(replace "traveled to" with "lives in" as appropriate)* an area with risk of Zika within the past 12 weeks and you have had *(replace 'have had' with "during your pregnancy you previously developed" as appropriate)* symptoms of Zika. Since you may have been exposed to Zika and are experiencing symptoms *(replace "are experiencing" with 'during your pregnancy you previously experienced" as appropriate)*, I think it is best to move forward with testing you for Zika. Before we begin, I would like to tell you what to expect throughout this process.
Patients should be informed that a combination of Zika tests will be required before a final result is determined	You will need a combination of tests to determine whether or not you have Zika. Finding out if you have Zika can require up to three different kinds of tests because the result of one test may require more testing to find out if you recently had a Zika infection. The tests we use to detect Zika can detect other similar viruses often found in the same areas with risk of Zika. Sometimes even after several tests, we may not know which type of virus you were infected with. Each test result is important, because it may help me decide how best to care for you during pregnancy. I want to be sure we take all of the necessary steps to make sure your results are accurate. Each test can take different amounts of time to receive results, which I know can be frustrating. As your healthcare provider I am here to answer any questions you may have. • Reassure the patient that this method of testing is normal • Consider providing the fact sheet *What You Should Know About Zika Virus Testing for Pregnant Women with Symptoms of Zika.*
Let the patient know that you will be ordering two tests; one to look for Zika RNA and one to look for Zika antibodies. Define these terms as they may be unfamiliar	I am going to start the testing process by ordering two tests: • The first test looks for genetic material of Zika virus, known as RNA. RNA can be found in blood and urine. • The second test looks for Zika antibodies, which are proteins that your body makes to fight off a Zika infection. Zika test results can be difficult to interpret. If you've had exposure to Zika virus or another similar virus before this pregnancy, it's possible that you've been infected before, and this could affect today's test results.

Recommendation	Sample Script
Patients should be informed that it can be challenging to understand test results and that previous exposure to Zika could affect their test results	Scientists have learned that Zika antibodies can stay in your blood for several months after infection. Antibodies show evidence that your body fought off a recent Zika infection. It is possible that you may have already developed antibodies against Zika virus if you've lived in or frequently traveled to an area with risk of Zika before becoming pregnant. Because of this, it is possible that your Zika antibody test results may not tell me if you were infected in the past or if you were infected more recently during your current pregnancy. This means if you test positive, we may not know if you are currently infected or not. *Ask the patient if she has any questions before you move forward with providing information on the testing process.*
Inform the patient of what the possible results of the Zika RNA and antibody tests may be	• If your Zika RNA test comes back with a positive result, regardless of your test result for Zika antibodies, it most likely means that you have recently been infected with Zika. • If your Zika RNA test comes back negative and your antibody test is positive, we will need to do one more round of testing to figure out whether or not you actually have or recently had Zika. A positive antibody test may mean that you had Zika but the virus is no longer in your body or it could mean that you had an infection with another similar virus. • If your Zika RNA test and your antibody test are both negative, it means there is no evidence that you have Zika or another similar virus and I will continue evaluating you to find out what may be causing your symptoms. *Ask the patient if they have any questions before you move forward with providing information on step two of testing.*
If the patient requires further testing after the Zika RNA and Zika antibody test, inform the patient and provide them with information on what to possibly expect next.	If you test negative for Zika RNA and your antibody test is positive, I will need to order a third test to confirm whether the antibodies are for Zika or a similar virus. This test takes the longest to receive results because I have to send the results to a specialized lab and then work with the state or local health department to interpret the results. *Ask the patient if they have any questions on what to expect during each step of the testing process.*
Inform patients of each what each test result could mean for their pregnancy.	Now we'll go over what each test result could mean for your pregnancy.
If Zika test results are positive	If you test positive for Zika, I will need to watch your pregnancy more closely. I may do more ultrasounds or other tests to check for your fetus's growth and development.
If Zika test results are not clearly positive or negative	Sometimes test results will not come back as a clear negative or positive. If this happens, I'd rather be more cautious and still do more ultrasounds and other tests to closely monitor your pregnancy.
If Zika test results are negative.	If your test results are negative, I will do an ultrasound to check the growth and development of your fetus and check for any signs of Zika virus infection. If I see any signs of Zika during the ultrasound, then I may order additional tests. If there are no signs of Zika, we will continue with routine prenatal care.

APPENDIX K

INTERIM GUIDANCE FOR ZIKA VIRUS TESTING* OF FORMALIN-FIXED, PARAFFIN-EMBEDDED PLACENTAL, FETAL, OR INFANT AUTOPSY TISSUES†

For completed pregnancies with possible maternal Zika virus exposure § during pregnancy ¶

MATERNAL ZIKA VIRUS TEST RESULTS ON NONTISSUE CLINICAL SPECIMENS (e.g., serum, urine)					
Pregnancy outcome	**Acute Zika virus infection ****	**Zika virus infection; timing of infection cannot be determined ††**	**Flavivirus infection; timing of infection cannot be determined**	**> 12 weeks after symptom onset or exposure,§§ with either negative maternal Zika virus IgM, or no maternal testing conducted**	**No evidence of Zika virus infection ¶¶**
TESTING OF PLACENTAL TISSUES					
Live birth, possible Zika virus–associated birth defects ***	Not indicated †††	Should be considered to aid in maternal diagnosis.			Not indicated †††
Live birth, no obvious Zika virus–associated birth defects at birth	Not indicated	May be considered to aid in maternal diagnosis on a case-by-case and jurisdictional basis. Not routinely recommended for asymptomatic women with possible Zika virus exposure but *without ongoing* possible exposure.			Not indicated
TESTING OF PLACENTAL AND FETAL TISSUES					
Pregnancy loss, possible Zika virus–associated birth defects	May be considered to aid in fetal diagnosis.	May be considered to aid in fetal and maternal diagnosis.			Not indicated †††
Pregnancy loss, no obvious Zika virus–associated birth defects	May be considered to aid in fetal diagnosis.	May be considered to aid in fetal and maternal diagnosis.			Not indicated †††
TESTING OF PLACENTAL AND INFANT AUTOPSY TISSUES					
Infant death following live birth	Should be considered to aid in infant diagnosis.	Should be considered to aid in infant and maternal diagnosis.			Not indicated †††

Abbreviations: IHC = immunohistochemistry; NAT = nucleic acid testing; RT-PCR = reverse-transcription polymerase chain reaction.

* Zika virus testing on formalin-fixed, paraffin embedded tissue specimens is conducted at CDC's Infectious Diseases Pathology Branch (IDPB) and includes Zika virus RT-PCR on placental and fetal/infant tissues. Zika virus IHC may be performed on placental tissues into the second trimester, fetal tissues from any gestational age, and infant autopsy tissues.

† Placental tissues include placental disc, umbilical cord, and fetal membranes. Zika virus RNA can be focal within placental tissues, and testing of three sections of placenta, one section of umbilical cord, and one section of fetal membrane is recommended (https://www.cdc.gov/zika/laboratories/test-specimens-tissues.html). For pregnancy losses and infant deaths, submission of placental tissues in addition to fetal or infant autopsy tissues, if available, is preferred, but if not available will not preclude placental testing.

§ Possible Zika virus exposure includes travel to or residence in an area with risk for Zika virus transmission (https://www.cdc.gov/zika/geo/index.html) during pregnancy or the periconceptional period (8 weeks before conception [6 weeks before the last menstrual period]), or sex without a condom, during pregnancy or the periconceptional period, with a partner who traveled to, or resides in an area with risk for Zika virus transmission. Persons with ongoing possible exposure include those who reside in or frequently travel (e.g., daily or weekly) to an area with risk for Zika virus transmission.

¶ Zika virus testing is not routinely recommended for asymptomatic pregnant women with recent possible Zika virus exposure but ***without ongoing*** possible exposure and who have a fetus or infant without Zika virus–associated birth defects.

** In the event of a confirmed maternal acute Zika virus infection or confirmed congenital Zika virus infection in the infant (e.g., a positive NAT), placental testing from live births is not indicated. Currently, placental testing does not routinely provide additional diagnostic information in the setting of a maternal or infant diagnosis of acute or congenital Zika virus infection, respectively.

†† For women with no possible Zika virus exposure before the current pregnancy, a positive IgM result likely represents acute Zika virus infection, and placental testing is not indicated.

§§ All or part of possible maternal Zika virus exposure, or symptom onset occurred >12 weeks before maternal serum specimen was collected.

¶¶ Includes pregnant women with negative Zika virus NAT and negative Zika virus IgM ≤12 weeks after symptom onset or exposure.

*** Possible Zika virus–associated birth defects that meet the CDC surveillance case definition include the following: brain abnormalities and/or microcephaly, intracranial calcifications, ventriculomegaly, neural tube defects and other early brain malformations, eye abnormalities, or other consequences of central nervous system dysfunction including arthrogryposis (joint contractures), congenital hip dysplasia, and congenital deafness (https://www.cdc.gov/zika/geo/pregnancy-outcomes.html). In all cases, infants or fetuses with possible Zika virus–associated birth defects should also be evaluated for other etiologies of congenital anomalies.

††† Testing may be considered on a case-by-case basis, consult CDC for case-specific questions https://www.cdc.gov/zika/laboratories/test-specimens-tissues.html.

www.cdc.gov/mmwr/volumes/66/wr/mm6629e1.htm?s_cid=mm6629e1_w

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

Instructions for Zika (pregnant mother at time of birth)

Los Angeles County Public Health Laboratories
12750 Erickson Avenue, Downey, CA 90242
After Hours, call County Operator at 213-974-1234 and ask for Dr. Nicole Green (Laboratory Director)

1. Complete Zika epidemiological and test request form and send with specimens
   http://publichealth.lacounty.gov/acd/Diseases/EpiForms/ZikaInfoTestReq.pdf

2. Complete a **test request form for each specimen type**. You will need multiple forms since are several specimen types.

SPECIMEN	GENERAL INSTRUCTIONS	NOTES	STORAGE
Placenta and fetal membranes (fixed)	Several full thickness pieces including **at least 3** full thickness pieces (0.5–1 cm x 3–4 cm in depth) from middle third of placental disk and **at least 1** from the placental disk margin 5 x 12 cm strip of fetal membranes Please include sections of the placental disk, fetal membranes, and pathologic lesions when possible.	Please include information about placenta weight and sample both maternal and fetal side of the placenta Label all specimens to identify location of sample Fix specimens in formalin Volume of formalin used should be about 10x mass of tissue. Place in 10% neutral buffered formalin for a minimum of 3 days. **Order histopathology**	Storage and transport at room temperature for fixed specimens
Umbilical cord	2.5 cm segments of cord **At least 4** specimens Umbilical cord segments should be obtained proximal, middle, and distal to umbilical cord insertion site on the placenta	Label all specimens to identify location of sample. Fix specimens in formalin Volume of formalin used should be about 10x mass of tissue. Place in 10% neutral buffered formalin for a minimum of 3 days **Order histopathology**	Storage and transport at room temperature for fixed specimens
Infant urine	1-5 mL in sterile container (bagged urine transferred to sterile container)	Collection recommended within first 2 days after birth. Specimens collected up to 12 weeks will be tested. **Order PCR**	Store in fridge Transport on cold pack
Infant serum	At least 1mL collected in red top pediatric microtainer tube	Collection recommended within first 2 days after birth. Specimens collected up to 12 weeks will be tested. **Order PCR and serology**	Store in fridge Transport on cold pack

ZIKA TEST REQUEST FORM

APPENDIX M

County of Los Angeles Public Health

Public Health Laboratories
12750 Erickson Avenue
Downey, CA 90242
Phone: 562-658-1330/1300
Fax: 562-401-5999

CA Certified PHL #335637
CLIA #05D1066369

FAILURE TO COMPLETE ALL FIELDS WILL RESULT IN SPECIMEN REJECTION OR DELAYED TESTING

SUBMIT A SEPARATE TEST REQUEST FOR EACH SPECIMEN TYPE

For Zika virus testing eligibility:
www.publichealth.lacounty.gov/acd/Diseases/EpiForms/ZikaEligibility.pdf
For Zika virus testing and notification information:
www.publichealth.lacounty.gov/acd/ZikaTesting.htm

PUBLIC HEALTH LAB USE ONLY

SUBMITTER INFORMATION

Date Submitted				
Requesting Physician Name (Last, First)	Requesting Physician Phone	Requesting Physician Email		
Facility Name	Facility Address (Street)	City	State	Zip
Facility Phone Number	Secure Fax Number For Results Reporting	Contact Person For Specimen and Phone Number		

PATIENT INFORMATION

Patient Name (Last, First, Middle Initial)	Date of Birth (mm/dd/yyyy)	Sex ☐ Male ☐ Female	
Patient Address (Street)	City	State	Zip
Patient Primary Telephone Number	Patient Alternate Phone Number	MRN/Patient ID	

LAB INFORMATION

Specimen Source
☐ Serum ☐ Cord Blood ☐ Amniotic Fluid
☐ Urine ☐ Placenta ☐ Other:_____

Specimen Collection Date/Time (hh:mm AM/PM)
____/____/____ _____:_____ **AM/PM**

Specimen Storage Condition
☐ Refrigerated
☐ Frozen (-20°C)

TEST(S) REQUESTED – Current Lab Testing Algorithms Available at http://www.cdc.gov/zika/laboratories/lab-guidance.html

☐ Arbovirus serology panel (with reflex to confirmatory PRNT or rRT-PCR if required) for Zika, Chikungunya, Dengue, and West Nile Viruses
☐ Arbovirus rRT-PCR (with reflex to serology or PRNT if required) for Zika, Chikungunya, and Dengue Viruses
☐ Immunohistochemistry (fixed tissue or paraffin block)
☐ Histopathology (fixed tissue or paraffin block)
☐ PRNT for Zika/Chikungunya/Dengue/West Nile Virus Confirmation (Previous IgM serology positive result(s) required for PRNT)

CLINICAL INFORMATION

PREGNANCY STATUS

☐ Yes: # Weeks Pregnant _____ OR Estimated Due Date: _____ ☐ Ultrasound Evidence of Microcephaly/Calcification
☐ Not Pregnant ☐ Not Applicable

SYMPTOMS (CHECK ALL APPLICABLE)

☐ Symptomatic: ☐ Fever ☐ Arthralgia ☐ Rash ☐ Conjunctivitis AND Symptom Onset Date: _____
☐ Asymptomatic
☐ Guillain-Barré Syndrome: Onset Date: _____
☐ Other, Specify:

FLAVIVIRUS HISTORY (CHECK ALL PREVIOUS KNOWN VACCINATIONS AND ILLNESS)

☐ Flavivirus History Unknown
☐ Tick-borne Encephalitis ☐ Yellow Fever ☐ Japanese Equine Encephalitis ☐ West Nile Virus ☐ Saint Louis Encephalitis ☐ Dengue

TRAVEL AND EXPOSURE HISTORY

See current areas with Zika transmission at http://www.cdc.gov/zika/geo/active-countries.html

Did patient travel to an area with Zika transmission (including U.S with ongoing local Zika spread) within 14 days of symptom onset? ☐ Yes ☐ No ☐ Unknown
List all cities/countries/areas of travel: _____ Last Date of Travel: _____
Did patient's sexual partner travel to area with Zika transmission (including U.S. with ongoing local Zika spread)? ☐ Yes ☐ No ☐ Unknown
List all cities/countries/areas of travel: _____ Last Date of Travel: _____
Last Date of Unprotected Sexual Intercourse: _____ OR ☐ Unknown
Is the patient an infant with any of the following? ☐ Yes ☐ No
1) ☐ A mother with laboratory evidence of Zika virus infection Specify Mother's Name & Date of Birth:_____
2) ☐ Evidence of microcephaly/other birth defect: _____ **AND** ☐ A mom with recent travel to an area with Zika or had unprotected sex with traveler

Los Angeles County Public Health Department

Laboratory Contact Information for Zika

Please notify the Los Angeles County Department of Public Health when a pregnant woman positive for ZIKA arrives at your hospital. Call 213-240-7941.

For questions regarding **ZIKA specimen collection,** please contact the Los Angeles County Public Health Laboratories:

Business hours, **562-658-1330**
After hours, **213-974-1234** (press # 8)

Remember:

- A separate **ZIKA Test Request Form** must accompany each specimen
- Mother must give consent in advance if the provider wants to collect placental specimens

To arrange courier service and pick up of ZIKA specimens, contact the Public Health Laboratory:

Business hours, **562-658-1460**
After hours, **213-974-1234** (press # 8)

For questions regarding the **Neonate Form**, call **626-569-6508**

THE U.S. ZIKA PREGNANCY REGISTRY
DATA SUBMISSION PROCESS
Neonate Assessment Form

The California Department of Public Health (CDPH) is participating in the U.S. Zika Pregnancy Registry and is the point of contact for California data submission to the Centers for Disease Control and Prevention (CDC).

Who Is Eligible for the Registry?

- Pregnant women in the United States with laboratory evidence of Zika virus infection (positive or equivocal test results, regardless of whether they have symptoms) and periconceptionally, prenatally, or perinatally exposed infants born to these women.
- Infants with laboratory evidence of congenital Zika virus infection (positive or equivocal test results, regardless of whether they have symptoms) and their mothers.

To participate, follow the directions below:

Healthcare Provider Instructions	Local Health Department Instructions
▪ Healthcare providers should contact their Local Health Department (LHD) for questions about data submission. ▪ Providers may be contacted by either the LHD or CDPH for Zika pregnancy and infant outcomes data collection. ▪ Click here for more information on reporting Zika pregnancy and infant outcomes to CDPH.	▪ Local Health Departments may choose to follow up with healthcare providers or ask CDPH staff to follow-up. LHDs should inform CDPH of the LHD preference at: ZikaOutcomes@cdph.ca.gov. ▪ Various methods (e.g., medical record abstraction, telephone interview) can be used to collect surveillance information for the Registry. ▪ LHDs contacting providers to complete the attached form should insert the LHD contact information below for provider submission. ▪ LHDs should ensure completion of the attached form and then submit to CPDH by e-mail or fax as instructed below.

FORM PROCESSING INSTRUCTIONS

Send this form to:

☐ **California Department of Public Health**
Fax: (510) 620-3152
Phone: (510) 620-3151
Email: ZikaOutcomes@cdph.ca.gov (Please send a message for instructions **before** submission).

☑ **My Local Health Department at the address below:**
Los Angeles County Department of Public Health
Children's Medical Services Division
Phone: (626) 569-6508 Fax: (626) 569-1909

Security note:
-Call prior to faxing forms to CDPH or Local Health Department.
*-Please **DO NOT** scan and email documents before receiving instructions.*

HIPAA Privacy Rule permits providers to disclose PHI without authorization to public health authorities for the purposes of preventing or controlling disease.
The CDPH California Birth Defects Monitoring Program (CBDMP) is authorized to conduct studies to investigate the causes of birth defects (H&S section 103840).

California Department of PublicHealth

Reset Form

Neonate Assessment Form

These data are considered confidential and will be stored in a secure database at the Centers for Disease Control and Prevention

Please return completed form via SAMS or secure FTP—request access from ZIKApregnancy@cdc.gov
The form can also be sent by encrypted email to this address or by secure fax to 404-718-1013 or 404-718-2200
Contact Pregnancy & Birth Defects Task Force phone number: 770-488-7100

NAD.1. Infant's State/Territory ID _____	**NAD.2. Mother's State/Territory ID** _____	**NAD.3. DOB:** _____ ☐Live birth ☐Stillbirth ≥20 weeks	**NAD.4. Sex:** ☐ Male ☐ Female ☐ Ambiguous/undetermined
NAD.5. Gestational age at delivery: _____ weeks _____ days	**NAD.6. Based on**: (*check all that apply*) ☐ LMP Date:_____ ☐ 1st trimester ultrasound ☐ 2nd trimester ultrasound ☐ 3rd trimester ultrasound ☐ Other_____		**NAD.7. Maternal age at delivery** ____ years
NAD.8. State/Territory reporting: Select State		**NAD.9. County reporting:** _____	
NAD.10. Delivery type: ☐ Vaginal ☐ Caesarean section **NAD.11.** Delivery complication: ☐ No ☐ Yes **NAD.12.** If yes, please describe: _____		**NAD.13. Arterial cord blood pH** (*if performed*): _____ **NAD.14. Venous cord blood pH** (*if performed*): _____	
NAD.15. Placental exam (based on path report): ☐ No ☐ Yes **NAD.16.** If yes, ☐ Normal ☐ Abruption ☐ Inflammation ☐ Other abnormality (*please describe*)			
NAD.17. Apgar score: 1 min _____ / 5 min _____		**NAD.18. Infant temp** (*if abnormal*): _____ °F **or** _____ °C	

Physical Examination (record earliest measurements taken)

NAD.19. Birth head circumference: _____☐ cm _____☐ in **NAD.20.** ☐ Molding present **NAD.21.** Physican report: ☐ Normal ☐ Abnormal **NAD.22.** HC percentile:_____	**NAD.23. Birth weight:** _____☐ grams _____☐ lbs/oz **NAD.24.** Birth weight percentile: _____	**NAD.25. Birth length:** _____ ☐ cm _____ ☐ in **NAD.26.** Birth length percentile:_____
NAD.27. *Repeat* head circumference: _____☐ cm _____☐ in **NAD.28.** Date performed: _____ *or* Age _____ day(s) **NAD.29.** Physican report: ☐ Normal ☐ Abnormal **NAD.30**. HC percentile:_____	**NAD.31. Admitted to Neonatal Intensive Care Unit:** ☐ No ☐ Yes *If yes,* reason: _____ **NAD.32. Neonatal death:** ☐ No ☐ Yes **NAD.33.** Date: _____ *or* Age at death_____ days **NAD.34.** Cause of death: _____	
NAD.35. Microcephaly (head circumference <3%ile): ☐ No ☐ Yes	**NAD.36. Seizures:** ☐ No ☐ Yes	
NAD.37. Neurologic exam: (*check all that apply*) ☐ Not performed ☐ Unknown ☐ Normal ☐ Hypertonia/Spasticity ☐ Hyperreflexia ☐ Irritability ☐ Tremors ☐ Other neurologic abnormalities **NAD.38.** (*please describe below*)		

Infant's State/Territory ID_____ Mother's State/Territory ID _____

U.S. Zika Pregnancy Registry and Birth Defects Surveillance — Integrated Neonate Assessment Form

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NAD.39. Splenomegaly *by physical exam*: ☐ No ☐ Yes ☐ Unknown **NAD.40.** (*please describe*)	**NAD.41. Hepatomegaly** *by physical exam*: ☐ No ☐ Yes ☐ Unknown **NAD.42.** (*please describe*)	**NAD.43. Skin rash** *by physical exam:* ☐ No ☐ Yes ☐ Unknown **NAD.44.** (*please describe*)

NAD.45. Other abnormalities identified: *please check all that apply*

☐ Fetal Brain Disruption Sequence (collapsed skull, overlapping sutures, prominent occipital bone, scalp rugae)
☐ Encephalocele ☐ Anencephaly/ Acrania ☐ Spina bifida ☐ Holoprosencephaly/arhinencephaly
☐ Microphthalmia/Anophthalmia ☐ Arthrogryposis (congenital joint contractures)
☐ Congenital Talipes Equinovarus (clubfoot) ☐ Congenital hip dislocation/developmental dysplasia of the hip
☐ Other abnormalities

NAD.46. (*please describe below*)

Neonate Imaging and Diagnostics

NAD.47. Hearing screening : (Date:_____) *or* Age _____ day(s)

NAD.48. ☐ Pass ☐ Fail ☐ Inconclusive/Needs retest ☐ Not performed

NAD.49. Please describe

NAD.50. Audiological evaluation: ☐ Not performed ☐ Auditory brainstem response (ABR) test performed ☐ Otoacoustic emisions (OAE) test performed ☐ Acoustic stapedius reflex (ASR) test performed ☐ Unknown

NAD.51. If performed: Date: _____ **NAD.52.** ☐ Normal ☐ Abnormal

NAD.53. Please describe

NAD.54. Retinal exam (with dilation): ☐ Not Performed ☐ Performed ☐ Unknown

NAD.55. *If performed:* (Date: _____) *or* Age _____ day(s)

NAD.56. *please check all that apply:* ☐ Normal

☐ Microphthalmia/Anophthalmia ☐ Coloboma ☐ Cataract ☐ Intraocular calcifications

☐ Chorioretinal atrophy, scarring, macular pallor, gross pigmentary mottling, or retinal hemorrhage, excluding retinopathy of prematurity ☐ Other retinal abnormalities

☐ Optic nerve atrophy, pallor ☐ Other optic nerve abnormalities

NAD.57. (*please describe below)*

NAD.58. Imaging study: ☐ Cranial ultrasound ☐ MRI ☐ CT ☐ Not Performed

NAD.59. (Date: _____) *or* Age _____ day(s)

NAD.60. Findings: *check all that apply* ☐ Normal

☐ Microcephaly ☐ Intracranial calcification ☐ Cerebral / cortical atrophy

Infant's State/Territory ID_____ Mother's State/Territory ID _____

U.S. Zika Pregnancy Registry and Birth Defects Surveillance — Integrated Neonate Assessment Form

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☐ Abnormal cortical gyral patterns (lissencephaly, pachygyria, agyria, microgyria, polymicrogyria, schizencephaly)

☐ Corpus callosum abnormalities ☐ Cerebellar abnormalities ☐ Porencephaly

☐ Hydranencephaly ☐ Moderate or severe ventriculomegaly/hydrocephaly

☐ Fetal Brain Disruption Sequence (collapsed skull, overlapping sutures, prominent occipital bone, scalp rugae)

☐ Other major brain abnormalities

☐ Encephalocele ☐ Holoprosencephaly/ Arhinencephaly

☐ Other abnormalities

NAD.61. (*please describe below*)

NAD.62. Imaging study: ☐ Cranial ultrasound ☐ MRI ☐ CT ☐ Not Performed

NAD.63. (Date: _____) *or* Age _____ day(s)

NAD.64. Findings: *check all that apply* ☐ Normal

☐ Microcephaly ☐ Intracranial calcification ☐ Cerebral / cortical atrophy

☐ Abnormal cortical gyral patterns (lissencephaly, pachygyria, agyria, microgyria, polymicrogyria, schizencephaly)

☐ Corpus callosum abnormalities ☐ Cerebellar abnormalities ☐ Porencephaly

☐ Hydranencephaly ☐ Moderate or severe ventriculomegaly/hydrocephaly

☐ Fetal Brain Disruption Sequence (collapsed skull, overlapping sutures, prominent occipital bone, scalp rugae)

☐ Other major brain abnormalities

☐ Encephalocele ☐ Holoprosencephaly/ Arhinencephaly

☐ Other abnormalities

NAD.65. (*please describe below*)

NAD.66. Imaging study: ☐ Cranial ultrasound ☐ MRI ☐ CT ☐ Not Performed

NAD.67. (Date: _____) *or* Age _____ day(s)

NAD.68. Findings: *check all that apply* ☐ Normal

☐ Microcephaly ☐ Intracranial calcification ☐ Cerebral / cortical atrophy

☐ Abnormal cortical gyral patterns (lissencephaly, pachygyria, agyria, microgyria, polymicrogyria, schizencephaly)

☐ Corpus callosum abnormalities ☐ Cerebellar abnormalities ☐ Porencephaly

☐ Hydranencephaly ☐ Moderate or severe ventriculomegaly/hydrocephaly

☐ Fetal Brain Disruption Sequence (collapsed skull, overlapping sutures, prominent occipital bone, scalp rugae)

☐ Other major brain abnormalities

☐ Encephalocele ☐ Holoprosencephaly/ Arhinencephaly

Infant's State/Territory ID_____ Mother's State/Territory ID _____

U.S. Zika Pregnancy Registry and Birth Defects Surveillance — Integrated Neonate Assessment Form

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☐ Other abnormalities
NAD.69. (*please describe below*)

NAD.70. Was a lumbar puncture performed: ☐ Yes ☐ No ☐ Unknown **NAD.71.** (Date: _____)
or Age _____ day(s)

Postnatal Infection Testing (includes urine culture for CMV)		
NAD.72.	Toxoplasmosis infection:	☐ No ☐ Yes ☐ Unknown
NAD.73.	Cytomegalovirus infection:	☐ No ☐ Yes ☐ Unknown
NAD.74.	Herpes Simplex infection:	☐ No ☐ Yes ☐ Unknown
NAD.75.	Rubella infection:	☐ No ☐ Yes ☐ Unknown
NAD.76.	Lymphocytic choriomeningitis virus infection:	☐ No ☐ Yes ☐ Unknown
NAD.77.	Syphilis infection:	☐ No ☐ Yes ☐ Unknown

NAD.78. If yes for any postnatal infection testing, please describe results:

Postnatal (Infant) Cytogenetic Testing

NAD.79. Cytogenetic Test	**NAD.80. Date:** / **NAD.81. Infant Age:**	**NAD.82. Specimen**	**NAD.83. Test Result**
☐ Karyotype ☐ FISH ☐ CGH microarray ☐ Other, specify _____	_____ **NAD.81. Infant Age:** _____ **months**	☐ Cord blood ☐ Peripheral blood ☐ Tissue ☐ Other, specify _____	☐ Normal ☐ Abnormal ☐ Unknown

NAD.84. Description of cytogenetic test findings (verbatim):

Infant's State/Territory ID_____ Mother's State/Territory ID _____

U.S. Zika Pregnancy Registry and Birth Defects Surveillance — Integrated Neonate Assessment Form

These data are considered confidential and will be stored in a secure database at the Centers for Disease Control and Prevention

NAD.85. Other tests/results/diagnosis (*include dates*):

Birth Defects Diagnosed or Suspected (Include Chromosomal Abnormalities and Syndromes)		
Diagnostic Code	**Certainty**	**Verbatim Description**
	☐Definite ☐Possible/Probable	
	☐Definite ☐Possible/Probable	
	☐Definite ☐Possible/Probable	
	☐Definite ☐Possible/Probable	
	☐Definite ☐Possible/Probable	
	☐Definite ☐Possible/Probable	

Health Department Information

NAD.86. Name of person completing form: _____

NAD.87. Phone: _____

NAD.88. Email: _____ NAD.89. Date of form completion_____

FOR INTERNAL CDC USE ONLY

Mother ID: **State/territory ID:**

Appointment Reminders

Be sure to include your Zika exams during regular well-child visits at:

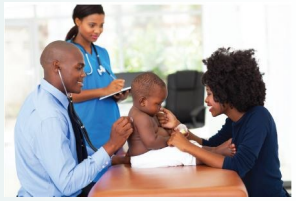
- ❑ **2 months** well-child visit & **Zika exam**
  Date: _____
- ❑ **6 months** well-child visit & **Zika exam**
  Date: _____
- ❑ **12 months** well-child visit & **Zika exam**
  Date: _____
- ❑ **18 months** well-child visit & **Zika exam**
  Date: _____
- ❑ **24 months** well-child visit & **Zika exam**
  Date: _____

Questions or Concerns, Contact:

Los Angeles County
Maternal, Child, Adolescent Health

Call:
(213) 639-6441

Email:
Zika-MCAH@ph.lacounty.gov



County of Los Angeles Public Health

Congratulations on the birth of your baby!

Information for When You Test Positive for the Zika Virus

County of Los Angeles Public Health

Zika Pregnancy Registry

Par. cipate in the free Los Angeles County US Zika Pregnancy Registry.

All women exposed to the Zika virus during pregnancy are encouraged to join.

Purpose of Zika Pregnancy Registry

Every day, we are learning more about how the Zika virus can aff ct babies.

The purpose of the registry is to:

- Learn more about the eff cts of Zika virus infectio during pregnancy
- Learn more about the eff cts of Zika virus on baby's development

Los Angeles County will use this information o help mothers and babies exposed to Zika. All information will be confid nti l.

Learn more about Zika:
http ://www.cdc.gov/zika/

What Should I Expect?

Well-child appointments will be scheduled with your provider. A Zika exam will be performed during these visits at 2, 6, 12, 18, and 24 months.

The Zika exams will monitor your baby's growth and development.

Your baby's doctor will make any needed referrals.

Recordatorios de visitas

Asegúrese de incluir su exámen de Zika durante las visitas de rutina para su bebé a:

- ❑ **2 meses** visita de rutina y **Examen de Zika**
  Fecha: _____
- ❑ **6 meses** visita de rutina y **Examen de Zika**
  Fecha: _____
- ❑ **12 meses** visita de rutina y **Examen de Zika**
  Fecha: _____
- ❑ **18 meses** visita de rutina y **Examen de Zika**
  Fecha: _____
- ❑ **24 meses** visita de rutina y **Examen de Zika**
  Fecha: _____

Si tiene alguna pregunta o problema

Llame al:
(213) 639-6441

O mande un correo electrónico:
Zika-MCAH@ph.lacounty.gov

CONDADO DE LOS ANGELES Salud Pública

¡Felicidades por el nacimiento de su bebé!

Información para mamás expuestas al virus del Zika durante el embarazo

CONDADO DE LOS ANGELES Salud Pública

Registro de casos de Zika en el embarazo

Parti ipe en el registro ***gratuito*** de casos de Zika en el embarazo del condado de Los Angeles.

Se recomienda a todas las mujeres que fueron expuestas al virus del Zika que parĀcipen.

Objetivos del registro de casos de Zika en el embarazo

Cada día aprendemos más sobre cómo el virus del Zika puede afectar a los bebés.

Los objetivo del registro son:

- Aprender más sobre los efecto que puede tener el virus del Zika durante el embarazo
- Aprender más sobre el desarrollo de los bebés nacidos a mujeres infectadas con el virus del Zika durante el embarazo

El condado de Los Angeles usará esta información para ayudar a mamás y bebés que han sido expuestos al virus del Zika.

Informese más sobre el Zika:
hĀps://espanol.cdc.gov/enes/zika/

¿Qué puedo esperar?

Las visitas de rutin del bebé serán programadas con su doctor. Se realizará un examen de Zika durante estas visitas a los 2, 6, 12, 18 y 24 meses.

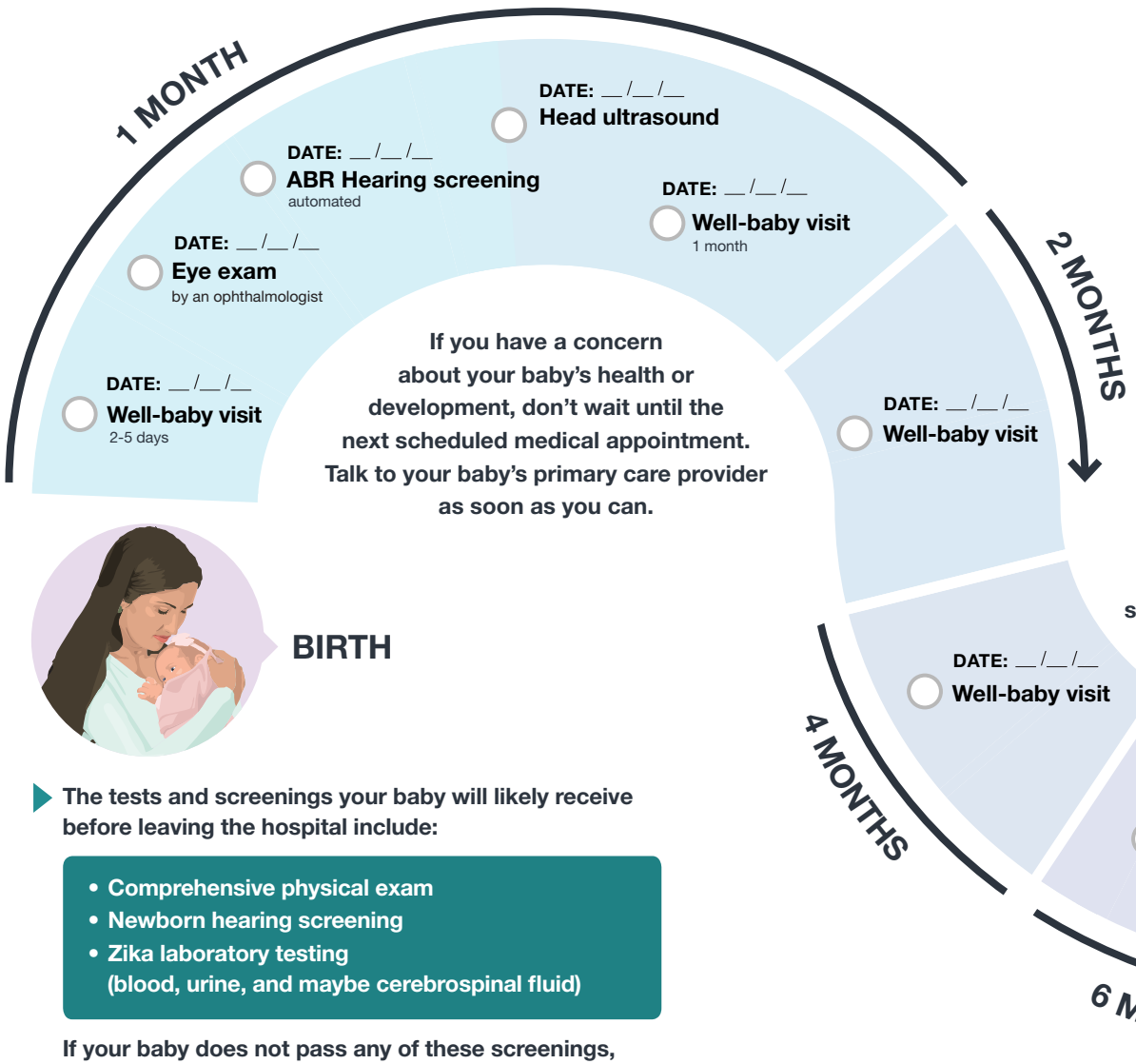
Los exámenes de Zika miden el crecimiento y desarrollo de su bebé.

Si es necesario, el doctor de su bebé la referirá a un especialista.

ROADMAP FOR BABIES WITH CONGENITAL ZIKA INFECTION

This document should be used as a guide to discuss the screening and testing your baby may receive with his or her primary care provider. Each baby is different, and it is possible that your baby may need more tests or fewer tests. This roadmap outlines care for 1) babies who are born with birth defects or other clinical findings related to Zika virus infection during pregnancy 2) babies who test positive for Zika virus infection but may look healthy at birth.

Follow the roadmap to ✓ check off each recommended doctor's visit for the first year of follow up.



BIRTH

- **Routine well-baby visits** include an exam of how your baby is growing and developing, routine immunizations, guidance about what you might expect, and support for mental and social well-being.
- You might be referred to a developmental specialist, family support services, and early intervention services. **Your baby's doctor also might recommend you take your baby to a specialist,** or someone who is an expert in a certain type of medicine. Your baby might be referred to an infectious disease specialist, clinical geneticist, neurologist, or other doctor based on the results of his or her screenings and tests.
- **Talk to your baby's primary care provider about establishing a medical home for your baby.** A medical home is not a place. It is an approach to healthcare that makes sure your baby gets the best, most appropriate services.

- **The tests and screenings your baby will likely receive before leaving the hospital include:**

  - **Comprehensive physical exam**
  - **Newborn hearing screening**
  - **Zika laboratory testing (blood, urine, and maybe cerebrospinal fluid)**

If your baby does not pass any of these screenings, you may be referred for additional follow-up.

APPOINTMENT LOG

Use this table to keep track of your baby's medical appointments.

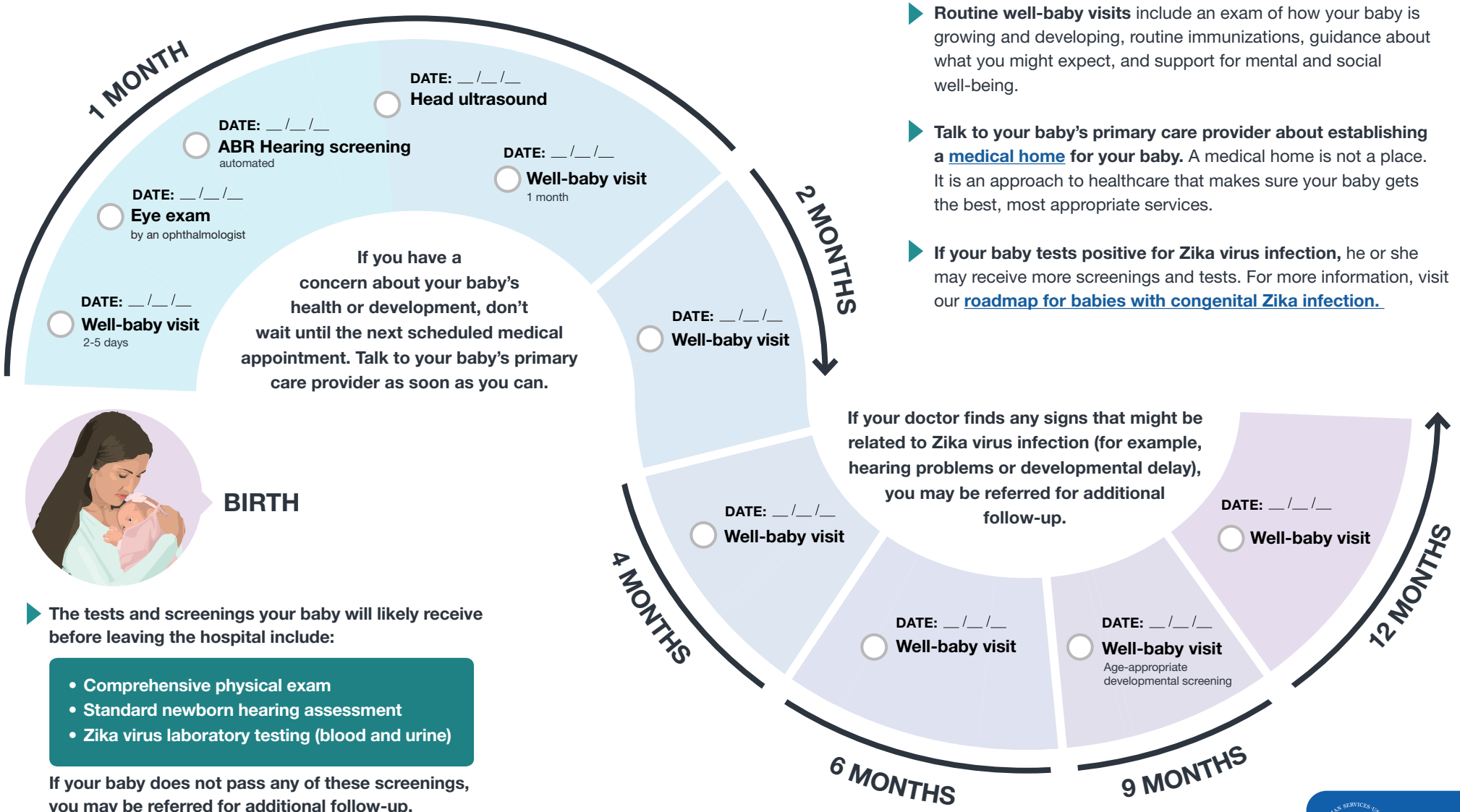
DATE	PROVIDER OR CLINIC	NOTES (Reason for visit, tests performed, care provided, etc.)	NEXT APPOINTMENT DATE	CLINIC PHONE NUMBER

ROADMAP FOR BABIES OF MOTHERS INFECTED WITH ZIKA DURING PREGNANCY WHO APPEAR HEALTHY

This document should be used as a guide to discuss the screening and testing your baby may receive with his or her primary care provider. Each baby is different, and it is possible that your baby may need more tests or fewer tests.

Follow the roadmap to ✓ check off each **recommended** doctor's visit for the first year of follow up.

- **Routine well-baby visits** include an exam of how your baby is growing and developing, routine immunizations, guidance about what you might expect, and support for mental and social well-being.
- **Talk to your baby's primary care provider about establishing a medical home for your baby.** A medical home is not a place. It is an approach to healthcare that makes sure your baby gets the best, most appropriate services.
- **If your baby tests positive for Zika virus infection,** he or she may receive more screenings and tests. For more information, visit our **roadmap for babies with congenital Zika infection.**



- **The tests and screenings your baby will likely receive before leaving the hospital include:**
  - **Comprehensive physical exam**
  - **Standard newborn hearing assessment**
  - **Zika virus laboratory testing (blood and urine)**

If your baby does not pass any of these screenings, you may be referred for additional follow-up.

APPOINTMENT LOG

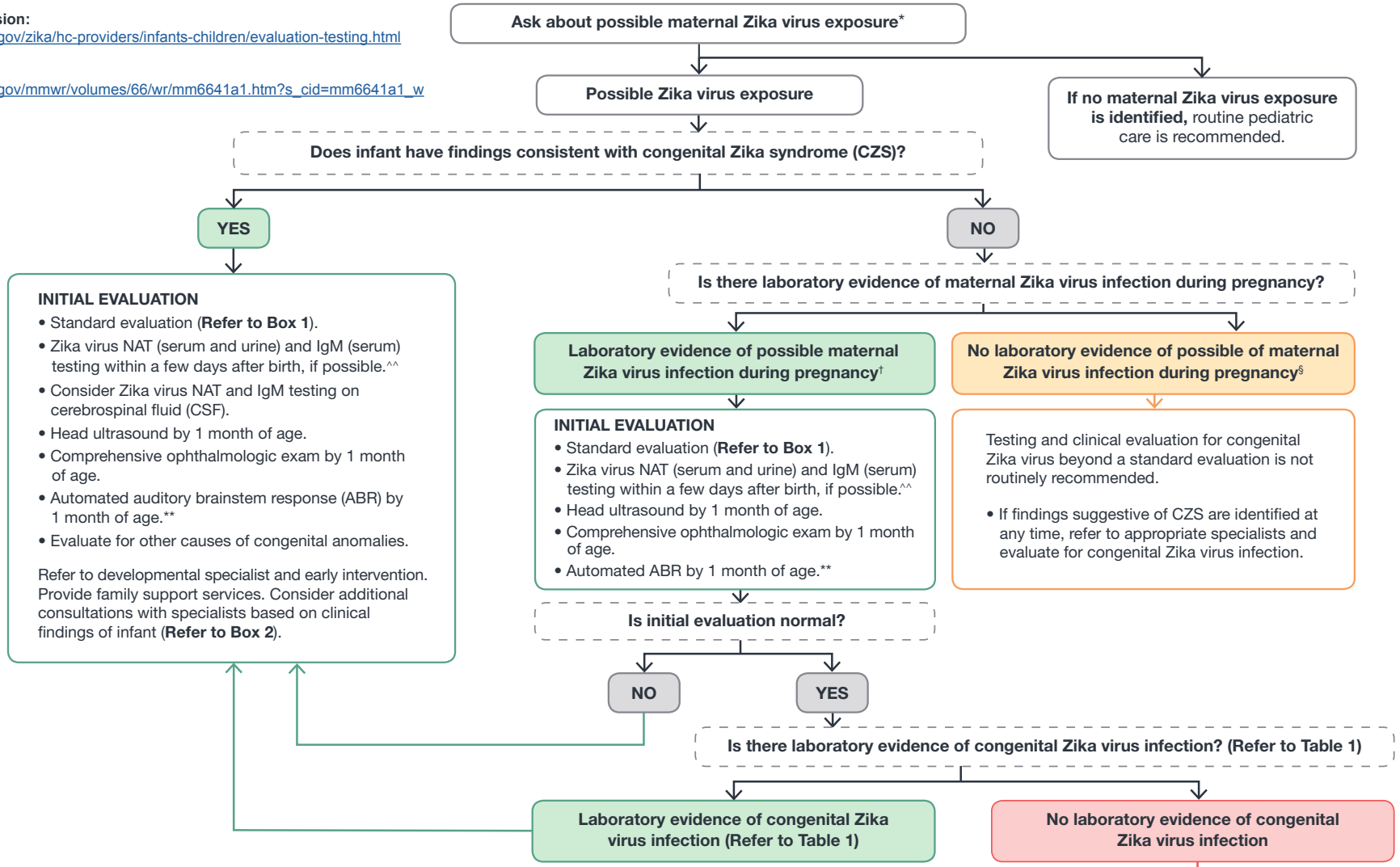
Use this table to keep track of your baby's medical appointments.

DATE	PROVIDER OR CLINIC	NOTES (Reason for visit, tests performed, care provided, etc.)	NEXT APPOINTMENT DATE	CLINIC PHONE NUMBER

EVALUATION FOR INFANTS WITH POSSIBLE CONGENITAL ZIKA VIRUS INFECTION

Accessible Version:
https://www.cdc.gov/zika/hc-providers/infants-children/evaluation-testing.html

MMWR:
https://www.cdc.gov/mmwr/volumes/66/wr/mm6641a1.htm?s_cid=mm6641a1_w



* Possible Zika virus exposure includes travel to, or residence in an area with mosquito-borne Zika virus transmission or sex without the use of condoms with a partner who has traveled to or resides in an area with mosquito-borne Zika virus transmission

† Laboratory evidence of possible Zika virus infection during pregnancy is defined as 1) Zika virus infection detected by a Zika virus RNA NAT on any maternal, placental, or fetal specimen (referred to as NAT-confirmed), or 2) diagnosis of Zika virus infection, timing of infection cannot be determined or unspecified flavivirus infection, timing of infection cannot be determined by serologic tests on a maternal specimen (i.e., positive/equivocal Zika virus IgM and Zika virus PRNT titer ≥10, regardless of dengue virus PRNT value; or negative Zika virus IgM, and positive or equivocal dengue virus IgM, and Zika virus PRNT titer ≥10, regardless of dengue virus PRNT titer). The use of PRNT for confirmation of Zika virus infection, including in pregnant women, is not routinely recommended in Puerto Rico (https://www.cdc.gov/zika/laboratories/lab-guidance.html).

§ This group includes women who were never tested during pregnancy as well as those whose test result was negative because of issues related to timing or sensitivity and specificity of the test. Because the latter issues are not easily discerned, all mothers with possible exposure to Zika virus during pregnancy who do not have laboratory evidence of possible Zika virus infection, including those who tested negative with currently available technology, should be considered in this group.

** Automated ABR by 1 month of age if newborn hearing screen passed but performed with otoacoustic emission (OAE) methodology

^^ If CSF is obtained for other purposes, Zika virus NAT and IgM antibody testing should be performed on CSF.

CS284288 October 19, 2017

TABLE 1

Interpretation of results of laboratory testing of infant's blood, urine, and/or cerebrospinal fluid for evidence of congenital Zika virus infection		
Infant test results*		
NAT	**IgM**	**Interpretation**
Positive	Any result	Confirmed congenital Zika virus infection†
Negative	Nonnegative§	Probable congenital Zika virus infection¶,**
Negative	Negative	Congenital virus infection unlikely ¶,††

Abbreviations: NAT = nucleic acid test; IgM = immunoglobulin M

*Infant serum, urine, or cerebrospinal fluid.

† Distinguishing between congenital and postnatal infection is difficult in infants who live in areas where there is ongoing transmission of Zika virus and who are not tested soon after birth. If the timing of infection cannot be determined, infants should be evaluated as if they had congenital Zika virus infection.

§ Nonnegative serology terminology varies by assay and might include "positive," "equivocal," "presumptive positive," or "possible positive." For explanation of a specific interpretation, refer to the instructions for use for the specific assay performed.

¶ Laboratory results should be interpreted in the context of timing of infection during pregnancy, maternal serology results, clinical findings consistent with congenital Zika syndrome, and any confirmatory testing with plaque reduction neutralization testing.

**A negative Zika virus plaque reduction neutralization test suggests that the infant's Zika virus IgM test is a false positive.

†† Congenital Zika virus infection is unlikely if specimens are collected within the first few days after birth and the clinical evaluation is normal; however, health care providers should remain alert for any new findings of congenital Zika virus infection.

BOX 1. Standard evaluation recommended at birth and during each well visit for all infants with possible congenital Zika virus exposure during pregnancy

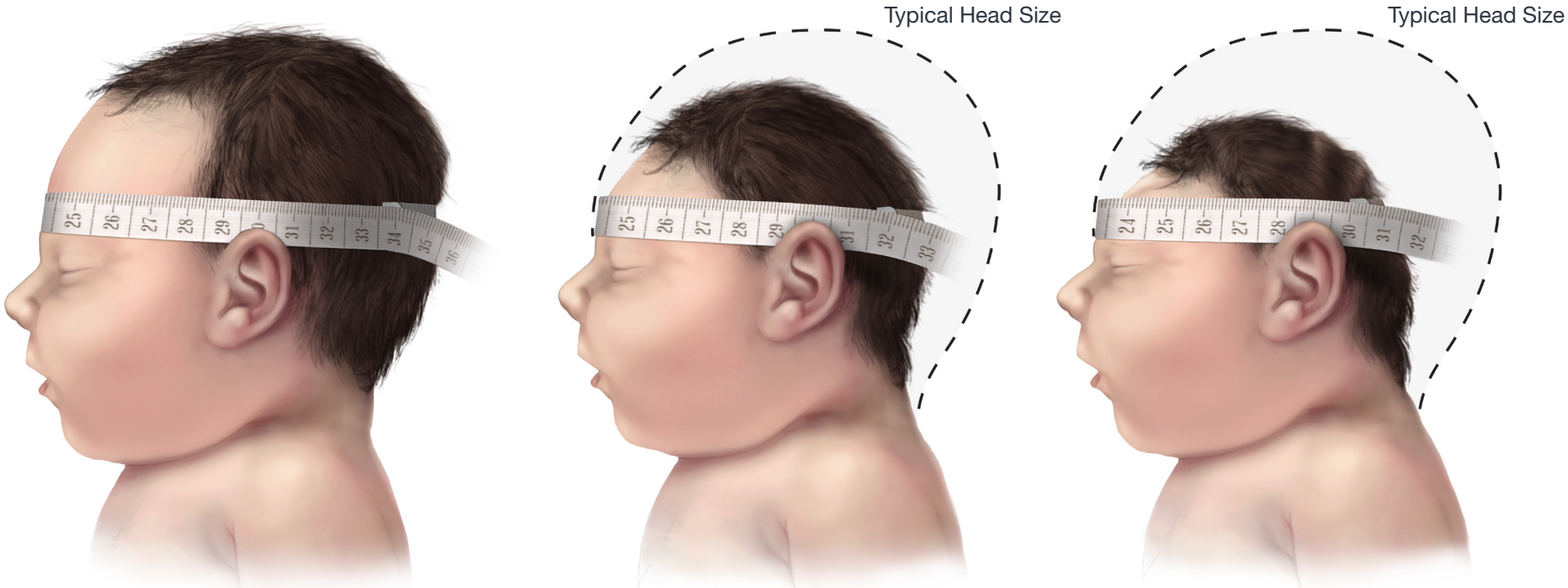
- Comprehensive physical exam, including growth parameters
- Developmental monitoring and screening using validated screening tools recommended by the American Academy of Pediatrics (https://www.aap.org/en-us/advocacy-and-policy/aap-health-initiatives/Screening/Pages/Screening-Tools.aspx)
- Vision screening as recommended by the American Academy of Pediatrics Policy Statement "Visual System Assessment in Infants, Children, and Young Adults by Pediatricians" (www.pediatrics.org/cgi/doi/10.1542/peds.2015-3596)
- Newborn hearing screen at birth, preferably with automated auditory brainstem response

BOX 2. Consultations for infants with clinical findings consistent with congenital Zika syndrome

- **Consider consultation with the following specialists:**
  - Infectious disease specialist for evaluation for other congenital infections (e.g., toxoplasmosis, syphilis, rubella, cytomegalovirus, or herpes simplex virus) and assistance with Zika virus diagnosis, testing, and counseling
  - Neurologist by age 1 month for comprehensive neurologic examination and consideration for other evaluations such as advanced neuroimaging and EEG
  - Ophthalmologist for comprehensive eye exam by age 1 month
  - Clinical geneticist for confirmation of the clinical phenotype and evaluation for other causes of microcephaly or congenital anomalies
  - Early intervention and developmental specialists
  - Family and supportive services
- **Additional possible consultations, based on clinical findings of the infant:**
  - Endocrinologist for evaluation of hypothalamic or pituitary dysfunction and consideration for thyroid testing
  - Lactation specialist, nutritionist, gastroenterologist or speech or occupational therapist for evaluation for dysphagia and management of feeding issues
  - Orthopedist, physiatrist, or physical therapist for the management of hypertonia, clubfoot or arthrogrypotic-like conditions
  - Pulmonologist or otolaryngologist for concerns about aspiration

CDC's Response to **Zika**

MEASURING HEAD CIRCUMFERENCE



Baby with Typical Head Size | **Baby with Microcephaly** | **Baby with Severe Microcephaly**

- Use a measuring tape that cannot be stretched
- Securely wrap the tape around the widest possible circumference of the head
  - » Broadest part of the forehead above eyebrow
  - » Above the ears
  - » Most prominent part of the back of the head
- Take the measurement three times and select the largest measurement to the nearest 0.1 cm
- Head circumference measurements should be taken on the first day of life because commonly-used birth head circumference reference charts by age and sex are based on measurements taken before 24 hours of age

For more information: www.cdc.gov/zika

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

Zika Hospital Toolkit for Los Angeles County. Los Angeles County Department of Public Health, Maternal, Child, and Adolescent Health Programs, Los Angeles, CA. 2018, March 20.