



ZIKA COLLABORATION MEETING: CLINICAL PERSPECTIVE

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DISCLOSURE STATEMENT

- The speakers, the speakers' spouses, and the planning committee have discussed no relationship with a commercial interest that would create a conflict of interest with this presentation.

OVERVIEW

- Zika Virus Disease
 - Transmission
 - Symptoms
 - Surveillance
- Congenital Zika Infections
 - Zika Pregnancy and Infant Registry
 - Clinical Evaluation
 - LDH Resources
- Zika Scenarios

ZIKA VIRUS

- Virus in the family Flaviviridae
- ~80% of infections are asymptomatic
- Those with symptoms are mild
- Hospitalization and death are rare
- Cause of birth defects in infants
- Associated with Guillian-Barré Syndrome

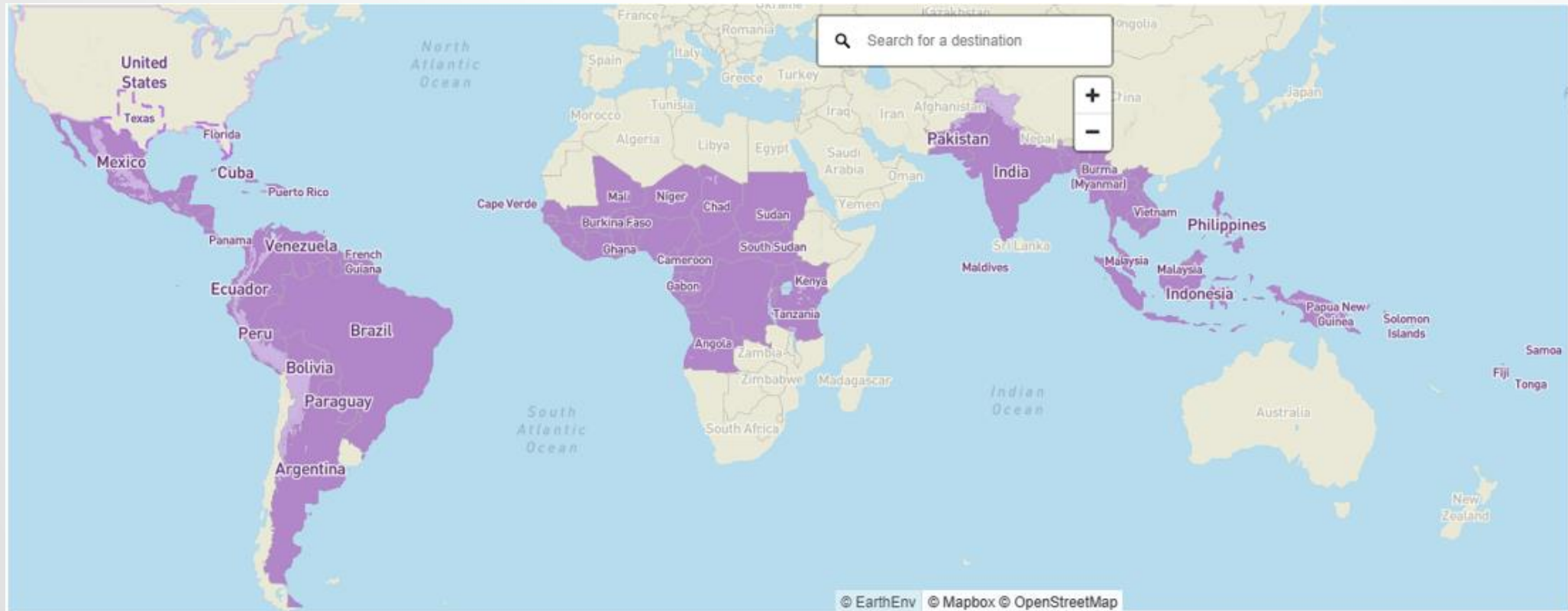
MOSQUITO BITES

- No known animal reservoir in US
 - Maintained in nature through mosquitoes and humans
- Bite of infected *Aedes aegypti* or *Aedes albopictus* mosquito
 - Ae. Aegypti primarily feeds on humans
 - Ae. Albopictus feeds on humans and animals
- Bite in the daytime and nighttime
- Prefer to lay eggs in man-made containers
 - Tires, birds baths, bottle caps

MOSQUITO PREVENTION

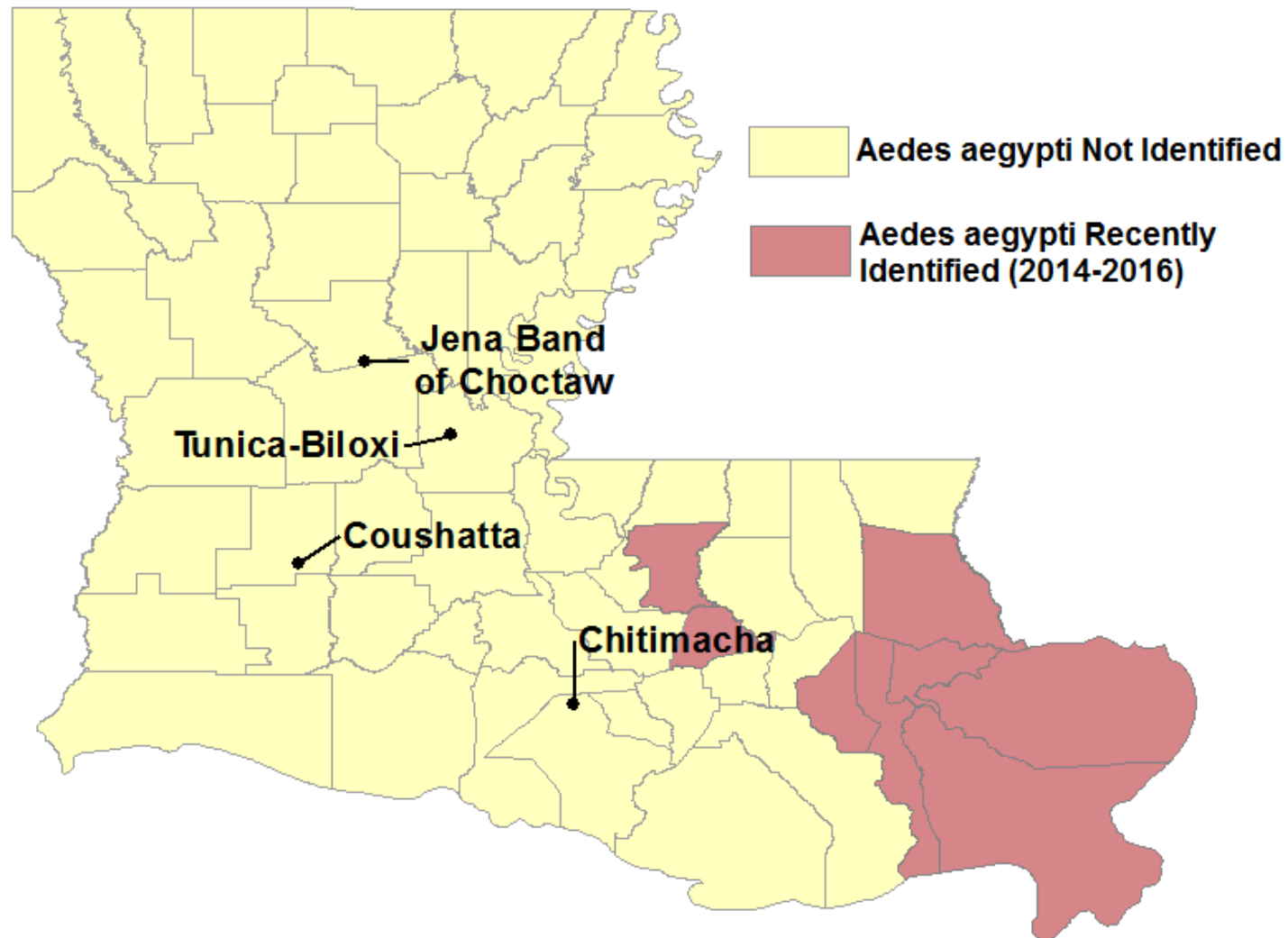
- Wear mosquito repellent and long-sleeved clothing to avoid mosquito bites three weeks after symptom onset or potential Zika exposure

ZIKA WORLD MAP



MOSQUITO POPULATION IN LOUISIANA

- **Ae. albopictus* have been identified in all parishes



MOTHER TO FETUS

- Transmitted vertically from an infected mother during pregnancy
- Infection in utero can cause microcephaly and other birth defects
 - Can be transmitted during any stage of pregnancy
- Virus found in breastmilk, but no reports of transmission

SEXUAL TRANSMISSION

- An infected person can transmit through unprotected sex, regardless of symptom status
 - Asymptomatic
 - Before, during or after symptoms develop
- Virus persists in semen longer than any other bodily fluid
 - Zika RNA has been detected in semen up to 188 days after illness onset
 - Ongoing studies are underway to determine how long Zika persists in genital fluids and how long it can be passed to a sexual partner

PREVENTION

- Men should use condoms or abstain from sex for 6 months after symptom onset or potential Zika exposure
- Women should use condoms or abstain from sex for 8 weeks after symptom onset or potential Zika exposure

BLOOD TRANSFUSION

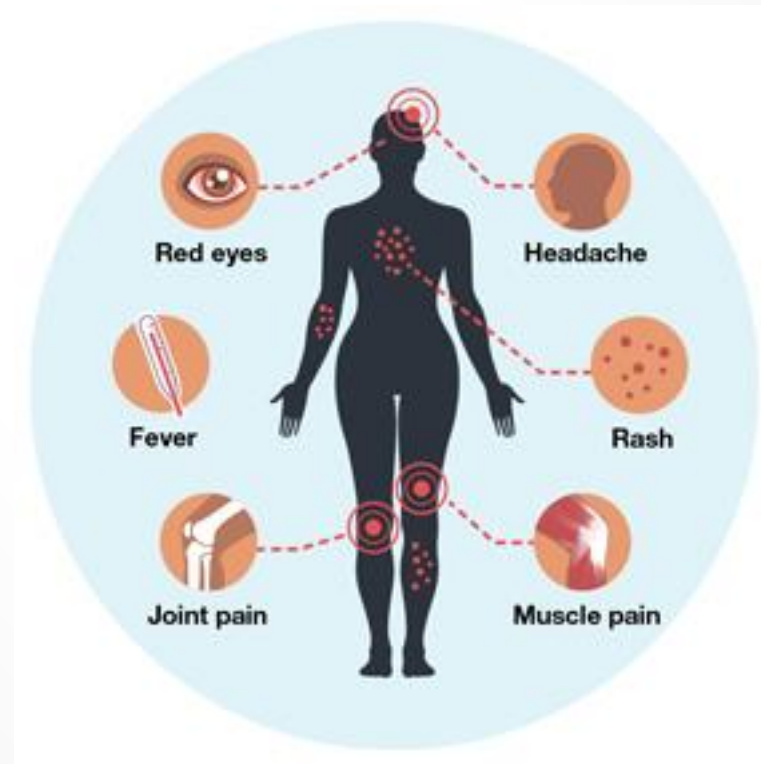
- As of today, no reports in the United States
 - Multiple cases in Brazil; investigation is ongoing
- All donations tested for Zika
- During the French Polynesian outbreak, 2.8% of blood donors tested positive for Zika

ASSOCIATED SYMPTOMS

- Fever
- Rash
- Arthralgia
- Conjunctivitis
- Guillian-Barré Syndrome
- Congenital Zika Syndrome

LOUISIANA'S ZIKA CASE COUNT

- 39 disease cases
 - Rash - 85%
 - Fever – 64%
 - Arthralgia -56%
 - Myalgia – 46%
 - Headache – 38%
 - Conjunctivitis – 28%
- 10 infection cases
 - Asymptomatic



TREATMENT

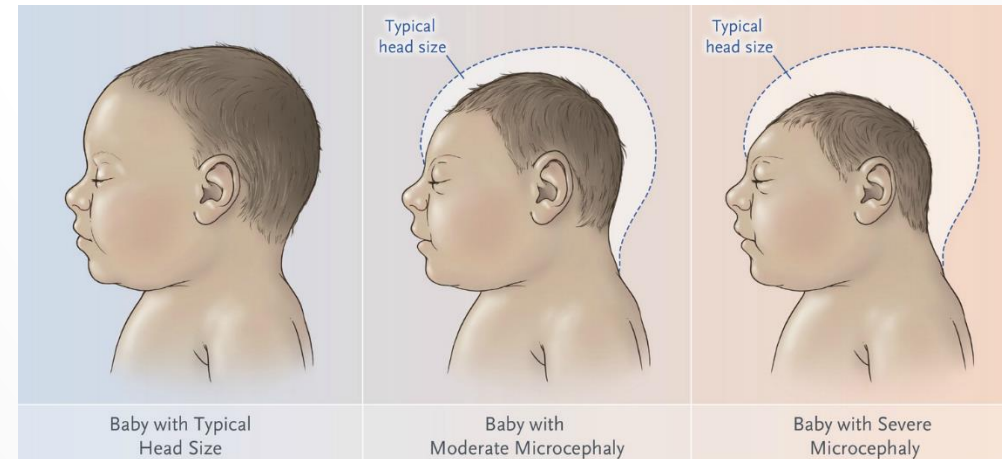
- No specific medicine or vaccine
- Only supportive care
 - Get plenty of rest
 - Drink fluids to prevent dehydration
 - Take medicine such as acetaminophen to reduce fever and pain
 - Do not take aspirin or other NSAIDs until dengue can be ruled out to reduce the risk of bleeding

GUILLAIN-BARRÉ SYNDROME

- Uncommon sickness of the nervous system in which a person's own immune system damages the nerve cells
 - Strongly associated with Zika but a small proportion of people get GBS as a result
- Weakness of the arms and legs
- In severe cases, can affect the muscles that control breathing
- Can last from a few weeks to several months
- Most people fully recover though some have permanent damage
- Very few people die from GBS

CONGENITAL ZIKA SYNDROME

- Pattern of birth defects found among fetuses and babies infected with Zika virus during pregnancy
- Louisiana Birth Defects Monitoring Network (LBDMN) has a list of ICD-9/10 codes to monitor these defects
- Some infants with a congenital Zika infection are born without defects and may experience the birth defects after birth



CONGENITAL ZIKA SYNDROME BIRTH DEFECTS

- Anencephaly/acrania
- Encephalocele
- **Microcephaly**
- Hydrocephaly
- Other CNS anomalies
- Spina bifida all sites with and without hydrocephalus
- Anophthalmia/microphthalmia
- Congenital cataract
- Coloboma of lens, coloboma of iris
- Other congenital malformations of anterior segment of eye
- Congenital malformation of posterior segment of eye
- Congenital malformations of ear causing hearing impairment
- Congenital deformities of the hip
- Talipes equinovarus, clubfoot, NOS; talipes, NOS
- Other congenital deformities of skull, face and jaw, skin
- Arthrogryposis multiplex congenital
- Optic nerve hypoplasia
- Conductive and sensorineural hearing loss
- Other and unspecified hearing loss

MICROCEPHALY

- Less than the 3rd percentile

INTERGROWTH-21st [Home](#) [Manual Entry](#) [Upload](#) [Languages](#) ▾

Newborn Sex:
 Male Female

Gestational age (weeks + days):

Length (cm):

Weight (kg):

Head circumference (cm):

[Compare to standards >](#) [Export](#)

Male 0 + 0 gestational age

Length (cm)

non specified

- z-score: 0.0000
- centile: 0.00

z-score centile

Weight (kg)

non specified

- z-score: 0.0000
- centile: 0.00

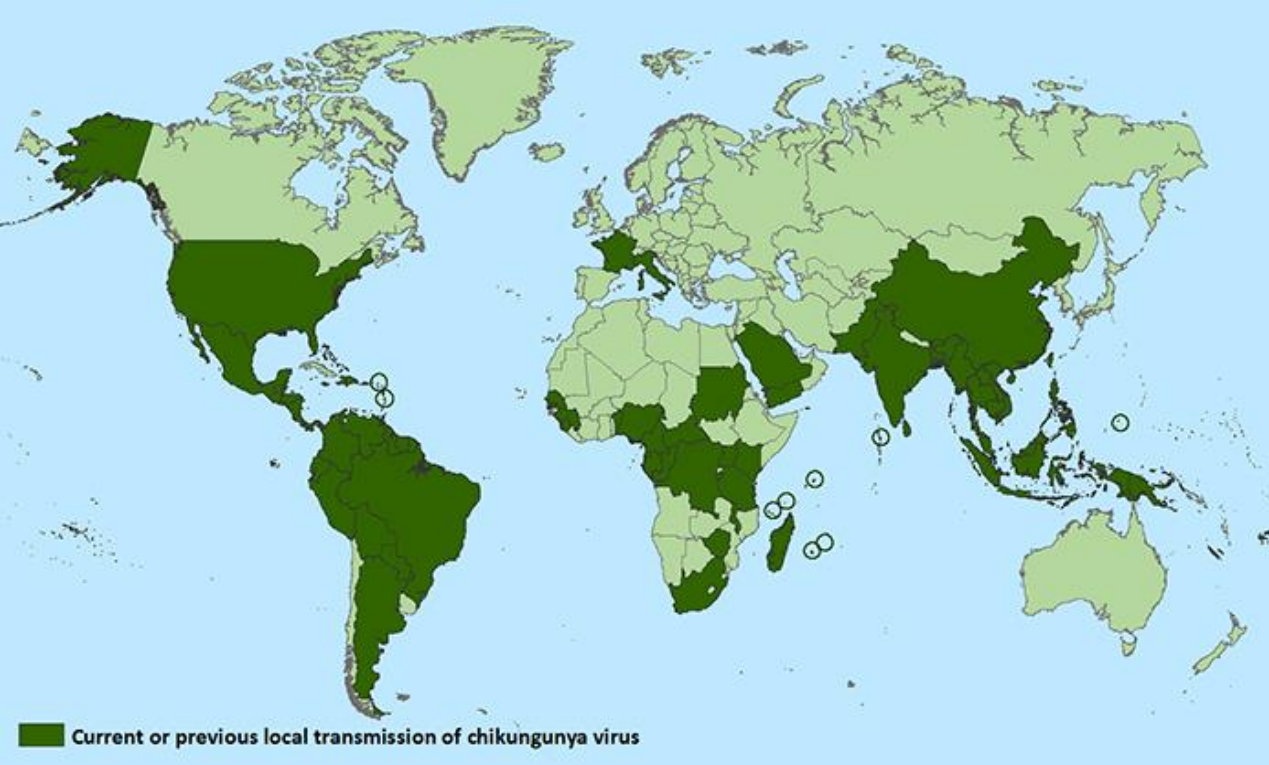
Head circumference (cm)

non specified

- z-score: 0.0000
- centile: 0.00

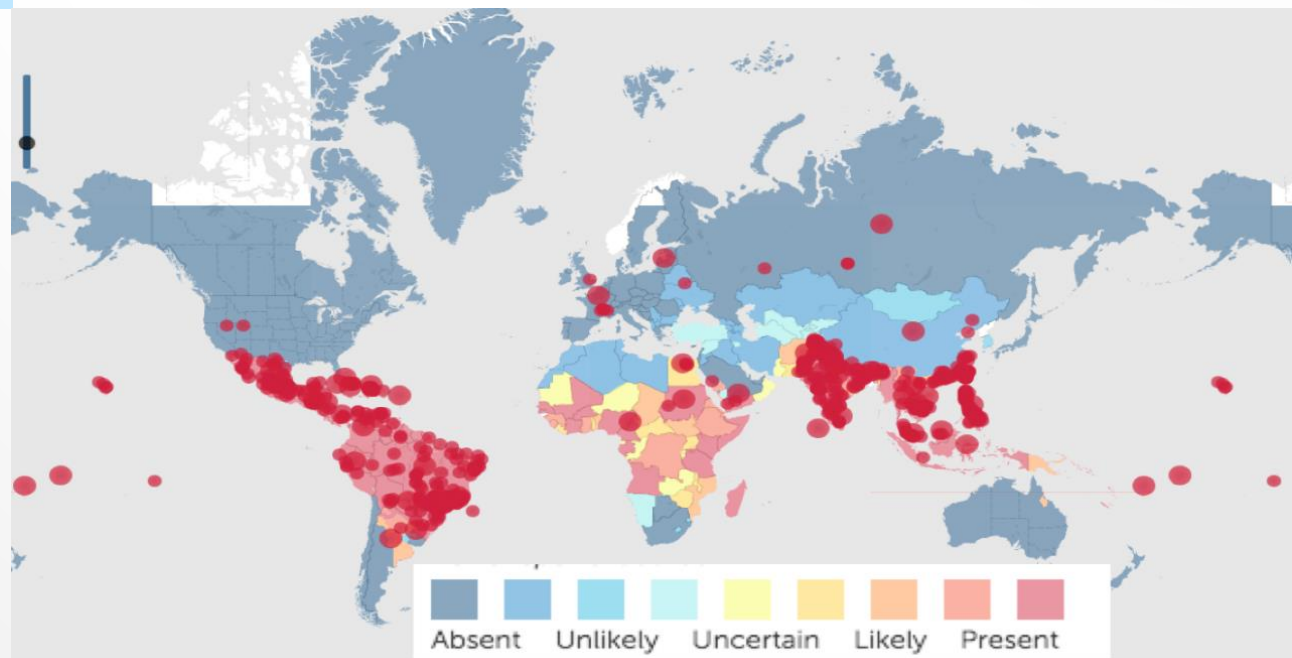
SURVEILLANCE

- Test all pregnant women with a potential Zika exposure
 - Travel to Zika affected area
 - Unprotected sexual contact with someone that traveled to a Zika affected area
- Test all travelers with a potential Zika exposure and one symptom
 - Fever
 - Rash
 - Joint pain
 - Red eyes
- Test for Chikungunya and Dengue viruses



Chikungunya Distribution

Dengue Distribution



COMPARISONS OF SYMPTOMS

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

ENHANCED SURVEILLANCE FOR LOCAL TRANSMISSION IN LOUISIANA

- Expect to identify local transmission through a symptomatic patient
 - In Miami-Dade, index case was a pregnant woman with fever, rash, and arthralgia
- Statewide
 - Patients with complaint of three Zika Symptoms
- Parishes that have identified *Ae. aegypti* mosquitoes
 - Parishes with complaint of two Zika symptoms
- Also test for WNV at OPH Lab

ID EPI ZIKA VIRUS DISEASE SUPPLEMENTAL FORM

Patient Name: Last: _____ First: _____

Date of Birth: _____ Gender: Male Female Pregnant, if yes: Gestational Weeks: _____

Ordering Provider: _____ Phone: _____

Ordering Facility: _____ Fax: _____

MRN: _____

<input type="checkbox"/> Asymptomatic <input type="checkbox"/> Symptomatic, Onset Date: _____ <input type="checkbox"/> Fever <input type="checkbox"/> Rash <input type="checkbox"/> Arthralgia <input type="checkbox"/> Conjunctivitis <input type="checkbox"/> Guillain-Barré Syndrome (GBS)* <input type="checkbox"/> Birth Defect: <input type="checkbox"/> Other:	<p style="text-align: center;">Travel: <input type="checkbox"/> Yes <input type="checkbox"/> No</p> Area: _____ Travel Dates: _____ Travel Reason: _____ <p style="text-align: center;">Sexual Partners with Travel to Affected Area</p> Area: _____ Travel Dates: _____ Date of Last Unprotected Sex: _____
FOR ID EPI USE ONLY Testing Approved: <input type="checkbox"/> Yes <input type="checkbox"/> No Reason: _____ Epidemiologist: _____ Date: _____	

Patient Information:

Race: White Black Asian Other: _____ Hispanic/Latino: Yes No

Language: English Spanish Other: _____

Street Address: _____

City: _____ Zip Code: _____

Parish: _____ Phone: _____

<p style="text-align: center;">Previous Infections</p> Dengue: <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown Chikungunya: <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown West Nile Virus: <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown	<p style="text-align: center;">Previous Vaccinations</p> Yellow Fever: <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown Japanese Encephalitis: <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown Tickborne Encephalitis: <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unknown
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*If GBS is suspected, collect: history and physical, CSF chemistry (WBC differential, glucose, & Protein), any labs (including negative bacteria and viruses) & recent neurology consult

PLEASE FAX THIS COMPLETED FORM TO (504) 568-8290 BEFORE SUBMITTING TO THE LAB.
 IF THERE ARE ANY ADDITIONAL QUESTIONS, PLEASE CONTACT EPI AT (800) 256-2748

Instructions for Collecting and Shipping Arboviral Samples

MUST HAVE APPROVAL FROM ID EPI BEFORE SHIPMENT

Serum: REFRIGERATE samples at 2-8°C†

- Draw blood in a serum separator tube. Follow manufacturer instructions for clot and centrifuge times.
- Aliquot at least 2 mL of serum off the clot and store in a sterile, screw cap tube. Refrigerate at 2-8°C.
- Complete [Lab Form 96](#).

Urine: REFRIGERATE samples at 2-8°C

- Submit at least 2 mL of urine in a sterile, screw cap tube. Refrigerate at 2-8°C.
- Complete [Lab Form 96](#).
- Must be paired with serum.

CSF: REFRIGERATE samples at 2-8°C

- Collect at least 2 mL of CSF in a sterile, screw cap tube. Refrigerate at 2-8°C.
- Complete [Lab Form 96](#).
- Zika IgM and JCV IgM samples must be paired with serum.

When testing for Zika, dengue testing should also be performed. Dengue IgM samples have to be received at OPH Lab within 48 hours of collection. Collection of serology samples on Fridays is not recommended. Outstanding samples will be rejected for Dengue IgM testing.

Each specimen should be labeled with:

- Patient name
- Date of birth
- Medical record or Chart number
- Date and time of collection
- Specimen source

All fields marked with bold print on [Lab Form 96](#) should be completed.

Select "Arbovirus Panel" under Specimen Information. The tests performed will be determined by specimens collected and epidemiologic criteria.

KEEP SPECIMENS REFRIGERATED AT 2-8°C AND SHIP TOGETHER

- Place samples in an insulated container and ship with [Lab Form 96](#).
- Ship specimens with 2 frozen ice packs, top and bottom, but wrapped in a thick barrier (i.e., bubble wrap or thick pads) to avoid direct contact.
- Ship to Attn: Virology Office of Public Health Laboratory
1209 Leesville Ave
Baton Rouge, LA 70802
(225) 219-5263

A secure fax form should be completed to receive the results directly. Please contact ID Epi for a form.

PERSISTENCE IN SERUM

- Virus
 - Detectable up to 2 weeks
- IgM Antibodies
 - Persist between 2-12 weeks after symptom onset or exposure
 - May persist longer in pregnant women
- Neutralizing Antibodies
 - Persist for many years

DIAGNOSTIC TESTS AT OPH LAB

- Molecular testing
 - Triplex RT-PCR
 - Very sensitive and specific test
 - Able to “time” infection
- Serologic testing
 - CDC Zika IgM MAC-ELISA
 - Cross reactivity with other flaviviruses
 - Unable to “time” infection
 - InBois DENV Detect IgM Capture ELISA
 - Genway Anti-Chikungunya Virus IgM Human μ -capture ELISA

LAB INTERPRETATION

- RT-PCR positive, confirmed Zika infection
- RT-PCR negative, no evidence of a Zika infection

- IgM positive, probable Zika infection
- IgM equivocal, possible Zika infection
- IgM negative, no evidence of a Zika infection
 - All non-negative results require additional testing

DIAGNOSTIC TESTS AT CDC

- Plaque Reduction Neutralization Test (PRNT)
 - More sensitive serologic test
 - Unable to “time” infection
 - Always ran against Dengue 1 & 2
- Zika ≥ 10 & Dengue < 10 , confirmed Zika infection
- Zika ≥ 10 & Dengue ≥ 10 , probable Zika infection
- Zika < 10 & Dengue < 10 , no infection

ZIKA PREGNANCY AND INFANT REGISTRY

- A surveillance system used to monitor outcomes of pregnancies among women with laboratory evidence of Zika virus infection and the infants born to these women in the US states, DC and US territories (excluding Puerto Rico)
- The data collected will provide additional, more comprehensive information to complement notifiable disease case reporting and will be used 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

PROVIDER FOLLOW-UP

- Obstetric and pediatric healthcare providers
 - Initial identification
 - During pregnancy
 - At delivery
 - Infant at 2, 6, 12, 18 & 24 months
 - Able to differentiate between maternal and infant antibodies ≥ 18 months

FUTURE OF THE ZIPR

- No longer entering new cases that have not had a pregnancy outcome by March 31, 2018
- LA will continue to follow pregnancies up until pregnancy outcome
 - Infant follow-up depends on clinical information at time of birth

EVALUATIONS RECOMMENDED AT BIRTH AND EACH WELL BABY VISIT

- Comprehensive physical exam, including growth parameters
- Developmental monitoring and screening using validated screening tools recommended by the American Academy of Pediatrics (AAP)
 - <https://www.aap.org/en-us/advocacy-and-policy/aap-health-initiatives/Screening/Pages/Screening-Tools.aspx>
- Vision screening as recommended by AAP
 - <http://pediatrics.aappublications.org/content/137/1/e20153596>
- Newborn hearing screen at birth, preferably with automated auditory brainstem response

INFANTS WITH CLINICAL FINDINGS CONSISTENT WITH CONGENITAL ZIKA SYNDROME

- Infectious disease specialist
- Neurologist by age 1 month
- Ophthalmologist by age 1 month
- Clinical geneticist
- Early intervention and developmental specialists
- Family and supportive services

TABLE. Population-based counts of cases of infants and fetuses with birth defects potentially related to Zika virus infection and prevalence per 1,000 live births — 15 U.S. jurisdictions,* 2016

Characteristic	Brain abnormalities or microcephaly [†] (N = 1,457; 49%)	Neural tube defects and other early brain malformations [§] (N = 581; 20%)	Eye abnormalities [¶] (N = 262; 9%)	Consequences of CNS dysfunction ^{**} (N = 662; 22%)	Total (N = 2,962; 100%)
Prevalence per 1,000 live births (95% CI)	1.5 (1.4–1.6)	0.60 (0.55–0.65)	0.27 (0.24–0.30)	0.68 (0.63–0.74)	3.0 (2.9–3.2)
Eye abnormalities No. (%)	144 (9.9)	24 (4.1)	—	0	430 (14.5)
Consequences of CNS dysfunction No. (%)	133 (9.1)	77 (13.3)	12 (4.6)	—	884 (29.8)
Pregnancy outcome^{††}					
Live births No. (%)	1,387 (95.2)	427 (73.5)	257 (98.1)	645 (97.4)	2,716 (91.7)
Neonatal death (≤28 days) No.	89	92	8	30	219
Pregnancy loss ^{§§} No. (%)	65 (4.5)	149 (25.6)	5 (1.9)	16 (2.4)	235 (7.9)
Zika virus laboratory testing for infants or mothers					
Positive No. (%)	29 (2.0)	4 (0.69)	10 (3.8)	2 (0.30)	45 (1.5)
Negative No. (%)	65 (4.5)	20 (3.4)	3 (1.1)	8 (1.2)	96 (3.2)
No testing performed/NA ^{¶¶} No. (%)	1,363 (93.5)	557 (95.9)	249 (95.0)	652 (98.5)	2,821 (95.2)

Abbreviations: CI = confidence interval; CNS = central nervous system; NA = not available.

* 15 U.S. jurisdictions: Florida (selected southern counties), Georgia (selected metropolitan Atlanta counties), Hawaii, Iowa, Illinois, Massachusetts, New Jersey, New York (excluding New York City), North Carolina (selected regions), Puerto Rico, Rhode Island, South Carolina, Texas (Public Health Regions 1, 3, 9, and 11), Utah, and Vermont. Total live births = 971,685.

[†] Brain abnormalities or microcephaly (congenital microcephaly [head circumference <3rd percentile for gestational age and sex], intracranial calcifications, cerebral atrophy, abnormal cortical gyral patterns [e.g., polymicrogyria, lissencephaly, pachygyria, schizencephaly, gray matter heterotopia], corpus callosum abnormalities, cerebellar abnormalities, porencephaly, hydranencephaly, ventriculomegaly/hydrocephaly [excluding “mild” ventriculomegaly without other brain abnormalities], fetal brain disruption sequence [collapsed skull, overlapping sutures, prominent occipital bone, scalp rugae], other major brain abnormalities).

[§] Neural tube defects and other early brain malformations (anencephaly/acrania, encephalocele, spina bifida, and holoprosencephaly).

[¶] Structural eye abnormalities (microphthalmia/anophthalmia, coloboma, cataract, intraocular calcifications, and chorioretinal anomalies [e.g., atrophy and scarring, gross pigmentary changes, excluding retinopathy of prematurity]); optic nerve atrophy, pallor, and other optic nerve abnormalities.

^{**} Consequences of CNS dysfunction (arthrogryposis, club foot with associated brain abnormalities, congenital hip dysplasia with associated brain abnormalities, and congenital sensorineural hearing loss).

^{††} 11 unknown pregnancy outcomes not included.

^{§§} Includes miscarriages, fetal deaths, and terminations.

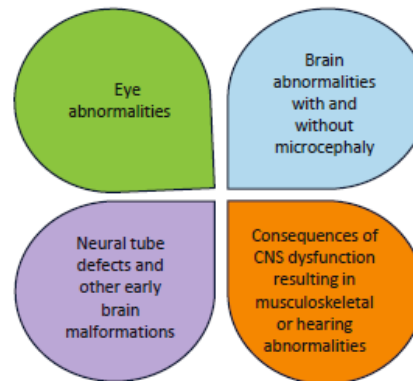
^{¶¶} Includes cases linked to lab data where no testing was performed or there was unknown testing status.

ZIKA BIRTH DEFECT SURVEILLANCE REPORTING: The Provider's Role

The role of the Provider is to help with access to medical health data for mothers and infants.

If you have a patient with a condition that fits into one of the four broad categories of anomalies to the right, you may receive a request from the Louisiana Birth Defects Monitoring Network (LBDMN) to access medical record data.

1. You will be contacted by a Data Collection Specialist (DCS) from LBDMN.
2. The DCS will make arrangements with you to share a patient's record based on your practice's preferences and your medical record release and storage policies.
3. For the most recent ICD-10 coding updates, please visit cdc.gov/nchs/icd/icd10cm.htm.



The role of public health is Zika-related birth defects data abstraction, surveillance, & mandated reporting.

1. **Louisiana Birth Defects Monitoring Network**
 - Collects data on all birth defects in Louisiana.
 - Contacts private providers if, during the abstraction process, data are found to be missing.
 - Sends monthly required reports to the Centers for Disease Control and Prevention (CDC).
2. **Infectious Disease Epidemiology Program (ID Epi)***
 - Extracts all Zika case data from LBDMN and maintains a Zika Pregnancy Registry (ZPR).
 - Tracks infants who test positive for Zika for two years to ensure diagnostics and screening are performed.
 - Provides a helpline for clinicians: (800) 256-2748.

*ID Epi is in the Louisiana Department of Health, Bureau of Infectious Disease

DATA SHARING: How does it help?

- By agreeing to data-share, you are facilitating early and fast reporting. This means early referral to care, needed resources, and follow-up for your patients.
- In the event of a Zika outbreak, early reporting facilitates and strengthens the state's response.
- The most up-to-date Zika clinical guidelines from CDC can be found at the Zika Healthcare Provider portal at cdc.gov/zika/hc-providers/index.html.



ABOUT THE LOUISIANA BIRTH DEFECTS MONITORING NETWORK

The Louisiana Birth Defects Monitoring Network (LBDMN) is part of the Louisiana Department of Health, Office of Public Health, Bureau of Family Health. LBDMN's mission is to prevent birth defects and birth defect-related disabilities in Louisiana's children through active surveillance, referral to services, and preventative education.

To learn more about the program, please visit ldh.la.gov/lbdmn.

KEY POINTS

- All pregnant women should be screened at all OB visits
 - Testing asymptomatic pregnant women is no longer routinely recommended due to limitations of IgM
- Arboviral panel should be considered when testing for Zika
- Louisiana is conducting enhanced surveillance for local transmission
- 3 of 1,000 pregnancies resulted in a birth defect
- LDH has resources for families affected by Zika

QUESTIONS?

ZIKA SCENARIO # 1

- 25 year old male comes to health clinic with complaints of a fever and headache. His symptoms began three days ago and he wants to be tested for Zika. He has not traveled outside of Louisiana in the past year.
 - Does this patient qualify for Zika testing?
 - What are the criteria for enhanced surveillance of Zika?
 - What other questions should he be asked?

ZIKA SCENARIO #1

- You ask the patient his sexual history and he states that his wife traveled to Honduras two weeks ago and that they have had unprotected three times since she has returned.
 - Does this patient now qualify for testing?
 - What other arboviruses should you test for?
 - What would you offer as treatment for his symptoms?

ZIKA SCENARIO #2

- A 37 year old woman comes in for her first obstetric visit after finding out that she is pregnant. She is 14 weeks gestation.
 - Do you screen this patient for Zika?
 - What questions should you ask her?
- You find out that she traveled to Brazil six weeks ago and developed a rash on her abdomen shortly after she returned home, but it resolved on its own.
 - Does she qualify for Zika testing?
 - Should she have molecular (RT-PCR) or serologic (IgM) testing performed?

ZIKA SCENARIO #2

- Her Zika results are in: she is RT-PCR negative and IgM positive.
 - Does she have Zika?
 - Why are we not sure?
- Her PRNT results are in: Zika ≥ 10 & Dengue < 10
 - Does she have Zika?
 - Is she entered into the Zika Pregnancy Registry? (Assuming she gives birth before March 31, 2018)

ZIKA SCENARIO #2

- She delivers a baby boy at 39 weeks gestation. His birth length is in the 47th percentile, his birth weight is in the 81st percentile and head circumference in the 12th percentile.
 - Does the baby have microcephaly?
 - Do we test the infant for Zika?
 - What other screenings should be performed?

ZIKA SCENARIO #3

- A baby girl is born at 41 weeks gestation to a mother that was not tested for Zika. The anthropometric birth measurements are within normal limits, but hydrocephaly was noticed on a head ultrasound.
 - Is this a birth defect associated with congenital Zika syndrome?
- You found out that the mother travelled to Mexico once a trimester while she was pregnant, but never developed any symptoms consistent with Zika.
 - Do you test the mother for Zika?
 - Do you test the infant for Zika?
 - What other specialists should be consulted?

ZIKA SCENARIO #3

- The RT-PCR and IgM are negative for the mother.
 - Was she infected with Zika?
 - Why are we not sure?
- The RT-PCR and IgM are negative for the infant, but the PRNT is positive.
 - Was the baby infected with Zika?
 - Why are we not sure?
- You repeat the PRNT on the baby at 18 months and the PRNT is positive.
 - Was the baby infected with Zika?

INFECTIOUS DISEASE EPIDEMIOLOGY

- Christine Scott-Waldron
- Sean Simonson
- Julius L. Tonzel
- (504) 568-8313 – main line
- (800) 256-2748 – on-call