MERCY HEALTH
SAINT MARY'S

West Michigan Health Forum
March 3rd, 2017

History of Zika

- Uganda Virus Research Institute
  - Established in 1936
  - Rockefeller Foundation

History of Zika

- UVRT discoveries
  - Chikungunya
  - West Nile Virus
  - Bwamba Virus
  - Semliki Virus
  - Developed yellow fever vaccine

History of Zika

- Sentinel rhesus macaque (Rhesus #766)
- 1947 first isolated from monkey
- 1948 isolated in *Aedes africanus*
- Described Zika virus in 1952

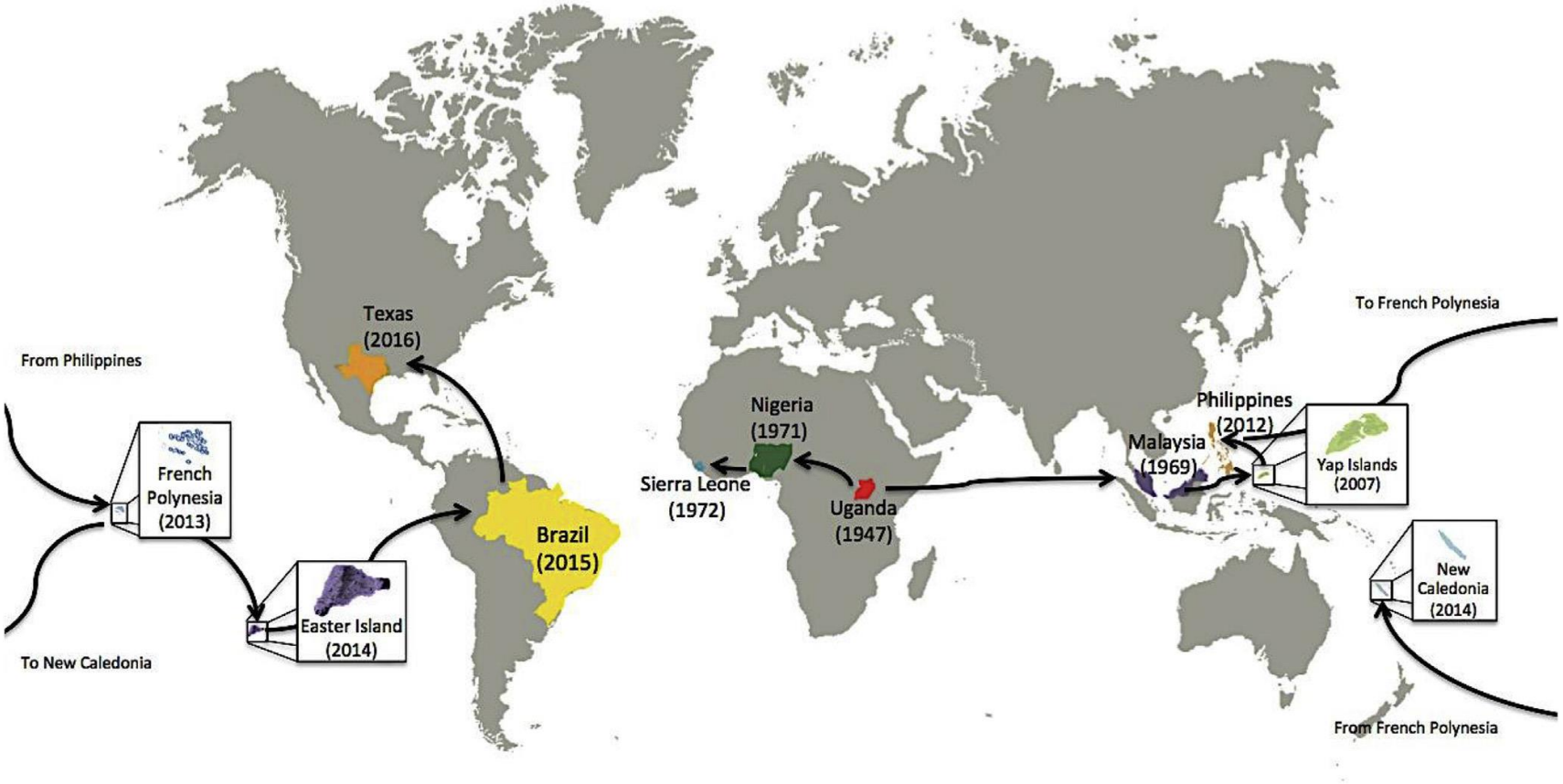
History of Zika

C. Chang et al. / Journal of Autoimmunity xxx (2016) 1e13 3

- 1952 isolated from 10 yo Nigerian girl
- 1956 documented lab transmission
- 1960-2006 about 20 cases described in humans
- 2007-2012 Yap Island Outbreak
  - 73% of population infection
  - Occasional travel spread

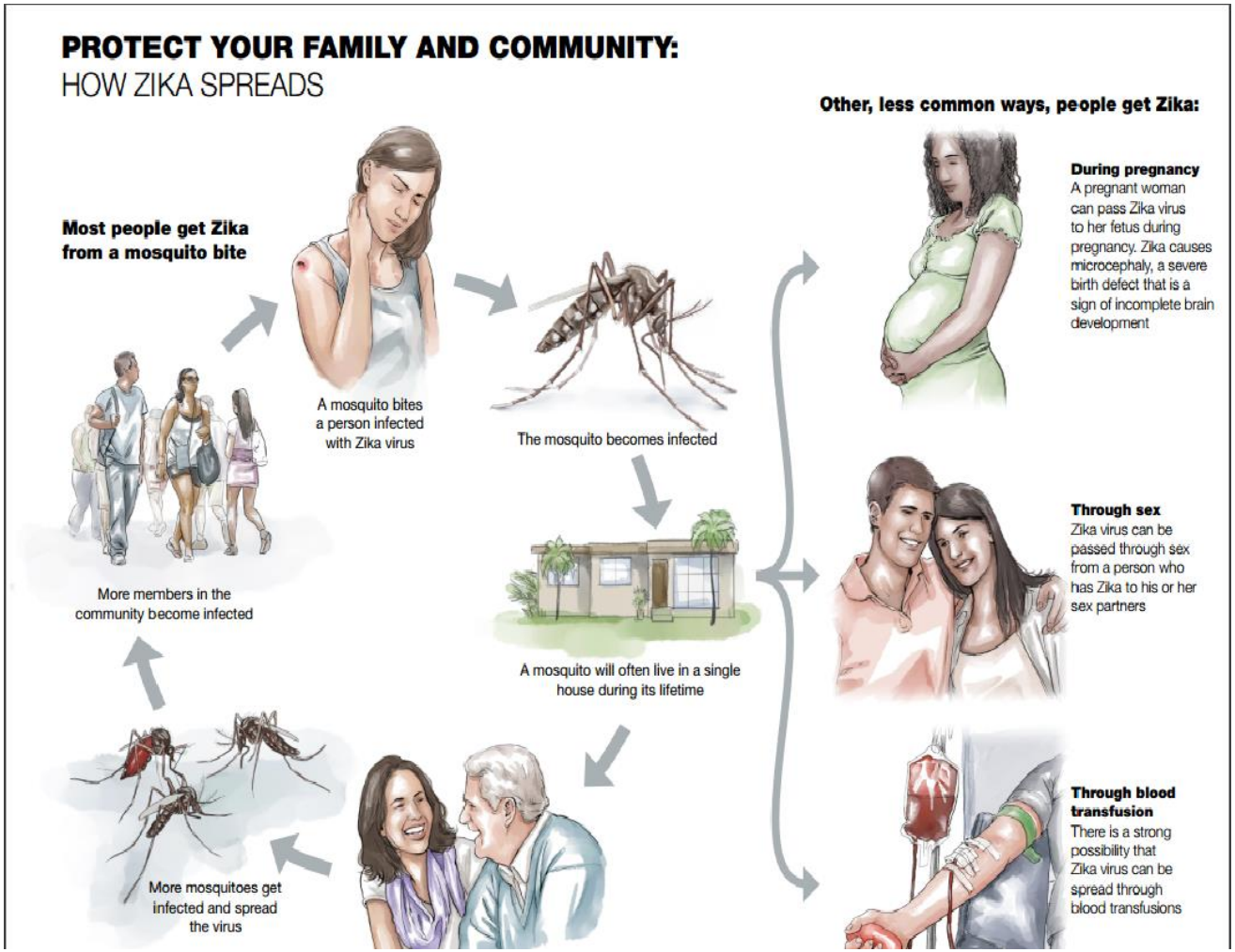
History of Zika

C. Chang et al. / Journal of Autoimmunity xxx (2016) 1e13 3



Zika Transmission

CDC



Typical Clinical Manifestations of Zika

- 80% Asymptomatic
- Most common symptoms
  - Fever, rash (descending macular/maculopapular), non-purulent conjunctivitis
  - Arthragia (65%) and puritis (94%)
  - Incubation period of 3-7 days
- 2-7 days of symptoms
- Labs
  - Leukopenia, thrombocytopenia, elevated LDH, elevated LFTs, increase inflammatory markers
- No NSAIDS (if Dengue possible)

Severe Manifestations of Zika

- Severe thrombocytopenia
- Zika Congenital Syndrome
- Guillain-Barre Syndrome
- Acute Myelitis

- Meningoencephalitis

Zika associated thrombocytopenia

Sarmiento-Ospina A et al. Zika virus associated death in Columbia. *The Lancet Infectious Diseases*. (2016) May; 523-524

- Idiopathic, presumed autoimmune
- 4 Zika associated deaths reported due to bleeding from Columbia
  - 2 year old girl
  - 30 year old woman
  - 61 year old woman
  - 72 year old woman

- Complicated by DIC, severe thrombocytopenia, ICH

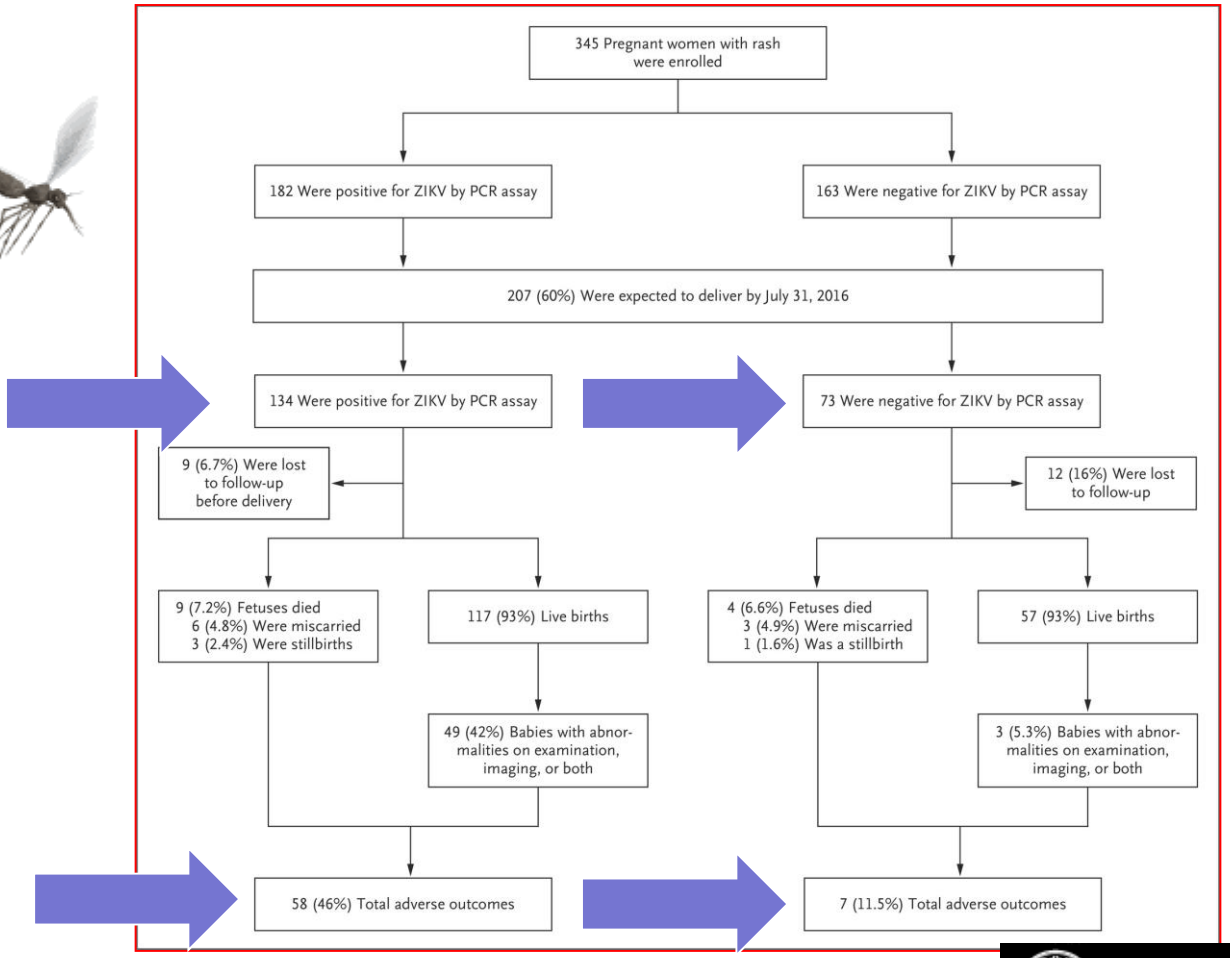
Zika Congenital Syndrome

- Pregnancy loss
- Microcephaly
- Intracranial calcifications
- Corpus callosum abnormalities
- Abnormal cortical formation
- Cerebral atrophy
- Hydrocephaly
- Cerebellar abnormalities
- Club foot
- Hypertonia

Zika Microcephaly Video (CBC News)

Cohort Study in Rio de Janeiro

Brasil et al



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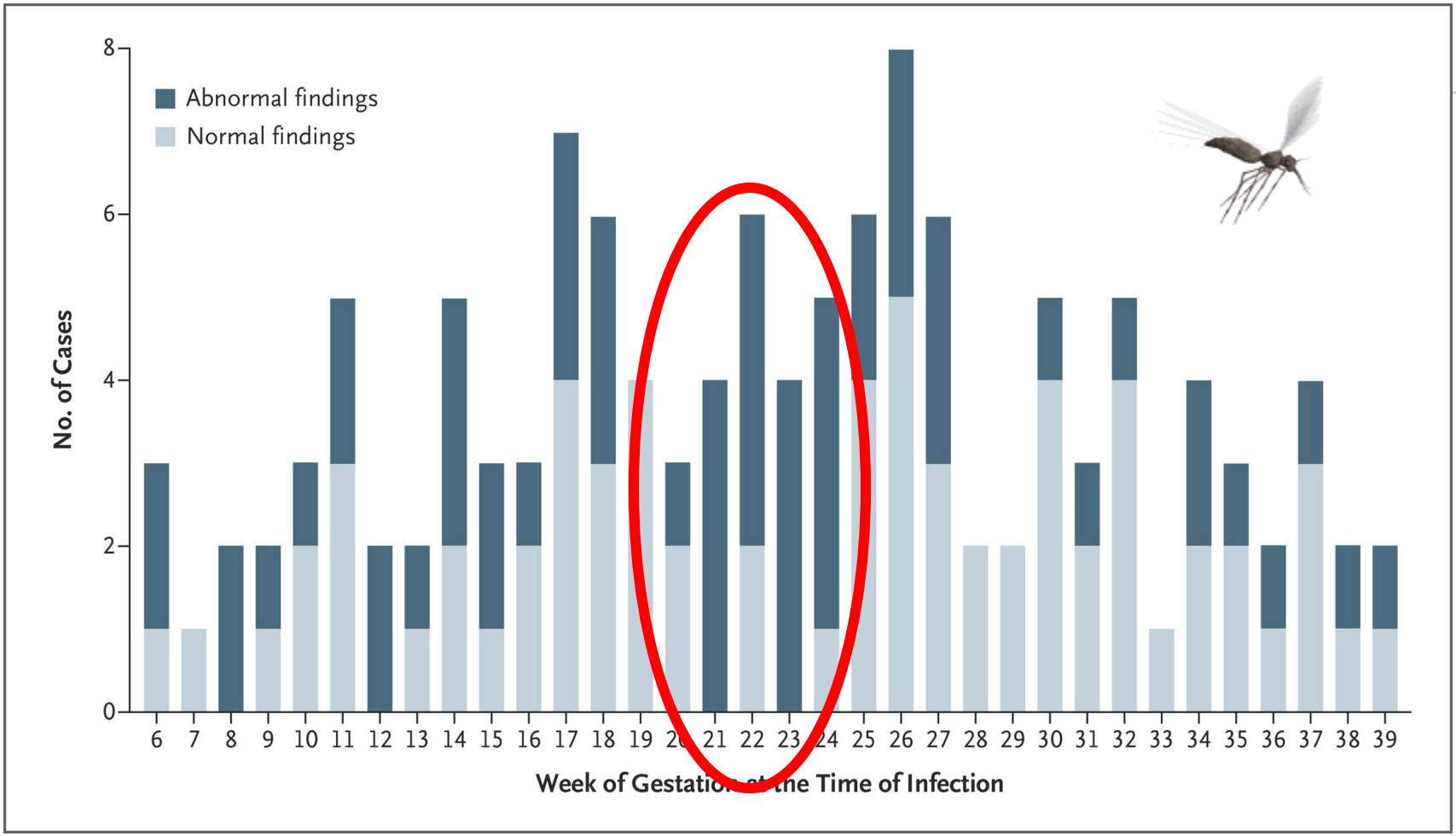

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Table 3. Infant Outcomes According to ZIKV Exposure.

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.

From: **Birth Defects Among Fetuses and Infants of US Women With Evidence of Possible Zika Virus Infection During Pregnancy**

JAMA. 2017;317(1):59-68. doi:10.1001/jama.2016.19006

Table 1. Pregnancy Outcomes for 442 Women With Completed Pregnancies With Laboratory Evidence of Possible Zika Virus Infection by Maternal Symptom Status and Timing of Symptom Onset or Exposure, US Zika Pregnancy Registry, December 2015-September 2016[a]

	No. of Pregnancies				
	Brain Abnormalities and/or Microcephaly[b]	Neural Tube Defects, Eye Abnormalities, and Consequences of Central Nervous System Dysfunction[c]	Total With ≥1 Birth Defect	Total Completed Pregnancies	Preliminary Estimates of Pregnancies With Birth Defects, % (95% CI)[d]
By maternal symptom status					
Maternal symptoms of Zika virus infection	8	2	10	167	6 (3-11)
No reported maternal symptoms of Zika virus infection	14	2	16	271	6 (4-9)
Unknown symptom status	0	0	0	4	
By timing of symptoms or exposure					
First trimester	8	1	9	85	11 (6-19)
Multiple trimesters including first trimester	13	2	15	211	7 (4-11)
Second trimester only	0	0	0	76	0 (0-5)
Multiple trimesters including second and third trimester	0	0	0	5	
Third trimester only	0	0	0	31	0 (0-11)
Periconceptional	0	0	0	7	
Unknown or missing data	1	1	2	27	
Total	22	4	26	442	6 (4-8)

[a] Pregnancies include live births, spontaneous abortions, terminations, and stillbirths. Outcomes for multiple-gestation pregnancies are counted once. Maternal, placental, or fetal or infant laboratory evidence of possible Zika virus infection is based on presence of Zika virus RNA on real-time reverse transcription–polymerase chain reaction or similar test, serological evidence of a recent Zika virus infection, serological evidence of a recent unspecified flavivirus infection, or immunohistochemistry staining in tissue indicating Zika virus.

[b] Includes all fetuses or infants with either microcephaly and/or brain abnormalities with or without the presence of additional birth defects; the 22 fetuses or infants included 4 with microcephaly and no reported neuroimaging, 14 with microcephaly and brain abnormalities reported, and 4 with brain abnormalities reported without a finding of microcephaly.

[c] Report of one of these birth defects in an infant with no report of brain abnormalities and/or microcephaly; the 4 fetuses or infants included 2 with encephalocele, 1 with eye abnormalities, and 1 with hearing abnormalities.

[d] Ninety-five percent confidence interval for a binomial proportion using Wilson score interval.

Table Title:

Pregnancy Outcomes for 442 Women With Completed Pregnancies With Laboratory Evidence of Possible Zika Virus Infection by Maternal Symptom Status and Timing of Symptom Onset or Exposure, US Zika Pregnancy Registry, December 2015–September 2016[a]

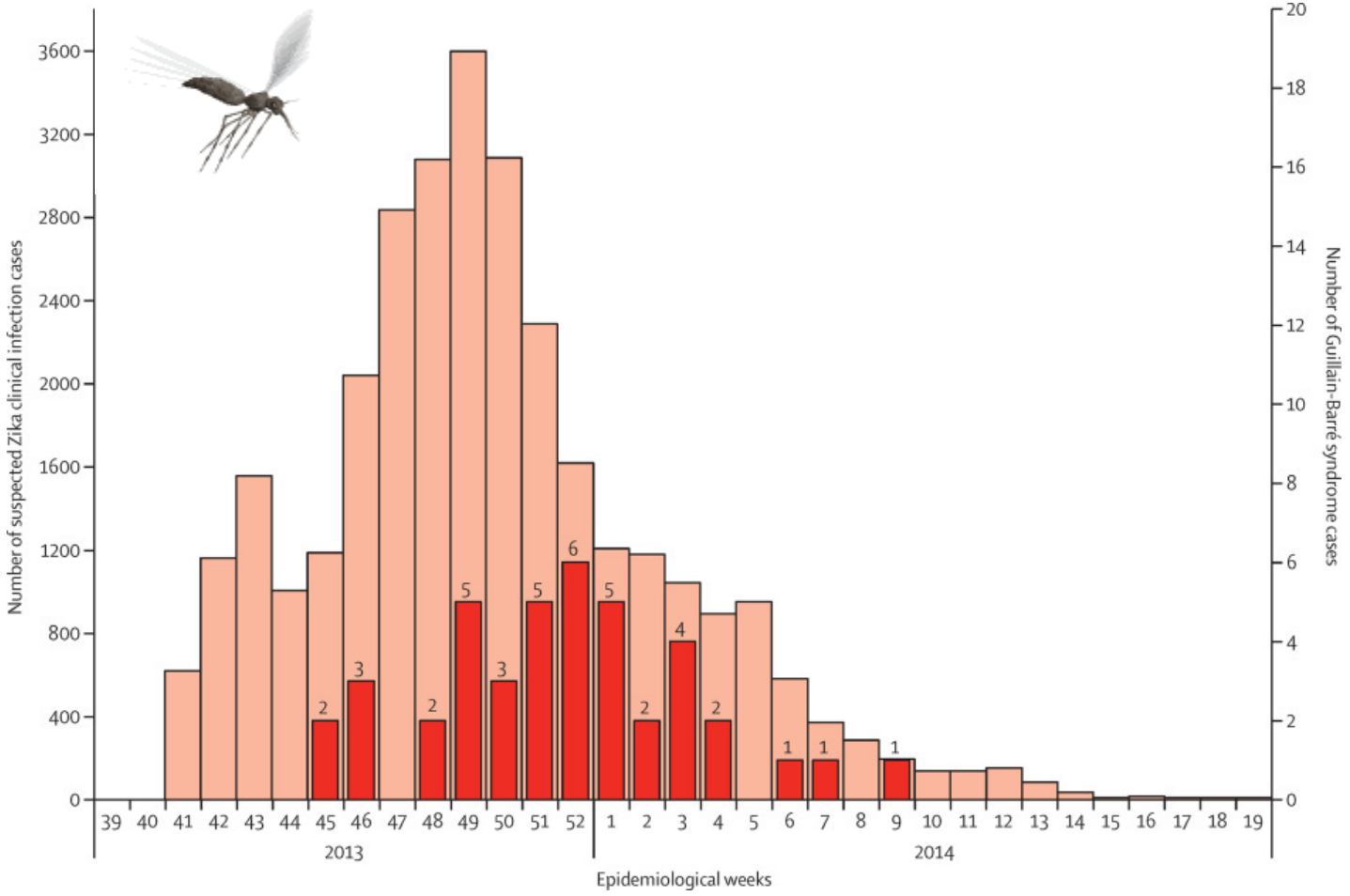
Guillain-Barre Syndrome

Cao-LormeauVM, BlakeA,Mons S, et al.

- 32,000 patients with Zika on Yap Island
  - 73% seropositive rate
  - Initial indication something was different
- Case-control study from outbreak in French Polynesia
- Nov 2013-Feb 2014
- 42 patients presented with GBS to the same hospital
- 98 patients in control group 1 (no Zika and matched)
- 0.24 cases of GBS per 1000 Zika infections

Epidemiology Curve

Cao-LormeauVM, BlakeA,Mons S, et al.

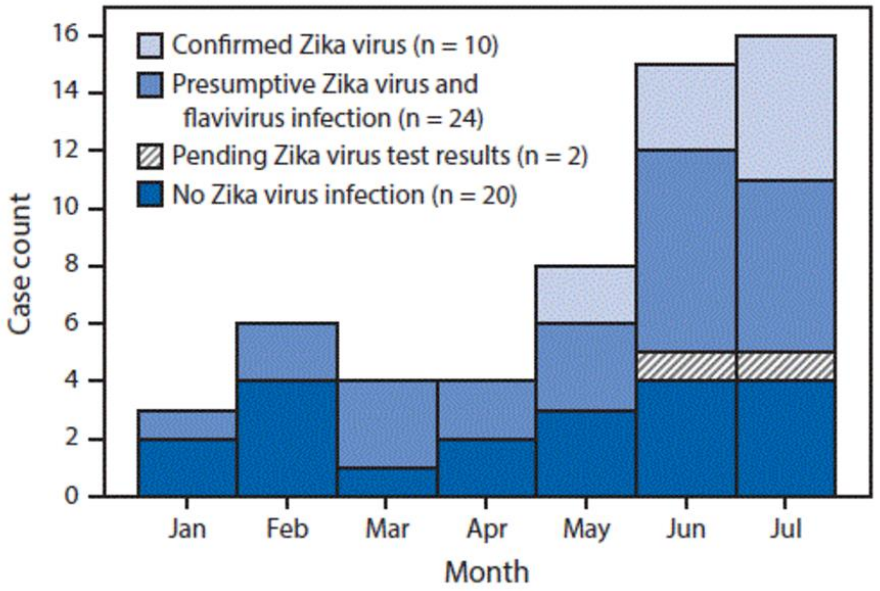


Guillain-Barre Syndrome

	Guillain-Barré syndrome*(n=42)	Control group 1 (n=98)	OR (95% CI)	OR†(95% CI)	Control group 2 (n=70)	OR (95% CI)	OR†(95% CI)
Zika virus IgM and/or IgG positivity	41 (98%)	35 (36%)	59·7 (10·4–+∞)	..	..	..	..
Positive Zika virus seroneutralisation	42 (100%)	54 (56%)	34·1 (5·8–+∞)	..	..	..	
Dengue virus IgG positivity	40 (95%)	87 (89%)	2·0 (0·4–19·9)	1·0 (0·2–11·5)	58 (83%)	6·0 (0·8–269·5)	4·0 (0·5–184·7)

Reported cases of confirmed and suspected Guillain-Barré syndrome (n = 56), by Zika virus laboratory result and month of onset of neurologic signs — Puerto Rico, January 1–July 31, 2016

- 3 expected cases per month (21)
- 54 actual cases
- 34 had confirmed Zika
  - –62% required ICU
  - –35% intubated
  - –1 death



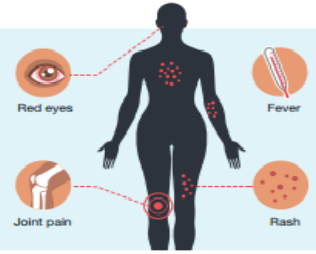
Acute Myelitis

Mecharles S, et al. Acute Myelitis due to Zika virus infection. *The Lancet*. Volume 387, Issue 10026, 2-8 April 2016

- Urinary retention
- Muscle weakness
- Zika PCR positive urine, serum, CSF

Who to test for Zika?

As a healthcare provider, you decide if a patient should be tested for Zika virus infection. The algorithm below will help you determine whether or not to test your patient for Zika virus infection. For information on which test to use, see CDC's interim guidance.



If your patient is

- Experiencing or has recently experienced symptoms of Zika*
- An asymptomatic pregnant woman

Ask the following questions

Does the patient live in or has the patient recently traveled to an area with Zika?

NO

YES

Test for Zika

Has the patient had unprotected sex with a partner who has lived in or traveled to an area with Zika?

NO

YES

Do Not Test for Zika

*Healthcare providers should review their local and state health jurisdiction guidelines regarding testing of patients with clinically compatible illness without known travel or sexual exposures.

CDC does not recommend Zika virus testing for asymptomatic

- Men
- Children
- Women who are not pregnant

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

How to test for Zika

- Symptomatic patients
  - RNA NAT <14 days of symptoms onset (urine and serum)
  - IgM if PCR negative or between 2-12 weeks after symptoms

- Asymptomatic pregnant women patients at risk
  - RNA NAT <14 days from last exposure
  - RNA NAT >14 days if IgM positive
  - IgM testing up to 12 weeks after exposure
  - Routine IgM testing in 1st and 2nd trimester with ongoing exposure risk
- Trioplex RT-PCR Assay
  - Zika, dengue, chikungunya RNA
  - No cleared by FDA but is under an EUA (emergency use authorization)
- Plaque Reduction Neutralization Test (PRNT)
  - Differentiates zika from other flavivirus

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