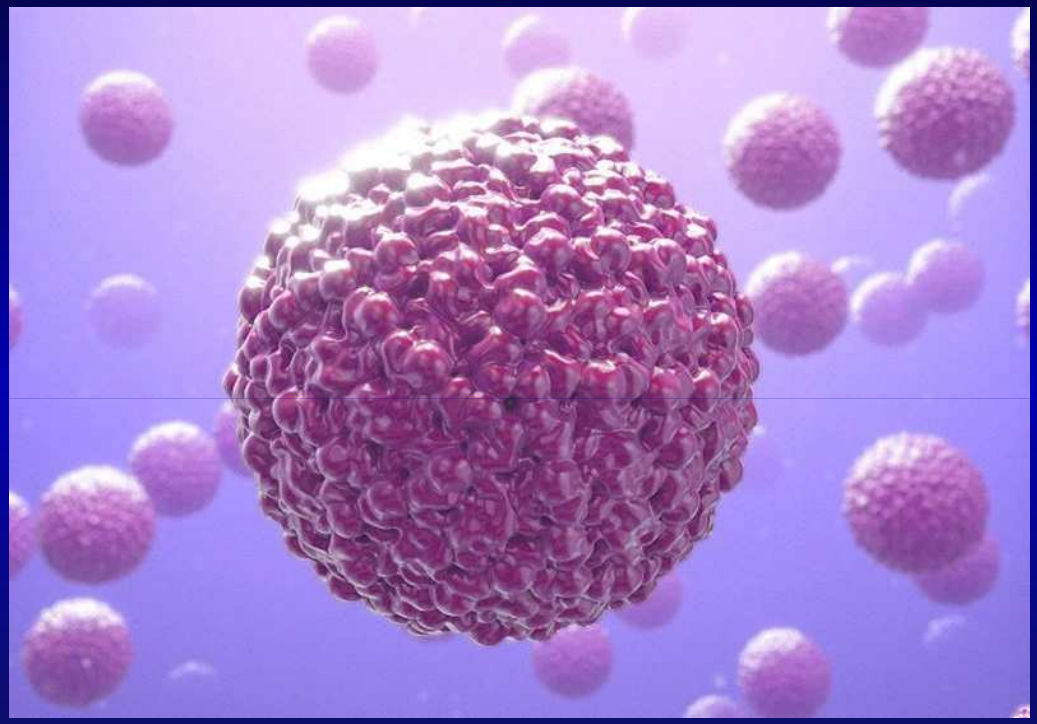
Zika Virus e Embarazo



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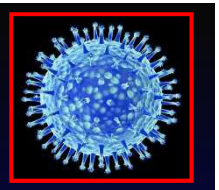
Santa Casa de São Paulo

I have no competing interests to declare for this presentattion

ZIKA VIRUS (ZIKV)



- ZIKV is a single-stranded RNA virus of the *Flaviviridae* family, *Flavivirus* genus (as DNV, YFV, JEV, WNV and SLE viruses).
- Two major lineages: African and Asiatic.
- Transmitted by arthropods, (*Aedes* genus).
- Other modes of transmission: transfusional, *in utero* and sexual transmission (male and female partners who become infected should use condoms for 6 months)[1-2].

ZIKV was detected among Neotropical primates, anticipating that they could act as reservoirs, similar to the sylvatic cycle of yellow fever in Brazil. Favoretto S et al. bioRxiv Apr. 20, 2016

1. http://wwwnc.cdc.gov/eid/article/20/6/14-0138_article
2. Cunha et al. Genome Announc 2016; 4(2):e00032

AMERICAN SOCIETY FOR MICROBIOLOGY | genomeAnnouncements

CrossMark

First Complete Genome Sequence of Zika Virus (*Flaviviridae*, *Flavivirus*) from an Autochthonous Transmission in Brazil

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M.S.C. and D.L.A.E contributed equally to this work.

We report here the genome sequence of Zika virus, strain ZikaSPH2015, containing all structural and nonstructural proteins flanked by the 5′ and 3′ untranslated region. It was isolated in São Paulo state, Brazil, in 2015, from a patient who received a blood transfusion from an asymptomatic donor at the time of donation.

Editorial

Zika Virus: What Have We Learned?

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Am J Perinatol 2016;33:1029–1031.

RAPID COMMUNICATIONS

Evidence of perinatal transmission of Zika virus, French Polynesia, December 2013 and February 2014

M Besnard[1], S Lastère[1], A Teissier[2], V M Cao-Lormeau[2], D Musso (dmusso@ilm.pf)[2]
1. Centre hospitalier de Polynésie française, Hôpital du Taaone, Tahiti, French Polynesia
2. Institut Louis Malardé, Tahiti, French Polynesia

Evidence of Sexual Transmission of Zika Virus

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Evidence for Transmission of Zika Virus by Platelet Transfusion

Clinical Manifestations

Asymptomatic presentations are frequent, but infection can cause a broad range of clinical symptoms, presenting as a "dengue-like" syndrome .

Fever, pruritic rash, arthralgia, conjunctival hyperemia. Other symptoms include muscle pain, headache, edema of extremities retro-orbital pain, and vomiting.

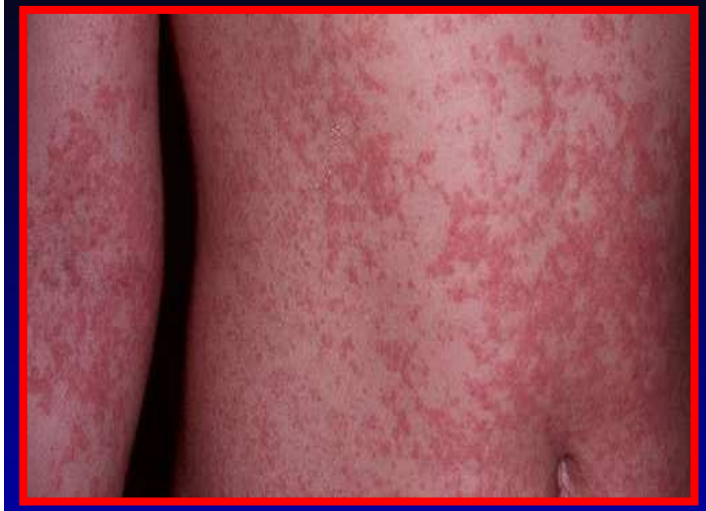
Comparison of symptoms for dengue fever, chikungunya, and Zika.
Clinique comparée de la dengue, du chikungunya et du Zika.

Symptoms	Dengue	Chikungunya	Zika
Fever	++++	+++	+++
Myalgia/arthralgia	+++	++++	++
Edema of extremities	0	0	++
Maculopapular rash	++	++	+++
Retro-orbital pain	++	+	++
Conjunctivitis	0	+	+++
Lymphadenopathies	++	++	+
Hepatomegaly	0	+++	0
Leukopenia/thrombopenia	+++	+++	0
Hemorrhage	+	0	0

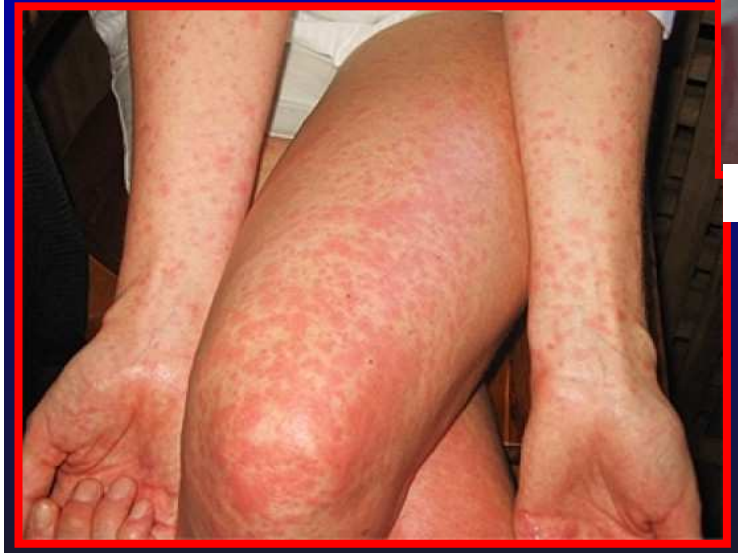
Adapted from Halstead, et al. and from the Yap State Department of Health Services presentation.

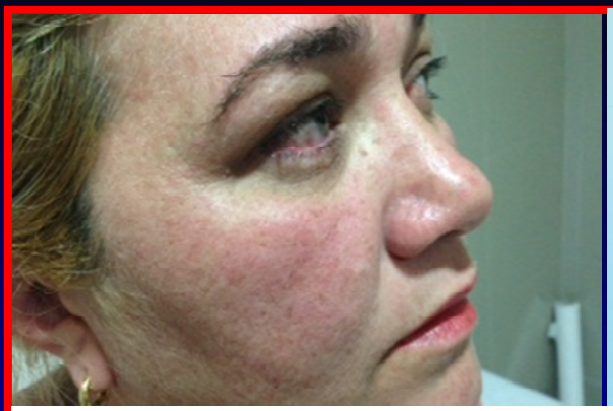
Ioos et al. Médecine et maladies infectieuses 44 (2014)

Clinical manifestations

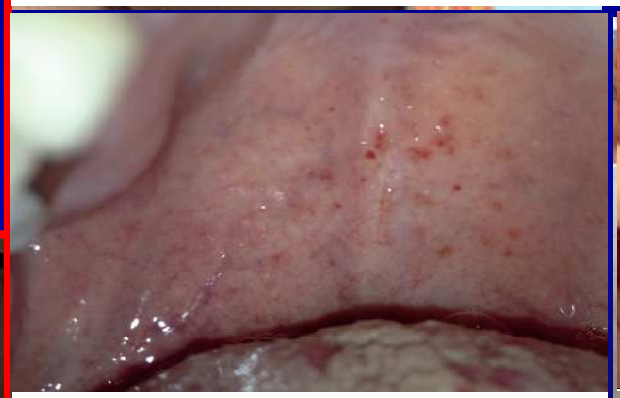


Macular rash

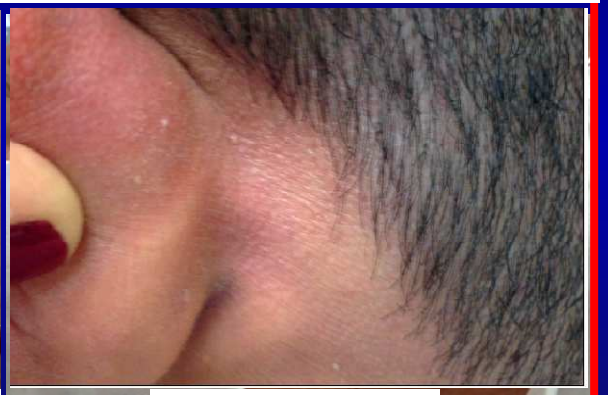




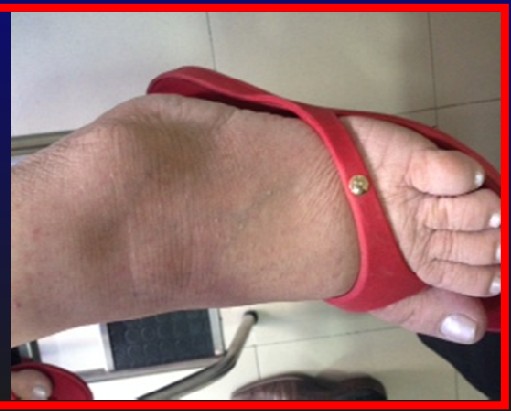
Edema and erythema of the malar region of the face and conjunctival injection.



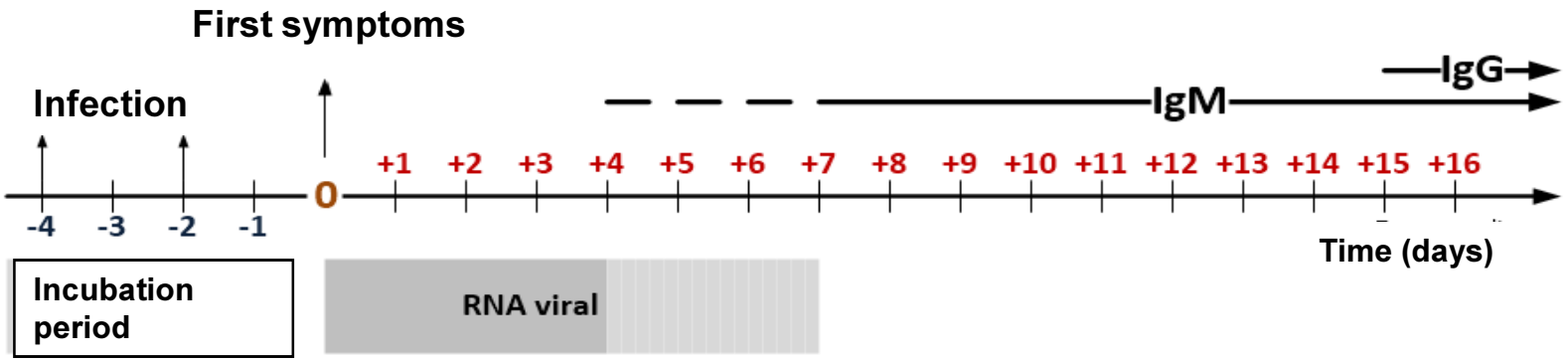
Hyperaemia/ petechiae in the palate



soft lymph node



Laboratory Diagnosis



Laboratory diagnosis by RT-PCR and serology (IgM and IgG) for Zika virus

- **RT-PCR**: During the first 5-7 days after the onset of symptoms, (acute phase, viremic period) RNA can be detected in serum. In urine ZIKV may persists longer.
- **Serology (ELISA or inmunofluerescence)**: IgM or IgG can be positive after 5 to 6 days following the onset of symptoms.
- Should be confirmed with neutralizing ZIKV antibody titers, at levels ≥4-fold higher than those against dengue virus. (cross-reactivity with other flaviviruses, especially dengue and yellow fever).

CDC, 2016

How Zika virus was introduced in Brazil?

Four Pacific countries (French Polynesia, New Caledonia, Cook Islands, and Easter Island) in which ZIKV circulated during 2013-2014 had teams engaged in this contest.

ZIKV sequences obtained in Brazil belonged to the Asian lineage and showed 99% identity with a sequence from a ZIKV isolate from French Polynesia (KJ776791)

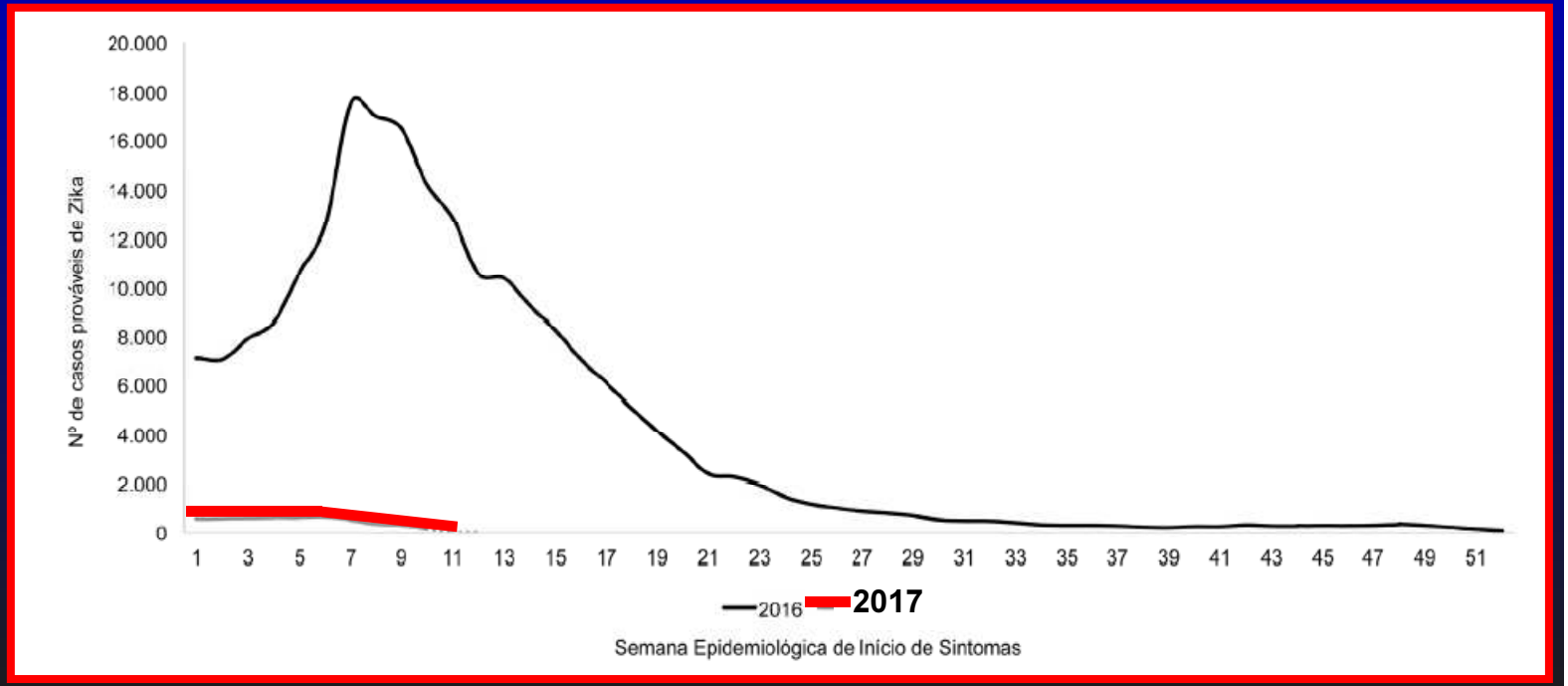
Campos et al. EID 2015

Phylogenetic and molecular clock analyses show a single introduction of ZIKV into the Americas, estimated to have occurred between May-Dec 2013. The estimated date of origin coincides with an increase in air passengers to Brazil from ZIKV endemic areas, and with reported outbreaks in Pacific Islands.

Faria N R *et al*., *Science* (2016).

Situação Epidemiológica

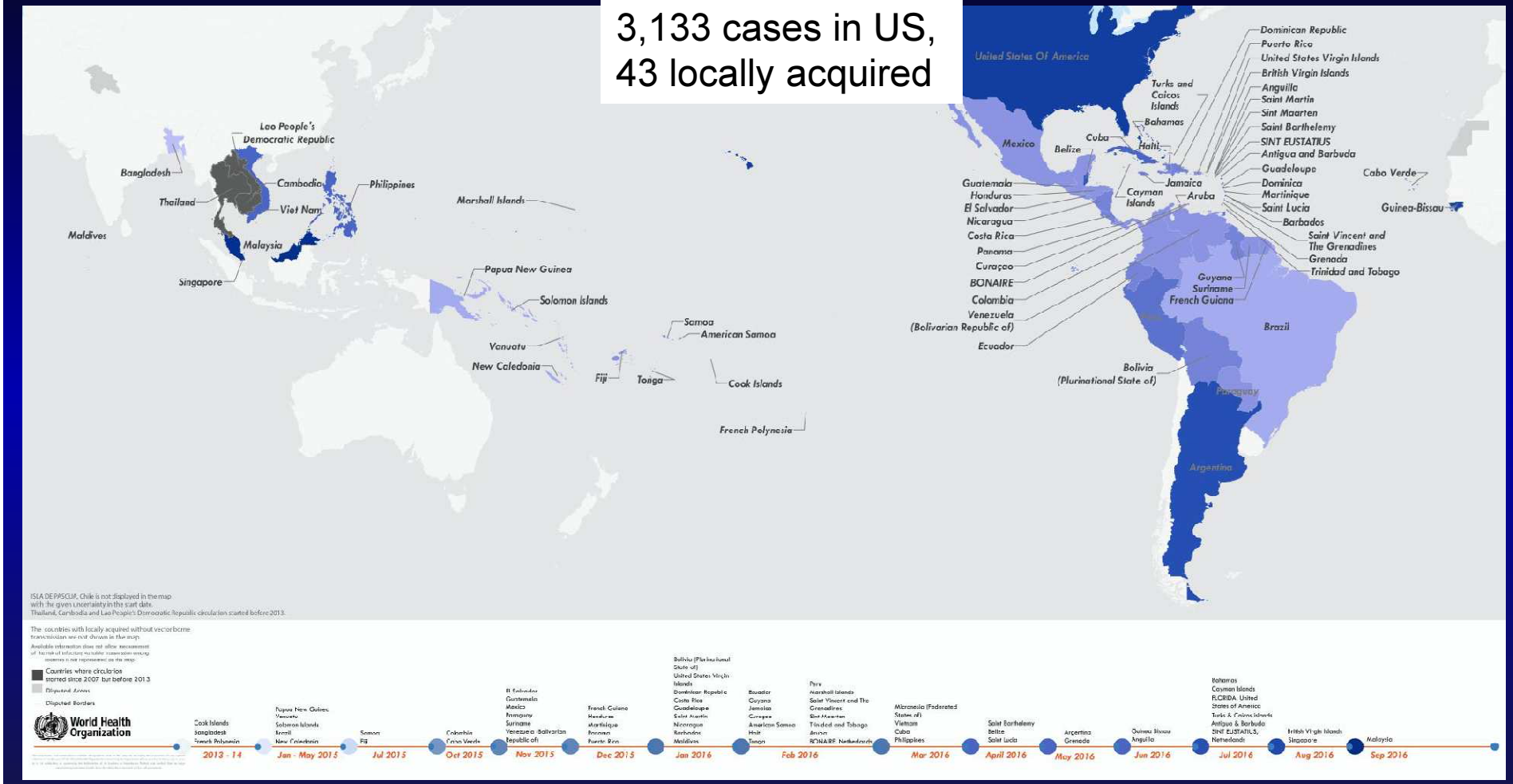
- In may 2015, autochthonous transmission was confirmed in Brazil[1].
- In 2016, until week 32, Brazil reported 215,317 probable cases of Zika, of which 130,701 confirmed.
- Incidence of 105 cases/100.000 hab.[1] Mato Grosso, Tocantins, Bahia e Rio de Janeiro
- In 2017, only 1,320 cases confirmed until week 12 (incidence is 30 times lower comparing to 2016).



MoH, Zika webpage. 2017

Epidemiologic Situation

3,133 cases in US,
43 locally acquired

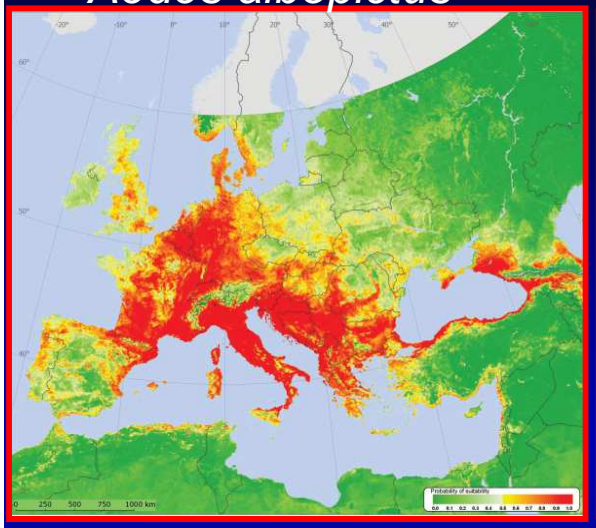


Global spread of Zika virus, 2016

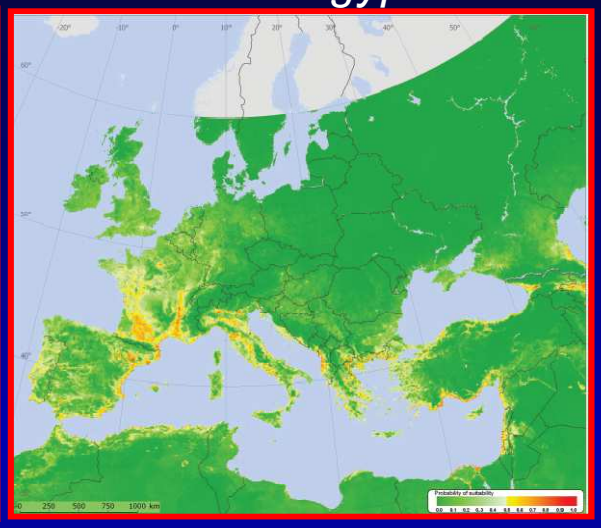
1. WHO 2016

Regional climatic suitability as habitats for *A. albopictus and A. aegypti*

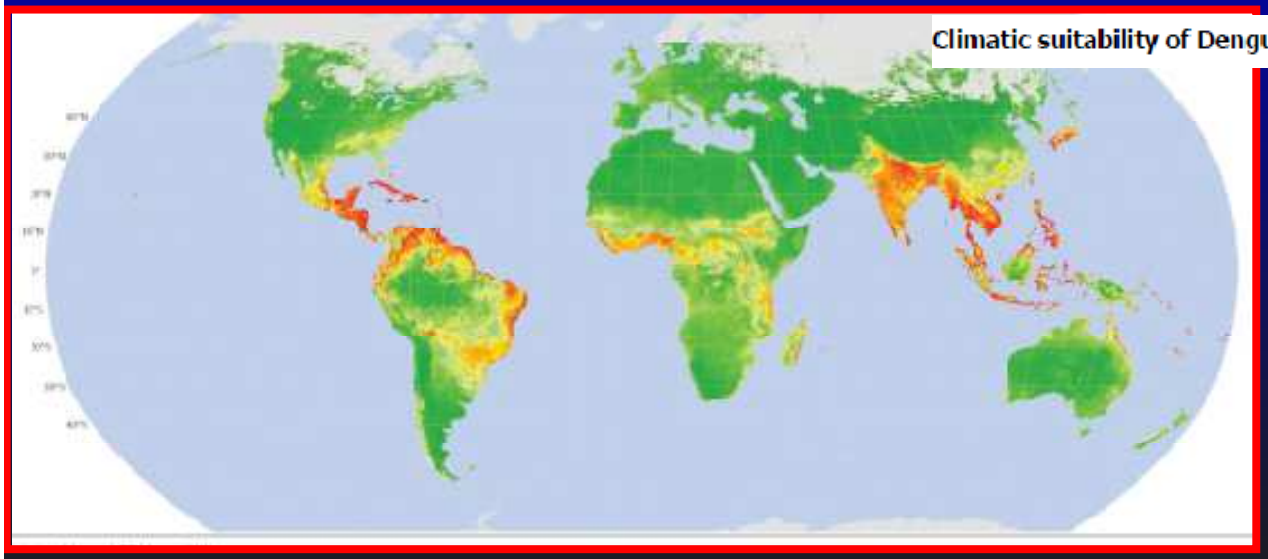
Aedes albopictus

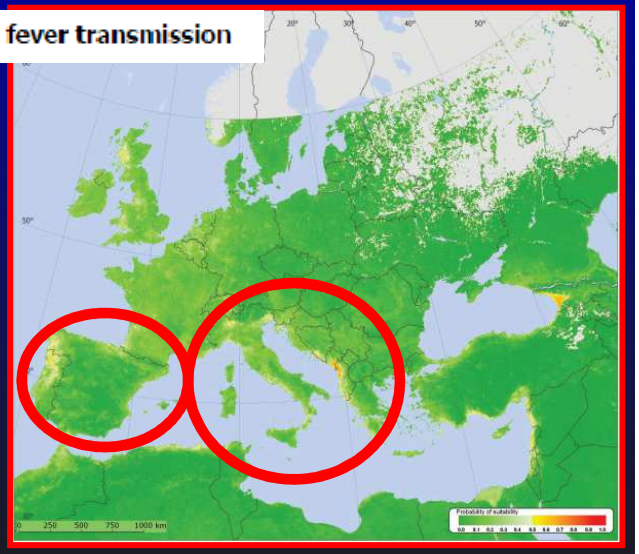


Aedes aegypti



Much of central and Mediterranean Europe is potentially climatically suitable as a habitat for *A. albopictus*. For *A. aegypti*, Mediterranean areas of Spain, France and Italy as well as south-eastern Europe could potentially be a suitable habitat.





ECDC, 2012

Guillain-Barré Syndrome outbreak associated with Zika virus infection in French Polynesia: a case-control study

Van-Mai Cao-Lormeau*, Alexandre Blake*, Sandrine Mons, Stéphane Lastère, Claudine Roche, Jessica Vanhomwegen, Timothée Dub, Laure Baudouin, Anita Teissier, Philippe Larre, Anne-Laure Vial, Christophe Decam, Valérie Choumet, Susan K Halstead, Hugh J Willison, Lucile Musset, Jean-Claude Manuguerra, Philippe Despres, Emmanuel Fournier, Henri-Pierre Mallet, Didier Musso, Arnaud Fontanet*, Jean Neil*, Frédéric Ghawché*

- Case control study providing evidence for Zika virus infection causing Guillain-Barré syndrome.
- The incidence of GBS cases during the French Polynesian outbreak was estimated to be 0.24 per 1000 Zika virus infections
- AMAN type, characterized by distal motor nerve involvement, the absence of typical patterns and levels of anti-glycolipid antibodies. (faster recovery).

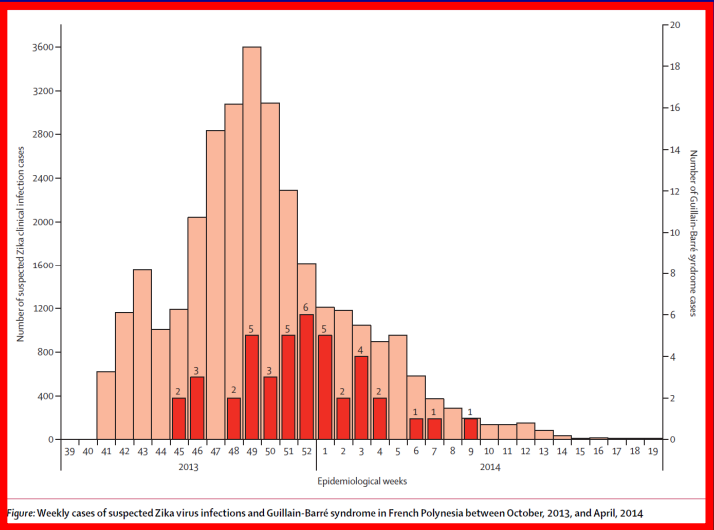


Figure: Weekly cases of suspected Zika virus infections and Guillain-Barré syndrome in French Polynesia between October, 2013, and April, 2014

Time between reported viral syndrome and onset of neurological symptoms: 6 days (4–10)
Median age: 42 years (36–56)
Previous viral syndrome: (88%)
Duration of hospital stay: 11 days (7–20)
Duration of hospital stay for patients admitted to intensive care: 51 days (16–70)

Lancet, 2016

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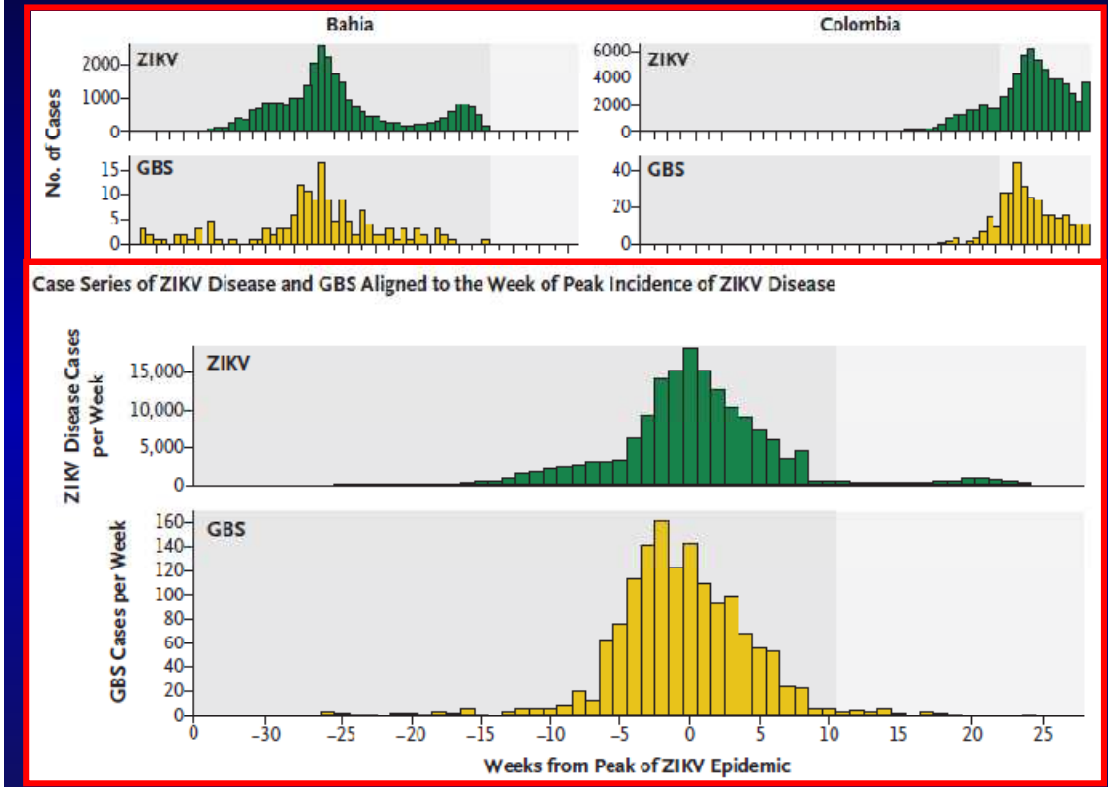
Zika Virus and the Guillain–Barré Syndrome — Case Series from Seven Countries



- Significant increases in the incidence of the Guillain–Barré syndrome compared with the pre-ZIKV baseline incidence:
  - Bahia, Brazil (172%),
  - Colombia (211%),
  - Dominican Rep (150%),
  - El Salvador (100%),
  - Honduras (144%),
  - Suriname (400%),
  - Venezuela (877%)

The incidence of the Guillain–Barré syndrome was 28% higher among males than among females (rate ratio, 1.28; 95% CI, 1.09 to 1.50) and consistently increased with age

Santos et al. NEJM 2016

In addition to its association with Guillain-Barré syndrome, new data from endemic areas suggests that ZIKV may be linked to other neurological outcomes

- Acute Myelitis

Mecharles S et al. Lancet 2016

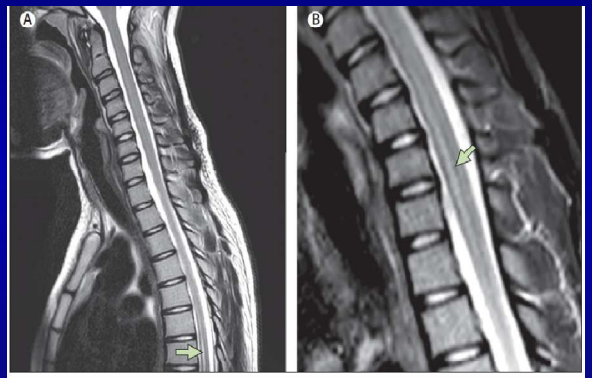
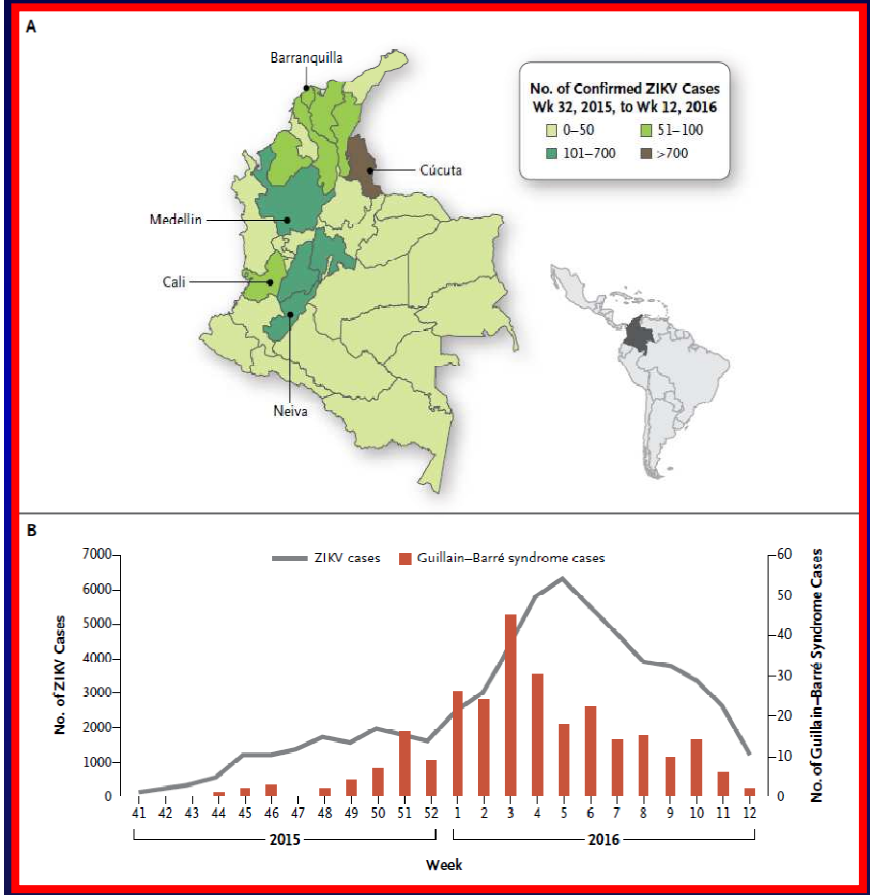


Figure: Magnetic resonance imaging (MRI) showing myelitis in Zika virus infection

- Acute Disseminated Encephalomyelitis (ADEM)

Ferreira ML et al. Abstract at AAN, 2016

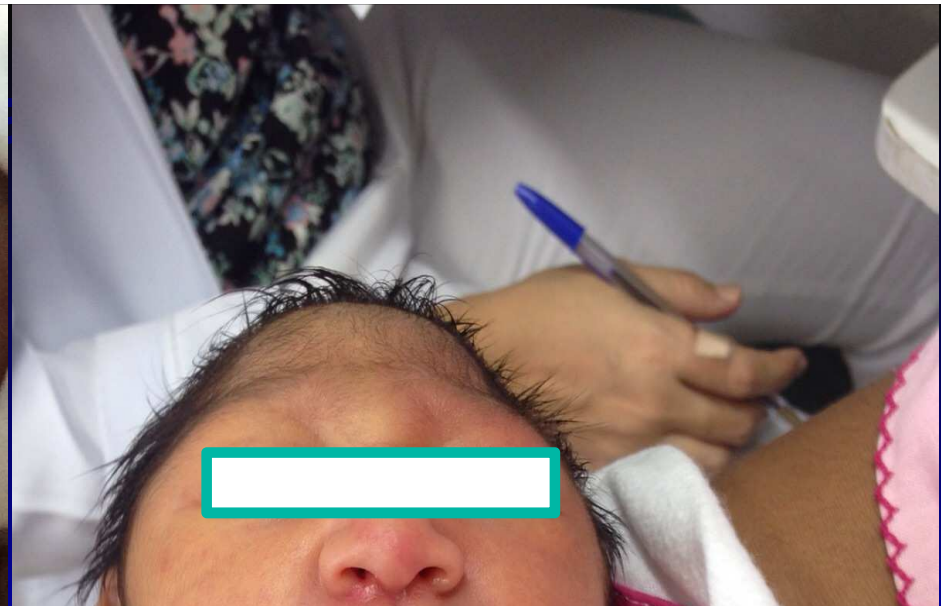
Guillain–Barré Syndrome Associated with Zika Virus Infection in Colombia



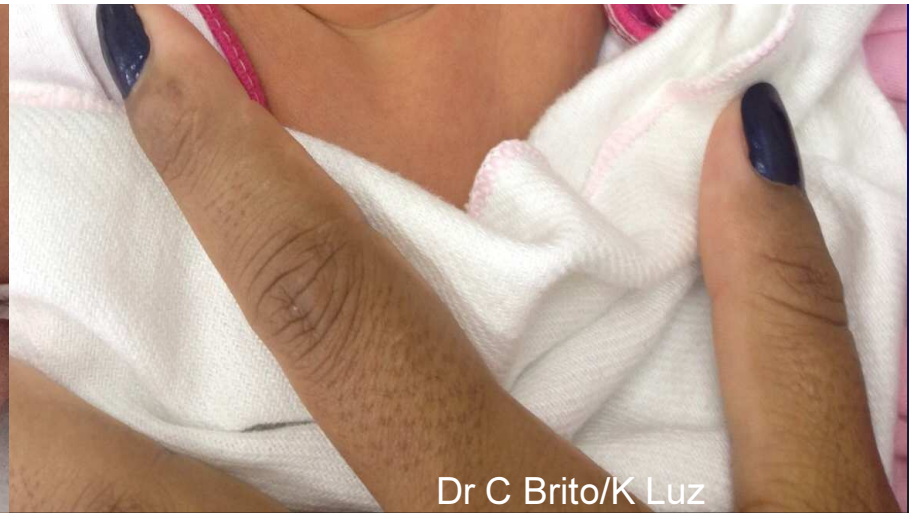
- Median age: 47 y (35–57)
- Median duration of ZIKV infection symptoms: 4 days (3–5)
- Median time from onset of ZIKV infection symptoms to onset of the GBS: 7 days (3–10)

Parra B et al. NEJM, October 5, 2016

- In October, 2015 several pediatricians from the northeast region started to observe a significant increased number of newborns with a congenital syndrome characterized by microcephaly and other neurological malformations, without a plausible cause.
- They postulated that those newborns could have been infected *in utero* with ZIKV (a ZIKV outbreak was occurring and several mothers reported a febrile rash during pregnancy).

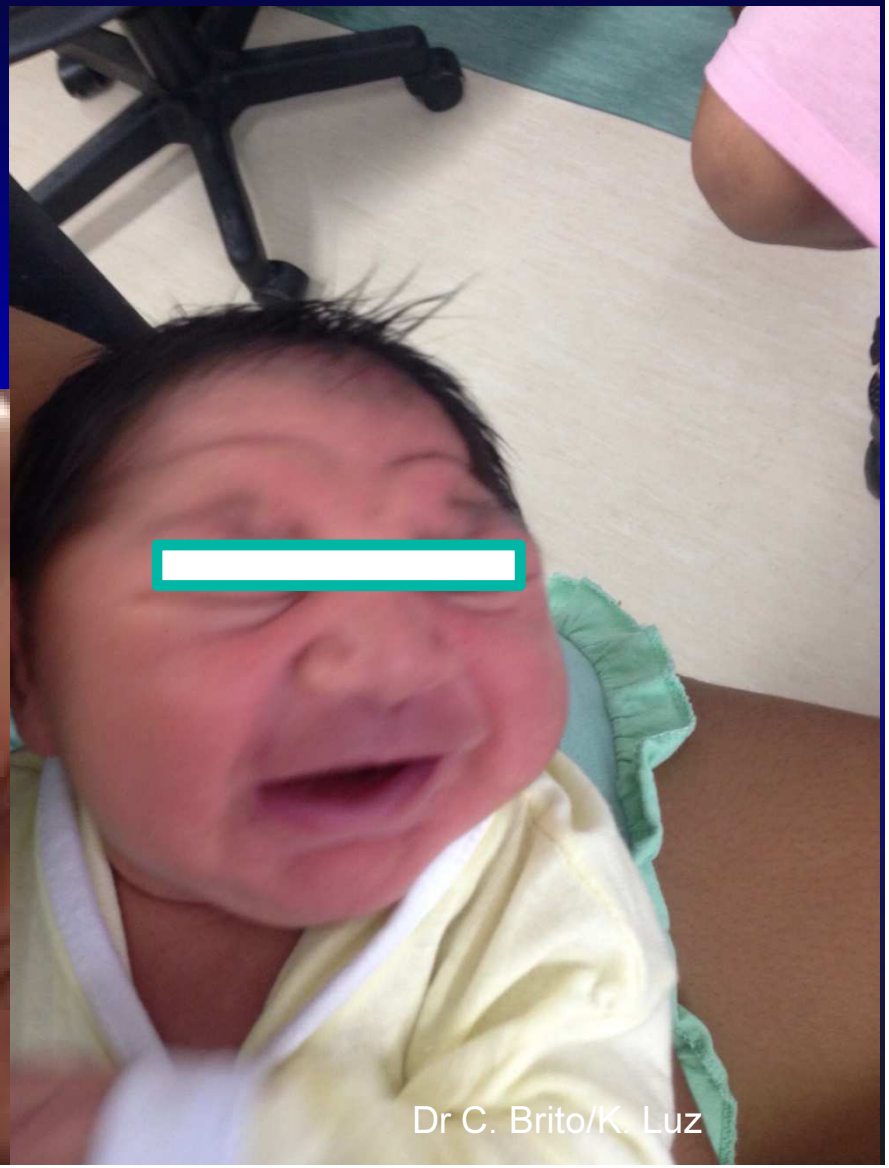


Neurological findings include microcephaly, calcifications in the periventricular parenchyma and thalamic areas, ventriculomegaly, lissencephaly with agenesis of corpus callosum, cerebellar alterations and pachigyria.

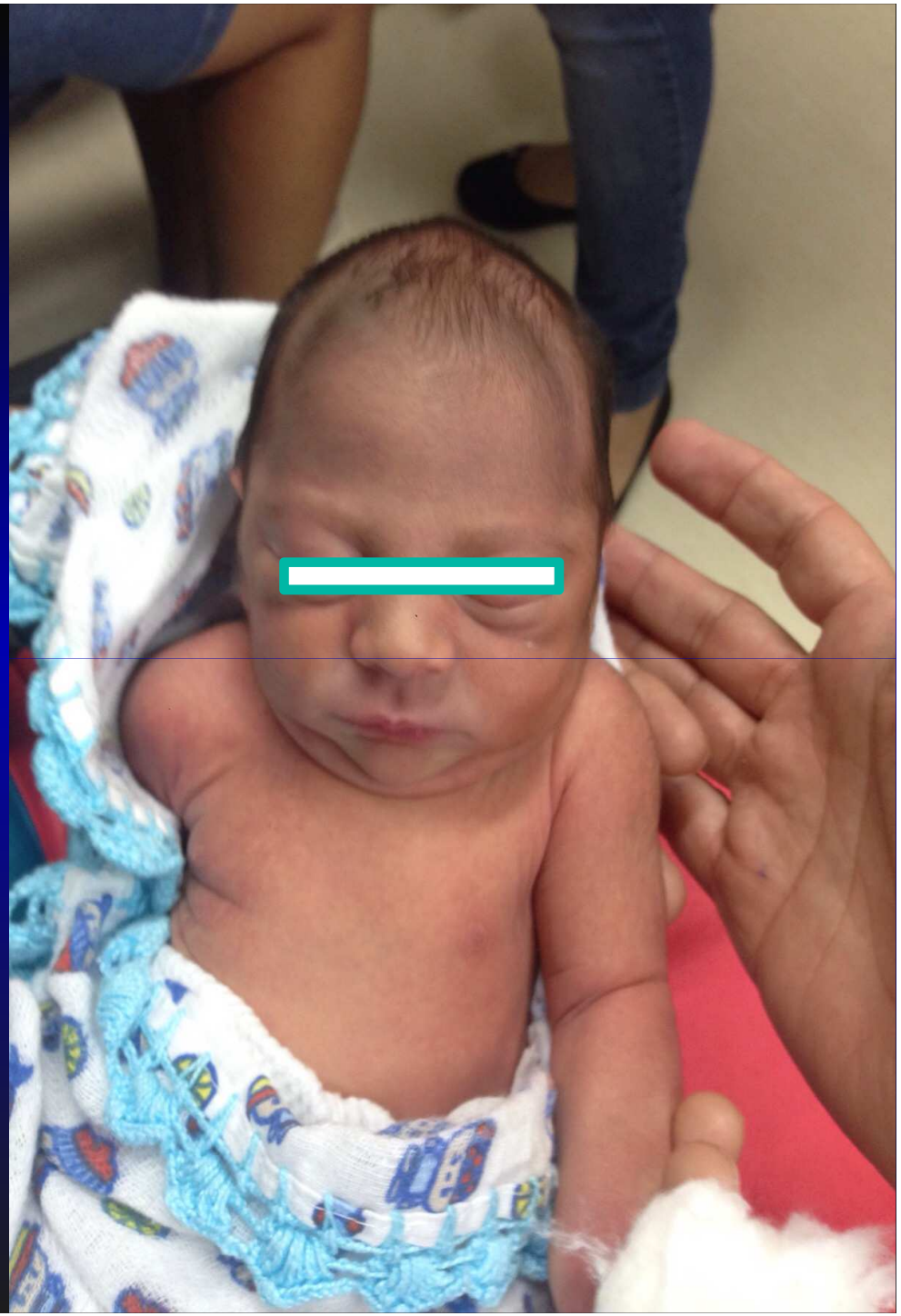


Dr C Brito/K Luz

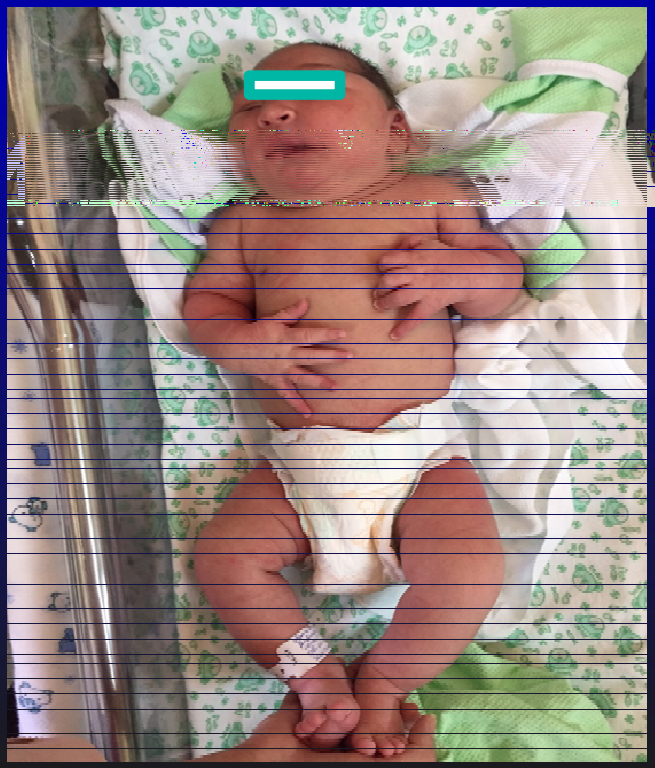
ova epidemia

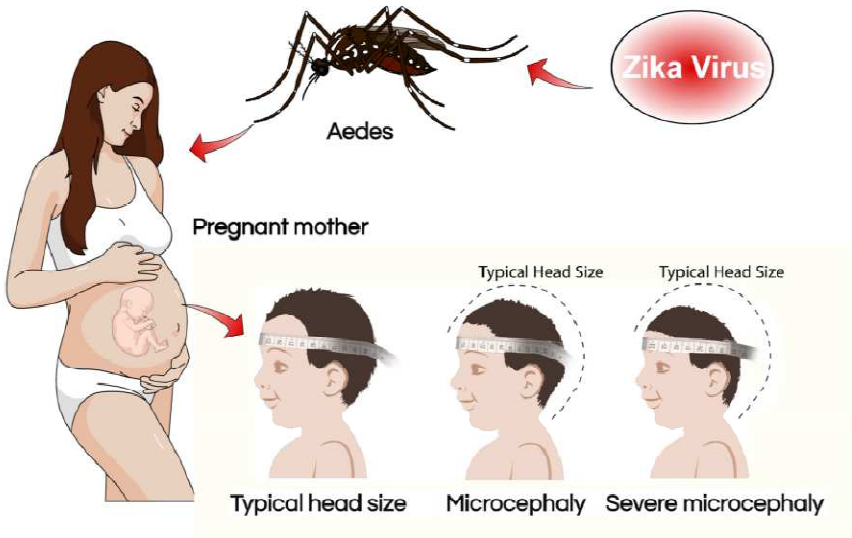


Dr C. Brito/K. Luz




cute





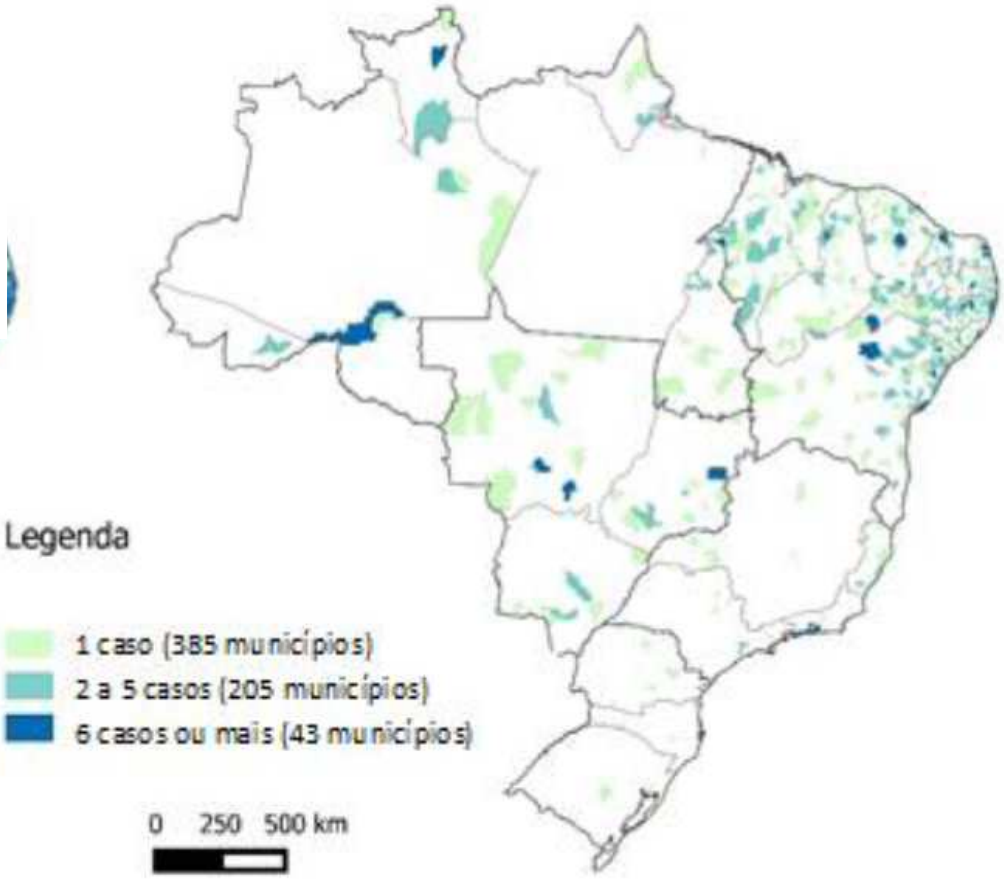
Microcephaly	-Below average head size -Sometimes failure of brain to grow at normal rate -At birth head circumference less than 32 cm

FIGURE 2 | Association of ZIKV with microcephaly in pregnant mothers.

ZIKV Microcephaly Burden in Brazil

- By April/2017: 13,364 suspected cases of microcephaly reported
- 2,621 confirmed, with 211 lab-confirmed for ZIKV.

Confirmed cases of microcephaly and/or neonatal CNS alterations suggestive of congenital infections



- Zika virus is highly neurotropic in mice and no virus has been recovered from tissues other than the brains of infected mice

- DICK GW, ZIKA VIRUS (II). PATHOGENICITY AND PHYSICAL PROPERTIES. TROPICAL MEDICINE AND HYGIENE. 46 (5): 521-534. No. 5. September, 1952

IgM ELISA for ZIKV in the CSF of 30 neonates with microcephaly in Brazil

- Samples of CSF and serum were tested for IgM specific for Zika virus using capture ELISA based on CDC Emergency Use Authorization protocol
- Zika-specific IgM was detected in 30 (97%) of 31 CSF samples and in 28 (90%) of 31 serum samples.

	Serum IgM		CSF IgM		
	Zika virus	Dengue virus type 1–4 mixture	Zika virus	Dengue virus type 1–4 mixture	Interpretation
1 day	17·0	2·7	12·1	1·5	Positive for Zika virus
1 day	20·6	2·9	16·1	2·4	Positive for Zika virus
1 day	20·6	7·8	14·8	4·2	Zika virus cross-reacting with dengue virus
1 day	5·2	0·7	9·3	1·0	Positive for Zika virus
1 day	8·2	1·7	16·3	3·4	Zika virus cross-reacting with dengue virus
2 days	6·2	0·9	15·0	1·5	Positive for Zika virus
2 days	6·2	0·9	14·5	2·7	Positive for Zika virus
2 days	7·5	0·9	16·1	2·9	Positive for Zika virus
2 days	4·7	0·9	14·2	1·7	Positive for Zika virus
2 days	12·7	1·2	15·9	2·9	Positive for Zika virus
2 days	10·5	1·7	15·8	2·1	Positive for Zika virus
3 days	10·5	1·1	14·8	2·4	Positive for Zika virus
3 days	15·6	2·6	14·8	2·4	Positive for Zika virus
3 days	16·0	1·6	16·4	1·9	Positive for Zika virus
4 days	3·2	0·6	13·5	1·9	Positive for Zika virus
5 days	3·9	0·8	9·3	0·8	Positive for Zika virus
5 days	11·4	5·5	15·5	4·6	Zika virus cross-reacting with dengue virus
7 days	5·9	0·7	13·1	1·2	Positive for Zika virus
7 days	2·1	0·9	15·0	0·9	Positive for Zika virus
7 days	15·4	2·2	13·5	1·6	Positive for Zika virus
8 days	9·6	1·8	15·7	1·7	Positive for Zika virus
10 days	4·0	1·5	14·5	6·6	Zika virus cross-reacting with dengue virus
11 days	0·9	1·8	0·6	1·9	Negative for Zika virus
12 days	16·1	6·2	15·7	5·0	Zika virus cross-reacting with dengue virus
13 days	15·3	2·6	12·1	1·3	Positive for Zika virus
17 days	6·4	1·8	16·1	1·4	Positive for Zika virus
17 days	16·0	2·8	14·8	3·0	Positive for Zika virus
22 days	4·1	1·2	15·5	2·7	Positive for Zika virus
23 days	3·4	2·6	16·1	5·7	Zika virus cross-reacting with dengue virus
36 days	2·1	0·9	15·6	1·9	Positive for Zika virus
40 days	12·2	1·1	13·3	0·8	Positive for Zika virus

ELISA values are patient optical densities divided by negative control densities (P/N); values less than 2 were considered negative, 2–3 equivocal, and more than 3 positive. CSF=cerebrospinal fluid.

Table: IgM against Zika virus and dengue virus in the serum and CSF of neonates with microcephaly, Pernambuco State, Brazil, 2015, by age (days) at testing

Cordeiro M et al. Lancet, 2016

The NEW ENGLAND JOURNAL of MEDICINE

BRIEF REPORT

Zika Virus Associated with Microcephaly

Jernej Mlakar, M.D., Misa Korva, Ph.D., Nataša Tul, M.D., Ph.D., Mara Popović, M.D., Ph.D., Mateja Poljšak-Prijatelj, Ph.D., Jerica Mraz, M.Sc., Marko Kolenc, M.Sc., Katarina Resman Rus, M.Sc., Tina Vesnaver Vipotnik, M.D., Vesna Fabjan Vodušek, M.D., Alenka Vizjak, Ph.D., Jože Pižem, M.D., Ph.D., Miroslav Petrovec, M.D., Ph.D., and Tatjana Avšič Županc, Ph.D.

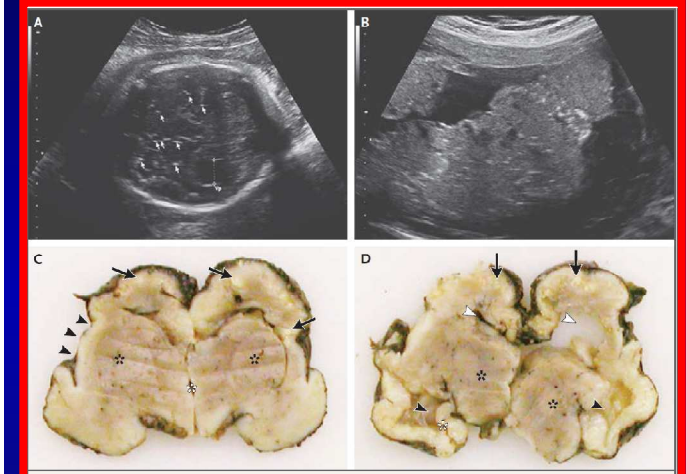


Figure 1. Prenatal Ultrasonographic Images and Photographs of Coronal Slices of Brain.

Panel A shows numerous calcifications in various parts of the brain (some marked with arrows) and the dilated occipital horn of the lateral ventricle (Vp, marked with a measurement bar) as seen on transverse ultrasonography. Panel B shows numerous calcifications in the placenta. Panel C shows multifocal cortical and subcortical white calcifications (arrows) and almost complete loss of gyration of the cortex. The basal ganglia are developed but poorly delineated (black asterisks), and the sylvian fissures are widely open on both sides (arrowheads on the left). The third ventricle is not dilated (white asterisk). Panel D shows dilated body of the lateral ventricles (white arrowheads); the left is collapsed. Temporal horns of the lateral ventricles (black arrowheads) are also dilated. The thalami (black asterisks) and the left hippocampus (white asterisk) are well developed, whereas the contralateral structure is not recognizable owing to autolysis.

centa. After the mother requested termination of the pregnancy, a fetal autopsy was performed. Micrencephaly (an abnormally small brain) was observed, with almost complete agyria, hydrocephalus, and multifocal dystrophic calcifications in the cortex and subcortical white matter, with associated cortical displacement and mild focal inflammation. ZIKV was found in the fetal brain tissue on reverse-transcriptase–polymerase-chain-reaction (RT-PCR) assay, with consistent findings on electron microscopy. The complete genome of ZIKV was recovered from the fetal brain.

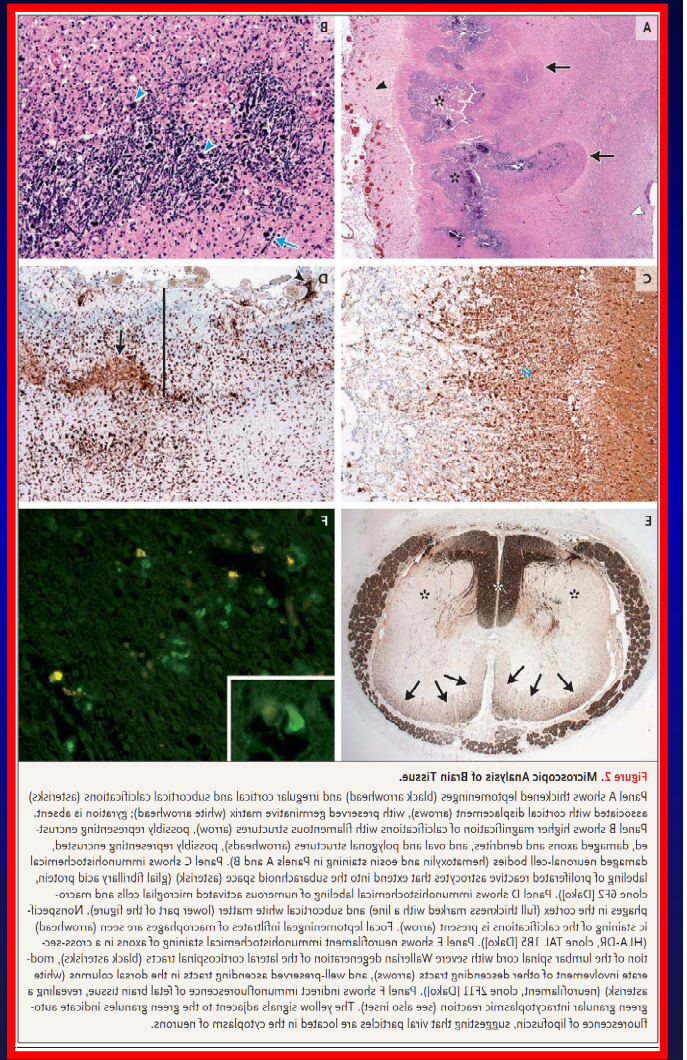


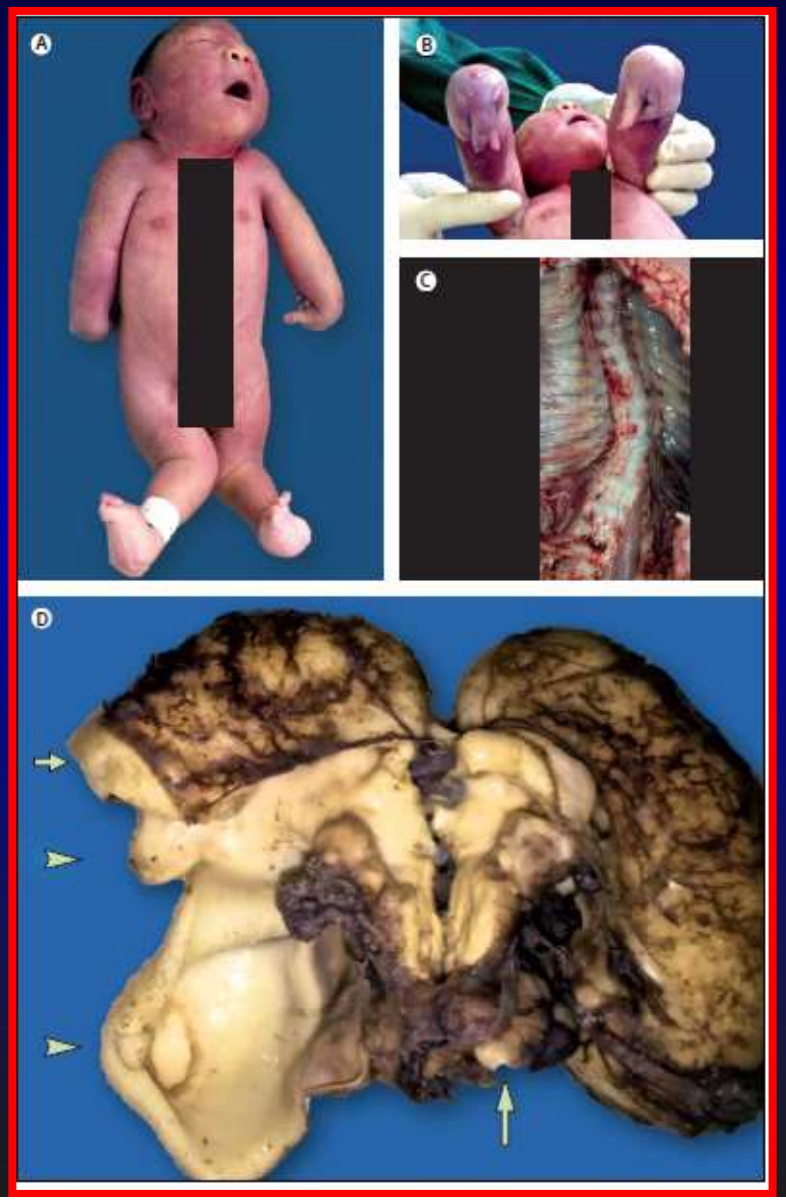
Figure 2. Microscopic Analysis of Brain Tissue.

Panel A shows thickened leptomeninges (black arrowhead) and irregular cortical and subcortical calcifications (asterisks) associated with cortical displacement (arrows), with preserved germinative matrix (white arrowhead); gyration is absent. Panel B shows higher magnification of calcifications with filamentous structures (arrow), possibly representing encrusted, damaged axons and dendrites, and oval and polygonal structures (arrowheads), possibly representing encrusted, damaged neuronal-cell bodies (hematoxylin and eosin staining in Panels A and B). Panel C shows immunohistochemical labeling of proliferated reactive astrocytes that extend into the subarachnoid space (asterisk) (glial fibrillary acid protein, clone GF2 [Dako]). Panel D shows immunohistochemical labeling of numerous activated microglial cells and macrophages in the cortex (full thickness marked with a line) and subcortical white matter (lower part of the figure). Nonspecific staining of the calcifications is present (arrow). Focal leptomeningeal infiltrates of macrophages are seen (arrowhead) (HLA-DR, clone TAL 185 [Dako]). Panel E shows neurofilament immunohistochemical staining of axons in a cross-section of the lumbar spinal cord with severe Wallerian degeneration of the lateral corticospinal tracts (black asterisks), moderate involvement of other descending tracts (arrows), and well-preserved ascending tracts in the dorsal columns (white asterisk) (neurofilament, clone 2F11 [Dako]). Panel F shows indirect immunofluorescence of fetal brain tissue, revealing granular intracytoplasmic reaction (see also inset). The yellow signals adjacent to the green granules indicate autofluorescence of lipofuscin, suggesting that viral particles are located in the cytoplasm of neurons.

NEJM, 2016

Pathology of congenital Zika syndrome in Brazil: a case series

Roosecelis Brasil Martines*, Julu Bhatnagar*, Ana Maria de Oliveira Ramos, Helaine Pompeia Freire Davi, Silvia D'Andretta Iglezias, Cristina Takami Kanamura, M Kelly Keating, Gillian Hale, Luciana Silva-Flannery, Atis Muehlenbachs, Jana Ritter, Joy Gary, Dominique Rollin, Cynthia S Goldsmith, Sarah Reagan-Steiner, Yolkabed Ermias, Tadaki Suzuki, Kleber G Luz, Wanderson Kleber de Oliveira, Robert Lanciotti, Amy Lambert, Wun-Ju Shieh, Sherif R Zaki



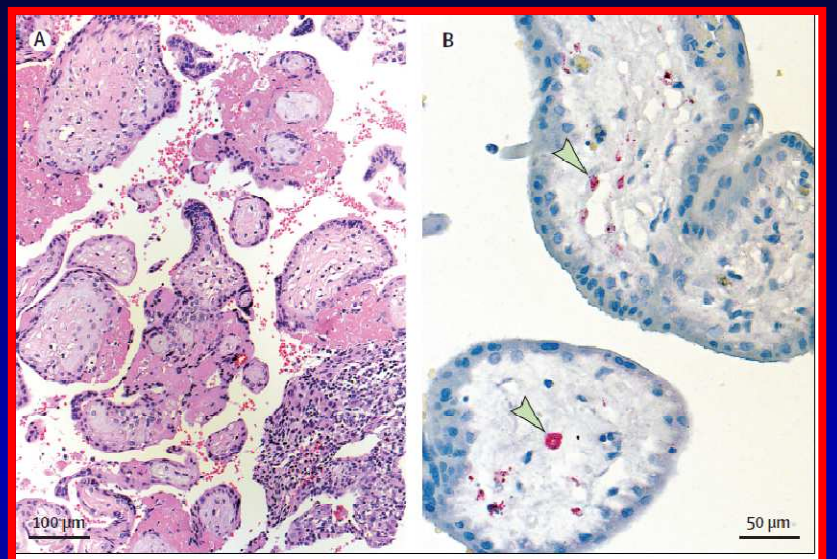


Figure 3: Case 4—histopathological and immunohistochemical findings of the placenta

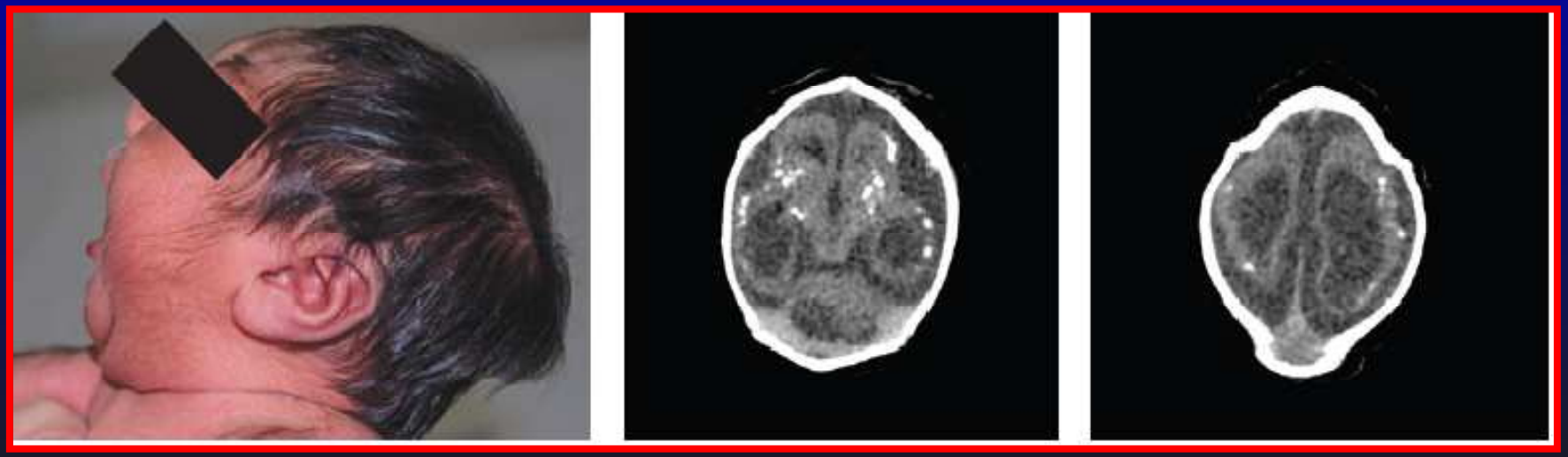
Evidence that maternal ZIKV infection during the first trimester of pregnancy can result in placental and fetal damage and loss.

Lancet, August 2016

Association between Zika virus infection and microcephaly in Brazil, January to May, 2016: preliminary report of a case-control study

	Cases (n=32)	Controls (n=62)	p value
RT-PCR or Zika virus-specific IgM (cerebrospinal fluid or serum)			
Positive	13 (41%)	0	<0·0001
Negative*	19 (59%)	62 (100%)	
RT-PCR or Zika virus-specific IgM (serum)			
Positive	9 (28%)	0	<0·0001
Negative	23 (72%)	62 (100%)	

Data suggest that the microcephaly epidemic is a result of congenital Zika virus infection



Araujo T et al. Lancet Infect Dis 2016; 16: 1356–63

Zika virus in Brazil and macular atrophy in a child with microcephaly

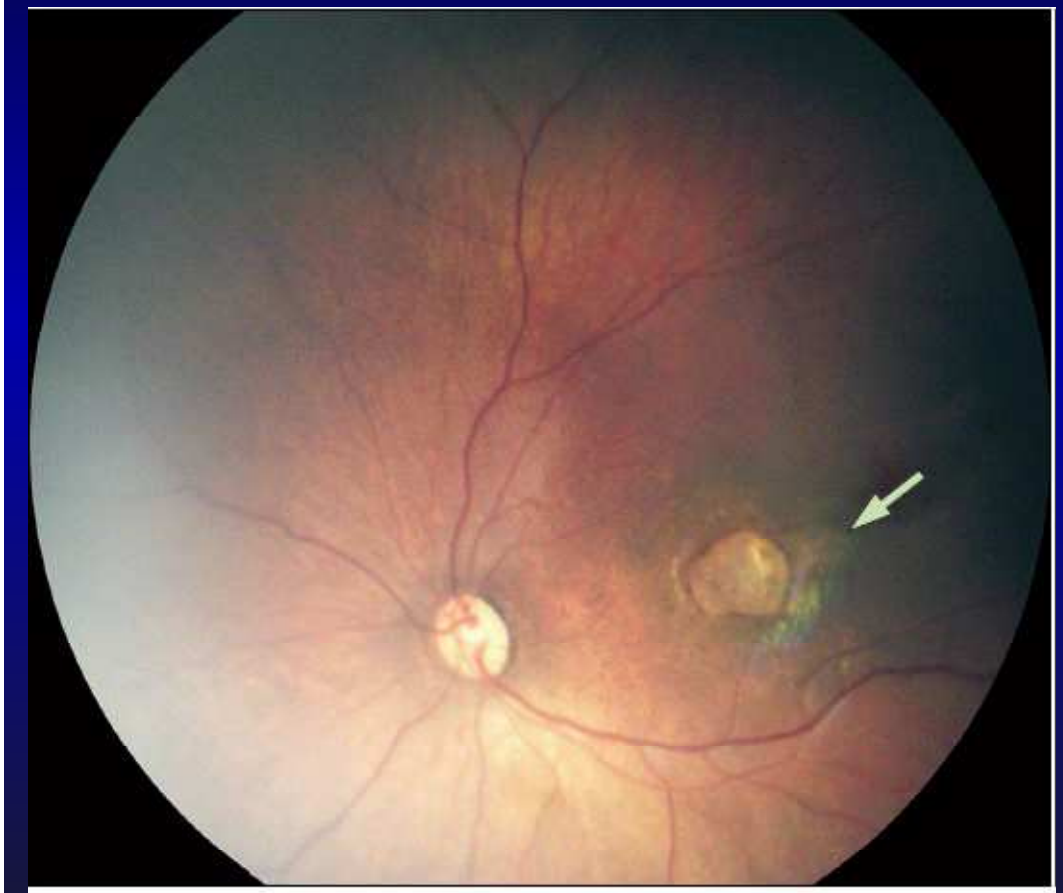
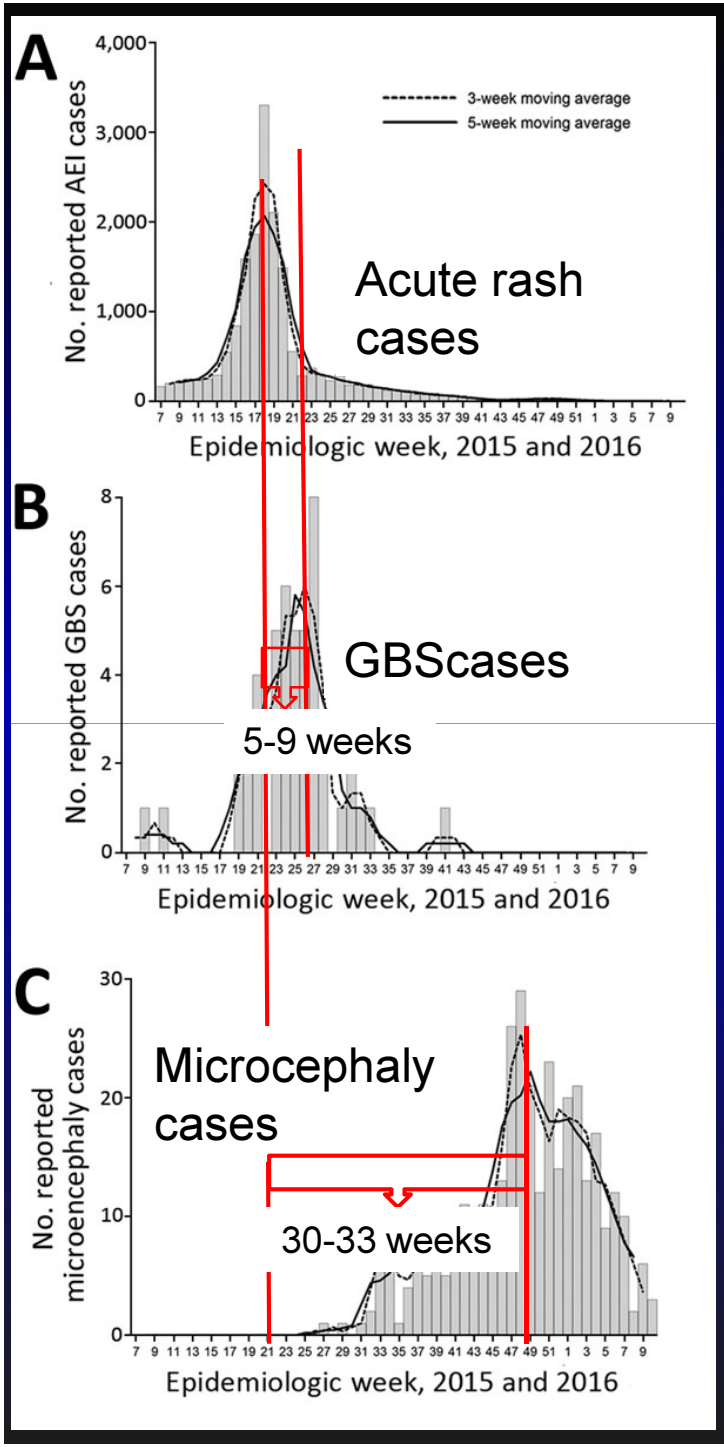


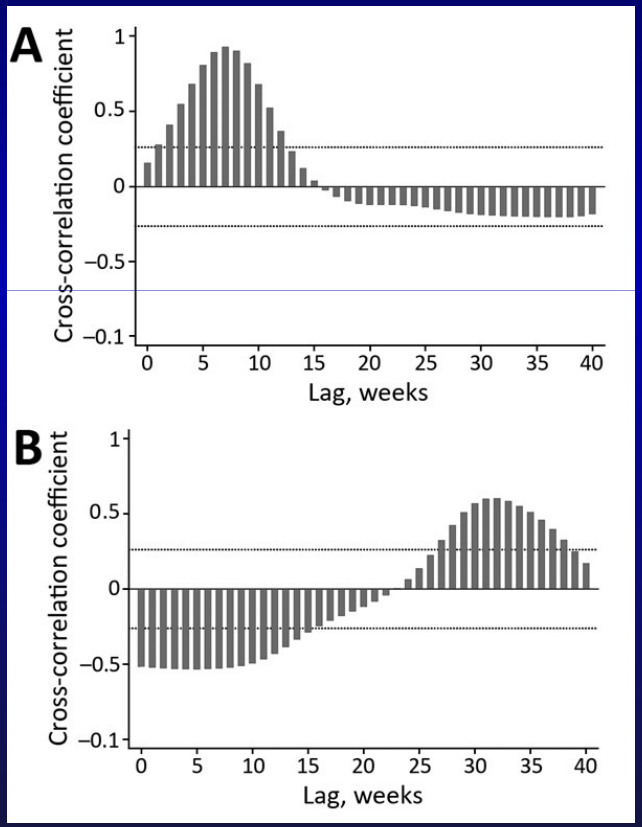
Figure: Severe macular neuroretinal atrophy in an infant with microcephaly

- 3 infants with microcephaly and unilateral ocular findings involving the macular region.

Vbentura C. Lancet, 2016

Time Lags between Exanthematous Illness Attributed to Zika Virus, Guillain-Barré Syndrome, and Microcephaly, Salvador, Brazil





- Cross-correlation of acute rash illness with A) GBS and B) microcephaly, Brazil, 2015–2016.
- Dotted horizontal lines indicate 95% tolerance intervals for a null model of no association

Paploski IAD, et al. Emerg Infect Dis. 2016 Aug

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 15, 2016 VOL. 375 NO. 24

Zika Virus Infection in Pregnant Women in Rio de Janeiro

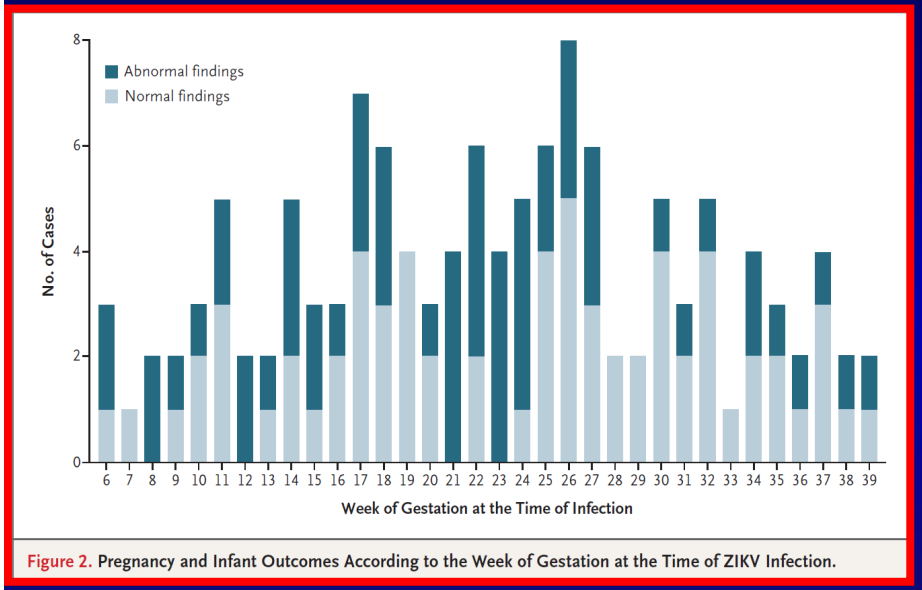


Figure 2. Pregnancy and Infant Outcomes According to the Week of Gestation at the Time of ZIKV Infection.

116 ZIKV infected pregnant women.
Abnormal clinical and/or brain imaging findings in 42% of the live infants.

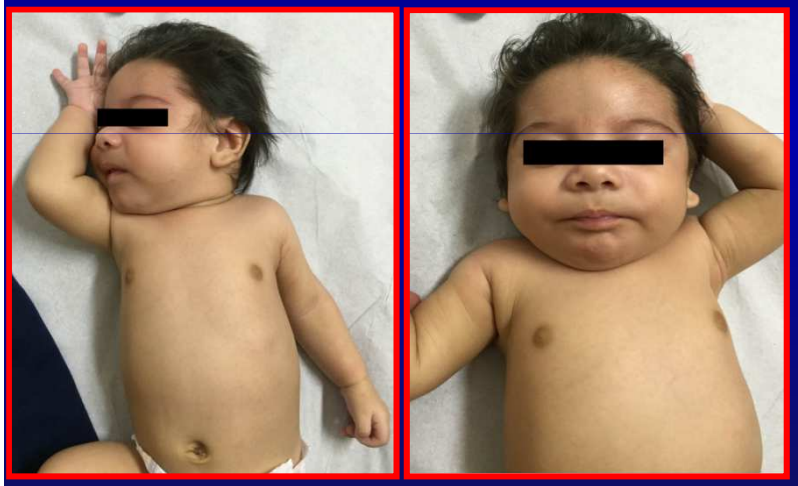
(55% of pregnancies had adverse outcomes after maternal infection in the first trimester, 52% after infection in the second trimester, and 29% after infection in the third trimester).

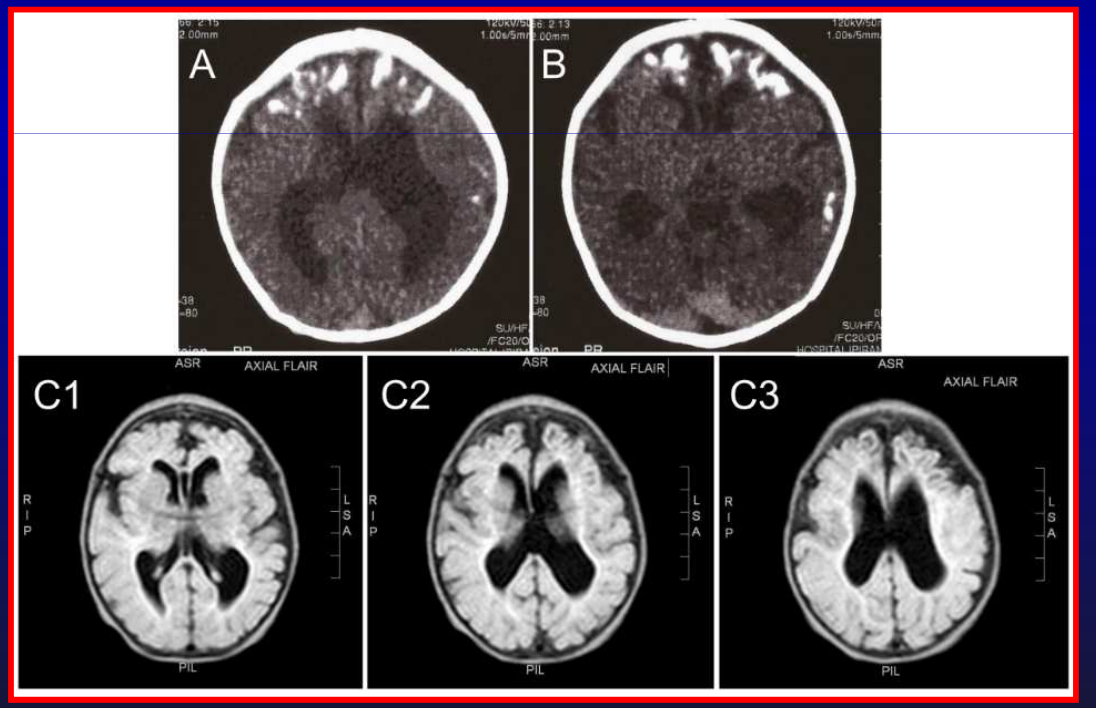
Brasil P et al. NEJM, 2016

The NEW ENGLAND JOURNAL of MEDICINE

Prolonged Shedding of Zika Virus Associated with Congenital Infection

Male, 2 months old. Born in 02/Jan/2016 at 40 weeks of gestation, with 3,095g; 48cm; HC 32.5cm. Mother reported a febrile rash around the 26th week of the gestation. Her husband presented a similar disease 3 weeks earlier, after returning from a trip to northeast Brazil.





Positive results for ZIKV genome (PCR) in sera; saliva; urine and plasma at 55 days and again at 70 days of life. IgM+ and IgG +

NEJM, 2016

This case report in intriguing since it brings to discussion two key points:

1. The true burden of the congenital disease associated with ZIKV is probably underestimated assuming that it is likely that a significant proportion of the affected newborns have subclinical manifestations at birth, without microcephaly, preventing these infants to be diagnosed by the current ascertainment methods, at least until later stages of the childhood / adolescence

2. If persistent viremia is present in these congenitally infected infants, can we expect further impact of the virus on CNS, eyes, etc?

Why the occurrence of microcephaly and other neurological congenital malformations related to maternal ZIKV infection during pregnancy was not detected before the outbreak in Brazil?

- In French Polynesia, the annual birth cohort is 4,000 newborns

Taking in account the baseline incidence of microcephaly and assuming a 10-fold higher incidence rate we would see only 4-8 cases per year!!!!!

- In Brazil, the annual birth cohort is ~ 2.8 million newborns,

Capitals in the northeast are densely populated, facilitating the identification of an increased number of newborns with neurological malformations

- Population in Brazil was naive to ZIKV, 100% susceptible to infection.

If ZIKV infection is associated with life long immunity, in places where the virus is circulating for years, a proportion of the women in childbearing age is likely to be previously infected, limiting the number of susceptible women.

Association between Zika virus and microcephaly in French Polynesia, 2013–15: a retrospective study

Simon Cauchemez, MarianneBesnard, Priscillia Bompard, Timothée Dub, Prisca Guillemette-Artur, Dominique Eyrolle-Guignot, Henrik Salje, Maria D Van Kerkhove, Véronique Abadie, Catherine Garel, Arnaud Fontanet*, Henri-Pierre Mallet*

	Baseline prevalence of microcephaly per 10 000 neonates	Number of microcephaly cases per 10 000 women infected in the period of risk	Risk ratio (95% CI)	p value*	AICc for model fit†
Trimester 1	2 (0–8)	95 (34–191)	53·4 (6·5–1061·2)	0·0007	0
Trimesters 1 and 2	2 (0–8)	50 (17–101)	26·4 (3·0–352·0)	0·0015	1·37
Trimesters 1, 2, and 3	2 (0–9)	42 (13–86)	20·8 (2·1–424·1)	0·0032	2·73
Trimester 2	4 (0–12)	84 (12–196)	23·2 (1·4–407·8)	0·02	5·76
Trimesters 2 and 3	4 (0–13)	53 (0–135)	11·9 (0–177·5)	0·05	7·67
Trimester 3	10 (3–18)	0 (0–251)	0 (0–49·3)	1·0	11·43
No association	10 (5–18)	..	..	..	7·15

Six scenarios were considered for the "period of risk" during pregnancy when infection of the mother with Zika virus might increase the risk of microcephaly. A last scenario assumed no association between infection and microcephaly. AICc=Akaike information criterion with a correction for small sample size. *Compared with no association. †Quality of fit increases with decreasing value, with differences in values ≥4 indicating substantial improvement in fit.[31]

Table 2: Prevalence and risk of microcephaly associated with Zika virus infection for different periods of risk during pregnancy

The risk of microcephaly related to ZIKV infection was ~1% for women infected in the first trimester.

Lancet, 2016 Published online March 15, 2016

Table 3. Countries and territories reporting microcephaly and/or CNS malformation cases potentially associated with Zika virus infection

Reporting country or territory	Number of microcephaly and/or CNS malformation cases suggestive of congenital Zika infections or potentially associated with a Zika virus infection	Probable location of infection
Brazil	1857[6]	Brazil
Cabo Verde	9	Cabo Verde
Canada	1	Undetermined
Costa Rica	1	Costa Rica
Colombia	38[7]	Colombia
Dominican Republic	3	Dominican Republic
El Salvador	4	El Salvador
French Guiana	3[8]	French Guiana
French Polynesia	8	French Polynesia
Haiti	1	Haiti
Honduras	1	Honduras
Marshall Islands	1	Marshall Islands
Martinique	10[8]	Martinique
Panama	5	Panama
Paraguay	2[9]	Paraguay
Puerto Rico	1	Puerto Rico
Slovenia	1[10]	Brazil
Spain	2	Colombia, Venezuela (Bolivarian Republic of)
Suriname	1	Suriname
United States of America*	21[11]	Undetermined**

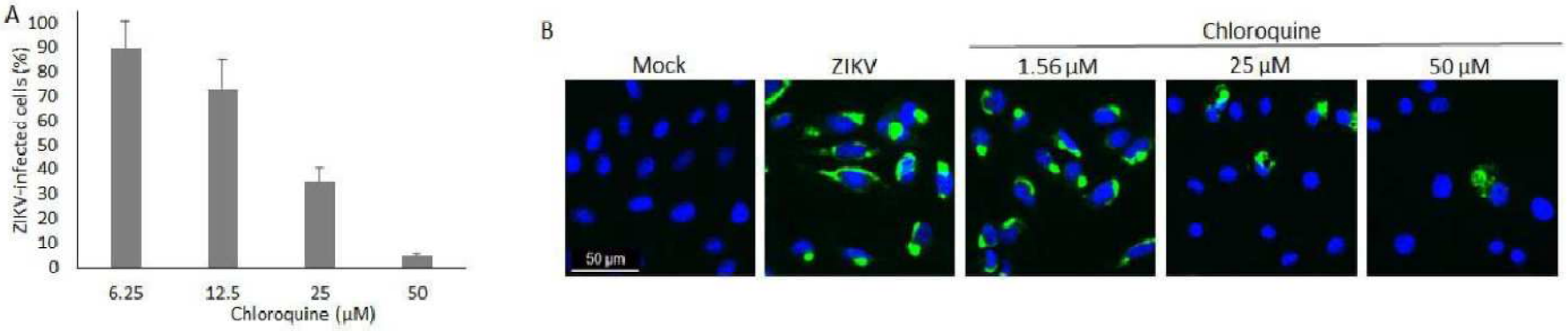
Hearing Loss in Infants with Microcephaly and Evidence of Congenital Zika Virus Infection — Brazil, November 2015–May 2016

- Among 70 infants with microcephaly and laboratorial evidence of congenital ZIKV infection , 4 out of 69 (5.8%) presented neuro-sensorial hearing loss without other possible causes.
- Trend to increased risk in women infected during the first trimester of pregnancy and in more severe microcephaly cases

MMWR Morb Mortal Wkly Rep 2016;65:917–919

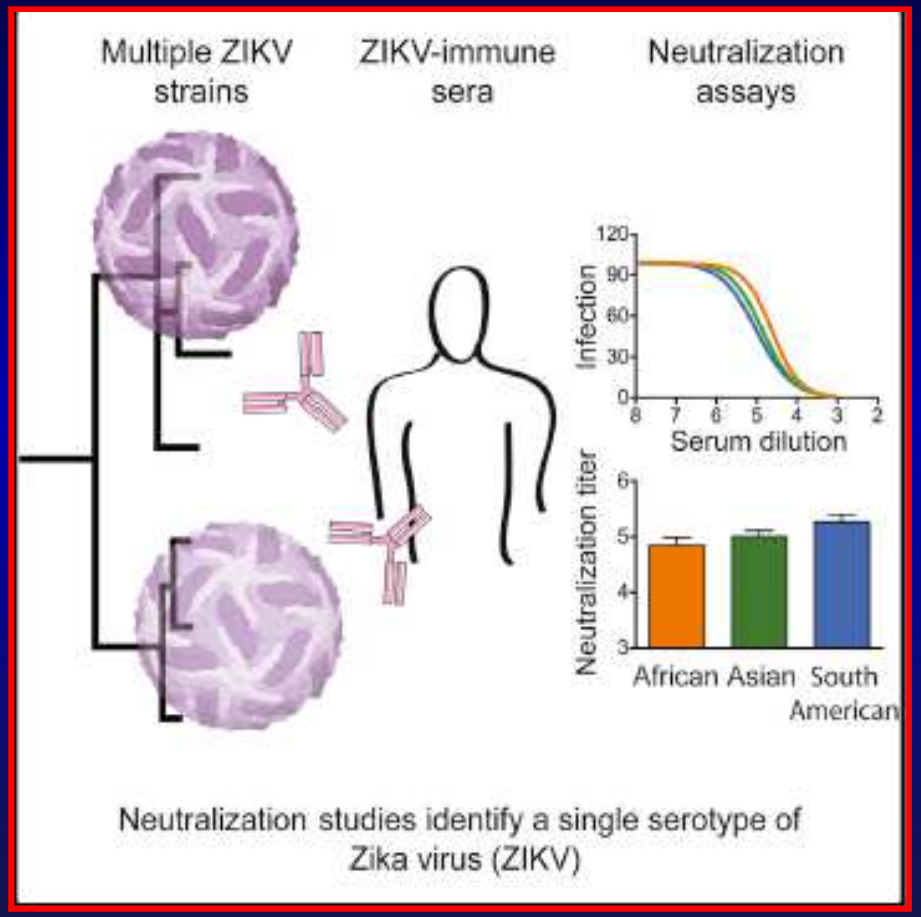
Potential therapeutic interventions

- Chloroquine exhibited antiviral activity against ZIKV in VERO, human brain microvascular endothelial, and neural stem cells.
- Chloroquine reduced *in vitro* the number of ZIKV-infected cells, virus production and cell death promoted by ZIKV infection without cytotoxic effects



Delvecchio R et al. bioRxiv, May. 2, 2016

Broadly Neutralizing Activity of Zika Virus-Immune Sera Identifies a Single Viral Serotype



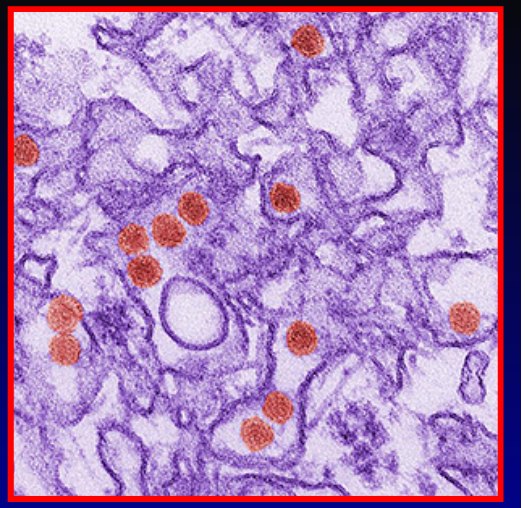
Neutralization studies identify a single serotype of Zika virus (ZIKV)

- Neutralization studies with convalescent ZIKV-immune sera identify a single serotype
- Infection with a single ZIKV strain elicits broadly neutralizing antibodies
- Strain selection may not be a critical parameter for ZIKV vaccine development

Cell Reports *16*, 1485–1491, August 9, 2016

Vaccines

- ✓ DNA-based vacines (NIH)
- ✓ Inactivated vacines
- ✓ Live attenuated, chimeric vaccines



Science

RESEARCH ARTICLES

Cite as: Abbink *et al.*, *Science*
10.1126/science.aah6157 (2016).

Protective efficacy of multiple vaccine platforms against Zika virus challenge in rhesus monkeys

urgent global health priority. Here we demonstrate that three different vaccine platforms protect against ZIKV challenge in rhesus monkeys. A purified inactivated virus vaccine induced ZIKV-specific neutralizing antibodies and completely protected monkeys against ZIKV strains from both Brazil and Puerto Rico. Purified immunoglobulin from vaccinated monkeys conferred passive protection in adoptive transfer studies. A plasmid DNA vaccine and a single-shot recombinant rhesus adenovirus serotype 52 vector expressing ZIKV prM-Env also elicited neutralizing antibodies and completely protected monkeys against ZIKV challenge. These data support the rapid clinical development of ZIKV vaccines for humans.

Key points

- ✓ Co-circulation of dengue, zika and chikungunya occurred for the first time in Brazil.
- ✓ The only intervention currently available to decrease the burden of ZIKV disease and other arboviruses is mosquito control, which, for *Aedes* spp mosquitoes has been unsuccessful in our setting.
- ✓ The true burden of the congenital disease associated to ZIKV is probably underestimated
- ✓ The potential teratogenicity of the ZIKV was established in Brazil for the very first time.
- ✓ We still have unanswered questions: the role of co-infections, previous infections and other risk factors in the neurological outcomes and for congenital disease.
- ✓ Case-control and cohort studies are on going to address these issues


Obrigado!
Gracias!