1º SIMPÓSIO GAÚCHO
DA SÍNDROME DA
ZIKA CONGÊNITA

# A epidemia de Zika no Brasil e a Síndrome da Zika Congênita

**Prof. Lavínia Schuler-Faccini**
Universidade Federal do Rio Grande do Sul
Presidente – Rede Latinoamericana de Genetica Humana

**Prof. Maria Teresa Vieira Sanseverino**
Pontificia Universidade Catolica Porto Alegre
Hospital de Clinicas de Porto Alegre

PPGBM Programa de Pós-Graduação em Genética e Biologia Molecular da UFRGS 50 ANOS

REALIZAÇÃO:

GENÉTICA
SERVIÇO DE GENÉTICA MÉDICA
HOSPITAL DE CLÍNICAS DE PORTO ALEGRE

25 anos SBG

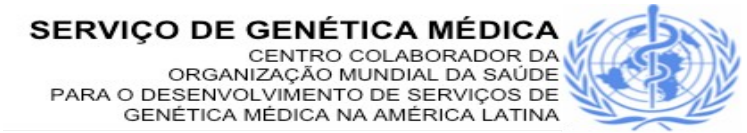
GOVERNO DO ESTADO DO RIO GRANDE DO SUL
TODOS PELO RIO GRANDE
SECRETARIA DA SAÚDE

# Disclosure: No conflicts of interest

## Funding and support:







Sistema Nacional de Informação sobre Agentes Teratogênicos

20 anos

# Gravidez Segura .org

HOSPITAL DE CLÍNICAS PORTO ALEGRE RS

UFRGS UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL


Apoio financeiro: CNPq, PROPEXT

# siat@gravidez-segura.org


Gravidez Segura.org

HOSPITAL DE CLÍNICAS
PORTO ALEGRE RS

UFRGS
UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL

**55 51 3359-8008**

**http://gravidez-segura.org**

**siat@gravidez-segura.org**

**www.facebook.com/gravidez.segura**

Apoio financeiro: CNPq, PROPEXT

Available online at www.sciencedirect.com
ScienceDirect
Reproductive Toxicology 25 (2008) 120–123
Reproductive Toxicology
Developmental Basis of Health and Disease
www.elsevier.com/locate/reprotox

# Prospective evaluation of pregnant women vaccinated against rubella in southern Brazil

Lenice Minussi [a,b,c], Renate Mohrdieck [d], Marilina Bercini [d], Tani Ranieri [d], Maria Teresa Vieira Sanseverino [c], Wakana Momino [a,b], Sidia Maria Callegari-Jacques [b,e], Lavínia Schuler-Faccini [a,b,c,*]

[a] Genetics Department, Universidade Federal do Rio Grande do Sul, Brazil
[b] Genetics and Molecular Biology Post-Graduate Program, Universidade Federal do Rio Grande do Sul, Brazil
[c] Teratogen Information Service, Medical Genetics Service, Hospital de Clinicas de Porto Alegre, Brazil
[d] Division of Epidemiological Surveillance, Centro Estadual de Vigilância em Saúde, Secretaria de Saúde do Rio Grande do Sul, Brazil
[e] Statistics Department, Universidade Federal do Rio Grande do Sul, Brazil

Received 16 May 2007; received in revised form 3 September 2007; accepted 13 September 2007
Available online 16 September 2007

**Vacinas**

**Infecções Congênitas**

OPEN ACCESS Freely available online
PLOS | ONE

# Impact on Pregnancies in South Brazil from the Influenza A (H1N1) Pandemic: Cohort Study

André Anjos da Silva[1,2], Tani Maria Schilling Ranieri[3], Fernanda Duarte Torres[1], Fernanda Sales Luiz Vianna[1], Graziella Rangel Paniz[1], Paula Baptista Sanseverino[1], Paulo Dornelles Picon[4], Pietro Baptista de Azevedo[1], Marta Haas Costa[1], Lavinia Schuler-Faccini[1,2]*, Maria Teresa Vieira Sanseverino[1]

# Brief history

**1947 – Virus isolated (Rhesus monkey)**

**1948 – Virus isolated from *Ae. africanus***

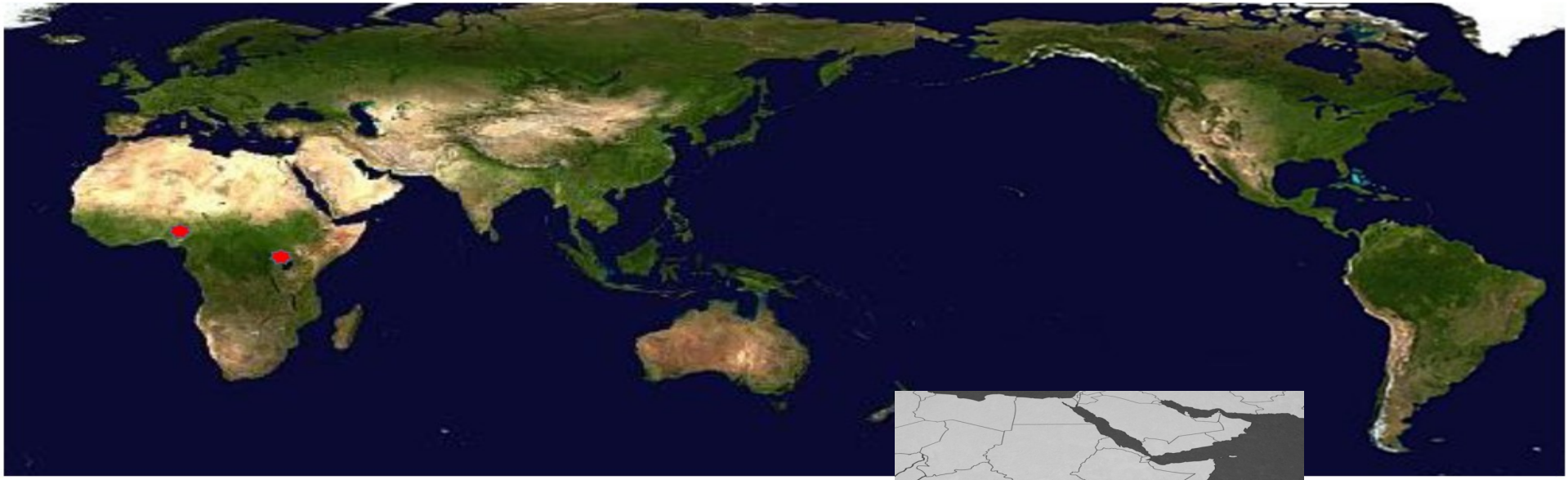



# Brief history

**1947 – Virus isolated (Rhesus monkey)**

**1948 – Virus isolated from *Ae. africanus***

**1954 – 1st human case, Nigeria**



# Brief history

**1947 – Virus isolated (Rhesus monkey)**
**1948 – Virus isolated from *Ae. africanus***

**1954 – 1st human case, Nigeria**

**Next 50 yrs – other areas in Africa/Asia**

**2007-14 – Reach Pacific Islands**

# Brief history

**1947 – Virus isolated (Rhesus monkey)**
**1948 – Virus isolated from *Ae. africanus***

**1954 – 1st human case, Nigeria**

**Next 50 yrs – other areas in Africa/Asia**

**2007-14 – Reach Pacific Islands**

**2015 – 1st cases in the Americas (arrival of the virus could have been in 2013)**

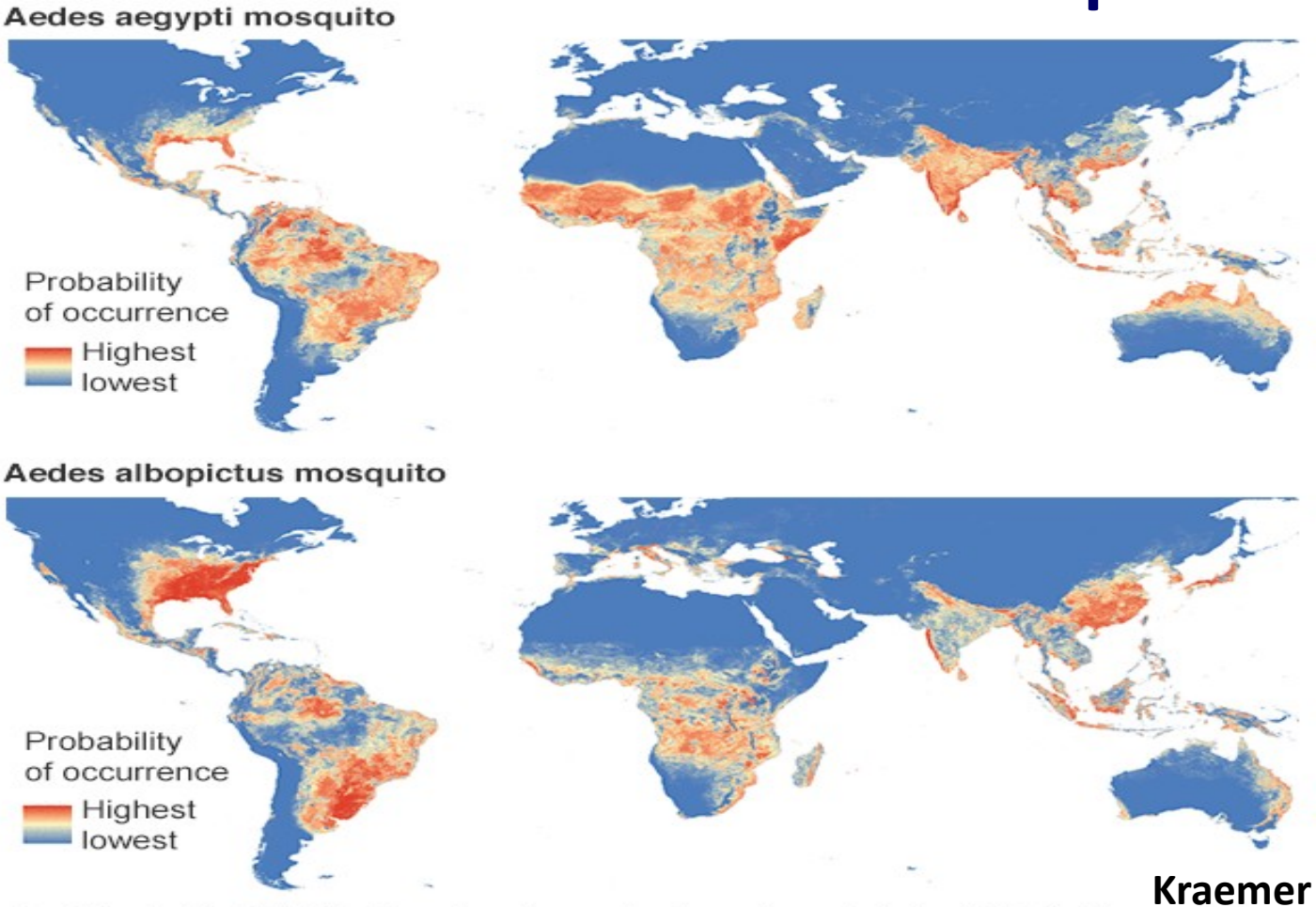
# Zika virus

- **Flavivirus**
  - **Dengue, West Nile, Japanese encephalitis, Yellow fever**
- **Primarily transmitted through the bite of an infected *Aedes* mosquito**
  - **Other modes: sexual transmission (importance?)**
- **Most common symptoms (usually mild): fever, rash, joint pain, conjunctivitis**
- **Many people infected with Zika virus present NO symptoms**

# Zika virus

- **Treatment:**
  - **There is no medicine to treat ZIKV**
- **Prevention:**
  - **There is no vaccine to prevent ZIKV**
    - **Long lasting immunity**
  - **Reduce exposure to vector (repellent)**
  - **Vector control**

# Global Distribution of *Aedes* Mosquitoes




Kraemer et al, 2015

# Zika Virus Outbreak, Bahia, Brazil

**Gubio S. Campos, Antonio C. Bandeira, Silvia I. Sardi**

Authors affiliations: Federal University of Bahia, Salvador, Bahia, Brazil (G.S. Campos, S.I. Sardi); Hospital Aliança, Salvador (A.C. Bandeira)

DOI: http://dx.doi.org/10.32301/eid2110.150847

**To the Editor:** Zika virus (ZIKV) is a mosquito-borne flavivirus related to yellow fever virus, dengue virus (DENV), and West Nile virus (WNV). It is a single-stranded positive RNA virus (10,794-nt genome) that is closely related to the Spondweni virus and is transmitted by many *Aedes* spp. mosquitoes, including *Ae. africanus*, *Ae. luteocephalus*, *Ae. hensilli*, and *Ae. aegypti*. The virus was identified in rhesus monkeys during sylvatic yellow fever surveillance in the Zika Forest in Uganda in 1947 and was reported in humans in 1952 (*1*).

In 2007, an outbreak of ZIKV was reported in Yap Island, Federated States of Micronesia (*2*). ZIKV also caused a major epidemic in the French Polynesia in 2013–2014 (*3*), and New Caledonia reported imported cases from French Polynesia in 2013 and reported an outbreak in 2014 (*4*).

A new challenge has arisen in Brazil with the emergence of ZIKV and co-circulation with others arboviruses (i.e., DENV and chikungunya virus [CHIKV]). We report ZIKV infection in Brazil associated with a recent ongoing outbreak in Camaçari, Bahia, Brazil, of an illness characterized by maculopapular rash, fever, myalgias/arthralgia, and conjunctivitis.

On March 26, 2015, serum samples were obtained from 24 patients (Table) at Santa Helena Hospital in Camaçari who were given a presumptive diagnosis of an acute viral illness by emergency department physicians. These

ZIKV infections were assessed by sequencing partial ZIKV envelope gene regions of isolates. Phylogenetic analysis rooted with Spondwei virus showed that ZIKV sequences obtained belonged to the Asian l showed 99% identity with a sequence from a Z from French Polynesia (KJ776791) (*10*).

**Diagnosis:**

**PCR:** specific, but virus have short circulation in blood

**IgM / IgG:** cross-reaction flavivirus

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Early Release / Vol. 65
March 8, 2016

**Increase in Reported Prevalence of Microcephaly in Infants Born to Women Living in Areas with Confirmed Zika Virus Transmission During the First Trimester of Pregnancy — Brazil, 2015**

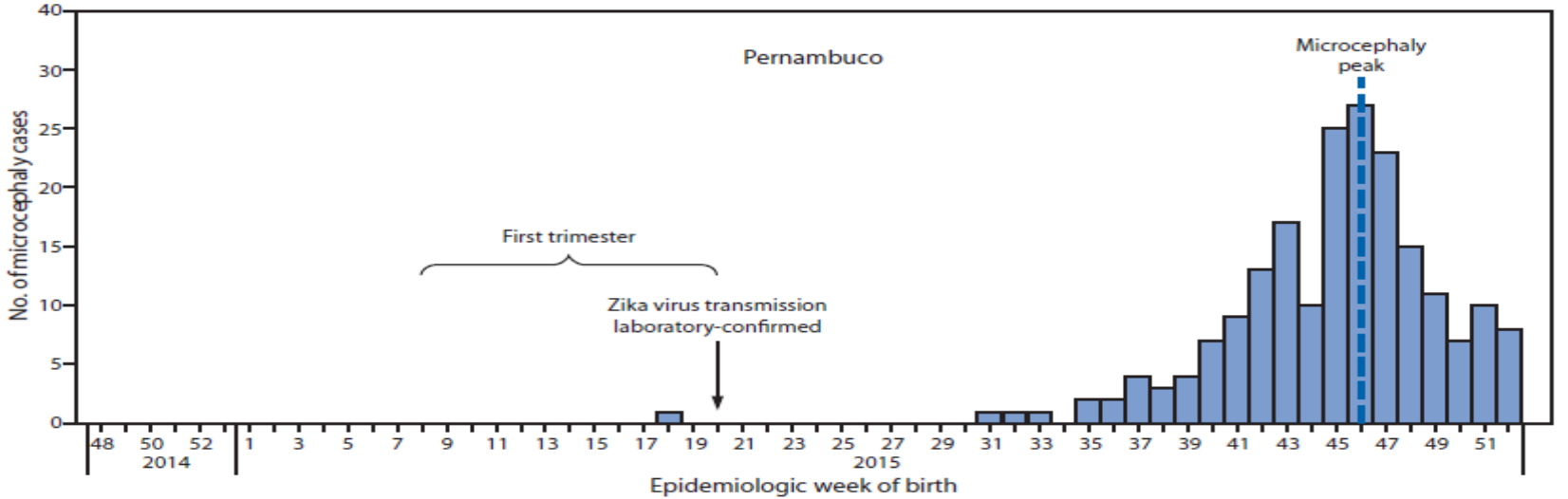
Wanderson Kleber de Oliveira, MSc[1]; Juan Cortez-Escalante, MD[2]; Wanessa Tenório Gonçalves Holanda De Oliveira, MSc[1]; Greice Madeleine Ikeda do Carmo, MSc[1]; Cláudio Maierovitch Pessanha Henriques, MD[1]; Giovanini Evelim Coelho, PhD[1]; Giovanny Vinícius Araújo de França, PhD[1]

# Limitações

Sub-registro antes do alarme
Super-registro depois do alarme

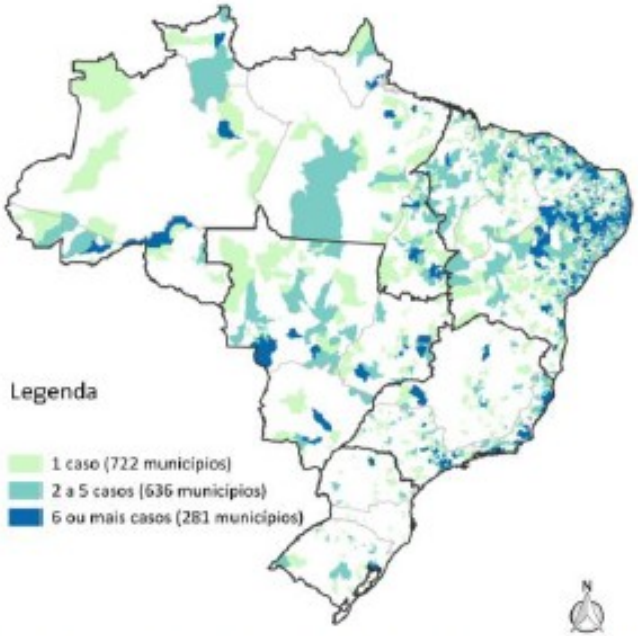
Mudança de critérios

**FIGURE 2. Number of reported cases of microcephaly* in full-term† newborns following laboratory-confirmed Zika virus transmission§ — Pernambuco, Paraíba, and Bahia states, Brazil, 2015**



# INFORME EPIDEMIOLÓGICO Nº 41 – SEMANA EPIDEMIOLÓGICA (SE) 34/2016 (21/08/2016 A 27/08/2016)
# MONITORAMENTO DOS CASOS DE MICROCEFALIA NO BRASIL

CASOS NOTIFICADOS (n = 1.639 municípios)




CASOS CONFIRMADOS (n = 639 municípios)

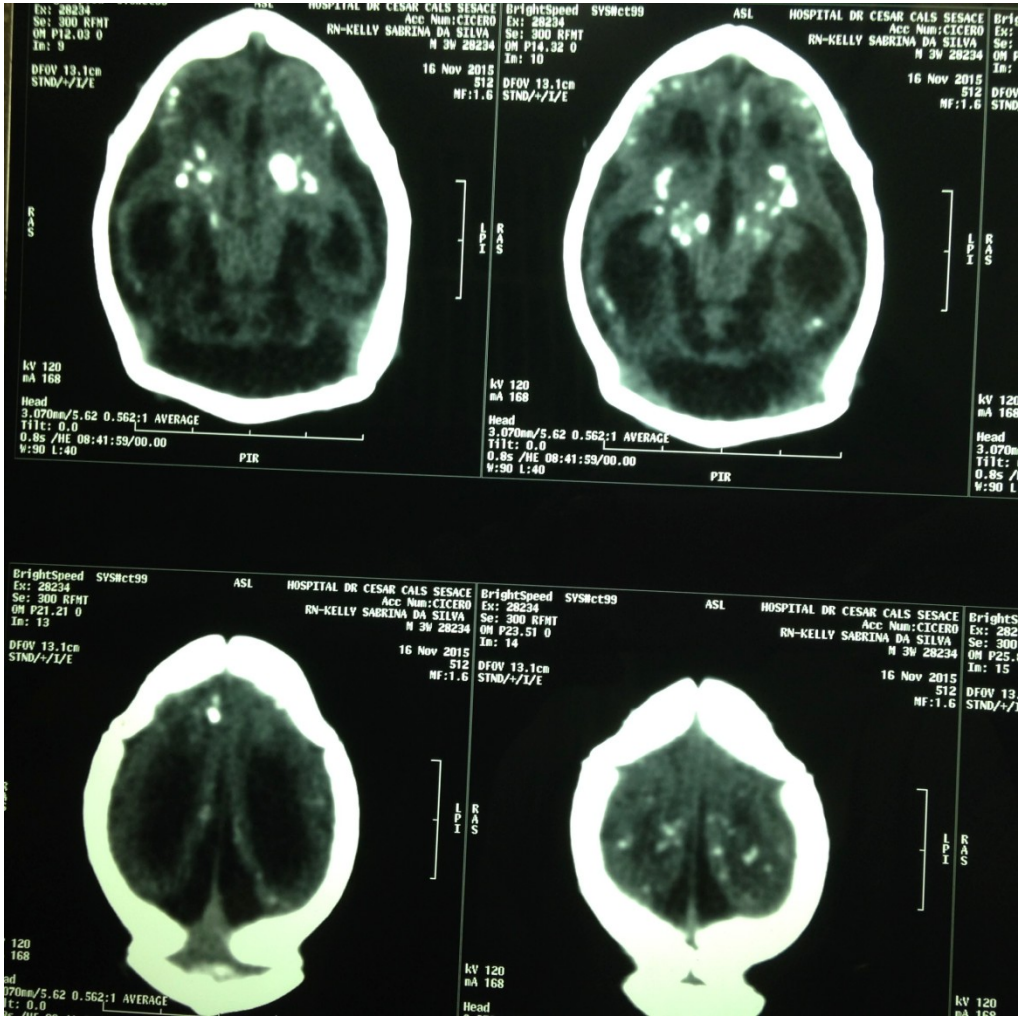




**Fonte:** Secretarias de Saúde dos Estados e Distrito Federal (dados atualizados até 27/08/2016).

# How to identify a new human teratogen?

**Dr. Erlane Ribeiro**


HOSPITAL DR CESAR CALS SESACE
Acc Num:CICERO
RN-KELLY SABRINA DA SILVA
N 3V 28234
16 Nov 2015
512
MF:1.6
BrightSpeed SYSMct99
ASL
kV 120
mA 168
Head
3.070mm/5.62 0.562:1 AVERAGE
Tilt: 0.0
0.8s /HE 08:41:59/00.00
W:90 L:40
PIR
RAS
LPI

Pan American Health Organization

World Health Organization

Regional Office for the Americas

# Epidemiological Alert

## Increase of microcephaly in the northeast of Brazil

17 November 2015

Given the unusual increase in cases of microcephaly in some northeast states of Brazil, the Pan American Health Organization (PAHO) / World Health Organization (WHO) calls upon Member States to remain alert to the occurrence of similar events in their territories and to notify its occurrence through the channels established under the International Health Regulations (IHR).

World Health Organization

# ZIKA SITUATION REPORT

## NEUROLOGICAL SYNDROME AND CONGENITAL ANOMALIES

**5 FEBRUARY 2016**

## GENERAL INFORMATION

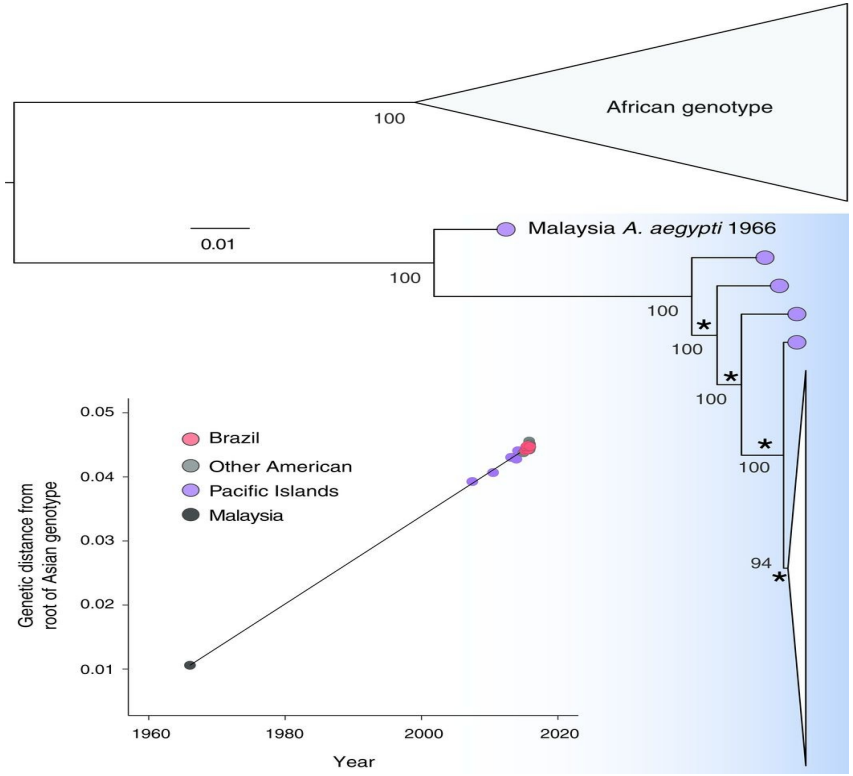
### Zika Virus

- Zika virus disease is caused by a virus transmitted by *Aedes* mosquitoes. Other transmission modes are still under investigation.
- People with Zika virus disease usually have a mild fever, skin rash (exanthema), and conjunctivitis. These symptoms normally last for 2-7 days.
- At present there is no specific treatment or vaccine currently available. The best form of prevention is protection against mosquito bites.
- Zika virus is known to circulate in Africa, the Americas, Asia, and the Pacific region. Zika virus had only been known to cause sporadic infections in humans until 2007, when an outbreak in Micronesia infected 31 people.


## ZIKA – MoH Brazil

- Emergency protocol for health attention for children being born with microcephaly associated to zika in pregnancy
- Mandatory report of all babies born with microcephaly
- Funding for epidemiological, clinic and experimental projects
- Special treatment and care of babies with microcephaly
- Improved birth defects reporting and surveillance

# Fig. 2 Maximum likelihood phylogeny of ZIKV complete coding region sequences.




Nuno Rodrigues Faria et al. Science 2016;352:345-349

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Early Release / Vol. 65
January 22, 2016

# Possible Association Between Zika Virus Infection and Microcephaly — Brazil, 2015

Lavinia Schuler-Faccini, PhD[1]; Erlane M. Ribeiro, PhD[2]; Ian M.L. Feitosa, MD[3]; Dafne D.G. Horovitz, PhD[4]; Denise P. Cavalcanti, PhD, MD[5]; André Pessoa[2]; Maria Juliana R. Doriqui, MD[6]; Joao Ivanildo Neri, MD[7]; Joao Monteiro de Pina Neto, PhD[8]; Hector Y.C. Wanderley, MD[9]; Mirlene Cernach, PhD[10]; Antonette S. El-Husny, PhD[11]; Marcos V.S. Pone, PhD[4]; Cassio L.C. Serao, MD[12]; Maria Teresa V. Sanseverino, PhD[13]; Brazilian Medical Genetics Society–Zika Embryopathy Task Force[14]

SBGM
Sociedade Brasileira de GENÉTICA MÉDICA

# Microcephaly: what the numbers tell us

Comment

## Microcephaly in Brazil: how to interpret reported numbers?

Brazil is facing its first outbreak of Zika virus, particularly in the northeast region. Most cases of Zika virus infection are self-limited and without sequelae, but there have been remain under investigation.[3] Although 36·2% seems to be a high rate of true positives, it has to be interpreted with caution because in the present situation newborn

Published Online
February 5, 2016
http://dx.doi.org/10.1016/
S0140-6736(16)00273-7

*Cesar Gomes Victora, Lavinia Schuler-Faccini, Alicia Matijasevich, Erlane Ribeiro, André Pessoa, Fernando Celso Barros

CPT: Pharmacometrics & Systems Pharmacology
Open Access
An official open access journal of the ASCPT and ISoP

Commentary

# Zika virus: A new human teratogen? Implications for women of reproductive age

1. L Schuler-Faccini[1,2,*],
2. MTV Sanseverino[1,2],
3. FSL Vianna[1,2],
4. AA da Silva[1,3],
5. M Larrandaburu[1,2],
6. C Marcolongo-Pereira[4] and
7. AM Abeche[1,5]

Version of Record online: 13 MAY 2016

DOI: 10.1002/cpt.386



Issue

The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL REPORT

# Zika Virus and Birth Defects — Reviewing the Evidence for Causality

Sonja A. Rasmussen, M.D., Denise J. Jamieson, M.D., M.P.H.,
Margaret A. Honein, Ph.D., M.P.H., and Lyle R. Petersen, M.D., M.P.H.

N ENGL J MED 374;20 NEJM.ORG MAY 19, 2016

# Congenital Zika virus syndrome in Brazil: a case series of the first 1501 livebirths with complete investigation

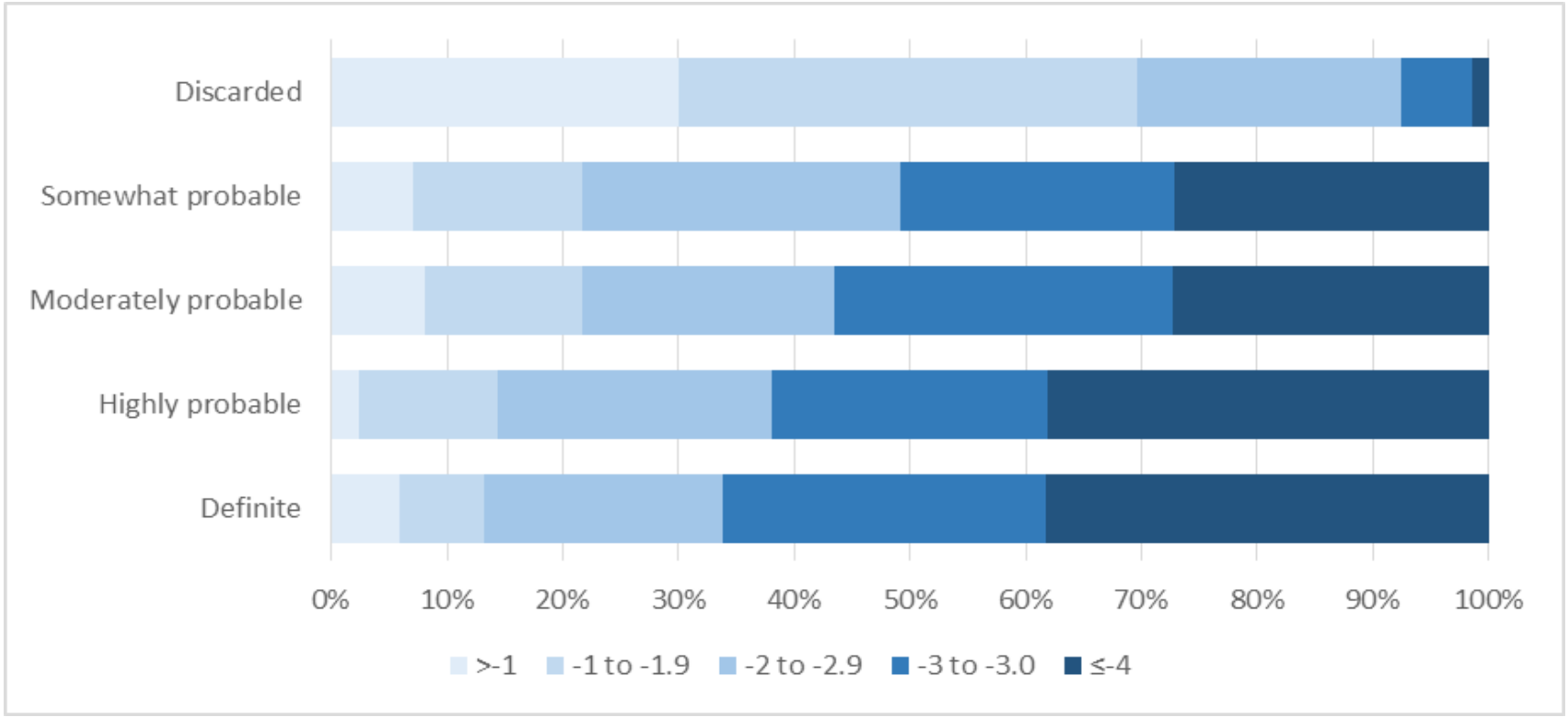
*Giovanny V A França, Lavinia Schuler-Faccini, Wanderson K Oliveira, Claudio M P Henriques, Eduardo H Carmo, Vaneide D Pedi, Marília L Nunes, Marcia C Castro, Suzanne Serruya, Mariângela F Silveira, Fernando C Barros, Cesar G Victora*

www.thelancet.com **Published online June 29, 2016 http://dx.doi.org/10.1016/S0140-6736(16)30902-3**

Published Online
June 29, 2016
http://dx.doi.org/10.1016/
S0140-6736(16)30902-3

See Online/Comment
http://dx.doi.org/10.1016/
S0140-6736(16)30931-X

# Head circumference Z scores by group



# Estimating risks

1. Symptomatic cases: 1- 39% of adverse outcome detected prenatally (US) or at birth – preliminary

2. Asymptomatic cases: We know some asymptomatic women had babies with microcephaly! We DON'T know how many asymptomatic women had NORMAL babies. Absolute risk?

3. Does the risks vary if the infection was asymptomatic in the mother?

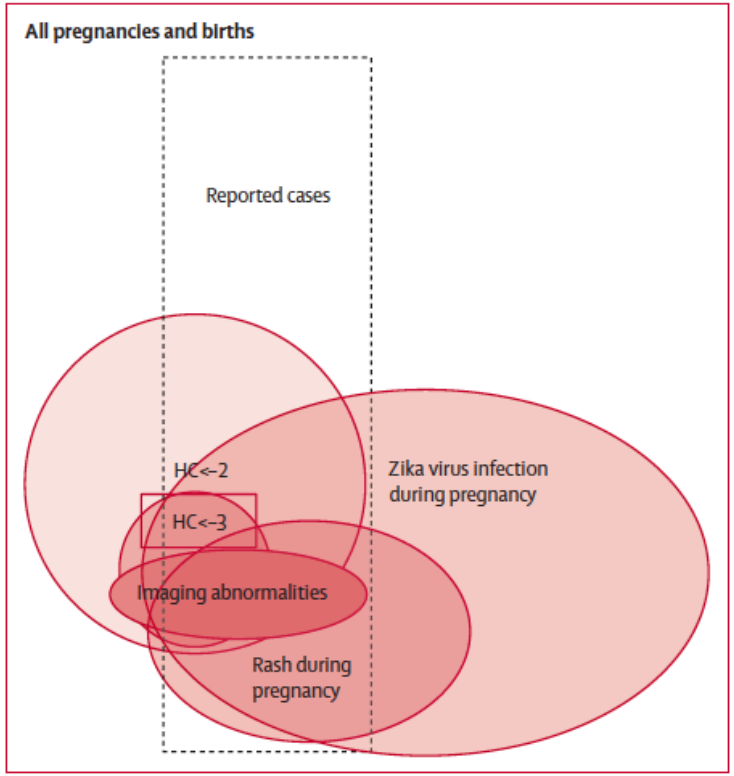



*Figure 3:* **Proposed overlap between Zika virus infection, rash during pregnancy, neuroimaging findings and head size**

# Estimating risks

## Timing of infection:

- First half of pregnancy: Brain Disruption Sequence
- Second half of pregnancy: Generally normal HC, but with possible postnatal developmental problems

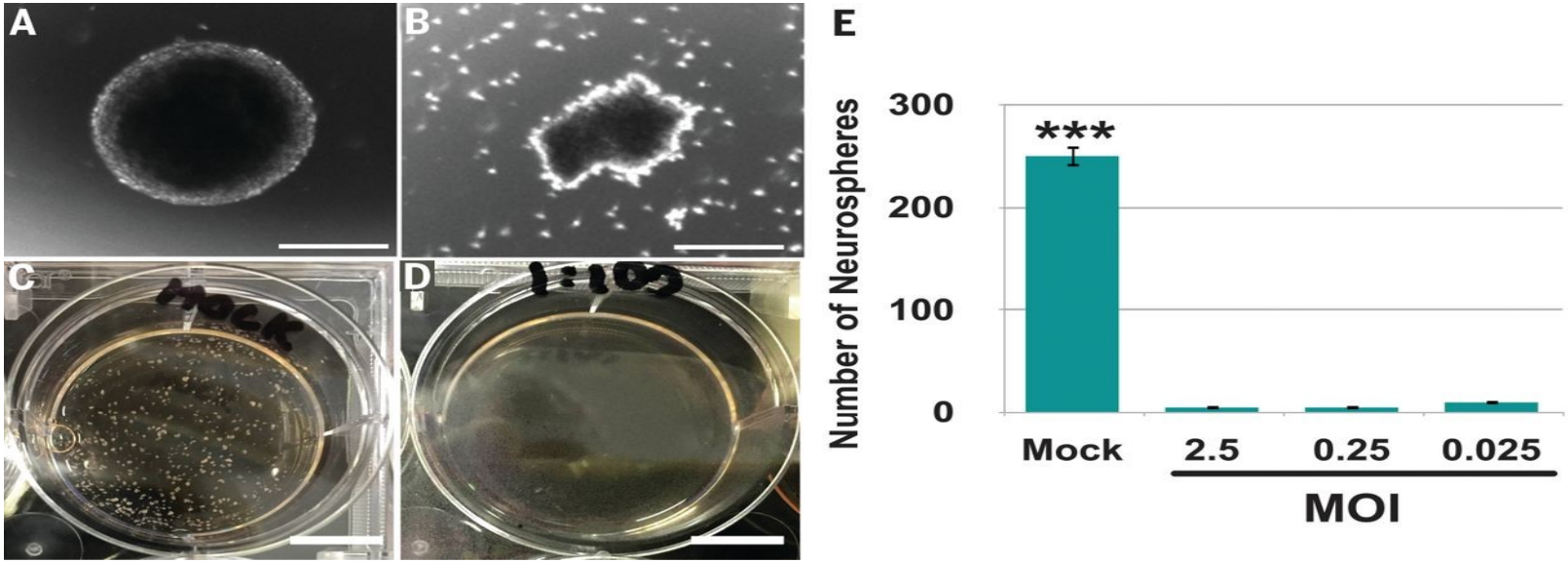
# Zika virus impairs growth in human neurospheres and brain organoids

*by Patricia P. Garcez, Erick Correia Loiola, Rodrigo Madeiro da Costa, Luiza M. Higa, Pablo Trindade, Rodrigo Delvecchio, Juliana Minardi Nascimento, Rodrigo Brindeiro, Amilcar Tanuri, and Stevens K. Rehen*

*Science*
*Volume 352(6287):816-818*
*May 13, 2016*

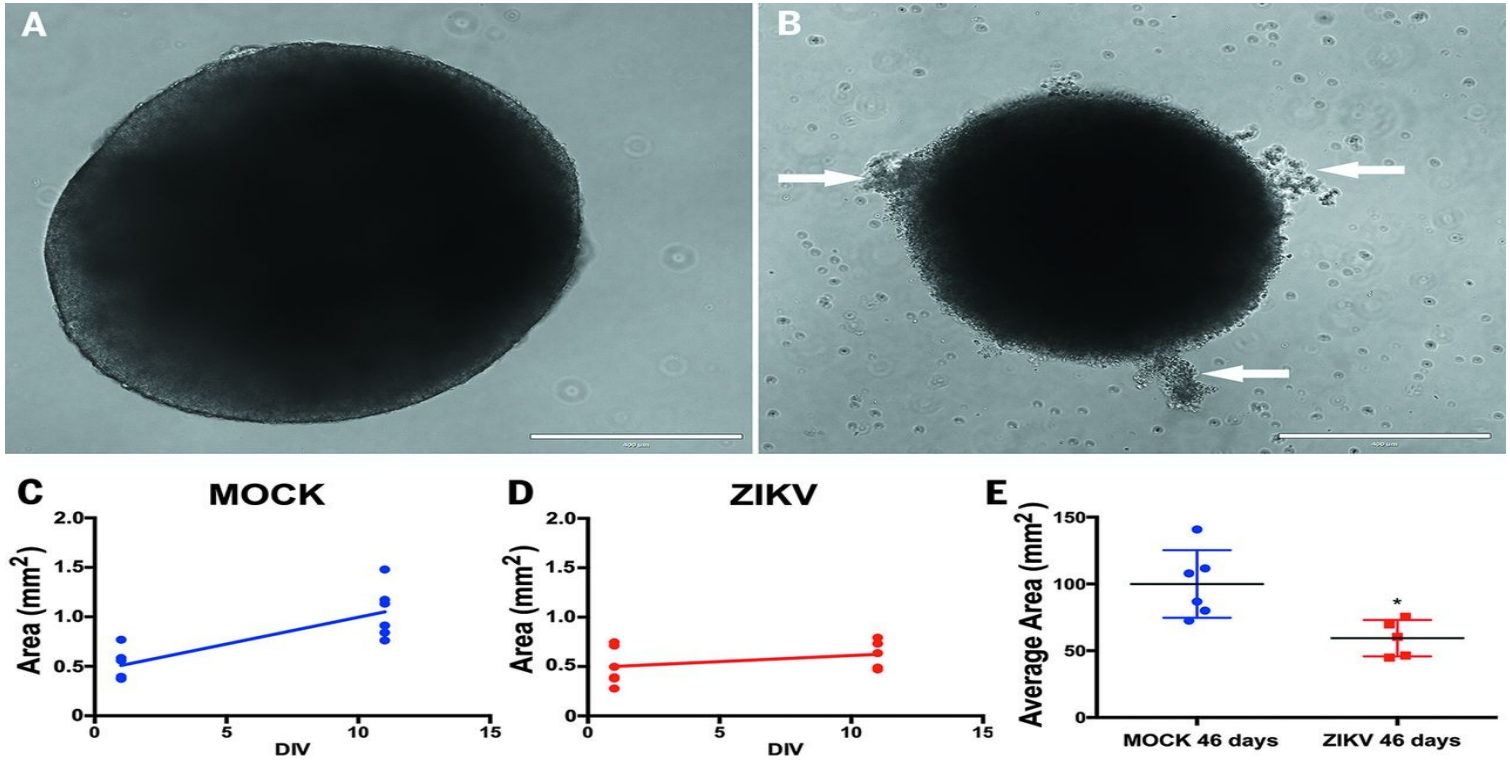
Published by AAAS

**Fig. 2 ZIKV alters morphology and halts the growth of human neurospheres.**




Patricia P. Garcez et al. Science 2016;352:816-818

## Fig. 4 ZIKV reduces the growth rate of human brain organoids.




Patricia P. Garcez et al. Science 2016;352:816-818

Published by AAAS

LETTER

doi:10.1038/nature18296

# The Brazilian Zika virus strain causes birth defects in experimental models

Fernanda R. Cugola[1]*, Isabella R. Fernandes[1,2]*, Fabiele B. Russo[1,3]*, Beatriz C. Freitas[2], João L. M. Dias[1], Katia P. Guimarães[1], Cecília Benazzato[1], Nathalia Almeida[1], Graciela C. Pignatari[1,3], Sarah Romero[2], Carolina M. Polonio[4], Isabela Cunha[4], Carla L. Freitas[4], Wesley N. Brandão[4], Cristiano Rossato[4], David G. Andrade[4], Daniele de P. Faria[5], Alexandre T. Garcez[5], Carlos A. Buchpigel[5], Carla T. Braconi[6], Erica Mendes[6], Amadou A. Sall[7], Paolo M. de A. Zanotto[6], Jean Pierre S. Peron[4], Alysson R. Muotri[2] & Patricia C. B. Beltrão-Braga[1,8]

Rodriguez-Morales et al.
Ann Clin Microbiol Antimicrob (2016) 15:13
DOI 10.1186/s12941-016-0128-2

Annals of Clinical Microbiology and Antimicrobials

EDITORIAL

Open Access

# The expanding spectrum of modes of transmission of Zika virus: a global concern

Alfonso J. Rodriguez-Morales[1,2*], Antonio Carlos Bandeira[3] and Carlos Franco-Paredes[4,5]

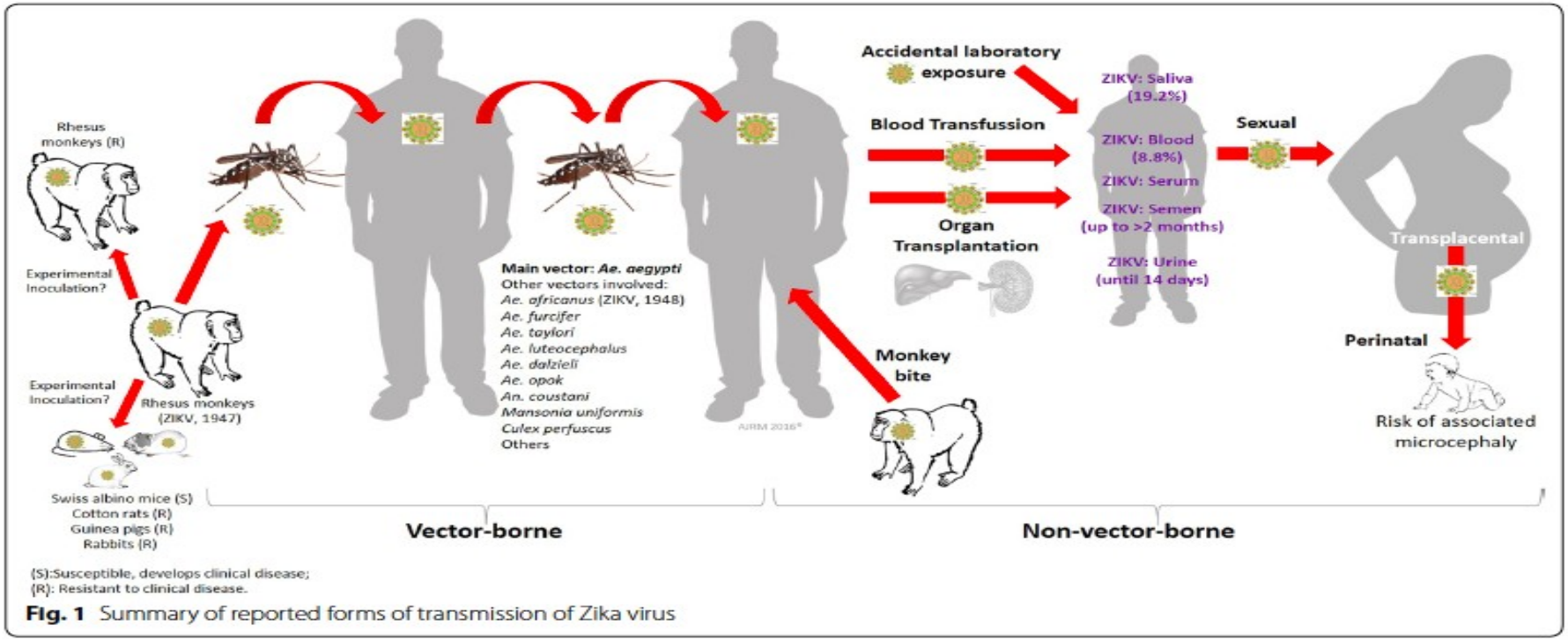



**Fig. 1** Summary of reported forms of transmission of Zika virus

**Thank you / Obrigada / Gracias**

SBGM
Sociedade Brasileira
de GENÉTICA MÉDICA

**www.sbgm.org.br**

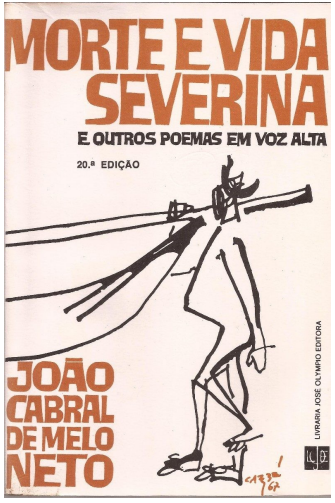

# A tribute to the Brazilian families

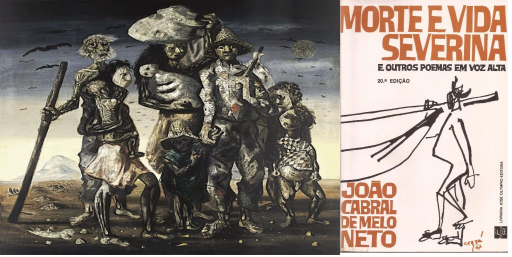
## Morte e Vida Severina
### Auto of Pernambucan Life

Joao Cabral de Melo Neto, 1955

— O meu nome é Severino,
como não tenho outro de pia.
Como há muitos Severinos,
que é santo de romaria,
deram então de me chamar
Severino de Maria;
como há muitos Severinos
com mães chamadas Maria,
fiquei sendo o da Maria
do finado Zacarias.

**Candido Portinari's**
**Retirantes**






# A tribute to the Brazilian families

E se somos Severinos
iguais em tudo na vida,
morremos de morte igual,
mesma morte Severina:
que é a morte de que se morre
de velhice antes dos trinta,
de emboscada antes dos vinte
de fome um pouco por dia
(de fraqueza e de doença
é que a morte Severina
ataca em qualquer idade,
e até gente não nascida).