

# CERPO

Centro de Referencia Perinatal Oriente  
Facultad de Medicina, Universidad de Chile



# Seminario N°79

## Infecciones congénitas IV:

### Virus Zika

Dra. Valentina Alvarez G., Dr. Daniel  
Martin N., Dr Juan Guillermo  
Rodriguez A., Dr. Paz Ahumada D.  
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# INTRODUCCION



Virus de la familia Flaviviridae

Genoma de ARN monocatenario

2 Linajes: Asiático y Africano

Transmitido por hembras mosquitos del género Aedes

Aedes Aegypti

También vector de: Dengue, fiebre Chikungunya y fiebre amarilla



# VIRUS ZIKA: HISTORIA



Tabla 1. Historia de la propagación de la infección por ZIKV en todo el mundo

1947	El ZIKV se detectó por primera vez en monos rhesus en Uganda.
1952	Se ha identificado el primer caso humano en Uganda.
1968	Se ha informado ZIKV en Nigeria.
1951-1981	Se han informado casos de este virus en varios países de Asia y África.
2007	El primer brote se notificó en las Islas Yap, parte de los Estados Federados de Micronesia.
2012-2014	Se han notificado casos en Tailandia.
2013	El virus se propagó a la Polinesia Francesa con un estimado de 28 000 casos. ZIKV se propaga rápidamente a las Islas Cook y la Isla de Pascua.
2015	La infección por el virus del Zika se diagnosticó por primera vez en Brasil. Se encontró que estaba asociado con microcefalia en los bebés de madres con sospecha de infección por ZIKV.
enero 2016	El primer caso de microcefalia por ZIKV ha sido reportado en Hawaii, Estados Unidos.

# VIRUS ZIKA: MECANISMOS DE TRANSMISION



Vector clave → mordedura diurna por el mosquito

## Transmisión sexual

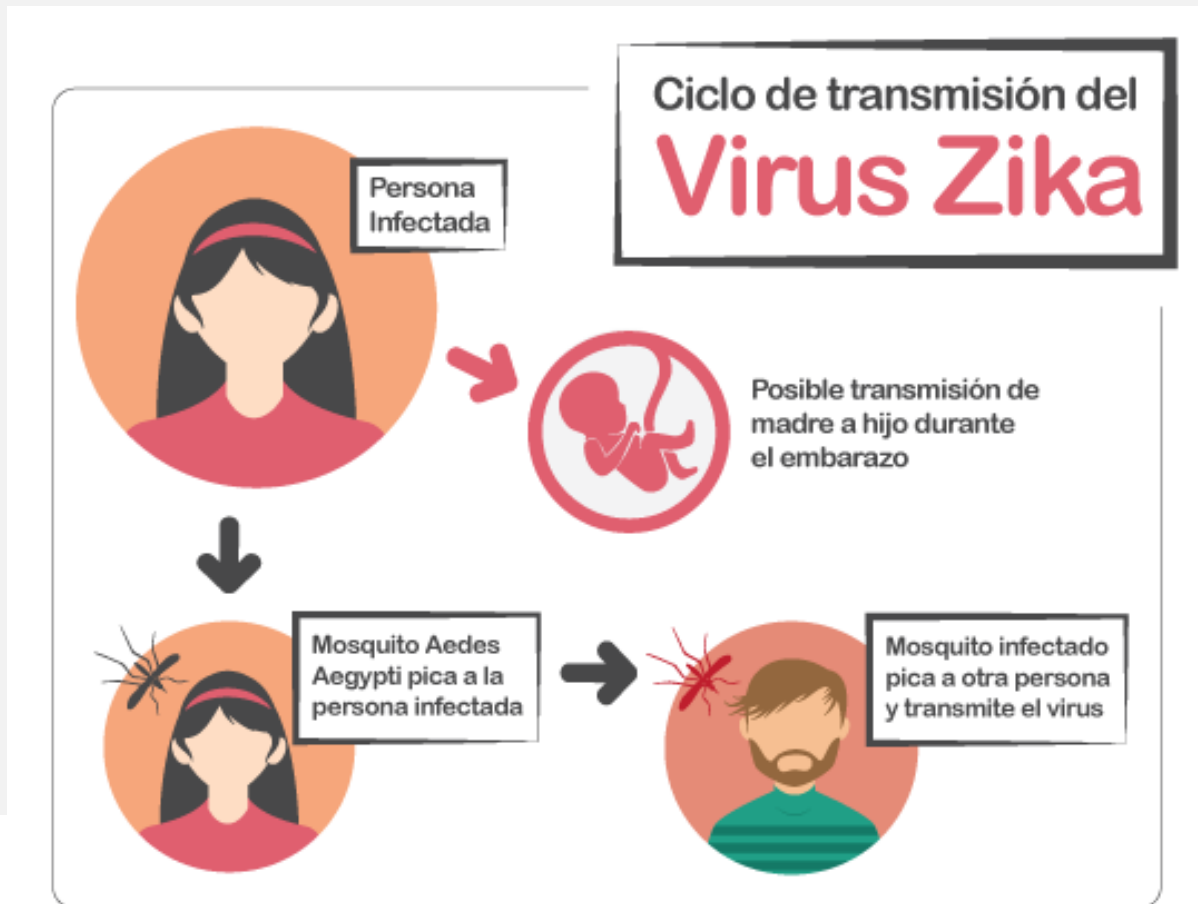
Aislamiento de virus en el semen 17 días posterior al diagnóstico clínico

## Transmisión Sanguínea

Se detectó el virus en donantes de sangre asintomáticos durante el brote en la polinesia francesa

Transmisión vertical: transplacentaria, durante el parto, lactancia?

# VIRUS ZIKA: CICLO TRANSMISION



# CLINICA



- Primeros síntomas generalmente 3-12 días luego de la picadura
- Sólo un 20% sintomáticos
- Duran entre 2-7 días

# CLINICA



- Fiebre
- Exantema maculopapular
- Artralgias
- Conjuntivitis no purulenta



# CASO PROBABLE



## **Box 4: Provisional case definition of suspected acute Zika virus infection. Pan American Health Organization<sup>49</sup>**

- Rash or increase in body temperature ( $>37.2^{\circ}\text{C}$ ), with any of the following not explained by other conditions:
- Arthralgia or myalgia
- Non-purulent conjunctivitis
- Conjunctival hyperaemia
- Headache
- Malaise



# SINTOMAS Y SIGNOS



- Mialgias
- Cefalea
- Dolor retroorbitario
- Dolor abdominal
- Nauseas
- Diarrea
- Ulceras mucosas
- Trombocitopenia
- Petequias
- Uveítis

Hajra, A., Bandyopadhyay, D., Heise, L. R., Bhadra, R., Ball, S., & Hajra, S. K. (2017). Zika and pregnancy: A comprehensive review. *American journal of reproductive immunology (New York, N.Y. : 1989)*, 77(2), 10.1111/aji.12607.

Basarab, M., Bowman, C., Aarons, E. J., & Cropley, I. (2016). Zika virus. *BMJ (Clinical research ed.)*, 352, i1049.

# COMPLICACIONES



- Neurológicas
  - Síndrome Guillian Barré
  - Mielitis
  - Meningoencefalitis

# DIAGNOSTICO



- rRT-PCR en suero: entre 2-7 días post infección
- rRT- PCR en Orina: positiva hasta 14 días después del inicio de los síntomas
- Pruebas serológicas
  - IgM (hasta 12 semanas post infección)
  - Reactividad cruzada con Ac de otros flavivirus ( FP por infección anterior por dengue o vacunación contra fiebre amarilla)

# DIAGNOSTICO



- rRT-PCR liquido amniótico
  - Mujeres (+) o con hallazgos ecográficos compatibles serían candidatas
  - Más sensible >21 semanas
  - Se desconoce el tiempo de duración de una PCR (+), por lo tanto, que esté (-) no descarta infección
  - Exámen histopatológico de placenta y cordón umbilical

# VIRUS ZIKA Y EMBARAZO



- Octubre 2015 Brasil → aumento RN con microcefalia
- 28 enero 2016 OMS: si bien no se ha establecido relación causal, se sospecha firmemente su asociación entre virus Zika, microcefalia y síndromes neurológicos
- Infección entre semana 7 y 13 fuertemente asociada a microcefalia

# VIRUS ZIKA Y EMBARAZO



- RCIU
- Calcificaciones cerebrales
- Doppler ACM y AU
- OHA

Se ha detectado virus en cerebro fetal → virus neurotrópico

Hajra, A., Bandyopadhyay, D., Heise, L. R., Bhadra, R., Ball, S., & Hajra, S. K. (2017). Zika and pregnancy: A comprehensive review. *American journal of reproductive immunology (New York, N.Y. : 1989)*, 77(2), 10.1111/aji.12607

Marrs, C., Olson, G., Saade, G., Hankins, G., Wen, T., Patel, J., & Weaver, S. (2016). Zika Virus and Pregnancy: A Review of the Literature and Clinical Considerations. *American journal of perinatology*, 33(7), 625–639..

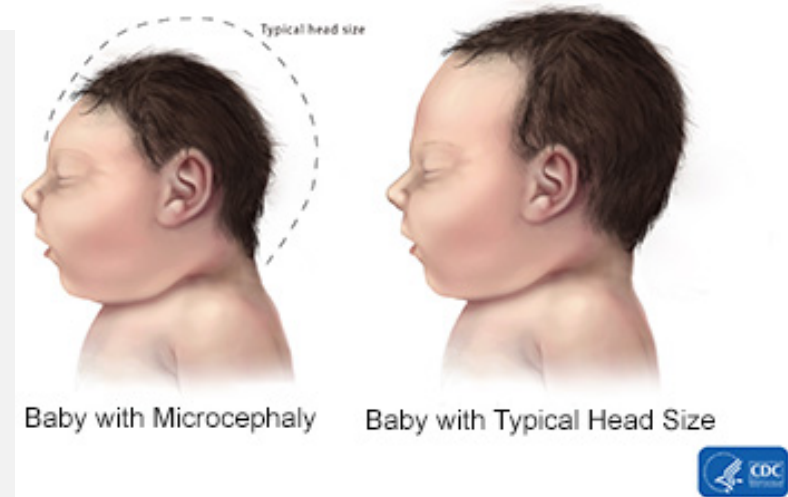
# TRANSMISION AL FETO



- Paso Transplacentario
  - Muestras amniocentesis (+) PCR viral
  - Muestras de LCR (+) IgM Zika en RN con microcefalia
  - se ha demostrado tejido trofoblastico infectado en I, II y III trimestre

# EFFECTOS SOBRE EL FETO

- Microcefalia
- Una vez RN
  - Irritabilidad
  - Hiperrreflexia
  - Hipertonía o espasticidad
  - Temblores y convulsiones





compromiso  
cerebral

1. Cuero cabelludo y pliegues cutáneos redundantes occipitales
2. occipucio prominente
3. Ventriculomegalia (cisterna magna agrandada)
4. Calcificaciones cerebrales multifocales (que involucran la sustancia blanca de los lóbulos frontales, calcificaciones sutiles alrededor de los ventrículos lateral y cuarto)
5. Agiria, lisencefalia, polimicrogiria
6. Degeneración y falta de visualización del cuerpo caloso
7. disgenesia vermiana
8. No visualización de tálamos
9. Adelgazamiento de la protuberancia y el tronco encefálico
10. Quiste de la bolsa de Blake

Compromiso  
ocular

1. Moteado de pigmento macular
2. Pérdida del reflejo foveal
3. nistagmo horizontal
4. exoforia
5. Hipoplasia del nervio óptico
6. Signo de doble anillo
7. Aumento de la relación copa-disco
8. Atrofia coriorretiniana

Otras  
participaciones

1. Pérdida de la audición
2. Pie zambo y artrogriposis



Morbidity and Mortality Weekly Report

## Pregnancy Outcomes After Maternal Zika Virus Infection During Pregnancy — U.S. Territories, January 1, 2016–April 25, 2017

Carrie K. Shapiro-Mendoza, PhD<sup>1</sup>; Marion E. Rice, MPH<sup>2,3</sup>; Romeo R. Galang, MD<sup>2</sup>; Anna C. Fulton, MPH<sup>2</sup>;  
Kelley VanMaldeghem, MPH<sup>2</sup>; Miguel Valencia Prado, MD<sup>4</sup>; Esther Ellis, PhD<sup>5</sup>; Magele Scott Anesi, MPH<sup>6</sup>; Regina M. Simeone, MPH<sup>2</sup>;  
Emily E. Petersen, MD<sup>1</sup>; Sascha R. Ellington, MSPH<sup>1</sup>; Abbey M. Jones, MPH<sup>2</sup>; Tonya Williams, PhD<sup>7</sup>; Sarah Reagan-Steiner, MD<sup>8</sup>;  
Janice Perez-Padilla, MPH<sup>9</sup>; Carmen C. Deseda, MD<sup>4</sup>; Andrew Beron, MPH, MLS<sup>5</sup>; Aifili John Tufa, MPH<sup>10</sup>; Asher Rosinger, PhD<sup>11,12</sup>;  
Nicole M. Roth, MPH<sup>2</sup>; Caitlin Green, MPH<sup>2</sup>; Stacey Martin, MSc<sup>9</sup>; Camille Delgado Lopez, MPH<sup>4</sup>; Leah deWilde<sup>5</sup>; Mary Goodwin, MA, MPA<sup>1</sup>;  
H. Pamela Pagano, DrPH<sup>1</sup>; Cara T. Mai, DrPH<sup>2</sup>; Carolyn Gould, MD<sup>9</sup>; Sherif Zaki, MD<sup>8</sup>; Leishla Nieves Ferrer, MPH<sup>4</sup>; Michelle S. Davis, PhD<sup>5</sup>;  
Eva Lathrop, MD<sup>2</sup>; Kara Polen, MPH<sup>2</sup>; Janet D. Cragan, MD<sup>2</sup>; Megan Reynolds, MPH<sup>2</sup>; Kimberly B. Newsome, MPH<sup>2</sup>; Mariam Marcano Huertas<sup>4</sup>;  
Julu Bhatangar, PhD<sup>8</sup>; Alma Martinez Quiñones, MPH<sup>4</sup>; John F. Nahabedian, MS<sup>2</sup>; Laura Adams, DVM<sup>9</sup>; Tyler M. Sharp, PhD<sup>9</sup>;  
W. Thane Hancock, MD<sup>13</sup>; Sonja A. Rasmussen, MD<sup>15</sup>; Cynthia A. Moore, MD, PhD<sup>2</sup>; Denise J. Jamieson, MD<sup>1</sup>; Jorge L. Munoz-Jordan, PhD<sup>9</sup>;  
Helentina Garstang, DCHMS<sup>16</sup>; Afeke Kambui, MPH<sup>10</sup>; Carolee Masao, DCHMS<sup>17</sup>; Margaret A. Honein, PhD<sup>2</sup>; Dana Meaney-Delman, MD<sup>14</sup>;  
Zika Pregnancy and Infant Registries Working Group



**TABLE 1. Pregnancy outcomes\* for 2,549 completed pregnancies† with laboratory evidence of recent possible maternal Zika virus infection, by symptom status and timing of symptom onset or specimen collection date — Zika Pregnancy and Infant Registries,‡ U.S. territories, January 1, 2016–April 25, 2017**

Characteristic	No. with brain abnormalities and/or microcephaly¶	No. with NTDs and early brain malformations, eye abnormalities, or consequence of CNS dysfunction without brain abnormalities or microcephaly	Total no. with ≥1 birth defect	Total no. of completed pregnancies	Percentage with Zika virus–associated birth defect, (95% CI**)
<b>Any laboratory evidence of recent possible Zika virus infection††</b>					
Total	108	14	122	2,549	5 (4–6)
<b>Maternal symptom status§§</b>					
Symptoms of Zika virus infection reported	68	11	79	1,561	5 (4–6)
No symptoms of Zika virus infection reported	38	3	41	966	4 (3–6)
<b>Timing¶¶ of symptoms or specimen collection date***</b>					
First trimester†††	27	5	32	536	6 (4–8)
Second trimester§§§	46	5	51	1,096	5 (4–6)
Third trimester¶¶¶	31	4	35	876	4 (3–6)
<b>Recent NAT-confirmed Zika virus infection in maternal, placental, fetal, or infant specimen****</b>					
Total	71	9	80	1,508	5 (4–7)
<b>Maternal symptom status††††</b>					
Symptoms of Zika virus infection reported	54	9	63	1,279	5 (4–6)
No symptoms of Zika virus infection reported	16	0	16	225	7 (4–11)
<b>Timing§§§§ of symptoms or specimen collection date***</b>					
First trimester†††	18	4	22	276	8 (5–12)
Second trimester§§§	34	2	36	726	5 (4–7)
Third trimester¶¶¶	17	3	20	494	4 (3–6)

**Abbreviations:** CI = confidence interval; CNS = central nervous system; IgM = immunoglobulin M; NAT = nucleic acid test; NTD = neural tube defect; RT-PCR = reverse transcription–polymerase chain reaction.

Shapiro-Mendoza, C. K., Rice, M. E., Galang, R. R., Fulton, A. C., VanMaldeghem, K., Prado, M. V., Ellis, E., Anesi, M. S., Simeone, R. M., Petersen, E. E., Ellington, S. R., Jones, A. M., Williams, T., Reagan-Steiner, S., Perez-Padilla, J., Deseda, C. C., Beron, A., Tufa, A. J., Rosinger, A., Roth, N. M., ... Zika Pregnancy and Infant Registries Working Group (2017). Pregnancy Outcomes After Maternal Zika Virus Infection During Pregnancy - U.S. Territories, January 1, 2016-April 25, 2017. *MMWR. Morbidity and mortality weekly report*, 66(23), 615–621. <https://doi.org/10.15585/mmwr.mm6623e1>



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**TABLE 2. Infant Zika virus testing and screening at birth for 2,464 live-born infants from completed pregnancies with laboratory evidence of recent possible Zika virus infection — Zika Pregnancy and Infant Registries,\* U.S. territories, January 1, 2016–April 25, 2017**

Testing and screening	Live-born infants		
	With birth defects <sup>†</sup> No. (%)	Without birth defects No. (%)	Total No. (%)
<b>Total</b>	116 (5)	2,348 (95)	2,464 (100)
<b>Infant Zika virus testing</b>			
≥1 infant specimen <sup>‡</sup> test result reported to Zika pregnancy and infant registries	64 (55)	1,381 (59)	1,445 (59)
<b>Infant screening at birth</b>			
Postnatal neuroimaging <sup>¶</sup> conducted and findings reported to Zika pregnancy and infant registries	69 (59)	1,219 (52)	1,288 (52)
Hearing screening conducted and results reported to Zika pregnancy and infant registries	105 (91)	1,840 (78)	1,945 (79)

\* U.S. Zika Pregnancy Registry and Puerto Rico Zika Active Pregnancy Surveillance System.

<sup>†</sup> Includes infants with one or more of the following birth defects potentially associated with Zika virus infection: brain abnormality and/or microcephaly or possible microcephaly, neural tube defect and other early brain malformation, eye abnormality, or consequence of central nervous system dysfunction.

<sup>‡</sup> Infant specimens include serum, urine, and cerebrospinal fluid.

<sup>¶</sup> Neuroimaging includes any imaging of the infant head, including cranial ultrasound, computed tomography, magnetic resonance imaging, or radiograph reported to the Zika pregnancy registries based on neuroimaging guidance published August 19, 2016. (Russell K, Oliver SE, Lewis L, et al. Update: interim guidance for the evaluation and management of infants with possible congenital Zika virus infection—United States, August 2016. *MMWR Morb Mortal Wkly Rep* 2016;65:870–8).

# DISCUSION

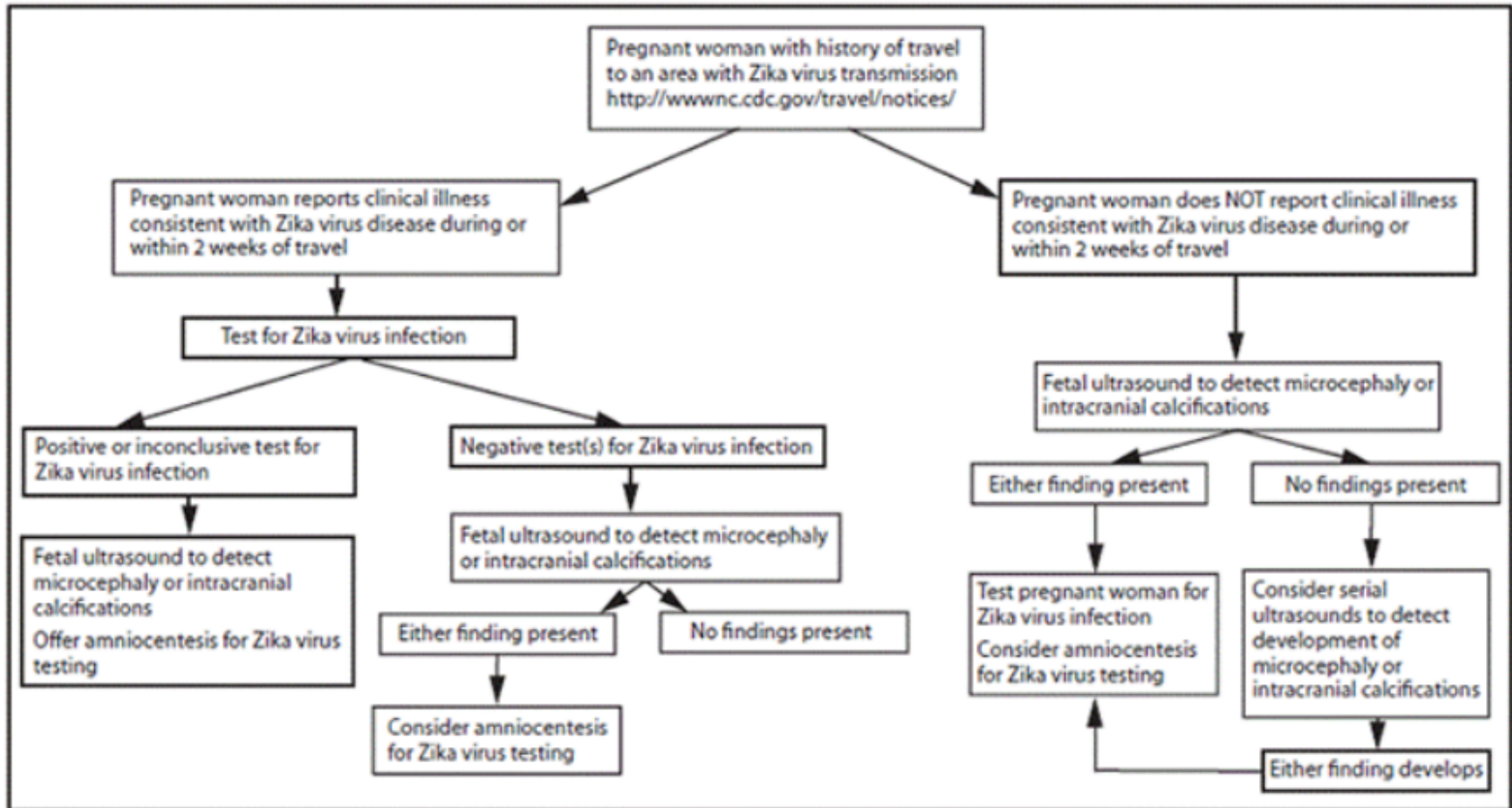


- Entre los embarazos con evidencia de infección materna 1 de cada 20 fetos tuvo un defecto de nacimiento
- Son mas frecuentes entre más precoz el embarazo
- Existen secuelas graves como perdida de audición y coriorretinitis

# ALGORITMO MANEJO



Interim guidance: testing algorithm<sup>\*,†</sup>, for a pregnant woman with history of travel to an area<sup>§</sup> with Zika virus transmission, with or without clinical illness<sup>\*\*</sup> consistent with Zika virus disease



# TRATAMIENTO EN EL EMBARAZO



- No existe tratamiento específico ni vacuna

# PATOGENIA Y OPCIONES DE TRATAMIENTO



- Infección de células neurales corticales: apoptosis mediada por caspasa 3 y desregulación ciclo celular
- Invade la célula a través de varios receptores: DC-SIGN, AXL y TIM-1
- AXL se expresa en gran medida en células del cerebro en desarrollo
- El aumento de muerte celular y reducción de la proliferación celular → microcefalia

- ❖ IFN- $\alpha$ , IFN- $\beta$  o IFN- $\gamma$
- ❖ Anticuerpos monoclonales específicos de ZIKA
- ❖ Emricasan → inhibidor de pancaspasas



# PREVENCION



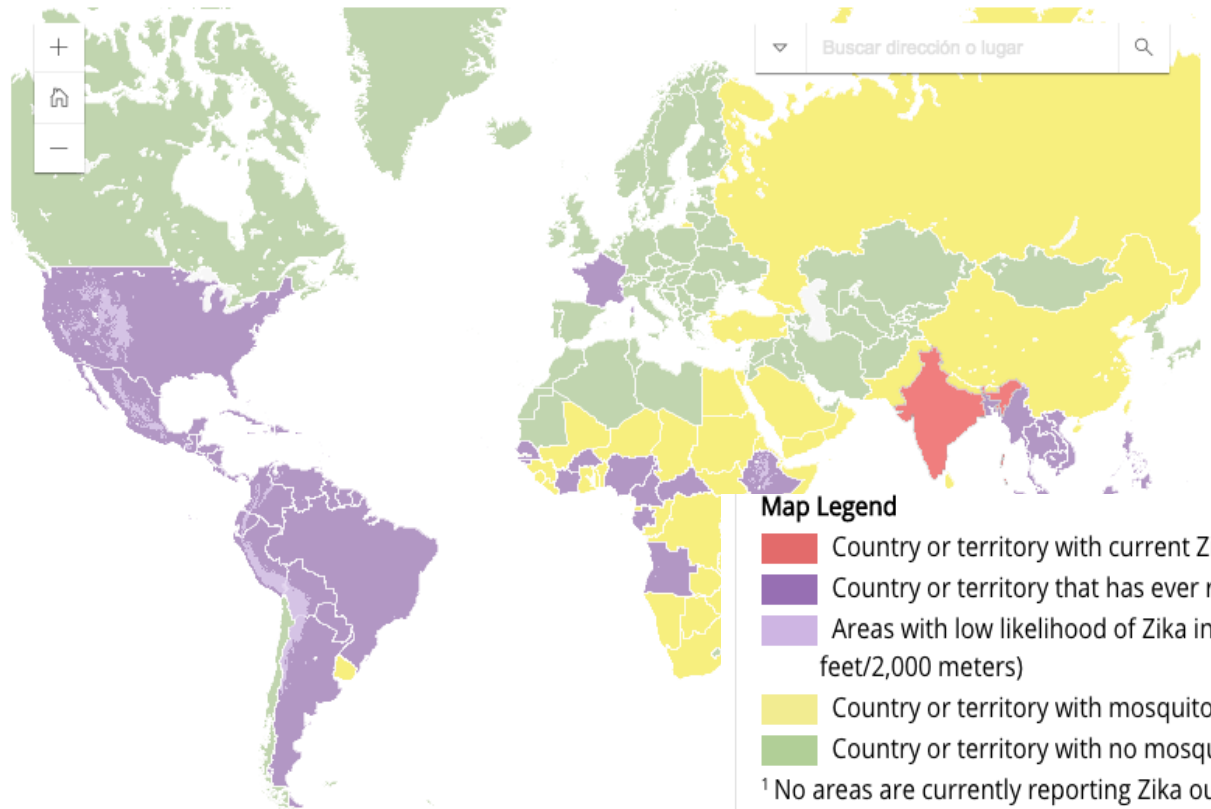
- Embarazadas deben evitar viajar a un área con transmisión activa
- Evitar las picadura de mosquitos ( poleras manga larga, repelente)
- Evitar transmision sexual → uso condón hasta 3 meses despues de un viaje si asintomático y hasta 6 meses sintomáticos
  - Evitar relaciones sexuales si embarazo

# PREVENCION



Click on your destination for Zika information

Search for a place by name or zoom and click on the map to see CDC's travel recommendations for Zika. Follow the links in the pop-up message to learn more.



### Map Legend

- Country or territory with current Zika outbreak<sup>1</sup>
- Country or territory that has ever reported Zika cases<sup>2</sup> (past or current)
- Areas with low likelihood of Zika infection because of high elevation (above 6,500 feet/2,000 meters)
- Country or territory with mosquito<sup>3</sup> but no reported Zika cases<sup>2</sup>
- Country or territory with no mosquitoes<sup>3</sup> that spread Zika

<sup>1</sup> No areas are currently reporting Zika outbreaks





<sup>2</sup> Locally acquired, mosquito-borne Zika cases

<sup>3</sup> *Aedes aegypti*

# PREVENCION



## Recommendations for US Residents Traveling Abroad

Traveler Type	Country Category			
	 Outbreak (Red)	 Current or Past Transmission but No Current Outbreak (Purple) <sup>1</sup>	 Mosquito Present but No Reported Cases (Yellow) <sup>2</sup>	 No Mosquito (Green) <sup>3</sup>
<b>Pregnant women</b>	Do not travel.	Talk to a health care provider about potential risks. If you decide to travel, prevent mosquito bites and sexual exposure to Zika.	Prevent mosquito bites during and <a href="#">after</a> travel.	No Zika precautions recommended.
<b>Women planning pregnancy</b>	Talk to a health care provider about potential risks. If you decide to travel, prevent mosquito bites and sexual exposure to Zika during and <a href="#">after</a> travel. If traveling without male partner, wait 2 months after return before becoming pregnant.			

# PREVENCION



<https://travelhealthpro.org.uk/countries>

**TRAVEL HEALTH PRO**

COUNTRY INFORMATION LATEST NEWS OUTBREAK SURVEILLANCE DISEASES IN BRIEF FACT FROM

## EASTER ISLAND (CHILE)

- General information
- Vaccine recommendations
- Other risks
- COVID-19
- Important news

An Introduction  
Capital City: H...  
Official Language  
Monetary Unit

Dengue

Influenza

Outdoor air quality

Zika Virus

Zika virus (ZIKV) is a viral infection transmitted by mosquitoes which predominantly feed between dawn and dusk. A small number of cases of sexual transmission of ZIKV have also been reported. Most people infected with ZIKV have no symptoms. When symptoms do occur they are usually mild and short-lived. Serious complications and deaths are not common. However, ZIKV is a cause of Congenital Zika Syndrome (microcephaly and other congenital anomalies) and neurological complications such as Guillain-Barré syndrome.

#### Zika virus in Easter Island

There is a **very low risk of ZIKV** in this country.

#### Prevention

- All travellers should avoid mosquito bites particularly between dawn and dusk.
- There is no vaccination or medication to prevent ZIKV infection.

Pregnant women should seek medical advice if they develop ZIKV symptoms or are concerned.

[Zika virus in brief](#)

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