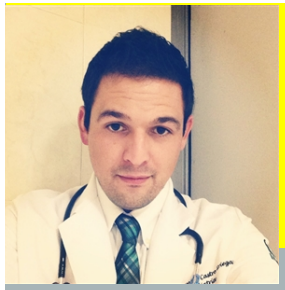
Emerging Dissese Part 2

Zika

Sören Thybo

Congenital syndrome

Query about this case from Dr. Marco Castro MD, general pediatrics



Congenital syndrome

Query from Dr. Marco Castro, general pediatrician

A primiparous 16 year old mother delivers a neonate with APGAR scores of 3, 1, 0 at 1, 5 & 10 minutes (??) of life. She had no prenatal care and the delivery was by emergency C-section due to severe fetal bradycardia. The infant was born at 34 weeks gestation, weight 1.8kg.

The examination reveals microcephaly, low nasal bridge, bilateral cataracts, low onset ears and a prominent and distended abdomen.

Mother had no pregnancy control nor had she taken vitamins or folates. She is from a very low income stratus and lives in an endemic area for Zika, dengue and chikungunya virus. After an exhaustive interrogation she recalls having had a rash involving head and trunk associated with fever in the 2nd trimester lasting for about 5 days. She has never been vaccinated. We concluded it was a rubella syndrome.

Can you help me figuring out other causes? What's your DDX?

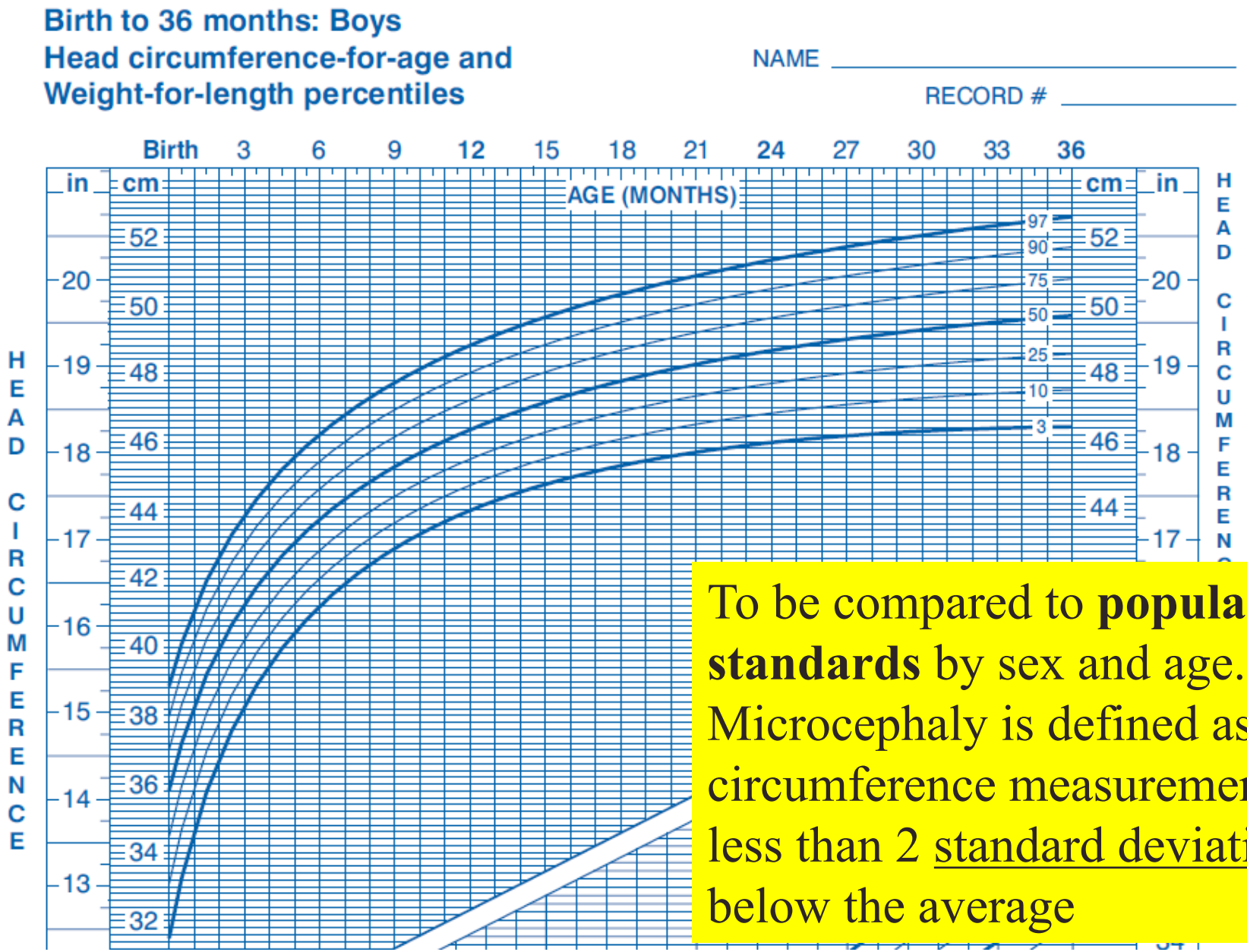
Congenital syndrome
Some causes of microcephaly:

- **Genetic/ Chromosomal abnormalities**, metabolic disorders
- **Congenital infections**
  - **TORCH** infections (toxoplasmosis, rubella, cytomegalovirus and herpes),
  - syphilis,
  - varicella–zoster,
  - parvovirus B19 and
  - human immunodeficiency virus (HIV).
- **Other non-genetic causes** include intrauterine exposure to teratogens such as alcohol and ionizing radiation.

ZIKA and Microcephaly

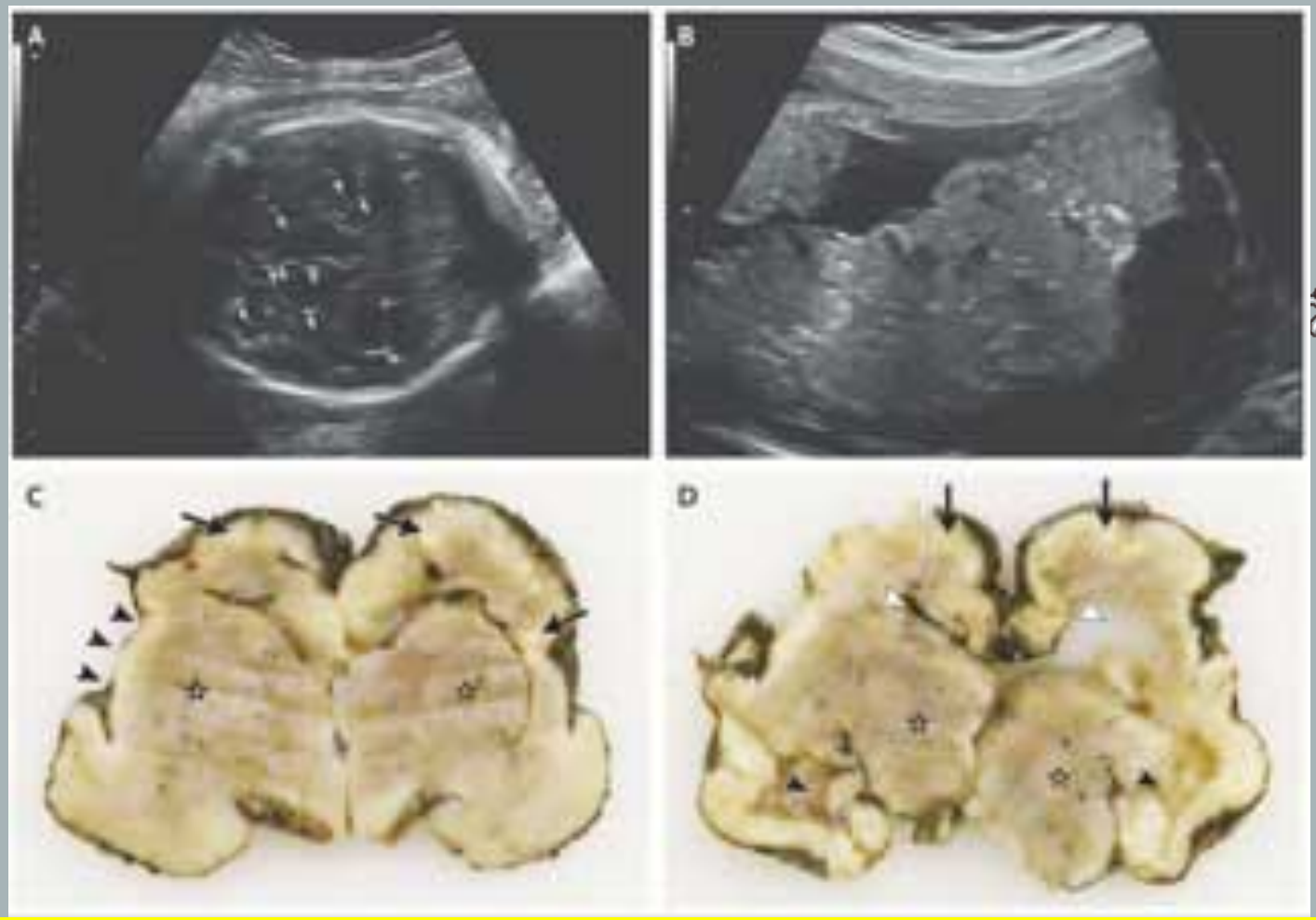
- **Zika has been associated with the appearance of a ”epidemic” of microcephaly cases, espec ially in Brazil**
- **However, in the beginning the reports did reflect different definition of trhe cut off for normal head circumference, and studies in different ethic groups.**
- **However, it seems documented beyopnd doubt that intrauterine ZIKA infection –especially inthe 1st. And 2nd. Trimester may have a devastation effect in gtrems of brain infection and destruction of nervous tissue of the fetus.**

Congenital syndrome
Microcephaly:



To be compared to **population standards** by sex and age.
Microcephaly is defined as a head circumference measurement that is less than 2 <u>standard deviations</u> (SDs) below the average

Congentital ZIKV CNS lesions



Credit: New England Journal of Medicine

Calcifications shown in the brain and placenta from prenatal ultrasonographic Images and photographs of coronal slices of brain.

ZIKA fear

- *The fear of Zika virus infection of the pregnant women has been very high.*
- *Zika virus has received an enormous amount of attention, not least in the USA, where locval transmission has been documented in southerne states.*

However real figures are low.

Congenital syndrome

USA statistics

Testing pregnant women for Zika virus (ZIKV) in the USA
Source:**www.cdc.gov click on "ZIKA"**

By Sept 22nd. 2016

No. of registered pregnant woman with lab evidence of ZIKV infection **808**

Live born with defects **1**

Includes microcephaly, calcium deposits in the brain indicating possible brain damage, excess fluid in the brain cavities and surrounding the brain, absent or poorly formed brain structures, abnormal eye development, or other problems resulting from damage to the brain that affects nerves, muscles and bones, such as clubfoot or inflexible joints, and confirmed hearing loss.

Pregnancy loses with birth defects **5**

ZIKV
USA statistics

US States

Locally acquired mosquito-borne cases reported: 59

Travel-associated cases reported: 3,565

Laboratory acquired cases reported: 1

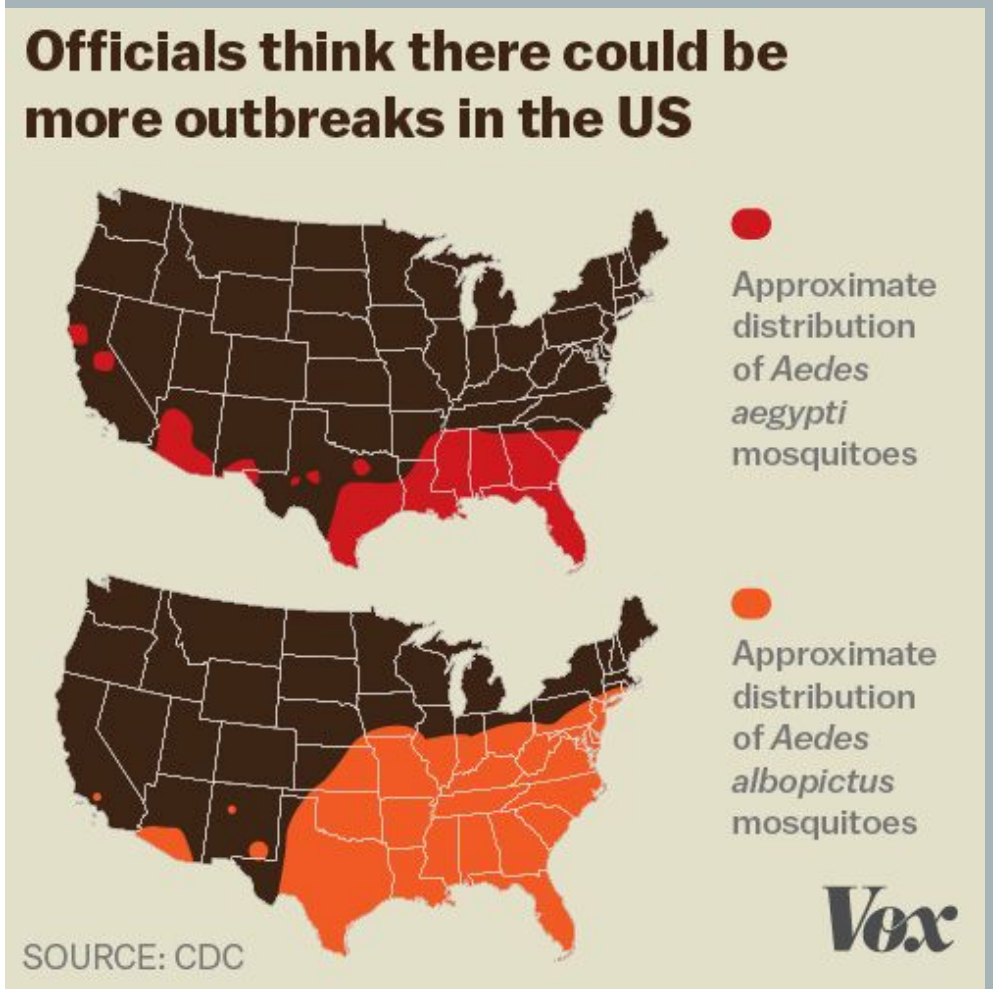
Total: 3,625

Sexually transmitted: 30
Guillain-Barré syndrome: 12

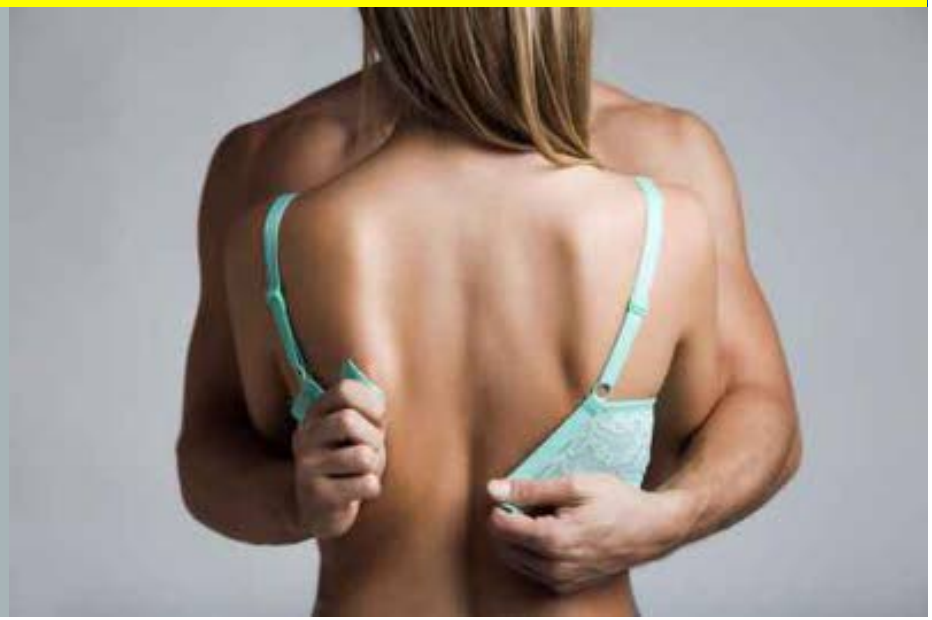
Zika-virus

Zika-virus Fear

Transmitted by Aëdes mosquitos and sex



A virologist has suggested that Zika virus infection is the only vector-borne disease that may be transmitted by sexual intercourse.

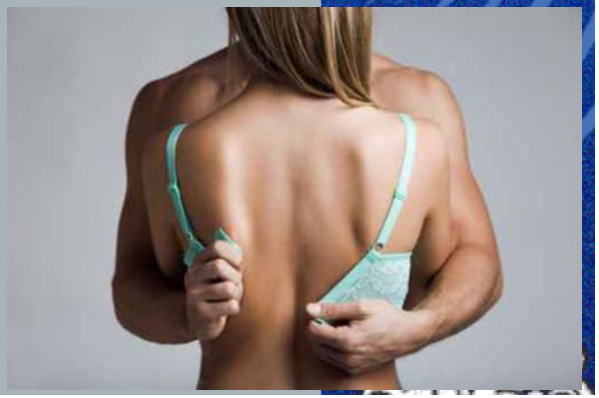


Zika-virus Fear

Transmitted by sex

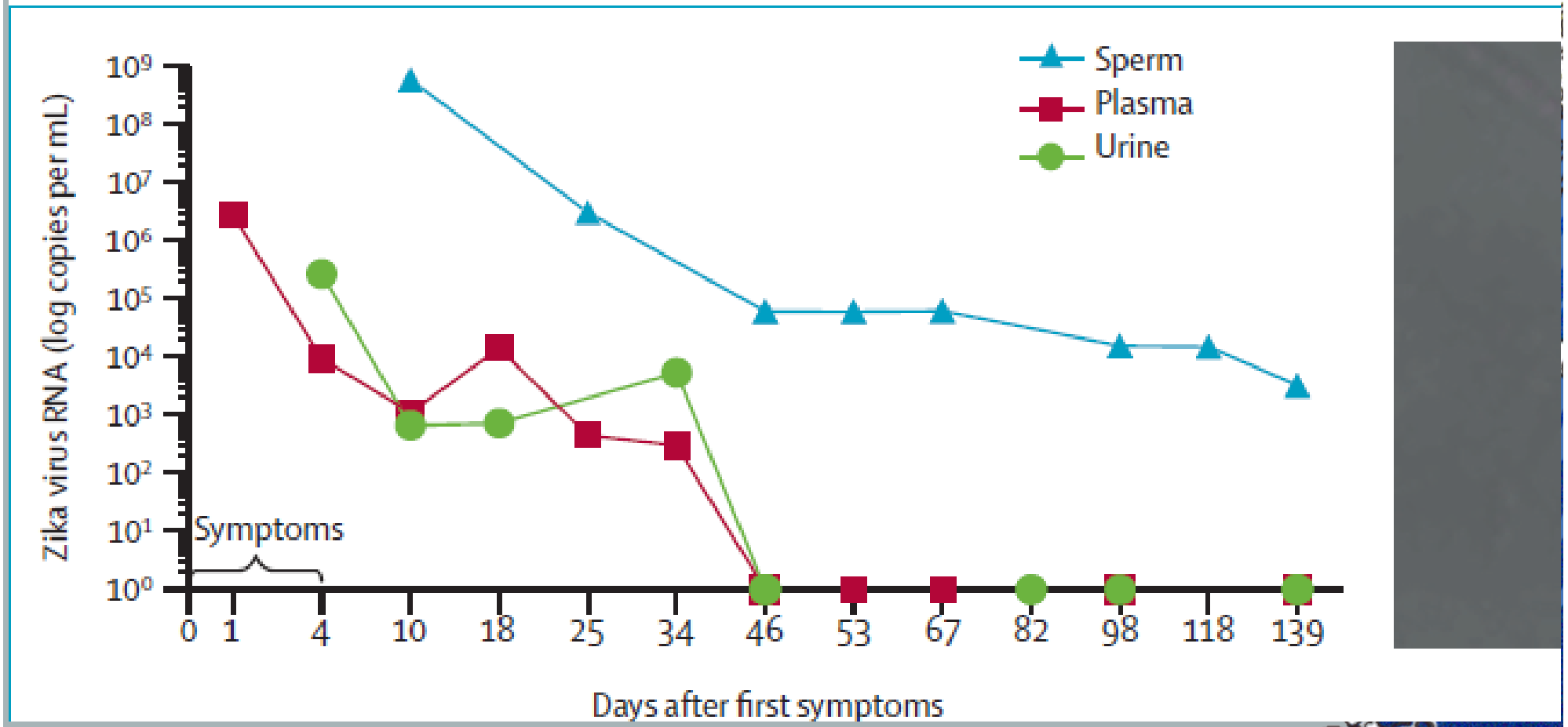
Table 2. Countries reporting non mosquito-borne Zika virus transmission since February 2016

Classification	WHO Regional Office	Country / territory	Total
Countries with evidence of person-to-person transmission of Zika virus, other than mosquito-borne transmission	AMRO/PAHO	Argentina, Canada, Chile, Peru, United States of America	5
	EURO	France, Germany, Italy, Netherlands, Portugal, Spain	6
	WPRO	New Zealand	1
Total			12



Zika-virus Fear

Transmitted by sex



Aedes sp. (e.g. aegypti and Albopictus)
Are the vectors involved-
Mosquitos that prefer urban environment

Anopheles sp.
and other mosquitos play
No role in ZIKA transmission

Global Demographics

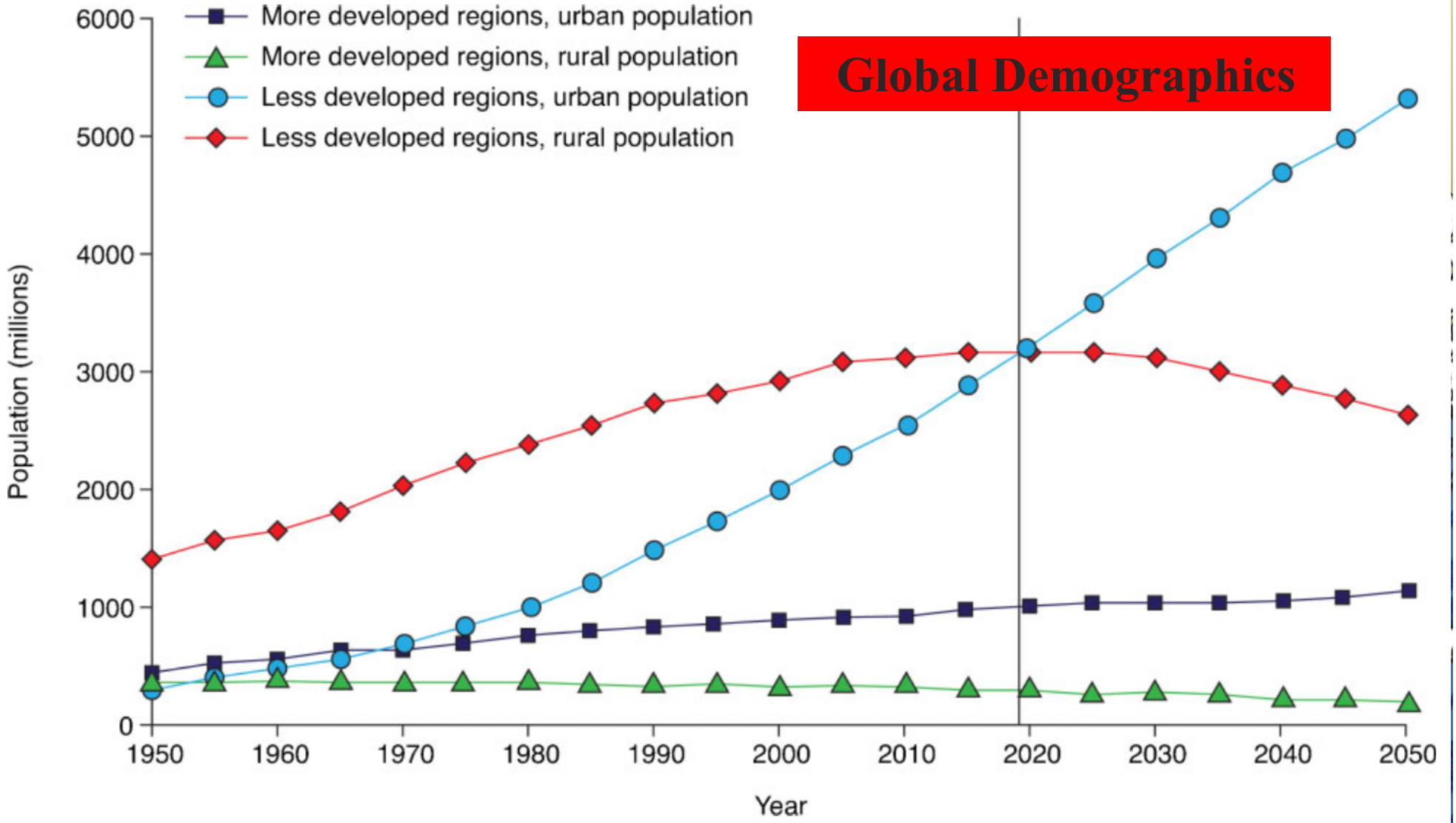
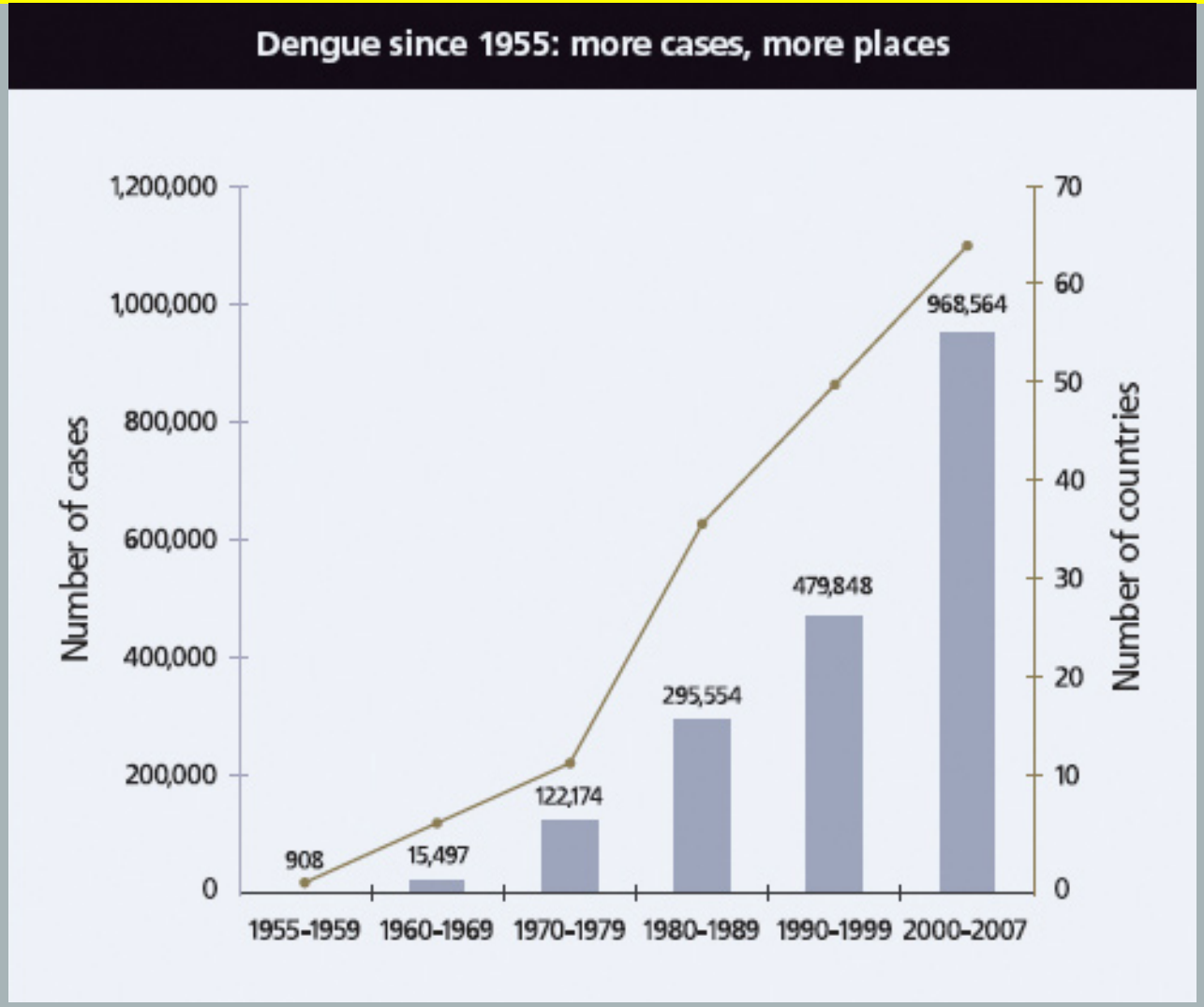


Figure 2 Global urban and rural population growth in developed and underdeveloped areas from 1950 to 2050.[11] Reprinted from Lancet Infect Dis, 11, Alirol E, Getaz L, Stoll B, Chappuis F, Loutan L, Urbanisation and infectious diseases in a globalised world, 131–241, Copyright 2012, with permission from Elsevier

Tapia-Conyer R et al. Dengue: an escalating public health problem in Latin America. Paed and Int. Health. 21012;32 (S1) 14-17

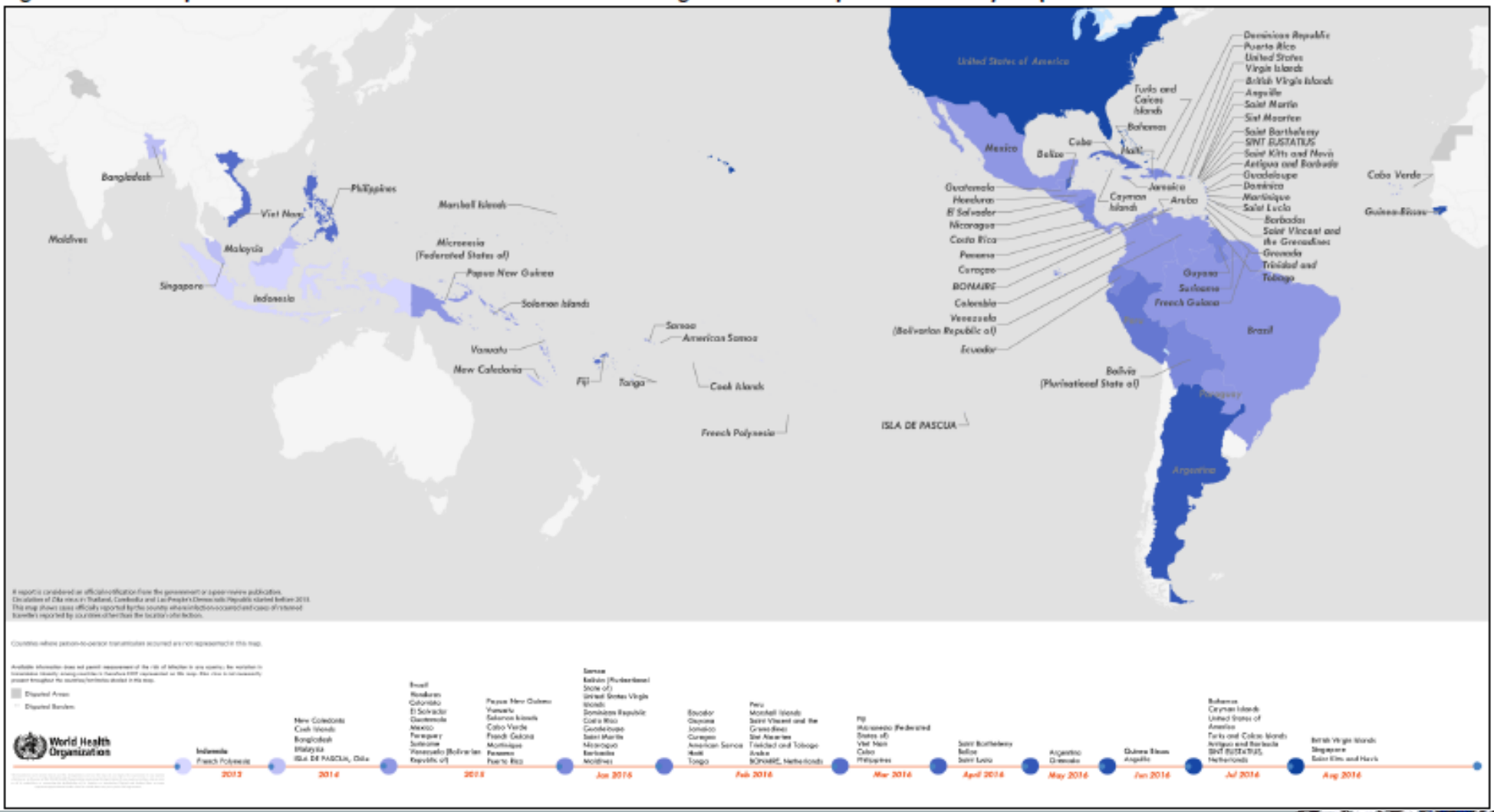
Dengue also an Aëdes transmitted disease- an stronglæy emerging infection

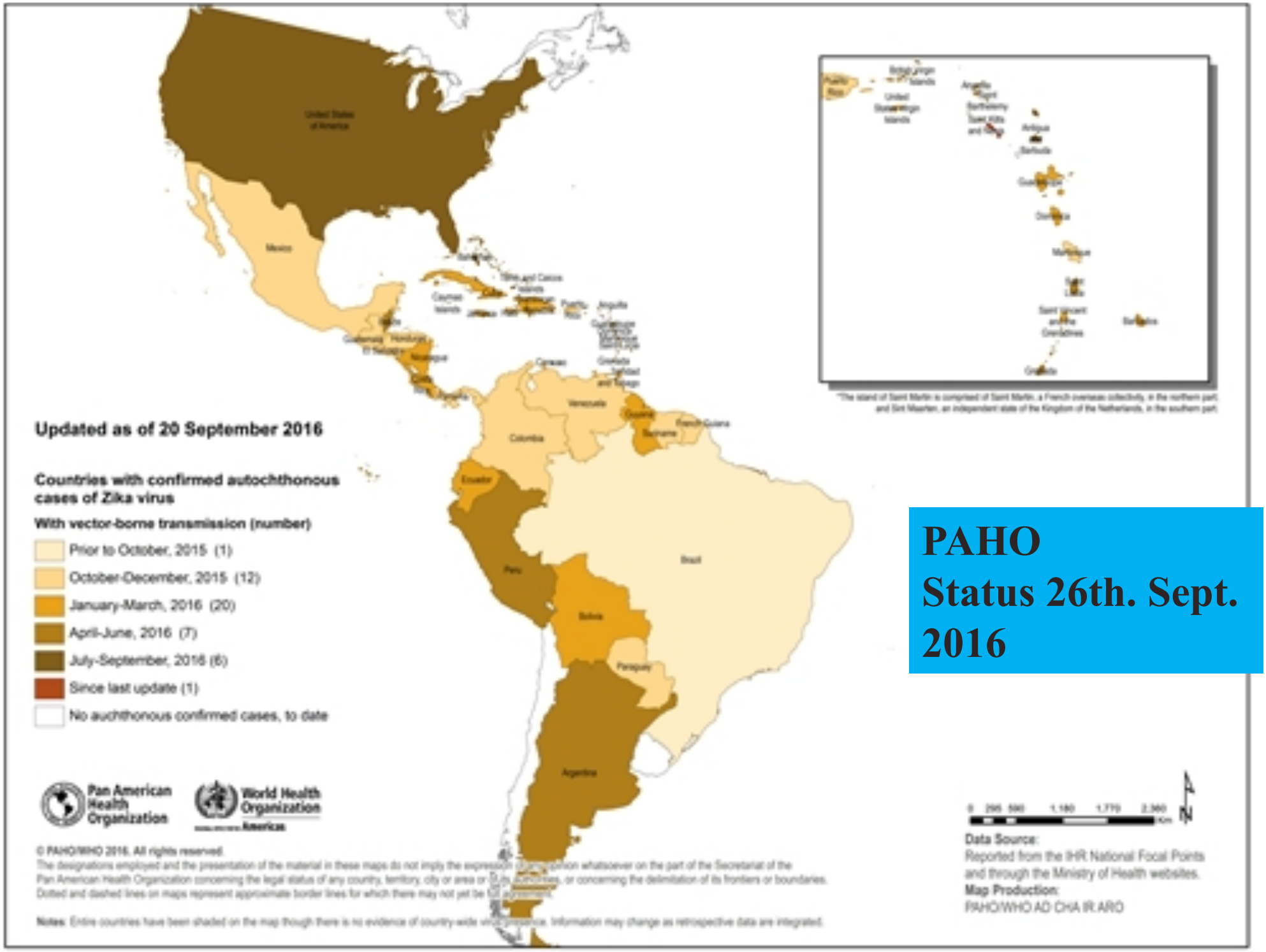


Graph from the World Health Organization

WHO ZIKV status 22nd. Sept. 2016

Figure 2. Global spread of Zika virus from 2013 to 2016 according to the first report of a locally-acquired infection




Updated as of 20 September 2016
Countries with confirmed autochthonous cases of Zika virus
With vector-borne transmission (number)
Prior to October, 2015 (1)
October-December, 2015 (12)
January-March, 2016 (20)
April-June, 2016 (7)
July-September, 2016 (6)
Since last update (1)
No auchthonous confirmed cases, to date
Pan American Health Organization
World Health Organization
Data Source:
Reported from the IHR National Focal Points and through the Ministry of Health websites.
Map Production:
PAHO/WHO AD CHA IR ARO
PAHO
Status 26th. Sept. 2016

Zika-virus Fear

- ***Brazil (March 2016)***:
  - *400 000 to 1 300 000 cases ???*
  - ***6776** cases of suspected **microcephaly***
  - *4291 still under investigation*
    - *(by 2nd. April 2016)*
  - *1541 discarded*
  - ***944 confirmed***

WHO (March *2016)Pregnant women should be advised not to travel to areas of ongoing Zika virus outbreaks*.

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

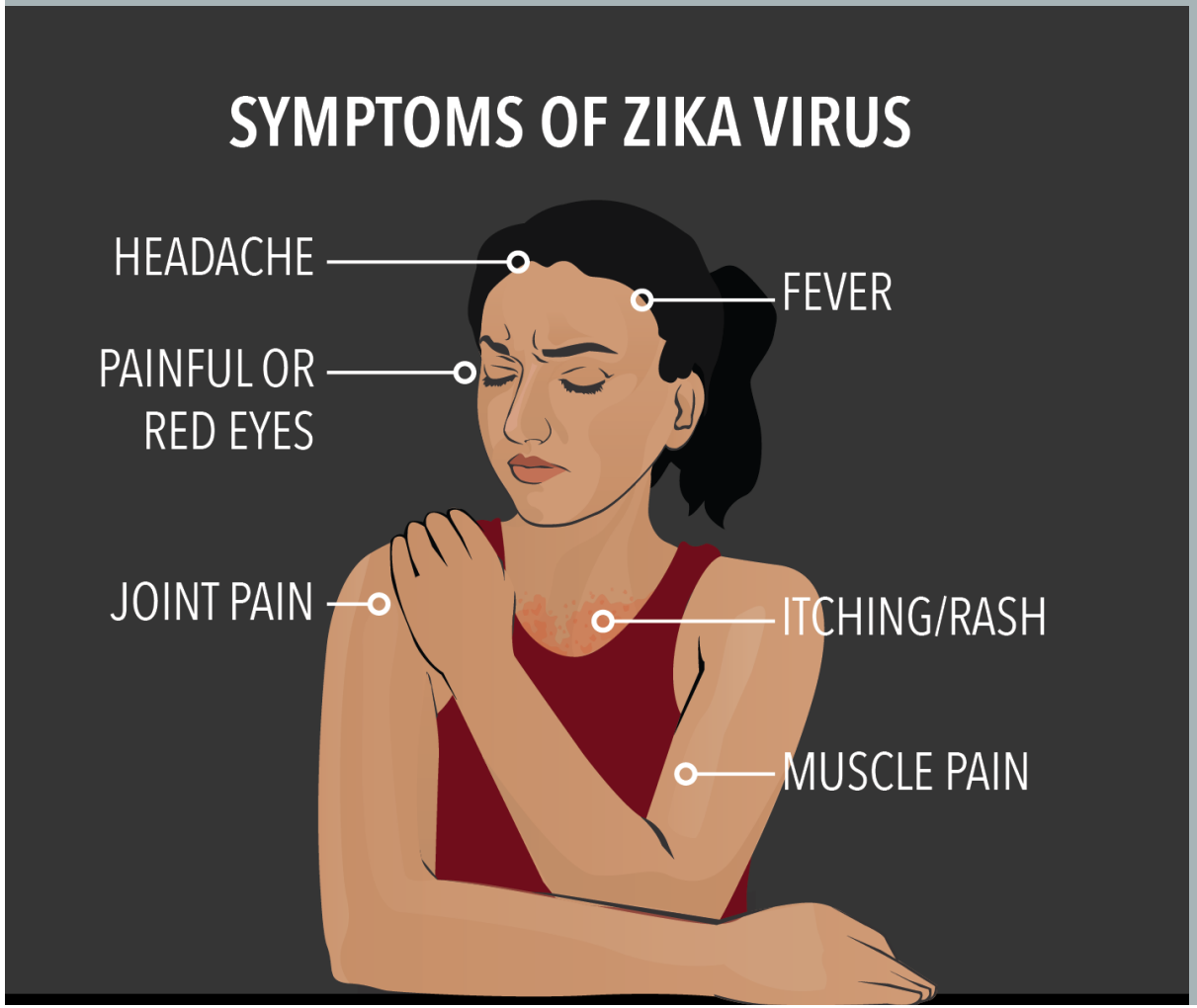
Reporting country or territory	Number of microcephaly and/or CNS malformation cases suggestive of congenital Zika infections or potentially associated with a Zika virus infection	Probable location of infection
Brazil	1911[2]	Brazil
Cabo Verde	9	Cabo Verde
Canada	1	Undetermined
Costa Rica	1	Costa Rica
Colombia	40[3]	Colombia
Dominican Republic	3	Dominican Republic
El Salvador	4	El Salvador
French Guiana	3[4]	French Guiana
French Polynesia	8	French Polynesia
Guatemala	17[5]	Guatemala
Haiti	1	Haiti
Honduras	1	Honduras
Marshall Islands	1	Marshall Islands
Martinique	12[5]	Martinique
Panama	5	Panama
Paraguay	2[6]	Paraguay
Puerto Rico	1	Puerto Rico
Slovenia	1[7]	Brazil
Spain	2	Colombia, Venezuela (Bolivarian Republic of)
Suriname	1	Suriname
United States of America	23[8]	Undetermined**

***The probable locations of three of the infections were Brazil (1 case), Haiti (1 case) and Mexico, Belize or Guatemala (1 case).*

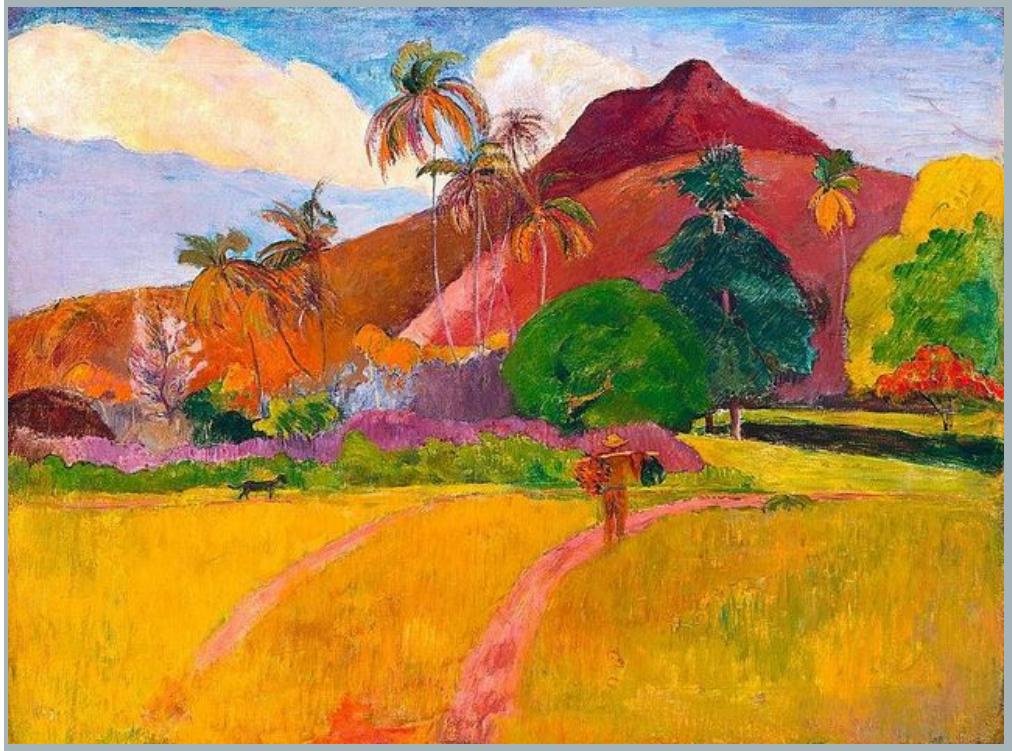
Zika-virus Fear

Zika-virus
Salienmt features and symptoms

The majority of ”cases” without symptoms !



Zika-virus
In the French Polynesia



Zika-virus
In the French Polynesia

French Polynesia
270 000
4500 km²

Zika-virus
In the French Polynesia

- *Well defined Zika epidemic*
  - ***Oct. 2014 until July 2015***
  - *Attack rate* ***66%*** *of the general population*
  - *Mathematical model building on baseline data and 8 cases of microencephalic children identified during that period of time*
  - *Well defined definition of microcephaly*

Cauchemez S et al. Association between Zika virus and microcephaæy in French Polynesia 2013-5. Lancet 2016

Zika-virus
French Polynesia / **MICROCEPAHLY**

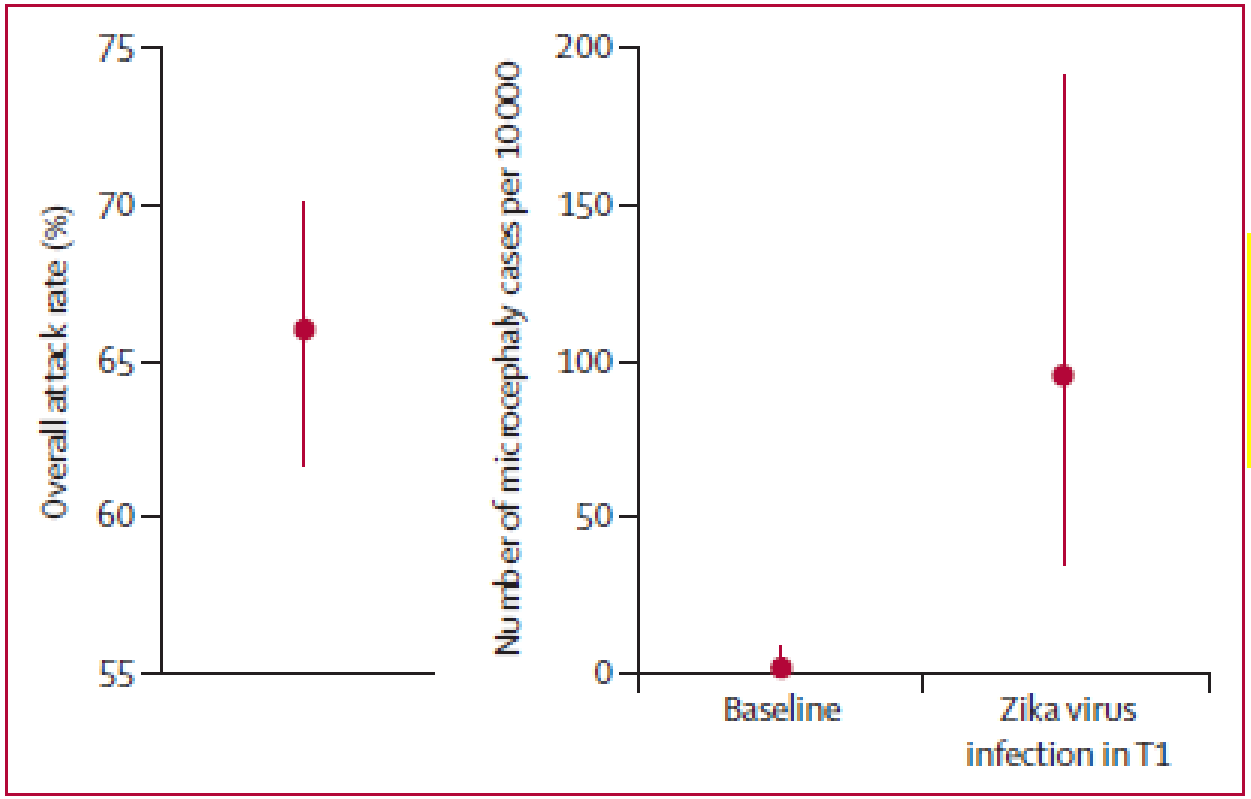


***Figure 2*: Attack rate and strength of the association between infection with Zika virus and microcephaly in French Polynesia**

(A) Final attack rate (95% CI) based on seroprevalence after the end of the outbreak. (B) Baseline prevalence of microcephaly (number per 10 000 neonates) and risk of microcephaly associated with Zika virus infection in mothers (number per 10 000 women infected in the first trimester of pregnancy). T=trimester.

Risk Ratio: 54.4
(95% CI 34-191)

Cauchemez S et al. Association between Zika virus and microcephaæy in French Polynesia 2013-5. Lancet 2016

Zika-virus
In the French Polynesia

- 42 patients were admitted to hospital with **Guillain-Barré syndrome** (GBS).

- **20-fold increase in incidence**
  - compared with the previous four years.
  - 38% required admission ICU
  - 29% on mechanical ventilation.
- Incidence: ≈ **16 / 100 000 inhab.**

WHO, April 2016

Zika-virus
In the French Polynesia

- **The duration of hospital stay**:
  - Non-ICU pats. 7 to 20 days (median=11).
  - ICU pats.16 to 70 days (median=51).
  - **No deaths** were reported.

  - The majority of these cases (88%) reported symptomatic Zika virus infection in the days (median=6) that preceded the onset of neurological symptoms.

WHO, April 2016

ZIKV-linked GBS in other countries as of September 2016 (WHO report)

Table 4. Countries and territories reporting Guillain-Barré syndrome (GBS) potentially associated with Zika virus infection

Classification	Country / territory
Reported increase in incidence of GBS cases, with at least one GBS case with confirmed Zika virus infection	Brazil, Colombia, Dominican Republic, El Salvador*, French Guiana, French Polynesia, Honduras, Jamaica, Martinique, Suriname**, Venezuela (Bolivarian Republic of)
No increase in GBS incidence reported, but at least one GBS case with confirmed Zika virus infection	Costa Rica, Ecuador, Grenada[9], Guadeloupe[10], Guatemala, Haiti, Panama, Puerto Rico

**GBS cases with previous history of Zika virus infection were reported by the International Health Regulations (2005) National Focal Point in United States of America.*

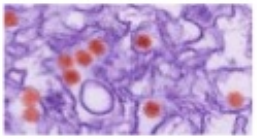
***One case living in continental Netherlands was diagnosed in mid-January 2016 and reported by the Netherlands.*

Zika-virus

- ***Diagnosis***:
- *Cross reaction with other Flaviviridae*
  - *Yellow fever, Dengue, West Nile*
- *PCR: positive in blood the first 4-5 days*
  - *And in urine and semen up to 28 days*

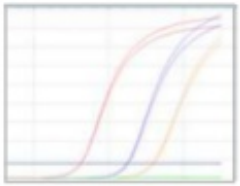
Zika Virus Diagnostic Testing

Culture for virus (generally not used clinically)



Acute phase (≤7 days after onset)

Zika specific polymerase chain reaction for viral RNA (PCR) in serum, saliva (may be more sensitive), or urine (may be positive longer)



CDC ZIKV assay consists of two PCR reactions; both reactions must be positive (analytical sensitivity 100 and 25 copies)

Subacute/Chronic phase (2-12 weeks)

IgM anti-ZikaV (ELISA) , 20-40% cross-reactivity with YFV, WNV, DENV; confirmatory plaque reduction neutralization test (PRNT) more specific

Screening, assessment and management of neonates and infants with complications associated with Zika virus exposure in utero

Rapid Advice Guideline
30 August 2016
WHO/ZIKV/MOC/16.3/Rev3

World Health Organization

1. Introduction

1.1 Background

On 1 February 2016, the World Health Organization

This guidance is intended to inform the development of national and local clinical protocols and health policies that relate to neonatal and infant care in the context of Zika virus transmission. It is not intended to provide a

Practical guidelines

Morbidity and Mortality Weekly Report

Update: Interim Guidance for the Evaluation and Management of Infants with Possible Congenital Zika Virus Infection — United States, August 2016

Kate Russell, MD[1,2]; Sara E. Oliver, MD[1,3]; Lillianne Lewis, MD[1,4]; Wanda D. Barfield, MD[5]; Janet Cragan, MD[6]; Dana Meaney-Delman, MD[7]; J. Erin Staples, MD, PhD[8]; Marc Fischer, MD[8]; Georgina Peacock, MD[9]; Titilope Oduyebo, MD[5]; Cynthia A. Moore, MD, PhD[6]; Sonja A. Rasmussen, MD

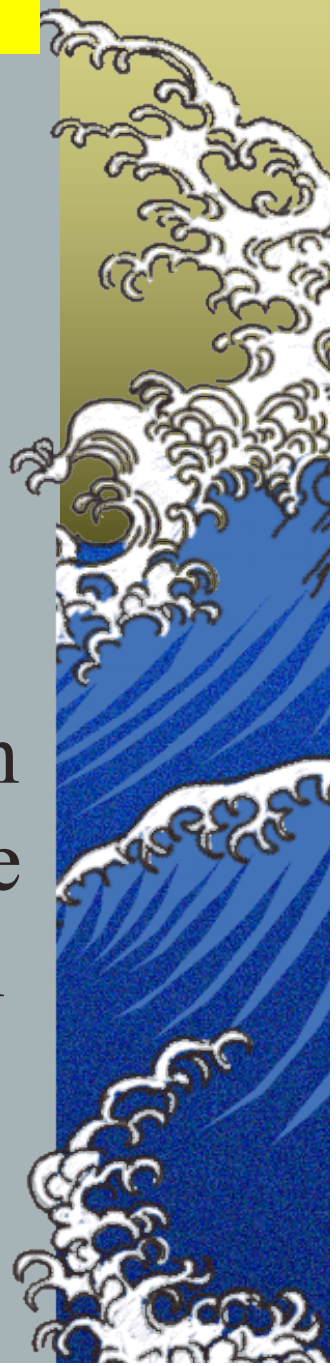
MMWR / August 26, 2016 / Vol. 65 / No. 33

On August 19, 2016, this report was posted as an MMWR

ongoing psychosocial support and assistance with coordina-

Zika-virus

- **Sundhedsstyrelsens opdaterede retningslinjer for håndtering af Zikavirus´**(15. februar 2016)
- Obstetrikere skal tilbyde **alle gravide**, der har **rejst i områder med udbrud af Zikavirus** under graviditeten, at få taget en **blodprøve** efter hjemkomst – uanset om de har haft symptomer på at have en infektion eller ej.
- A somewhat costly recommendation



STATENS SERUM INSTITUT

Virus - priser

Priser på undersøgelser vedr. virus og links til Diagnostisk Håndbog. Undersøgelserne er listet alfabetisk.

Undersøgelse	R-nr.	Art. nr.	Pris	Pris*
Influenza A + B virus (RNA)	299	49454	1301	*1142*
Chikungunya virus (RNA)	2022	96635	1550	*1361*
Chikungunya virus antistof (IgG, IgM)	2021	96633	1889	*1659*
Denquevirus (RNA) og antistof (IgG, IgM)	228	17061, 34934	1550	*1361*
Zika virus (RNA)	2027	97110	1550	*1361*
Zika virus antistof (IgG, IgM)	2017	96316	1889	*1659*

Sundhedsstyrelsens opdaterede retningslinjer for håndtering af Zikavirus´(2. August2016)

- **KVINDER**
- Gravide og kvinder, der aktuelt påtænker at blive gravide, **udskyder ikke-nødvendige rejser** til de berørte områder indtil efter graviditeten (se Statens Serum Instituts side om Zikavirus)

- Hvis rejsen ikke kan udskydes, skal gravide være særligt omhyggelige med at beskytte sig mod myggestik.

Sundhedsstyrelsens opdaterede retningslinjer for håndtering af Zikavirus´(2. August2016)

- **KVINDER**
- **Gravide**, som har rejst i de berørte områder under deres graviditet, skal informere deres læge og jordemoder om opholdet.
- Kvinder, der har rejst i de berørte områder, og som planlægger graviditet, opfordres til at vente to måneder efter hjemkomst med at blive gravide.
- .

Sundhedsstyrelsens opdaterede retningslinjer for håndtering af Zikavirus´(2. August2016)

- **MÆND**

- Mænd, der kommer hjem fra områder med udbrud af Zikavirus, og som har en **gravid partner**, anbefales at **anvende kondom i resten af graviditeten**. Det sker som en ekstra sikkerhed, fordi man endnu ved så lidt om en eventuel seksuel overførsel af smitte.

Sundhedsstyrelsens opdaterede retningslinjer for håndtering af Zikavirus´(2. August2016)

- **MÆND**

- Hvis **partneren er i den fertile alder**, men ikke er kendt gravid, anbefales det, at manden anvender kondom i mindst to måneder efter hjemkomsten. Hvis manden har eller har haft symptomer på infektion med Zikavirus er anbefalingen dog, at **han anvender kondom i minimum seks måneder.**

WHO secretary general Margareth Chan declares Zika Virus epidemic an international emergency

1st. Feb. 2016

In my påersonal view an exagerated measure but probably reflectiung all the deserved criticism the WHO received due to a very slow reaction during the Ebola Epidemic in W-Africa that cost > 11000 lives.


Ende gut, Alles gut.