ZIKA VIRUS UPDATE 2016

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Early Optimism about Antimicrobials

William H. Stewart, U.S. Surgeon General 1965-1969, is purported to have said, "We have closed the book on infectious disease."

The End of Infectious Disease

- Since 1967:
  - Legionnaire's disease
  - Toxic shock syndrome
  - AIDS
  - Lymedisease
  - West Nile encephalitis
  - SARS
  - Avian Flu
- Chronic diseases associated with pathogens:
  - Peptic ulcers (*Helicobacter pylori*)
  - Liver cancer (Hepatitis B and C)
  - Lymearthritis (*Borreliaburgdorferi*)

NEWLY IDENTIFIED INFECTIOUS DISEASES AND PATHOGENS (2)

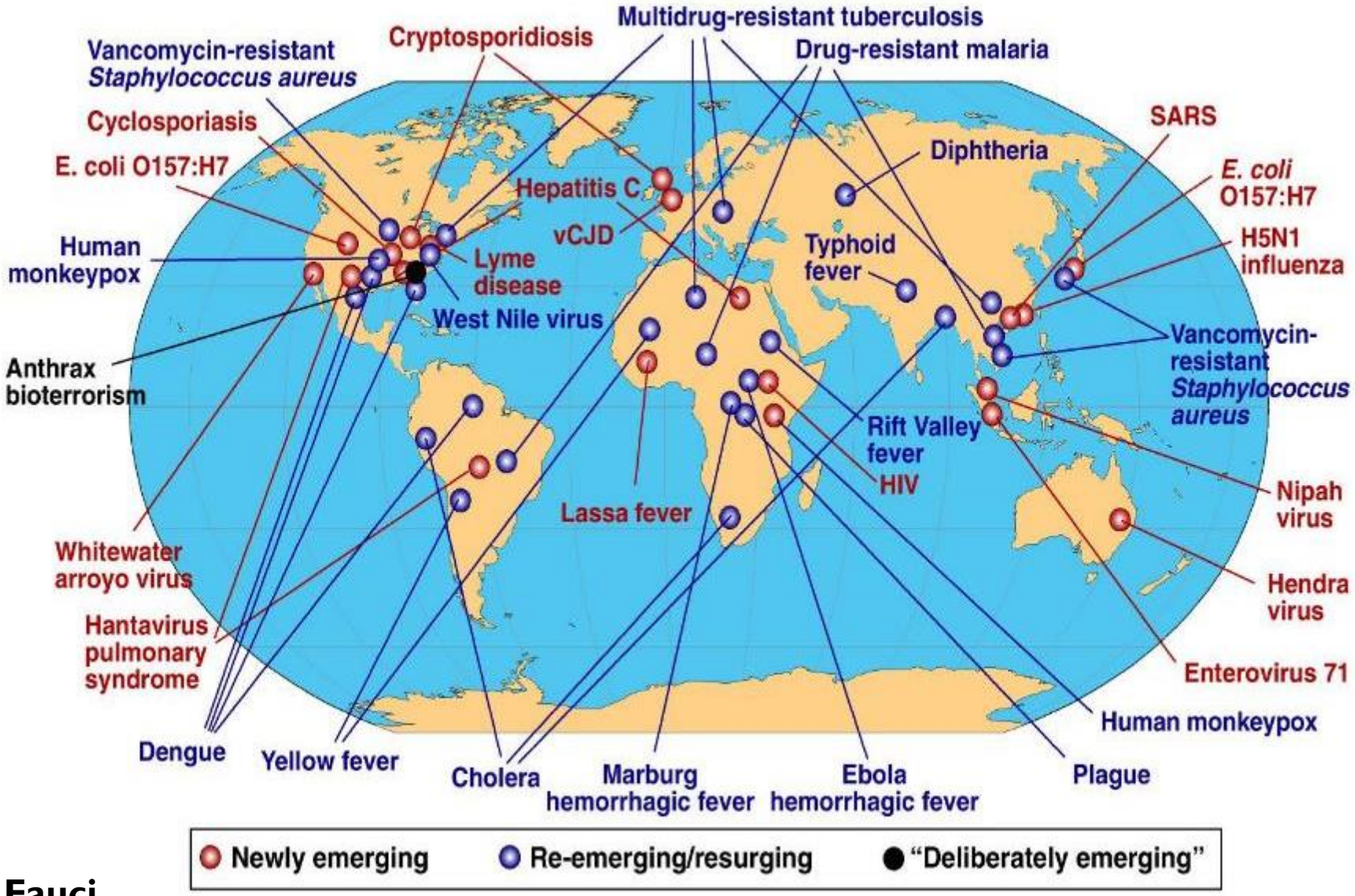
Year	Disease or Pathogen
2012	MERS-CoV
2009	H1N1
2004	Avian influenza (human cases)
2003	SARS
1999	Nipah virus
1997	H5N1 (avian influenza A virus)
1996	New variant Creutzfelt-Jacob disease; Australian bat lyssavirus
1995	Human herpesvirus 8 (Kaposi's sarcoma virus)
1994	Savia virus; Hendra virus

Source: Workshop presentation by David Heymann, World Health Organization, 1999

Emerging and Re-emerging Infectious Diseases

- Emerging infectious diseases: Infectious diseases that have newly appeared in a population.
- Global :
- Regional:
- Re-emerging Diseases: Diseases' incidence in human has increased during the last 20 years or threatens to increase in the near future.
- Global:
- Regional:

GLOBAL EXAMPLES OF EMERGING AND RE-EMERGING INFECTIOUS DISEASES



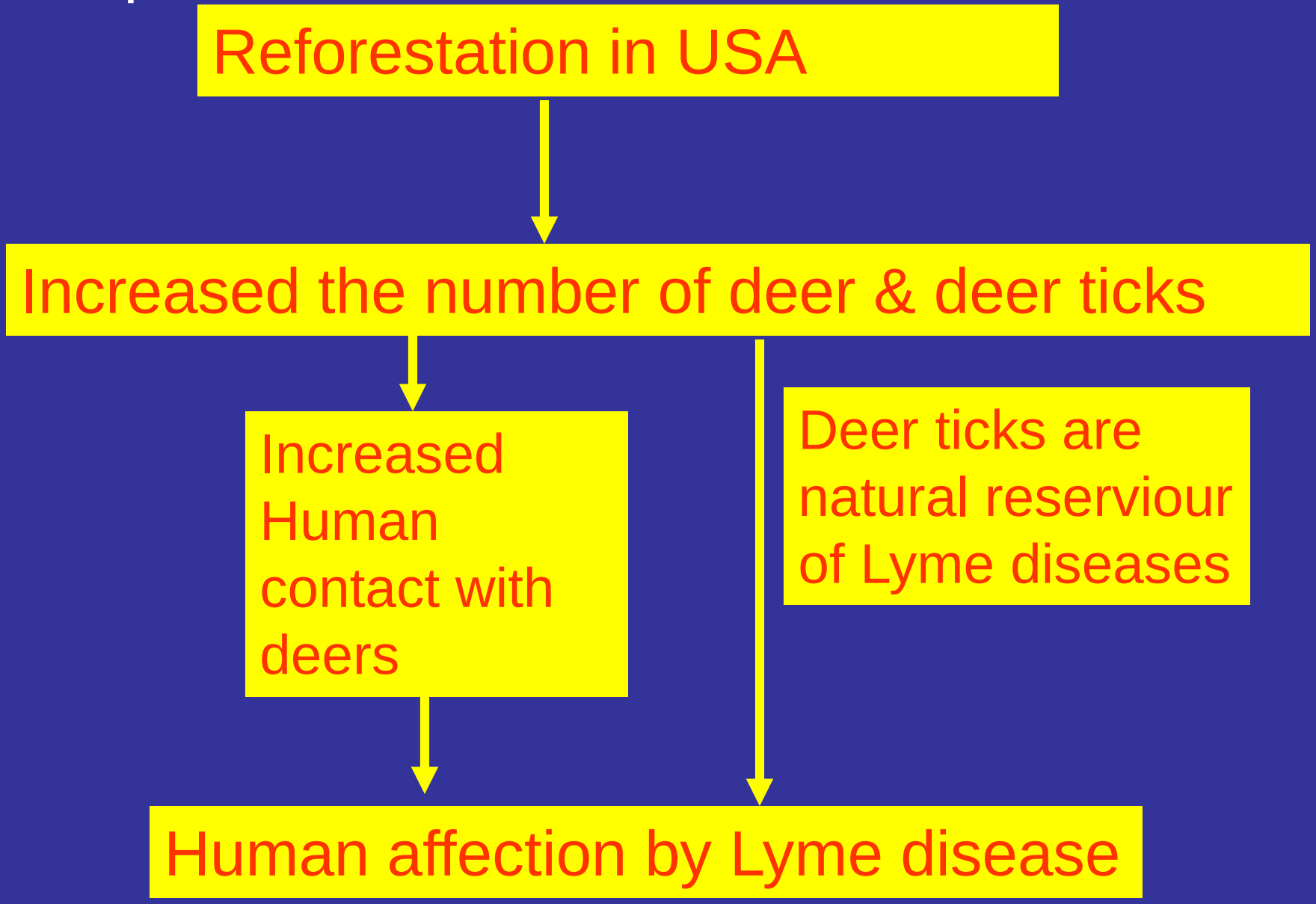
AS Fauci

Factors responsible for emerging of infections.

I-Ecological changes and Agricultural development.

Placing the people in contact with a natural reserviour or host of a hitherto unfamiliar, but usually already present,

Example 1 :


Reforestation in USA
Increased the number of deer & deer ticks
Increased Human contact with deers
Deer ticks are natural reserviour of Lyme diseases
Human affection by Lyme disease

II- Changes in Human demographics and behaviours

Inflation of population size

↓

Insufficient infrastructures

↓

Use open containers for water

↓

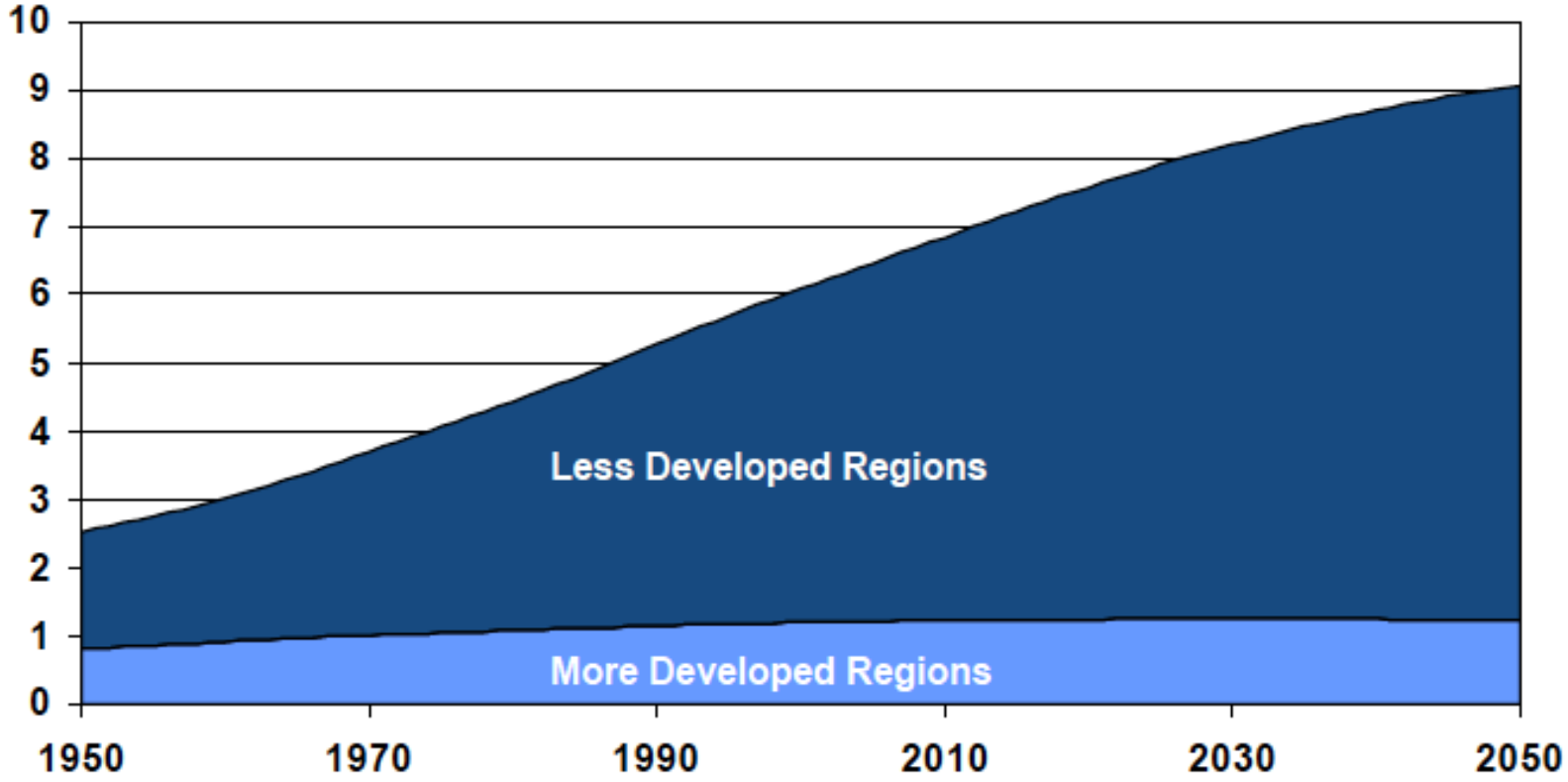
Breading mosquitos

↓

Dengue fever in Asia

Growth in More, Less Developed Countries

Billions



Source: United Nations, *World Population Prospects: The 2004 Revision* (medium scenario), 2005.

- **Urbanization-more people concentrated in cities-often without adequate infrastructure**

- **Increases in the elderly populations**

- **Increases in children in daycare: working woman with kids under 5 was 30% in 1970, is 75% in 2000.**

- **Fast paced Lifestyles- increase in convenience items and more stress**

- **High-risk behavior- Drug use and unprotected sex**

War and Famine

War refugees are a full 1% of the global population

War refuges are forced onto new areas where they are exposed to new microbes from vectors and people.

War and famine are closely linked.

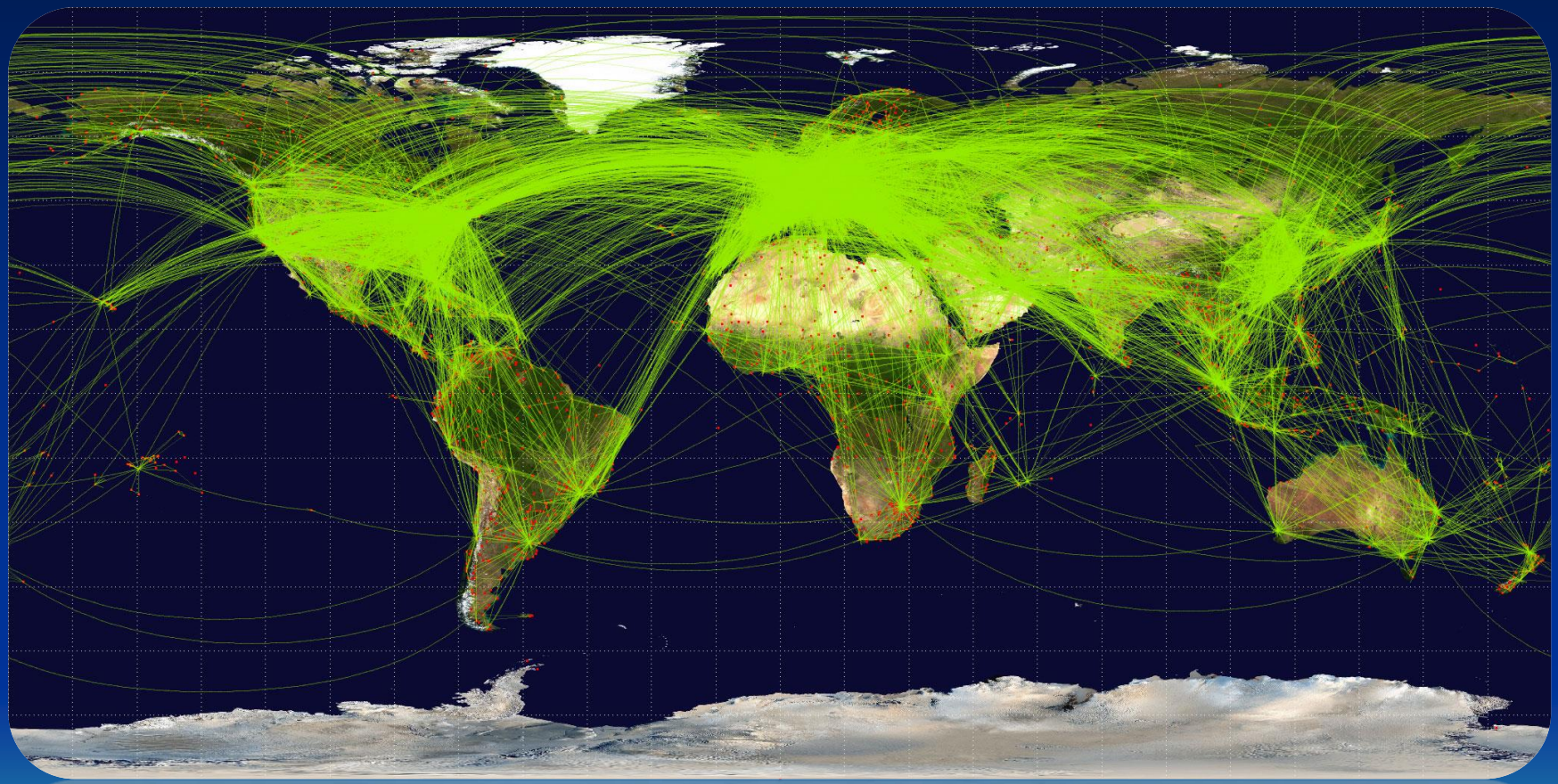
In 2001, tracking 16 countries with “food emergencies”, showed that 9 were because of civil unrest.

Famine is also caused by social, economic, and political forces.

- III-International travel and Commerce.
- **365 days to circumnavigate the globe…now it takes 36 hours**
- **-used to quarantine ships, but 36 h faster than disease incubation**

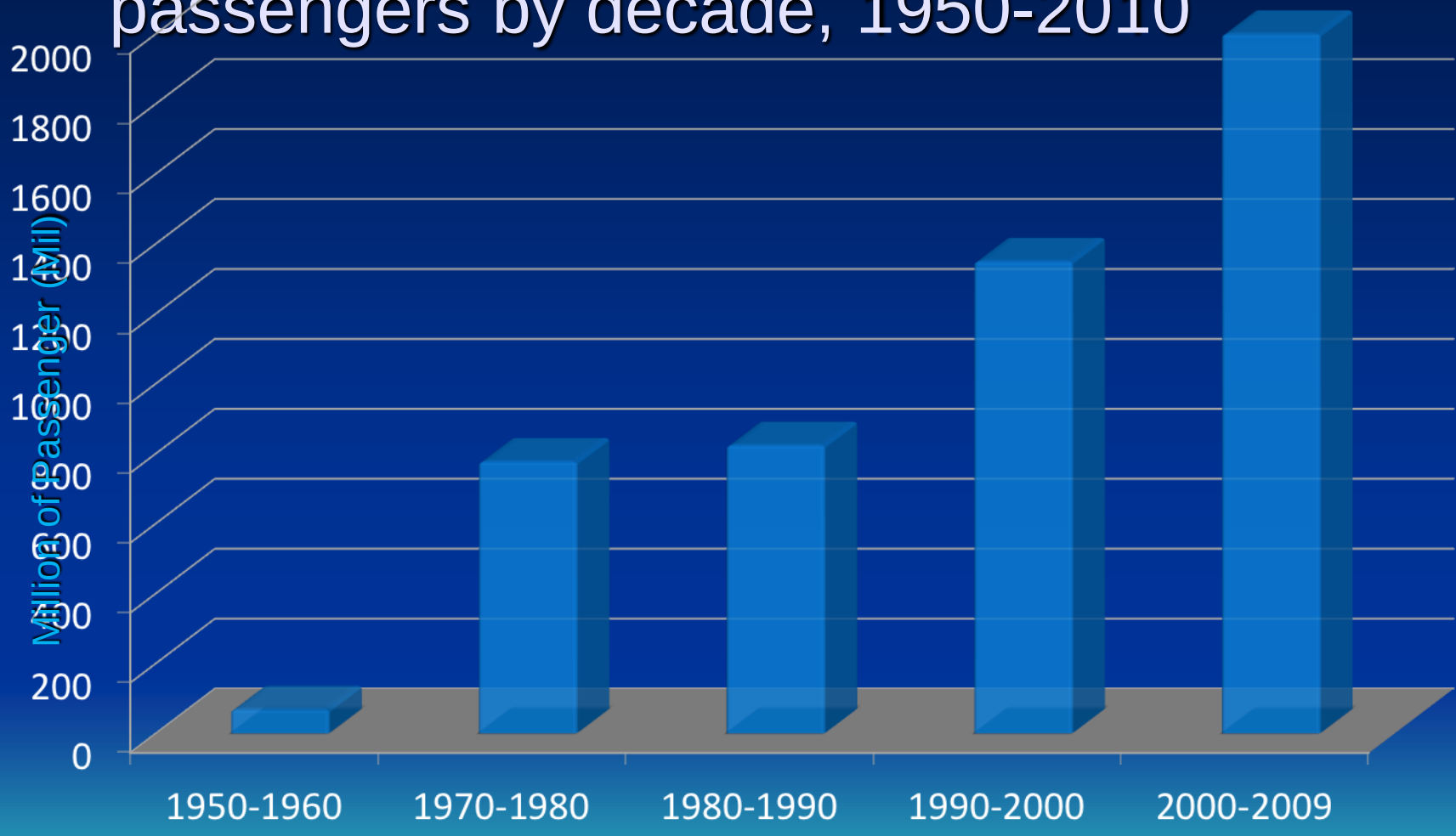
- **400 million people per year travel internationally**
- **increased incidence of both Tuberculosis and Influenza transmission on long flights**

The global air network



Commercial Air Traffic Over a 24 Hour Period

Average annual number of global airline passengers by decade, 1950-2010



- **-Transportation of products is an increased concern.**
- **-rapid transport of disease harboring fresh products.**
- **-transport of livestock facilitates movements of viruses and arthropods (especially ticks)**

Travel and HIV/AIDS.

-Silk route and plague.

-Slaves trade and yellow fever.

-Migration to new world and smallpox.

Cholera and Hajj.

IV- Technology and industry

- Modern mass production increased the chance of accidental contamination and amplifies the effect of such contamination.

  -Contamination of hamburger meat by E.coli strains causing haemolytic uraemic syndrome.

  -Feeding cattle by byproducts of sheep causing bovine spongiform encephalitis.

VI- Breakdown of public health measures.

- -Decrease in choline in water supplies lead to rapid spread of cholera in South America.

- Non functioning water plant in Wisconsin, USA lead to outbreak of waterborne cryptosporidium.

Major Factors Contributing to the Emergence of Infectious Diseases

1. Human demographics and behavior
2. Technology and industry
3. Economic development and land use
4. International travel and commerce
5. Microbial adaptation and change
6. Breakdown of public health measures

Institute of Medicine Report 1992


ZIKA
VIRUS

THE EMERGENCE OF ZIKA VIRUS

1947 – Isolation from Rhesus monkey, Zika forest, Uganda

1948 – Isolated from Aedes africanus mosquitos, Zika forest, 6% people in area test positive serologically

1952 – Nigeria, isolated from child, fever & headache

1956 – Human volunteer inoculation, limited febrile illness

1962 – Uganda, person with rash, fever, body pain

1960's – 1970's _ Africa and Asia febrile illness, sero +, Nigeria sero-prevalence 48% to 56%

RECENT ZIKA VIRUS EPIDEMICS

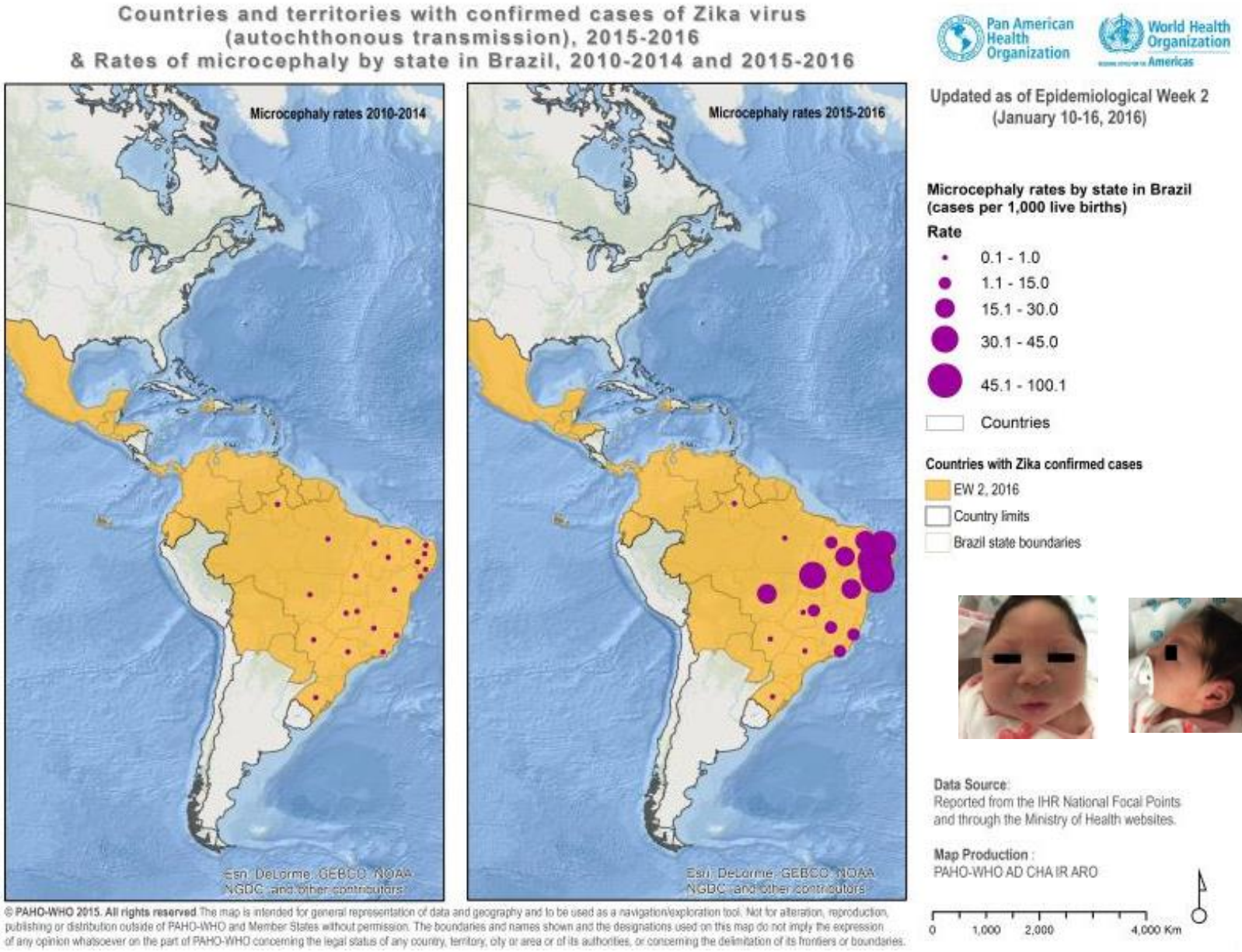
2007 – Yap Island, Micronesia (pop. 10,000), rash, fever, arthralgia, conjunctivitis, 73% inhabitants IgM antibodies, 19% clinical illness

2013 – French Polynesia islands (pop. 270,000), 28,000 cases, Guillain-Barre Syndrome (20% up)

2015 – NE Brazil, Americas & Caribbean, 33 countries

Feb 2016 – WHO microcephaly & neuro disorders (GBS), 4th international emergency

Rates of Microcephaly by State in Brazil 2010-2014 vs 2015-2016



Zika epidemic and GBS

Countries reporting increased incidence of Guillain-Barre Syndrome and Zika prevalence:

- **Brazil**
- **El Salvador**
- **Columbia**
- **Suriname**
- **Venezuela**
- Media reports in Puerto Rico and Honduras have not been confirmed
- Martinique has reported no increase of GBS,

GUILLAIN-BARRE SYNDROME and ZIKA VIRUS: Attributable Risk?

Table 1. Incidence of Guillain-Barré Syndrome Before and During the Zika Virus Outbreak in French Polynesia

Period (Date)		GBS Cases, n	Person, n	Year	Person-Year	GBS Incidence, n per 1000 Person-Year (95% Confidence Interval)[a]
Pre-ZIKV	(2009 to 2012)	21	268270[b]	4	1073080	0.02 (.01 to .03)
ZIKV outbreak	(October 2013 to April 2014)	42	177058.20	0·58	103283.95	0.41 (.29 to .55)

Abbreviations: GBS, Guillain-Barré syndrome; ZIKV, Zika virus.

[a] 95% confidence interval estimated using Byar approximation Poisson.

[b] Sensitivity analysis using 2007 census figures for 2009 to 2011 did not significantly change the result.

Guillain-Barré Syndrome During Ongoing Zika Virus Transmission — Puerto Rico, January 1–July 31, 2016

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

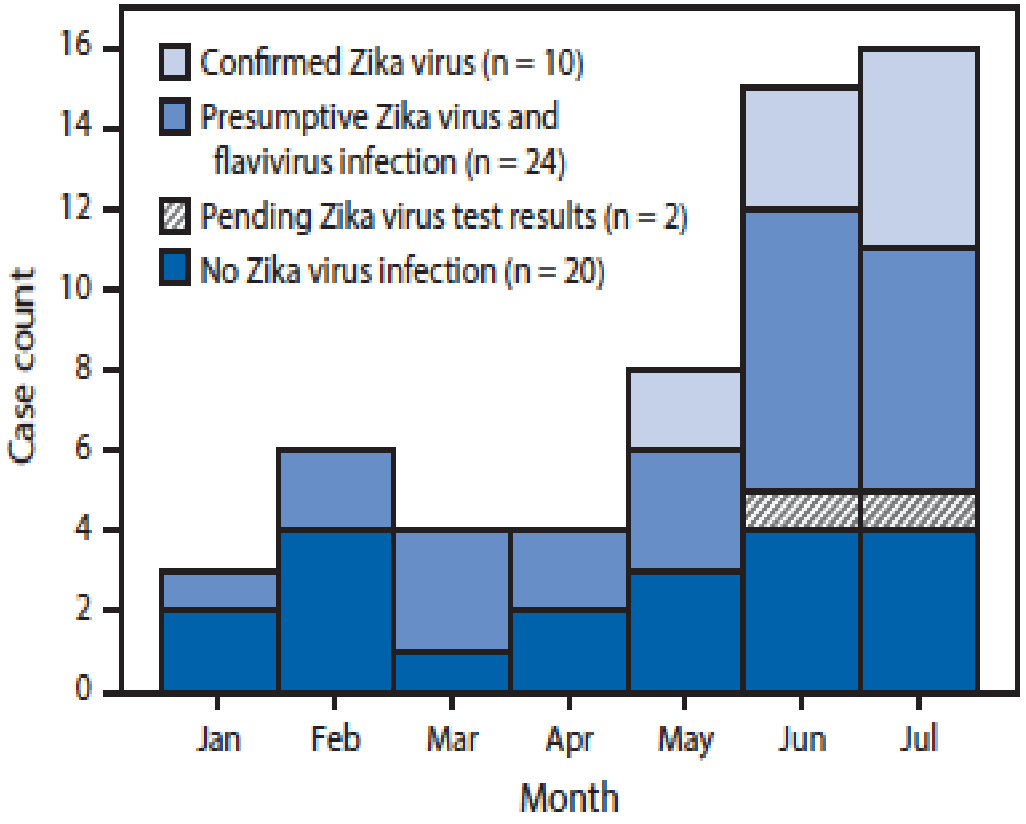
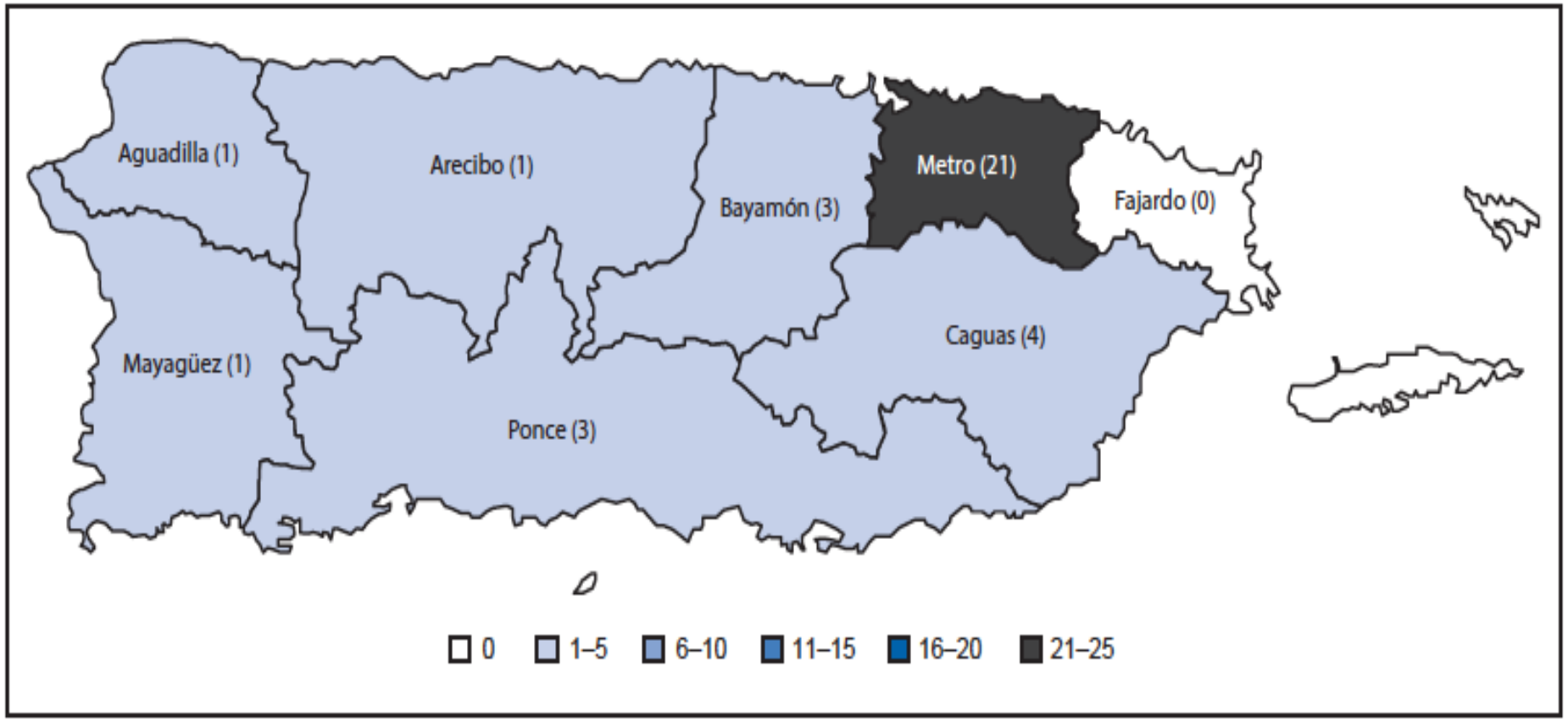


FIGURE 2. Reported cases of confirmed and suspected Guillain-Barré syndrome in persons with evidence of Zika virus or flavivirus infection, by public health region of residence — Puerto Rico, January 1–July 31, 2016 (N = 34)



The Vector

Aedes Aegypti

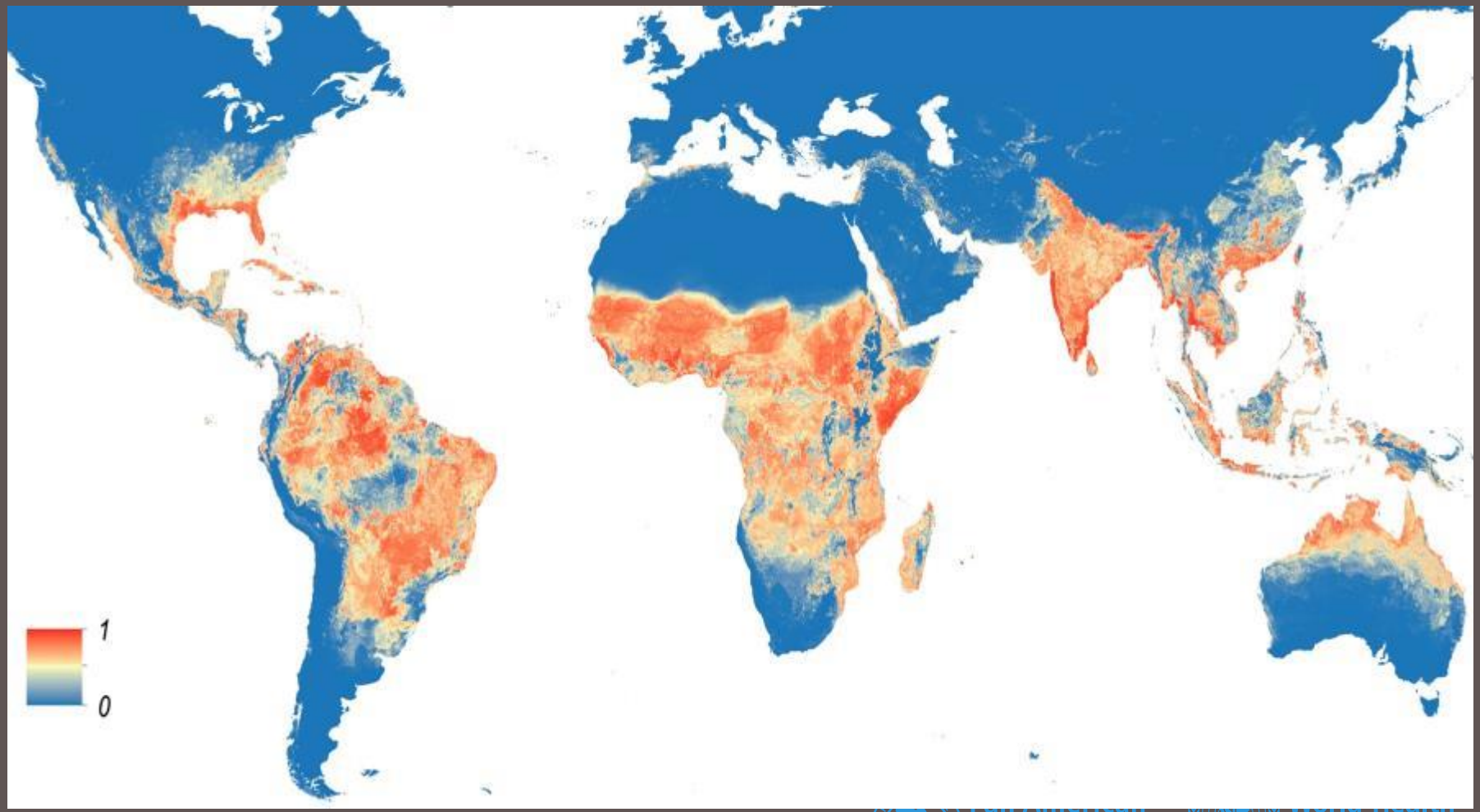
- Daytime mosquito – dawn and dusk; however due to LED light use is thought to be active at night
- Limited movement – flying radius of 500m
- Female lays ~80 eggs every 3 days
- Needs blood meal to lay eggs
- Eggs can survive several years out of water
- 4 stages of the lifecycle, 3 are water related
- Well adapted to human habitats (water storage, waste, white lights, air conditioning, bromeliads)

ZIKA VIRUS EPIDEMIOLOGY

Where has Zika virus been found?

- Before 2015, Zika outbreaks occurred in Africa, Southeast Asia, and the Pacific Islands.
- Currently outbreaks are occurring in many countries and territories.

Possible Geographic Distribution of *Aedes aegypti*

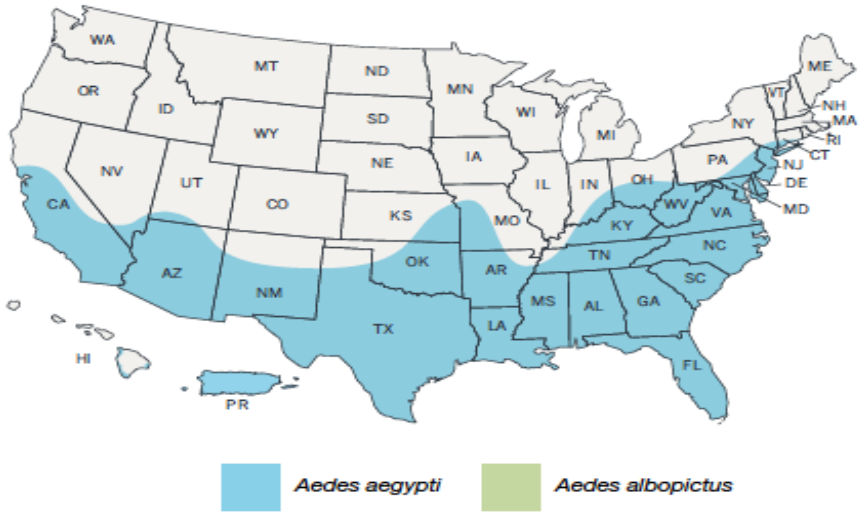


Kraemer MUG, *et alii*, eLife 2015;4:e08347

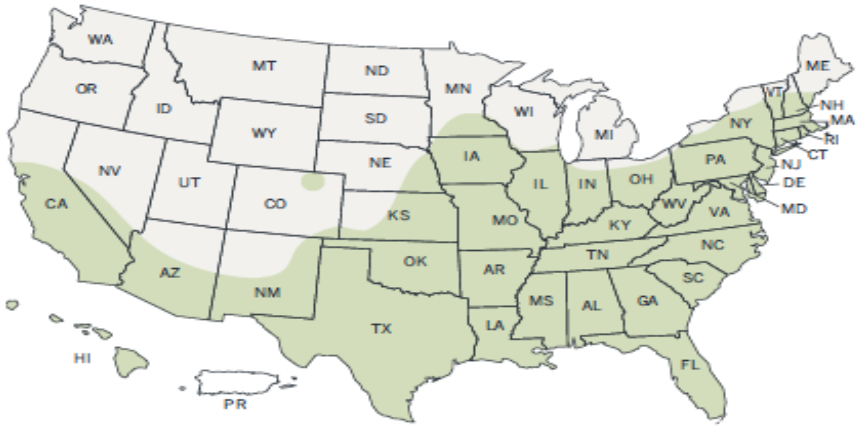
ALL COUNTRIES & TERRITORIES with ACTIVE ZIKA VIRUS TRANSMISSION

CDC's Response to **Zika**

ESTIMATED range of *Aedes albopictus* and *Aedes aegypti* in the United States, 2016*



Aedes aegypti | *Aedes albopictus*



* Maps have been updated from a variety of sources. These maps represent CDC's best estimate of the potential range of *Aedes aegypti* and *Aedes albopictus* in the United States. Maps are not meant to represent risk for spread of disease.

***Aedes aegypti* mosquitoes are more likely to spread viruses like Zika, dengue, chikungunya and other viruses than other types of mosquitoes such as *Aedes albopictus* mosquitoes.**

These maps DO NOT show

- Exact locations or numbers of mosquitoes living in an area
- Risk or likelihood that these mosquitoes will spread viruses

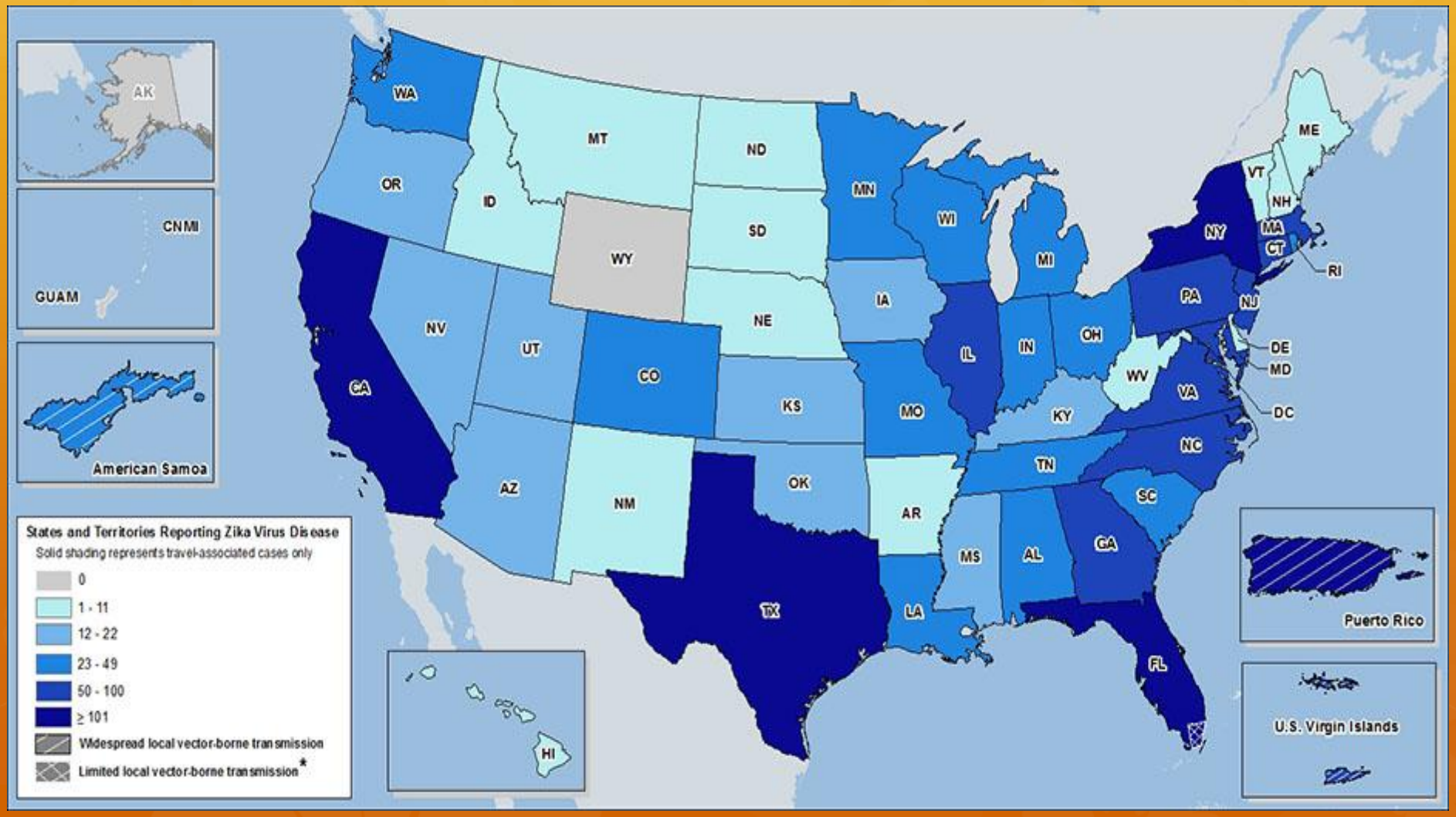
These maps show

- CDC's best estimate of the potential range of *Aedes aegypti* and *Aedes albopictus* in the United States
- Areas where mosquitoes are or have been previously found

CS264451-F
April 1, 2016

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

LABORATORY CONFIRMED ZIKA VIRUS CASES REPORTED TO ARBONET BY STATE OR TERRITORY AS OF SEPTEMBER 7, 2016



HOW MANY ZIKA CASES SO FAR…HOW ABOUT THE ASYMPTOMATIC CASES

Case Counts in the US (September 7, 2016)

US States

- Locally acquired mosquito-borne cases reported: 43
- Travel-associated cases reported: 2,920
- Laboratory acquired cases reported: 1
- Total: 2,964
  - Sexually transmitted: 24
  - Guillain-Barré syndrome: 7

US Territories

- Locally acquired cases reported: 15,809
- Travel-associated cases reported: 60
- Total: 15,869*
  - Guillain-Barré syndrome: 31

*Sexually transmitted cases are not reported for US territories because with local transmission of Zika virus it is not possible to determine whether infection occurred due to mosquito-borne or sexual transmission.

LABORATORY CONFIRMED ZIKA CASES UNITED STATES / TERRITORIES

Sept 7, 2016

States	Travel-associated cases* No. (% of cases in states) (N=2,921)	Locally acquired cases† No. (% of cases in states) (N=43)
Alabama	24 (1)	0 (0)
Arizona	22 (1)	0 (0)
Arkansas	9 (<1)	0 (0)
California	210 (7)	0 (0)
Colorado	27 (1)	0 (0)
Connecticut	58 (2)	0 (0)
Delaware	11 (<1)	0 (0)
District of Columbia	11 (<1)	0 (0)
Florida	571 (20)	43 (100)
Georgia	75 (3)	0 (0)
Hawaii	11 (<1)	0 (0)
Idaho	2 (<1)	0 (0)
Illinois	51 (2)	0 (0)
Indiana	32 (1)	0 (0)
Iowa	15 (1)	0 (0)
Kansas	13 (<1)	0 (0)
Kentucky	20 (1)	0 (0)
Louisiana	26 (1)	0 (0)
Maine	11 (<1)	0 (0)
Maryland	89 (3)	0 (0)
Massachusetts	67 (2)	0 (0)
Michigan	45 (2)	0 (0)
Minnesota	39 (1)	0 (0)
Mississippi	20 (1)	0 (0)
Missouri	26 (1)	0 (0)
Montana	7 (<1)	0 (0)
Nebraska	8 (<1)	0 (0)
Nevada	14 (<1)	0 (0)
New Hampshire	8 (<1)	0 (0)
New Jersey	91 (3)	0 (0)
New Mexico	4 (<1)	0 (0)
New York	661 (23)	0 (0)
North Carolina	52 (2)	0 (0)
North Dakota	1 (<1)	0 (0)
Ohio	36 (1)	0 (0)
Oklahoma	20 (1)	0 (0)
Oregon	19 (1)	0 (0)
Pennsylvania††	95 (3)	0 (0)
Rhode Island	29 (1)	0 (0)
South Carolina	31 (1)	0 (0)
South Dakota	1 (<1)	0 (0)
Tennessee	38 (1)	0 (0)
Texas	161 (6)	0 (0)
Utah	12 (<1)	0 (0)
Vermont	7 (<1)	0 (0)
Virginia	78 (3)	0 (0)
Washington	28 (1)	0 (0)
West Virginia	11 (<1)	0 (0)
Wisconsin	24 (1)	0 (0)

Territories	Travel-associated cases* No. (% of cases in territories) (N=60)	Locally acquired cases† No. (% of cases in territories) (N=15,809)
American Samoa	0 (0)	47 (<1)
Puerto Rico	59 (98)	15,541** (98)
US Virgin Islands	1 (2)	221 (1)

Pregnant Women with Any Laboratory Evidence of Possible Zika Virus Infection

US States and the District of Columbia	US Territories**
671	1080
*Includes aggregated data reported to the US Zika Pregnancy Registry as of Sept 1, 2016	**Includes aggregated data from the US territories reported to the US Zika Pregnancy Registry and data from Puerto Rico reported to the Zika Active Pregnancy Surveillance System as of Sept 1, 2016

Pregnancy Outcomes in the United States and the District of Columbia

Liveborn infants with birth defects*	Pregnancy losses with birth defects**
17	5
Includes aggregated data reported to the US Zika Pregnancy Registry as of Sept 1, 2016	Includes aggregated data reported to the US Zika Pregnancy Registry as of Sept 1, 2016

Pregnancy Outcomes in the United States Territories

Liveborn infants with birth defects*	Pregnancy losses with birth defects**
1	1
Includes aggregated data from the US territories reported to the US Zika Pregnancy Registry and data from Puerto Rico reported to the Zika Active Pregnancy Surveillance System as of Sept 1, 2016	Includes aggregated data from the US territories reported to the US Zika Pregnancy Registry and data from Puerto Rico reported to the Zika Active Pregnancy Surveillance System as of Sept 1, 2016

- Zika outbreak prompts travel warning for area of Miami
- 3:32 a.m. Tuesday, Aug. 2, 2016 | Filed in: News

ARE YOU SURPRISED ?

It's here: Florida 1st state with local

Zika cases, transmitted by mosquito

Palm Beach Post

CDC tells pregnant women to avoid Miami-Dade after latest outbreak

6:11 p.m. Friday, Aug. 19, 2016 | Filed in: **News**

Palm Beach County has first case of locally-acquired Zika virus

7:16 p.m. Monday, Aug. 8, 2016 | Filed in: News

Active Zika Virus Transmission in Florida

FDA says to check all blood donations for Zika

5:59 p.m. Friday, Aug. 26, 2016 | Filed in: **News**

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 65 / No. 28
July 22, 2016

Suspected Female-to-Male Sexual Transmission of Zika Virus — New York City, 2016

Pan American Health Organization

World Health Organization
REGIONAL OFFICE FOR THE Americas

Morbidity and Mortality Weekly Report

Likely Sexual Transmission of Zika Virus from a Man with No Symptoms of Infection — Maryland, 2016

In June 2016, the Maryland Department of Health and Mental Hygiene (DHMH) was notified of a nonpregnant woman who sought treatment for a subjective fever and an itchy rash, which was described as maculopapular by her provider. Laboratory testing at the Maryland DHMH Laboratories Administration confirmed Zika virus infection. Case investigation revealed that the woman had not traveled to a region with ongoing transmission of Zika virus, but did have sexual contact with a male partner who had recently traveled to the Dominican Republic. The male partner reported exposure to mosquitoes while traveling, but no symptoms consistent with Zika virus infection either before or after returning to the United States. The woman reported no other sex partners during the 14 days before onset of her symptoms and no receipt of blood products or organ transplants.

Modes of transmission

- Bite from an infected mosquito
- Maternal-fetal
  - Intrauterine
  - Perinatal
- Sexual transmission from infected male partners
- Laboratory exposure
- Theoretical: blood transfusion, organ and tissue transplant, fertility treatment, and breast feeding

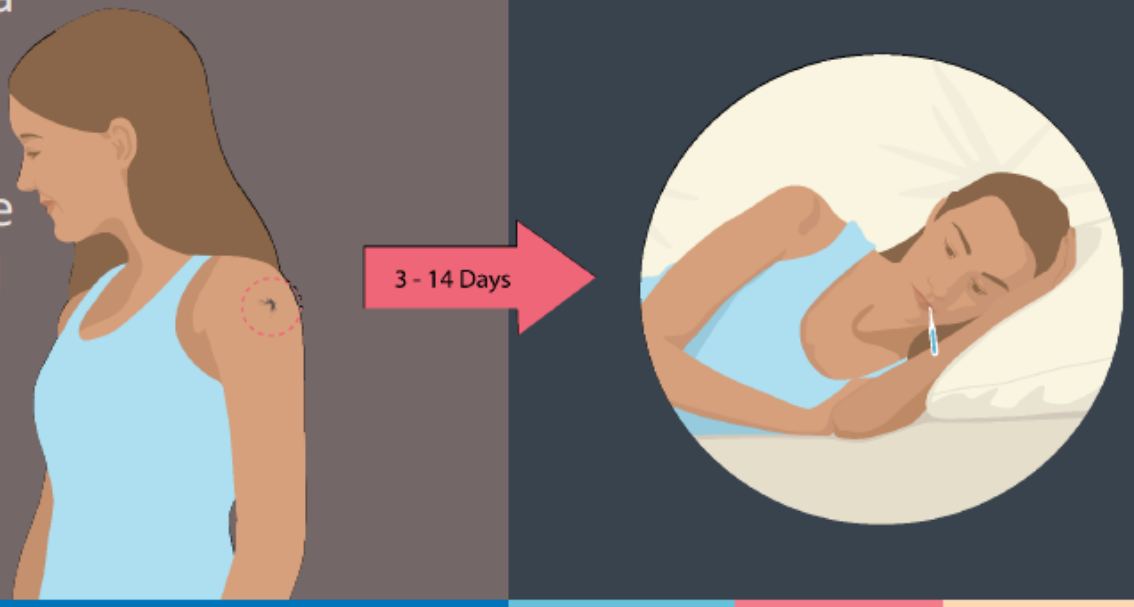
Example Zika virus incidence and attack rates, Yap 2007

- Infection rate: 73% (95% CI 68–77)
- Symptomatic attack rate among infected: 18% (95% CI 10–27)
- All age groups affected
- Adults more likely to present for medical care
- No severe disease, hospitalizations, or deaths

Note: Rates based on serosurvey on Yap Island, 2007 (population 7,391)

Incubation and viremia

- Incubation period for Zika virus disease is 3–14 days.
- Zika viremia ranges from a few days to 1 week.
- Some infected pregnant women can have evidence of Zika virus in their blood longer than expected.
- Virus remains in semen longer than in blood.

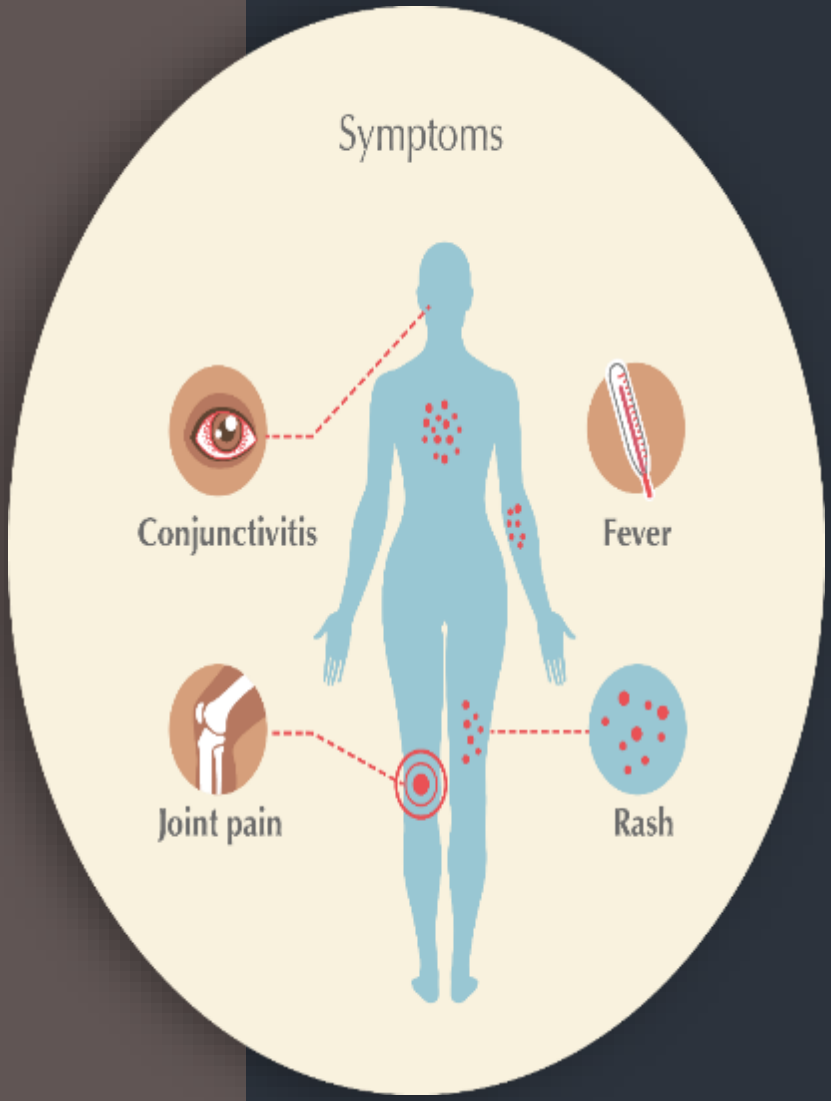


Zika virus clinical disease course and outcomes

- Clinical illness is usually mild.
- Symptoms last several days to a week.
- Severe disease requiring hospitalization is uncommon.
- Fatalities are rare.
- Guillain-Barré syndrome (GBS) reported in patients following suspected Zika virus infection.
  - Relationship to Zika virus infection is not known.

Symptoms

- Many infections asymptomatic.
- Most common symptoms
  - Acute onset of fever
  - Maculopapular rash
  - Joint pain
  - Conjunctivitis
- Other symptoms include muscle pain and headache.



Reported clinical symptoms among confirmed Zika virus disease cases

Symptoms	N (n=31)	%
Macular or papular rash	28	90%
Subjective fever	20	65%
Arthralgia	20	65%
Conjunctivitis	17	55%
Myalgia	15	48%
Headache	14	45%
Retro-orbital pain	12	39%
Edema	6	19%
Vomiting	3	10%

Yap Island, 2007

Duffy M. N Engl J Med 2009

Clinical Presentation of rash syndrome in Northeast Brazil, May 2015

Rash, swollen joints, and conjunctival hyperemia







Pan American Health Organization

World Health Organization
REGIONAL OFFICE FOR THE Americas

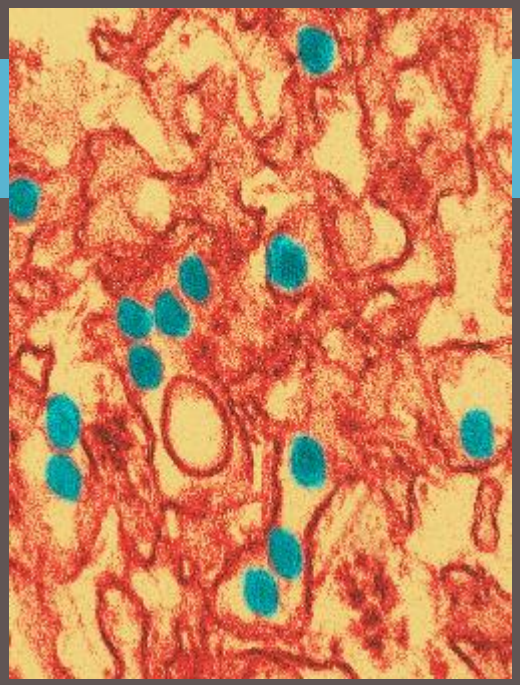
Source: Research team of the São Luís/MA municipal health office - From a presentation by the Ministry of Health of Brazil, 2015

Clinical features: Zika virus compared to dengue and chikungunya

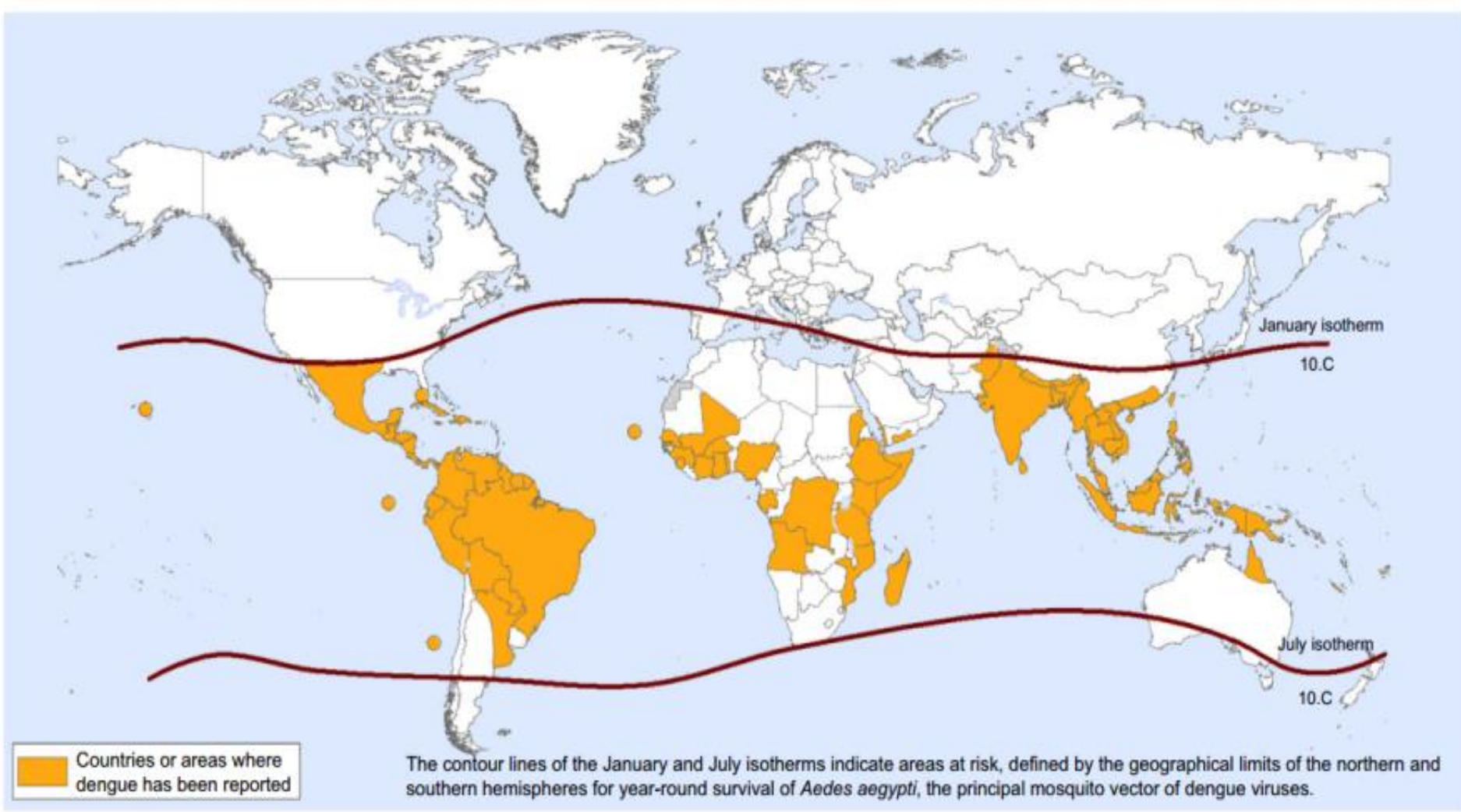
Features	Zika	Dengue	Chikungunya
Fever	++	+++	+++
Rash	+++	+	++
Conjunctivitis	++	-	-
Arthralgia	++	+	+++
Myalgia	+	++	+
Headache	+	++	++
Hemorrhage	-	++	-
Shock	-	+	-

Rabe, Ingrid MBChB, MMed "Zika Virus- What Clinicians Need to Know?" (presentation, Clinician Outreach and Communication Activity (COCA) Call, Atlanta, GA, January 26 2016)

DIAGNOSES AND TESTING FOR ZIKA



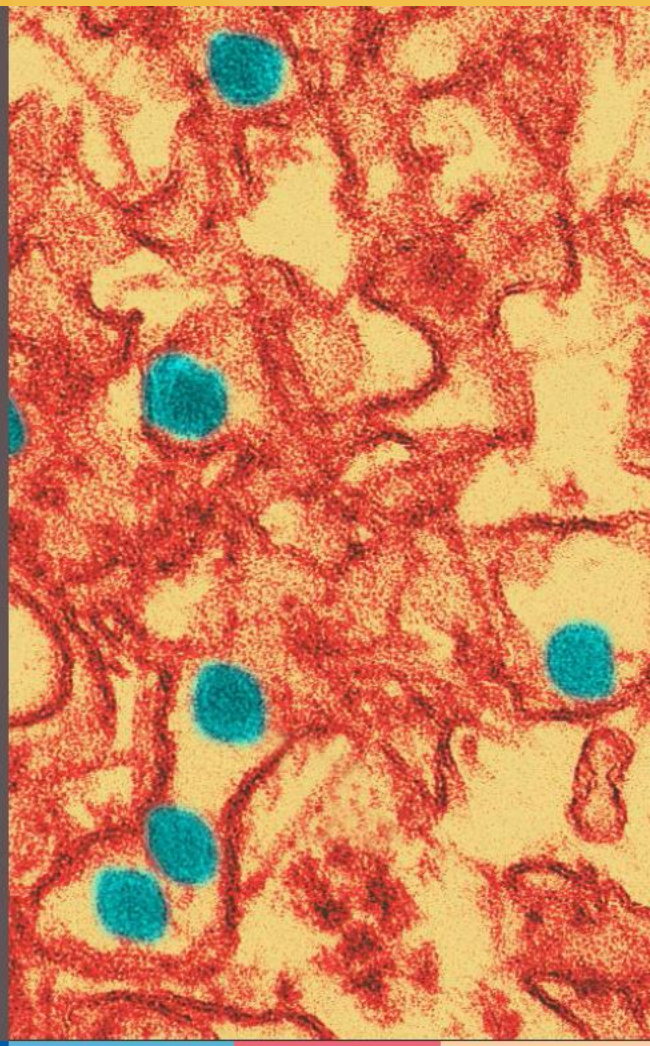
Risk of Dengue virus transmission = risk of Zika virus transmission



Differential diagnosis

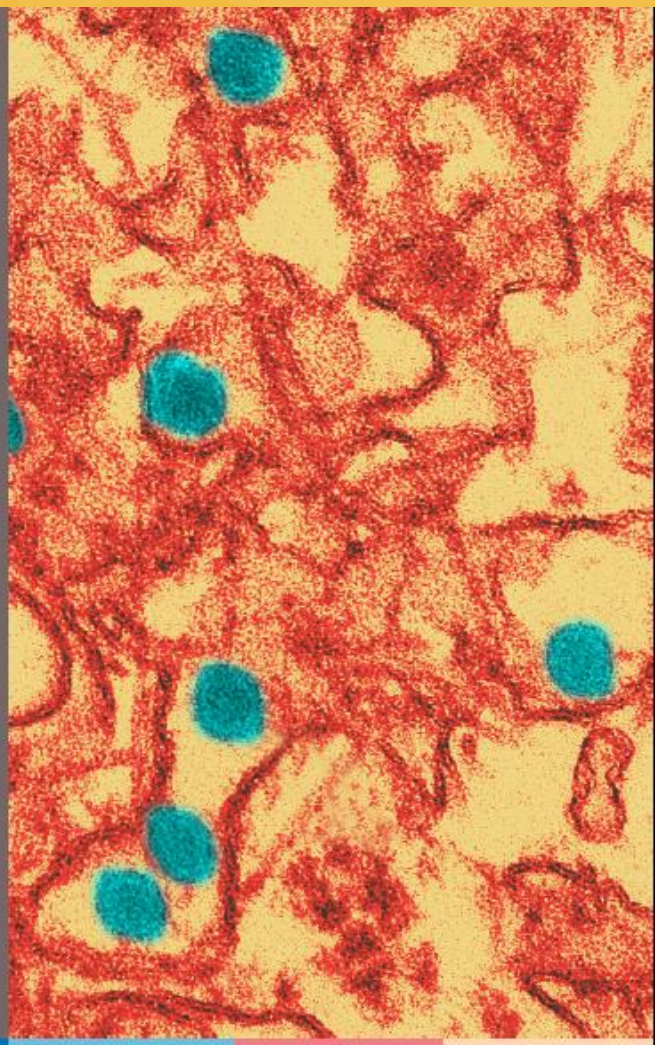
Based on typical clinical features, the differential diagnosis for Zika virus infection is broad. Considerations include

- Dengue
- Chikungunya
- Leptospirosis
- Malaria
- Riskettsia
- Group A Streptococcus
- Rubella
- Measles
- Parvovirus
- Enterovirus
- Adenovirus
- Other alphaviruses (e.g., Mayaro, Ross River, Barmah Forest, O'nyong-nyong, and Sindbis viruses)



Diagnostic testing for Zika virus

- During first two weeks after the start of illness, Zika virus infection can often be diagnosed by performing real-time reverse transcriptase polymerase chain reaction (rRT-PCR) on serum and urine.
- Serology for IgM and neutralizing antibodies in serum collected up to 12 weeks after illness onset
- Plaque reduction neutralization test (PRNT) for presence of virus-specific neutralizing antibodies in paired serum samples
- Immunohistochemical (IHC) staining for viral antigens or RT-PCR on fixed tissues



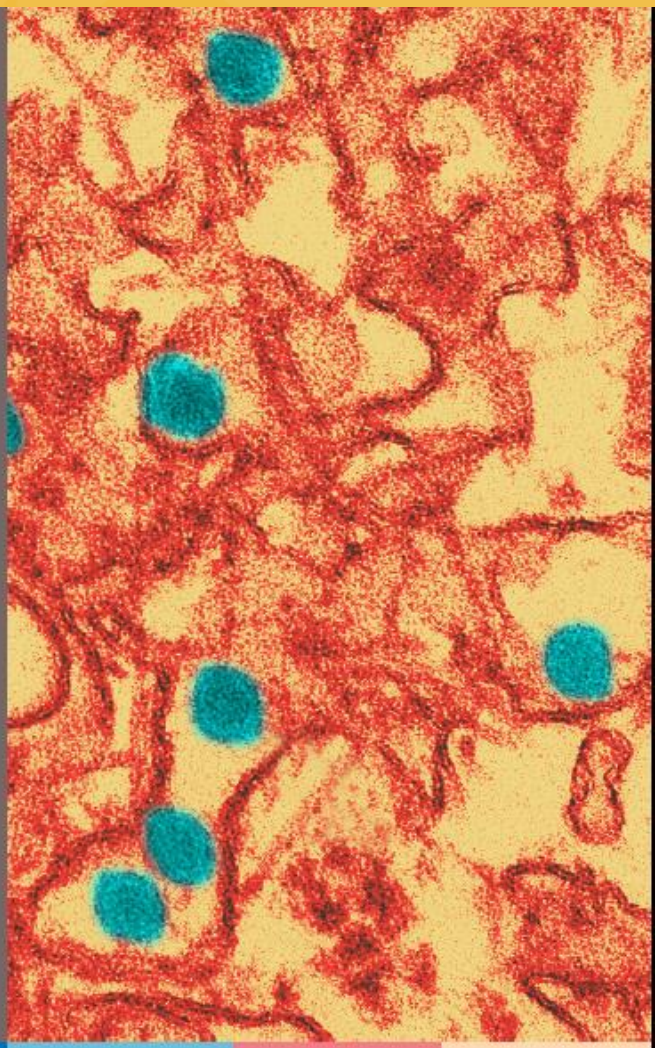
Comparison of Test Results for Zika Virus RNA in Urine, Serum, and Saliva Specimens from Persons with Travel-Associated Zika Virus Disease — Florida, 2016

TABLE 1. Results of Zika virus IgM antibody testing of serum specimens and RT-PCR testing of serum and urine specimens for Zika virus RNA, by days after symptom onset for 66 persons with travel-associated Zika virus disease — Florida, 2016

Days after onset	Serum IgM No. positive/No. tested (%)	Serum RT-PCR No. positive/No. tested (%)	Urine RT-PCR No. positive/No. tested (%)
0	0/1 (0)	0/1 (0)	1/1 (100)
1	2/7 (29)	6/7 (85)	7/7 (100)
2	3/12 (25)	8/12 (67)	11/12 (92)
3	5/10 (50)	4/10 (40)	10/10 (100)
4	3/12 (25)	8/12 (67)	12/12 (100)
5	9/13 (69)	5/13 (38)	11/13 (85)
6	2/2 (100)	0/2 (0)	2/2 (100)
7	4/4 (100)	0/4 (0)	3/4 (75)
9	2/3 (67)	0/3 (0)	3/3 (100)
14	1/1 (100)	0/1 (0)	0/1 (0)
20	1/1 (100)	0/1 (0)	1/1 (100)
Range of days			
0–5	22/55 (40)	31/55 (56)*	52/55 (95)*
6–10	8/9 (89)	0/9 (0)*	8/9 (89)*
11–15	1/1 (100)	0/1 (0)	0/1 (0)
16–20	1/1 (100)	0/1 (0)	1/1 (100)

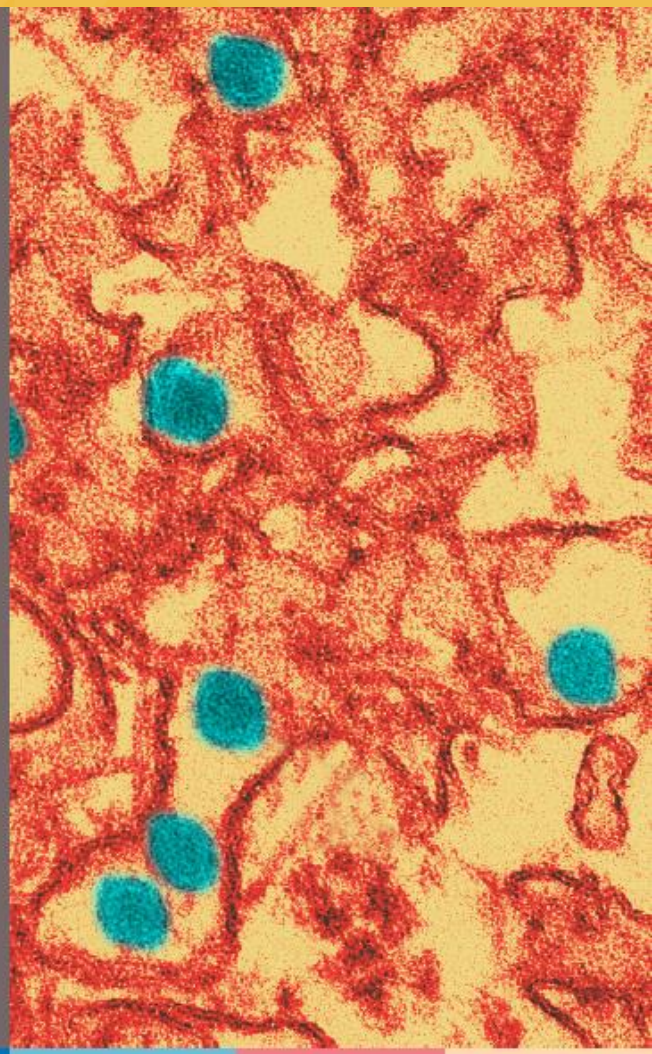
Serology cross-reactions with other flaviviruses

- Zika virus serology (IgM) can be positive due to antibodies against related *flaviviruses* (e.g., dengue and yellow fever viruses).
- As viremia decreases over time, a negative rRT-PCR collected after symptom onset does not preclude Zika; in this case, serologic testing should be performed.
- Neutralizing antibody testing may discriminate between cross-reacting antibodies in primary *flavivirus* infections.
- Difficult to distinguish infecting virus in people previously infected with or vaccinated against a related *flavivirus*



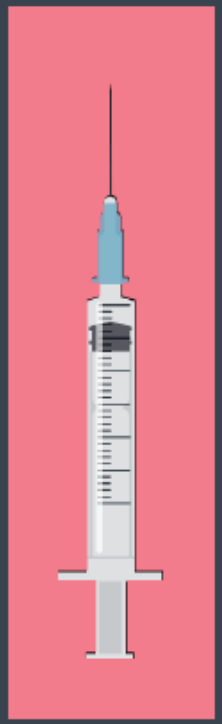
Laboratories for diagnostic testing

- Testing performed at CDC, select commercial labs, and a few state health departments
- CDC is working to expand laboratory diagnostic testing in states.
- Healthcare providers should work with their state health department to facilitate diagnostic testing and report results.



Recommendations

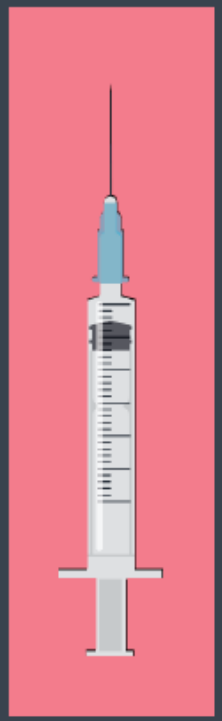
- CDC recommends Zika virus testing for
  - Symptomatic people who live in or recently traveled to an area with active Zika transmission, and
  - People who have had unprotected sex with someone confirmed to have Zika virus infection or who lives in or traveled to an area with active Zika transmission.
- All pregnant women in the US should be assessed for possible Zika exposure at each prenatal care visit.



Recommendations continued…

- Pregnant women with possible Zika exposure and signs or symptoms consistent with Zika virus disease should be tested based on time of evaluation relative to symptom onset in accordance with CDC guidance.

- Pregnant women with ongoing risk of possible Zika virus exposure and who do not report symptoms of Zika virus disease should be tested in the first and second trimester of pregnancy in accordance with CDC guidance.



REPORTING ZIKA CASES

Reporting cases

- Zika virus disease is a nationally notifiable condition. Report all confirmed cases to your state health department.

Zika pregnancy registry

- CDC established the US Zika Pregnancy Registry to collect information and learn more about pregnant women in the US with Zika and their infants.
- Data collected will be used to update recommendations for clinical care, plan for services for pregnant women and families affected by Zika, and improve prevention of Zika infection during pregnancy.
- CDC maintains a 24/7 consultation service for health officials and healthcare providers caring for pregnant women. To contact the service, call 770-488-7100 or email ZIKAMCH@cdc.gov
- CDC also established a similar system, the Zika Active Pregnancy Surveillance System, in Puerto Rico.

ZIKA AND PREGNANCY

Zika and pregnancy outcomes

- Zika virus can pass from a pregnant woman to her fetus during pregnancy or around the time of birth.
- Zika infection in pregnancy is a cause of microcephaly and other severe brain defects. Other problems include
  - Eye defects, hearing loss, impaired growth, and fetal loss.

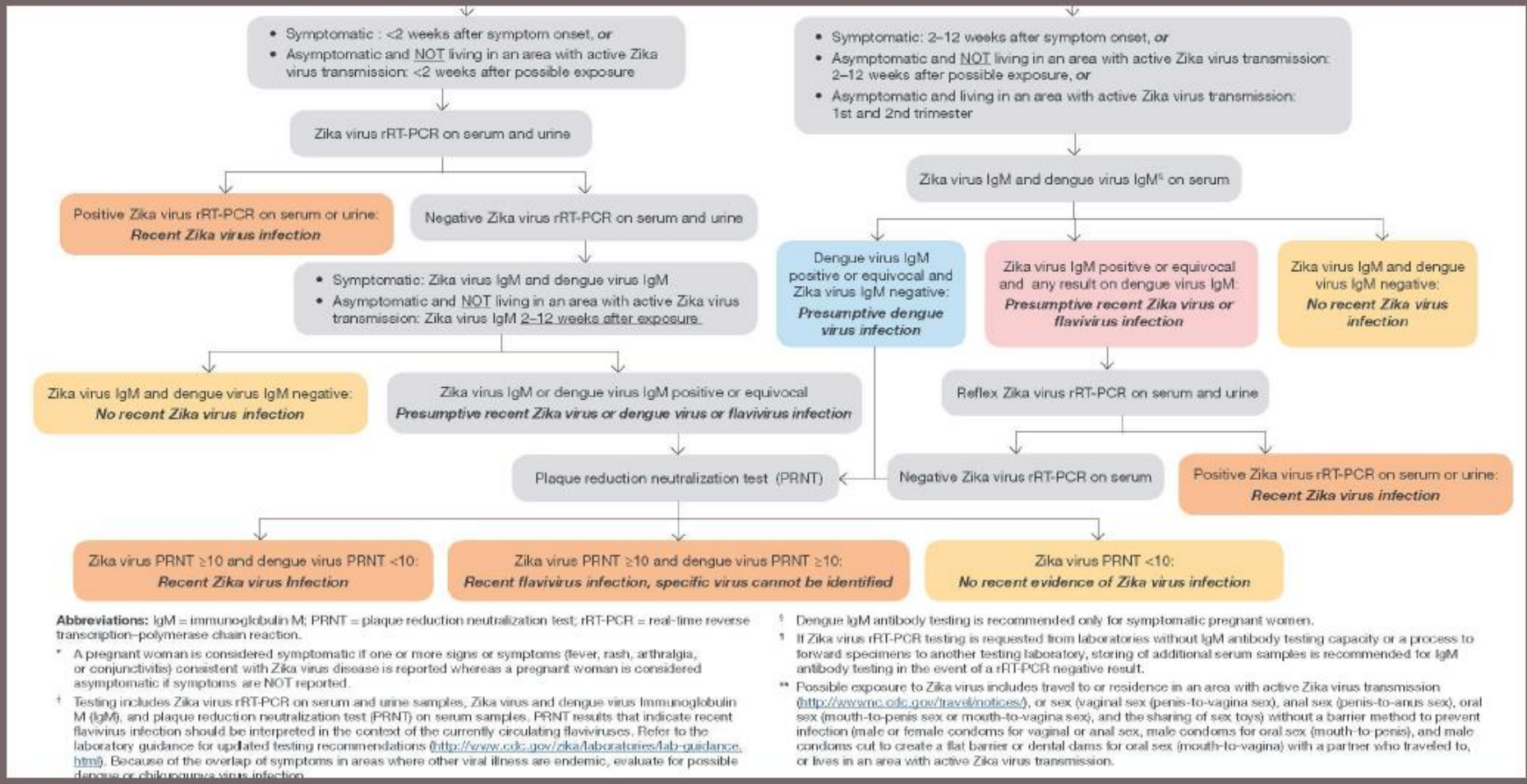
Zika and pregnancy outcomes

- Scientists are studying the full range of other potential health problems caused by Zika virus infection during pregnancy.
- No reports of infants getting Zika through breastfeeding.
- No evidence that previous infection will affect future pregnancies.

Who to test for Zika during pregnancy

- All pregnant women should be assessed for Zika at each prenatal care visit. They should be asked if they
  - Traveled to or live in an area with active Zika transmission
  - Had sex without a condom or other barrier method to prevent infection with a partner who lives in or traveled to an area with active Zika transmission

Testing guidance: Pregnant women with possible Zika exposure



Abbreviations: IgM = immunoglobulin M; PRNT = plaque reduction neutralization test; rRT-PCR = real-time reverse transcription–polymerase chain reaction.

* A pregnant woman is considered symptomatic if one or more signs or symptoms (fever, rash, arthralgia, or conjunctivitis) consistent with Zika virus disease is reported whereas a pregnant woman is considered asymptomatic if symptoms are NOT reported.

† Testing includes Zika virus rRT-PCR on serum and urine samples, Zika virus and dengue virus Immunoglobulin M (IgM), and plaque reduction neutralization test (PRNT) on serum samples. PRNT results that indicate recent flavivirus infection should be interpreted in the context of the currently circulating flaviviruses. Refer to the laboratory guidance for updated testing recommendations (http://www.cdc.gov/zika/laboratories/lab-guidance.html). Because of the overlap of symptoms in areas where other viral illness are endemic, evaluate for possible dengue or chikungunya virus infection.

§ Dengue IgM antibody testing is recommended only for symptomatic pregnant women.

¶ If Zika virus rRT-PCR testing is requested from laboratories without IgM antibody testing capacity or a process to forward specimens to another testing laboratory, storing of additional serum samples is recommended for IgM antibody testing in the event of a rRT-PCR negative result.

** Possible exposure to Zika virus includes travel to or residence in an area with active Zika virus transmission (http://wwwnc.cdc.gov/travel/notices), or sex (vaginal sex (penis-to-vagina sex), anal sex (penis-to-anus sex), oral sex (mouth-to-penis sex or mouth-to-vagina sex), and the sharing of sex toys) without a barrier method to prevent infection (male or female condoms for vaginal or anal sex, male condoms for oral sex (mouth-to-penis), and male condoms cut to create a flat barrier or dental dams for oral sex (mouth-to-vagina) with a partner who traveled to, or lives in an area with active Zika virus transmission.

Clinical management of a pregnant woman with suspected Zika virus infection

Interpretation of Laboratory Results*	Prenatal Management	Postnatal Management
Recent Zika virus infection	• Consider serial ultrasounds every 3–4 weeks to assess fetal anatomy and growth† • Decisions regarding amniocentesis should be individualized for each clinical circumstance§	**LIVE BIRTHS:** • Cord blood and infant serum should be tested for Zika virus rRT-PCR, Zika IgM, and dengue virus IgM antibodies. If CSF is obtained for other reasons, it can also be tested. • Zika virus rRT-PCR and IHC staining of umbilical cord and placenta is recommended.¶ **FETAL LOSSES:** • Zika virus rRT-PCR and IHC staining of fetal tissues is recommended.¶
Recent flavivirus infection; specific virus cannot be identified		
Presumptive recent Zika virus infection**	• Consider serial ultrasounds every 3–4 weeks to assess fetal anatomy and growth† • Amniocentesis might be considered; decision should be individualized for each clinical circumstance§	**LIVE BIRTHS:** • Cord blood and infant serum should be tested for Zika virus rRT-PCR, Zika IgM, and dengue virus IgM antibodies. If CSF is obtained for other reasons, it can also be tested. • Zika virus rRT-PCR and IHC staining of umbilical cord and placenta should be considered.¶ **FETAL LOSSES:** • Zika virus rRT-PCR and IHC staining of fetal tissues should be considered.¶
Presumptive recent flavivirus infection**		
Recent dengue virus infection	• Clinical management in accordance with existing guidelines (http://apps.who.int/iris/bitstream/10665/44188/1/9789241547871_eng.pdf).	
No evidence of Zika virus or dengue virus infection	• Prenatal ultrasound to evaluate for fetal abnormalities consistent with congenital Zika virus syndrome.† • Fetal abnormalities present: repeat Zika virus rRT-PCR and IgM test; base clinical management on corresponding laboratory results. • Fetal abnormalities absent: base obstetric care on the ongoing risk of Zika virus exposure to the pregnant woman.	

Zika and pregnancy: Clinical management for obstetricians

- Positive or inconclusive Zika virus testing results
  - Antepartum
    - Consider serial ultrasounds every 3-4 weeks.
    - Referral to maternal-fetal medicine specialist is recommended.
  - Postpartum
    - Histopathologic examination of the placenta and umbilical cord.
    - Testing of frozen placental tissue and cord tissue for Zika virus RNA.
    - Testing of cord serum for Zika and dengue virus IgM and neutralizing antibodies.

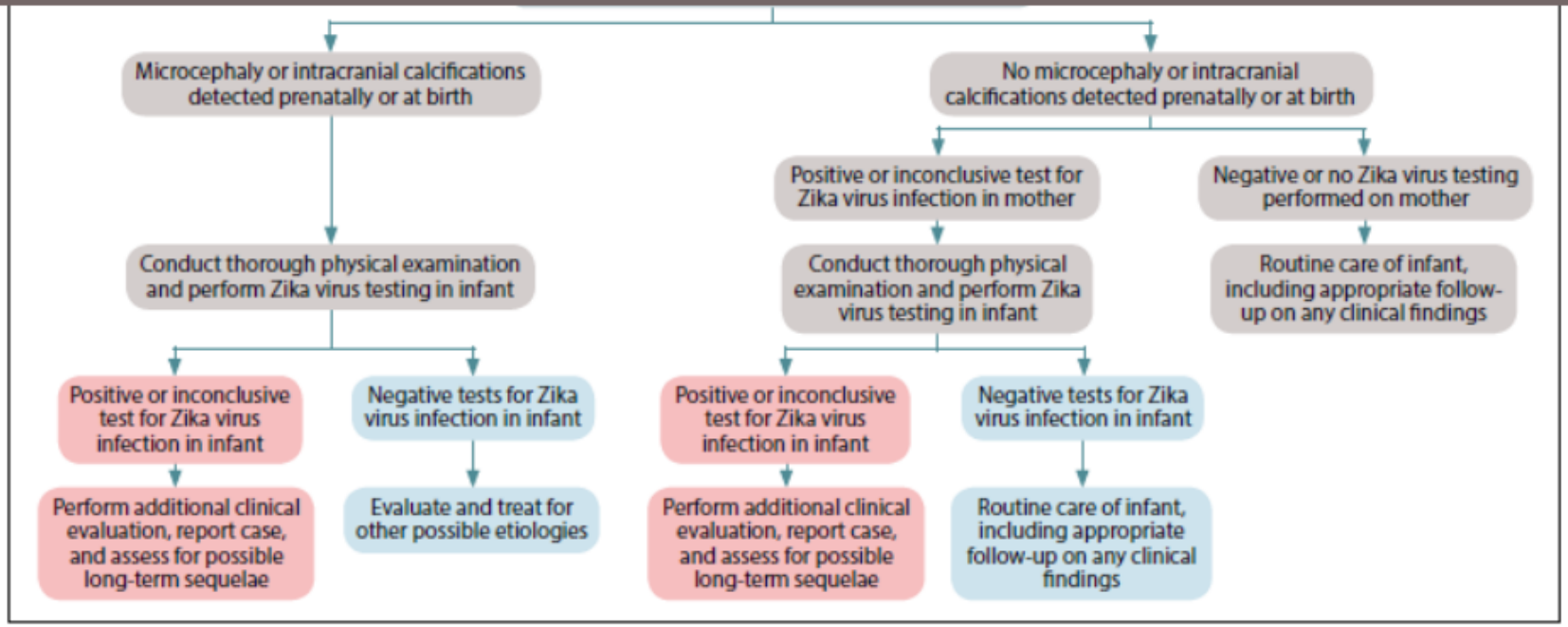
CLINICAL MANAGEMENT OF INFANTS WITH CONFIRMED OR POSSIBLE ZIKA INFECTION

Infants with confirmed or possible Zika infection

Doctors have found problems among fetuses and infants infected with Zika virus before birth, including

- Microcephlay
- Miscarriage
- Stillbirth
- Absent or poorly developed brain structures
- Defects of the eye
- Hearing deficits
- Impaired growth

Testing guidance for infants of women with possible exposure to Zika during pregnancy



*Areas with Zika virus transmission are listed on CDC's website at http://wwwnc.cdc.gov/travel/notices.

†Microcephaly defined as occipitofrontal circumference less than the third percentile for gestational age and sex based on standard growth curves, not explained by other etiologies.

§Laboraory evidence of Zika virus infection includes 1) detectable Zika virus, Zika virus RNA, or Zika virus antigen in any clinical specimen; or 2) positive Zika virus Immunoglobulin M (IgM) with confirmatory neutralizing antibody titers that are ≥4-fold higher than dengue virus neutralizing antibody titers in serum or cerebrospinal fluid. Testing is considered inconclusive if Zika virus neutralizing antibody titers are <4-fold higher than dengue virus neutralizing antibody titers.

More information on laboratory testing for Zika virus infection is available at http://www.cdc.gov/zika/state-labs/index.html.

Case definition of microcephaly

Definite congenital microcephaly for live births

- Head circumference (HC) at birth is less than the 3rd percentile for gestational age and sex.
- If HC at birth is not available, HC less than the 3rd percentile for age and sex within the first 6 weeks of life.

Definite congenital microcephaly for still births and early termination

- HC at delivery is less than the 3rd percentile for gestational age and sex.

Definitions for *possible* congenital microcephaly

Possible congenital microcephaly for live births

- If earlier HC is not available, HC less than 3rd percentile for age and sex beyond 6 weeks of life.

Possible microcephaly for all birth outcomes

- Microcephaly diagnosed or suspected on prenatal ultrasound in the absence of available HC measurements.

SEXUAL TRANSMISSION

About sexual transmission

- Zika virus can be passed through sex, even if the infected person does not have symptoms at the time.
- Sex includes vaginal, anal, and oral sex, and the sharing of sex toys.
- Condoms and other barriers* can reduce the chance of getting Zika from sex.
- Not having sex can eliminate the risk of getting Zika from sex.

* Barriers include male and female condoms and dental dams.

What we do not know about sexual transmission

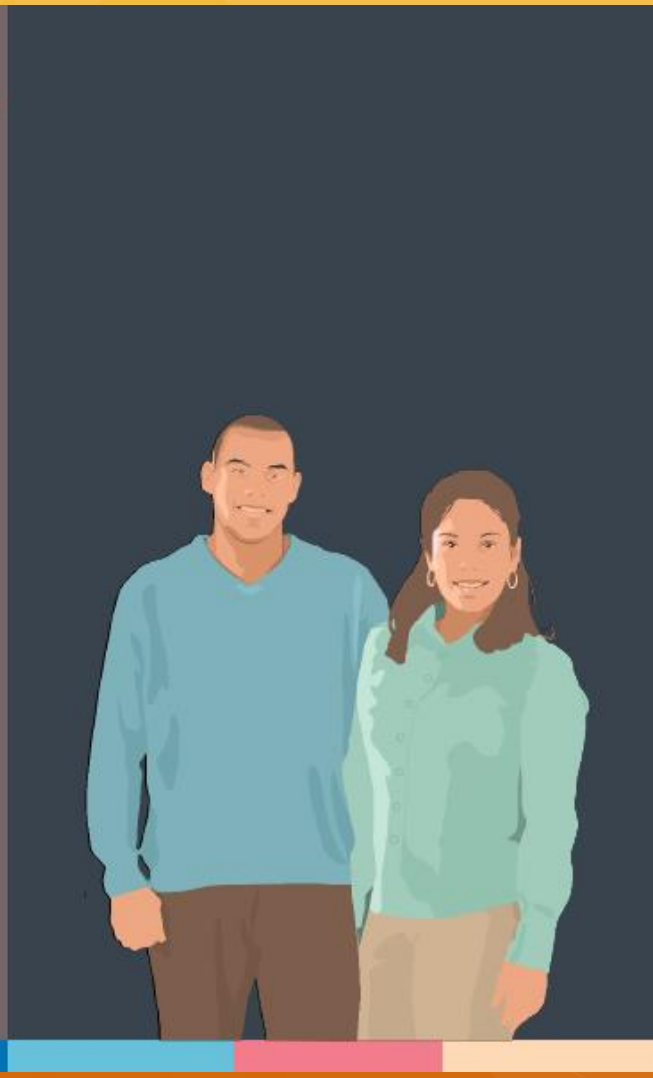
- We do not know how often people with Zika who never develop symptoms pass Zika through sex.
- We do not know if sexual transmission of Zika virus poses a different risk of birth defects than mosquito-borne transmission.

Non-pregnant couples with a partner who traveled to an area with Zika

- For non-pregnant couples with a partner who has **recently traveled** to an area with Zika
  - At least 8 weeks after a Zika diagnosis or start of symptoms if the traveling partner is female or if the traveling partner (male or female) has no symptoms.
  - At least 6 months after a Zika diagnosis or start of symptoms if the traveling partner is male. This long extended period is because Zika stays in semen longer than in other body fluids.

Non-pregnant couples with a partner who lives in an area with Zika

- Couples living in an area with Zika can use condoms or not have sex as long as there is Zika in the area. If either partner develops symptoms of Zika or has concerns, they should talk to a healthcare provider.



Update: Interim Guidance for Prevention of Sexual Transmission of Zika Virus — United States, July 2016

BOX. Recommendations for prevention of sexual transmission of Zika virus for couples in which one or both partners have traveled to or reside in an area with active Zika virus transmission

Couples in which a woman is pregnant

- Couples in which a woman is pregnant should use barrier methods against infection consistently and correctly or abstain from sex for the duration of the pregnancy.

Couples who are not pregnant and are not planning to become pregnant*

- Couples in which a partner had confirmed Zika virus infection or clinical illness consistent with Zika virus disease should consider using barrier methods against infection consistently and correctly or abstain from sex as follows:
  - Men with Zika virus infection for at least 6 months after onset of illness;
  - Women with Zika virus infection for at least 8 weeks after onset of illness.
- Couples in areas without active Zika transmission in which one partner traveled to or resides in an area with active Zika virus transmission but did not develop symptoms of Zika virus disease should consider using barrier methods against infection or abstaining from sex for at least 8 weeks after that partner departed the Zika-affected area.
- Couples who reside in an area with active Zika virus transmission might consider using barrier methods against infection or abstaining from sex while active transmission persists.

PRECONCEPTION GUIDANCE

Couples interested in conceiving who DO NOT reside in an area with active Zika virus transmission

- For Women with possible exposure to Zika virus
  - Discuss signs and symptoms and potential adverse outcomes associated with Zika
  - If Zika virus disease diagnosed or symptoms develop, wait at least 8 weeks after symptom onset to attempt conception.
  - If NO symptoms develop, wait at least 8 weeks after last date of exposure before attempting conception.
  - During that time, use condoms every time during sex or do not have sex to protect partner.

Couples interested in conceiving who DO NOT reside in an area with active Zika virus transmission

- For Men with possible exposure to Zika virus
  - If Zika virus disease diagnosed or symptoms develop, wait at least 6 months after symptom onset to attempt conception.
  - If NO symptoms develop, wait at least 8 weeks after exposure to attempt contraception.
  - During that time, use condoms every time during sex or do not have sex to protect partner.
  - Discuss contraception and use of condoms.

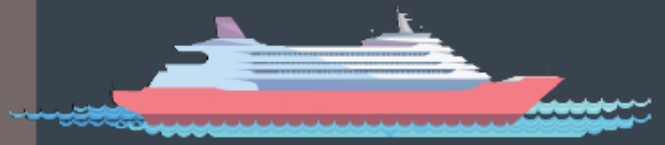
Couples interested in conceiving who reside in an area with active Zika virus transmission

- Women and men interested in conceiving should talk with their HCPs
- Factors that may aid in decision-making
    - Reproductive life plan
    - Environmental risk of exposure
    - Personal measures to prevent mosquito bites
    - Personal measures to prevent sexual transmission
    - Education about Zika virus infection in pregnancy
    - Risks and benefits of pregnancy at this time

WHAT TO TELL PATIENTS ABOUT ZIKA

Pregnant women

- Should not travel to areas with Zika.
- If they must travel to areas with Zika, tell pregnant patients to protect themselves from mosquito bites and take steps to prevent sexual transmission during and after travel.

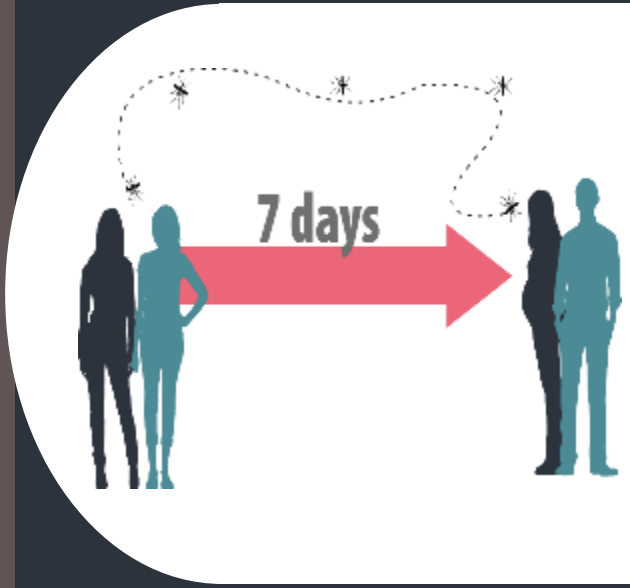


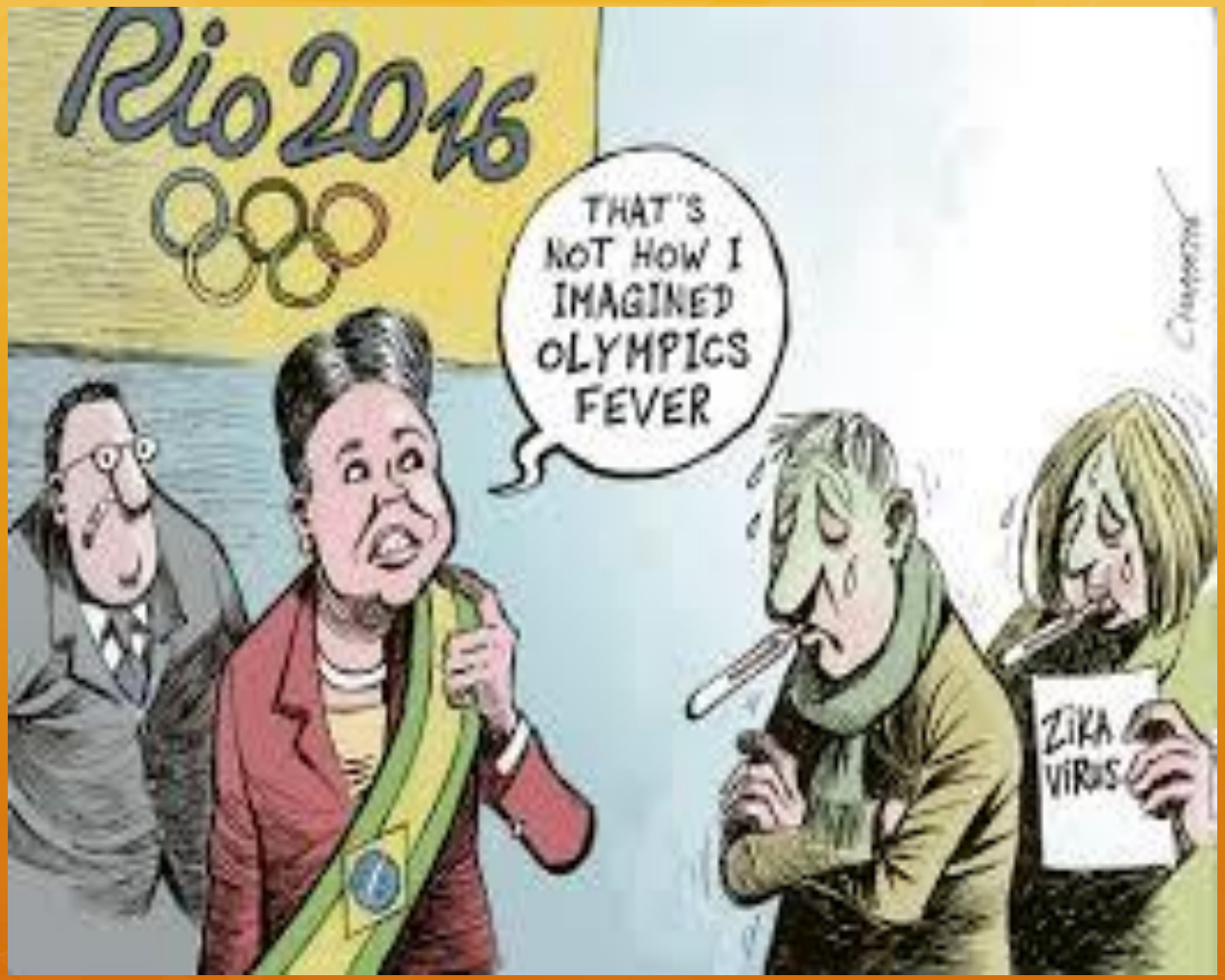
Treating patients who test positive

- There are no vaccine or medicine Zika.
- Treat the symptoms of Zika
  - Rest
  - Drink fluids to prevent dehydration
  - Take acetaminophen (Tylenol®) to reduce fever and pain
  - Do not take aspirin or other non-steroidal anti-inflammatory drugs (NSAIDS) until dengue can be ruled out to reduce the risk of bleeding.

Patients who test positive

- Protect from mosquito bites during the first week of illness, when Zika virus can be found in blood.
- The virus can be passed from an infected person to a mosquito through bites.
- An infected mosquito can spread the virus to other people.




Rio 2016
THAT'S NOT HOW I IMAGINED OLYMPICS FEVER
ZIKA VIRUS

Projected Zika Virus Importation and Subsequent Ongoing Transmission after Travel to the 2016 Olympic and Paralympic Games — Country-Specific Assessment, July 2016

BOX. CDC prevention recommendations for athletes and visitors to Rio de Janeiro, and other areas where Zika virus is circulating

- Pregnant women should not travel to any area where Zika virus transmission is ongoing.
- Travelers should take protective measures, including use of insect repellent, to prevent mosquito bites both during travel and for 3 weeks after returning to their home country. Such measures include wearing long-sleeved shirts and long pants; staying in places with air conditioning and window and door screens to keep mosquitoes outside; sleeping under a mosquito bed net, and using insect repellents with active ingredients (e.g., DEET).
- Travelers should prevent possible sexual transmission while at the 2016 Olympic and Paralympic Games and after returning home by correctly using condoms every time they have sex or by abstaining from sex. Males should use condoms for at least 8 weeks after travel or, if symptomatic for Zika virus infection, for 6 months from the start of symptoms.
- After returning from a country with Zika virus transmission, men with pregnant partners should use condoms or not have sex for the duration of the pregnancy.
- Couples who want to try to get pregnant after attending the Olympic and Paralympic Games should wait at least 8 weeks, and 6 months if the male partner has symptomatic Zika virus infection.

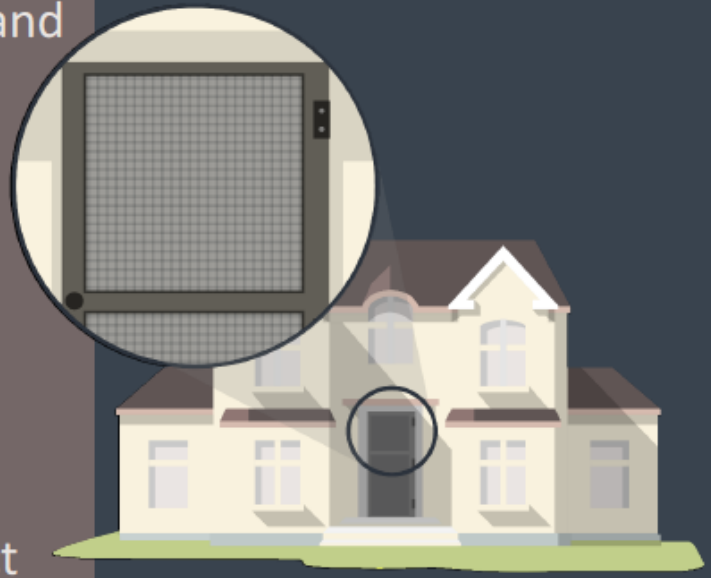
TABLE 2. Participating countries currently not reporting Zika outbreaks (n = 19) that met risk criteria for Zika virus importation and subsequent ongoing transmission attributed to travel to the Olympic and Paralympic Games, ranked by aviation travel volume* from Rio de Janeiro, Brazil — August 2016

Country	Total aviation travel from Rio de Janeiro in August 2015 (no. passenger-journeys)	No. of athletes for 2016 Games†	Estimated size of Olympic delegation for countries without aviation travel from Rio de Janeiro in August 2015 (no. persons)	Aviation travel from all Zika-affected countries in 2015§ No. passengers (% travel attributable to Rio de Janeiro¶)
Angola	2,841	21	NA	87,549 (3.25)
China	1,201	379	NA	308,238 (0.39)
Hong Kong**	229	32	NA	108,215 (0.21)
Sao Tome and Principe	104	2	NA	4,732 (2.20)
Oman	70	3	NA	2,300 (3.04)
Saudi Arabia	46	8	NA	7,688 (0.60)
Congo	22	6	NA	2,023 (1.09)
Myanmar	15	1	NA	733 (2.05)
Antigua and Barbuda	10	3	NA	61,312 (0.02)
Cayman Islands	10	3	NA	66,859 (0.01)
Ghana	10	6	NA	2,498 (0.40)
Rwanda	1	5	—	281 (0.36)
Eritrea	0	9	27	27 (100)
Yemen	0	4††	12	13 (92)
Djibouti	0	4	12	62 (19.35)
The Gambia	0	3	9	1,198 (0.75)
Chad	0	2††	6	19(31.6)
Mauritania	0	2††	6	201 (2.99)
Sudan	0	1	3	153 (1.96)

WHAT TO TELL PATIENTS ABOUT MOSQUITO BITE PROTECTION

Mosquito bite protection

- Wear long-sleeved shirts and long pants.
- Stay and sleep in places with air conditioning and window and door screens to keep mosquitoes outside.
- Take steps to control mosquitoes inside and outside your home (http://www.cdc.gov/zika/prevention/controlling-mosquitoes-at-home.html).
- Sleep under a mosquito bed net if you are overseas or outside and are not able to protect yourself from mosquito bites.



Mosquito bite protection

- Use Environmental Protection Agency (EPA)-registered insect repellents with one of the following active ingredients: DEET, picaridin, IR3535, oil of lemon eucalyptus, or para-menthane-diol.
- Always follow the product label instructions.
- Do not spray repellent on the skin under clothing.
- If you are also using sunscreen, apply sunscreen before applying insect repellent.

Mosquito bite protection

- Do not use insect repellent on babies younger than 2 months old.
- Do not use products containing oil of lemon eucalyptus or para-menthane-diol on children younger than 3 years old.
- Dress children in clothing that covers arms and legs.
- Cover crib, stroller, and baby carrier with mosquito netting.
- Do not apply insect repellent onto a child's hands, eyes, mouth, and cut or irritated skin.
  - Adults: Spray insect repellent onto your hands and then apply to a child's face.

The Medical Letter®
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Insect Repellents

Table 1. Some Insect Repellents

Repellent	Brand Name	Formulation	Duration of Protection[1] Mosquitoes	Ticks	Cost (Size)[2]
DEET	*Cutter Skinsations*	7% pump spray	1-3 hrs[3]	6 hrs[3]	$6.40 (7.5 oz)
	Repel Scented Family	15% aerosol spray	5-8 hrs[3]	8.5 hrs[3]	6.86 (6.5 oz)
	Off Deep Woods VIII	25% aerosol spray	8 hrs[3]	5 hrs[3]	7.38 (6 oz)
	Sawyer Ultra 30 Liposome Controlled Release	30% lotion	11 hrs	N.A.	8.49 (4 oz)
	Ultrathon[4]	34% lotion	12 hrs	N.A.	6.99 (2 oz)
Picaridin	*Cutter Advanced*	5.75% wipes	8 hrs	5 hrs	5.99 (18 wipes)
	Avon Skin So Soft Bug Guard Plus Picaridin	10% aerosol spray	8 hrs	12 hrs	6.99 (4 oz)
	Natrapel 8 hour	20% pump spray	8 hrs	8 hrs	5.59 (3.4 oz)
IR3535	*Avon Skin So Soft Bug Guard Plus IR3535*[5]	7.5% lotion	2 hrs	2 hrs	10.89 (4 oz)
	Coleman Skin Smart	20% pump spray	8 hrs	8 hrs	4.99 (5 oz)
Oil of lemon eucalyptus	*Coleman Botanicals*	30% pump spray	6 hrs	N.A.	8.94 (4 oz)
	Repel Lemon Eucalyptus	30% pump spray	7-8 hrs[3]	7 hrs[3]	4.99 (4 oz)
Permethrin	*Sawyer Premium Permethrin Clothing*	0.5% pump spray	—	—	14.99 (24 oz)
	Repel Permethrin Clothing and Gear	0.5% aerosol spray	—	—	7.42 (6.5 oz)

“There are risks and costs to action. But they are far less than the long range risks of comfortable inaction”.

John F. Kennedy

…But what are we asking congress to invest billions of dollars in??