Flaviviruses, An Overview

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WHO Meeting on Zika virus, 7-9 March, 2016

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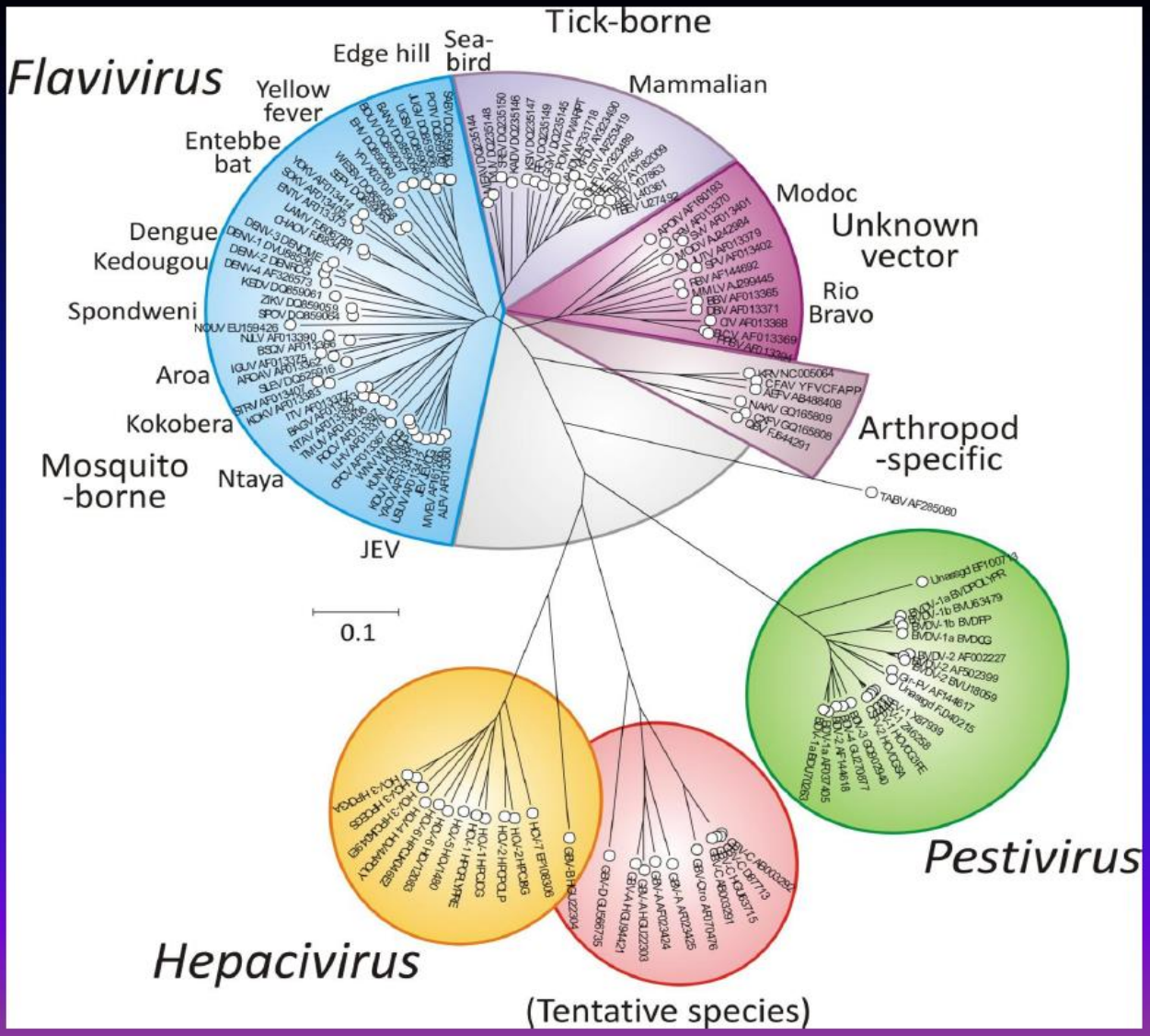
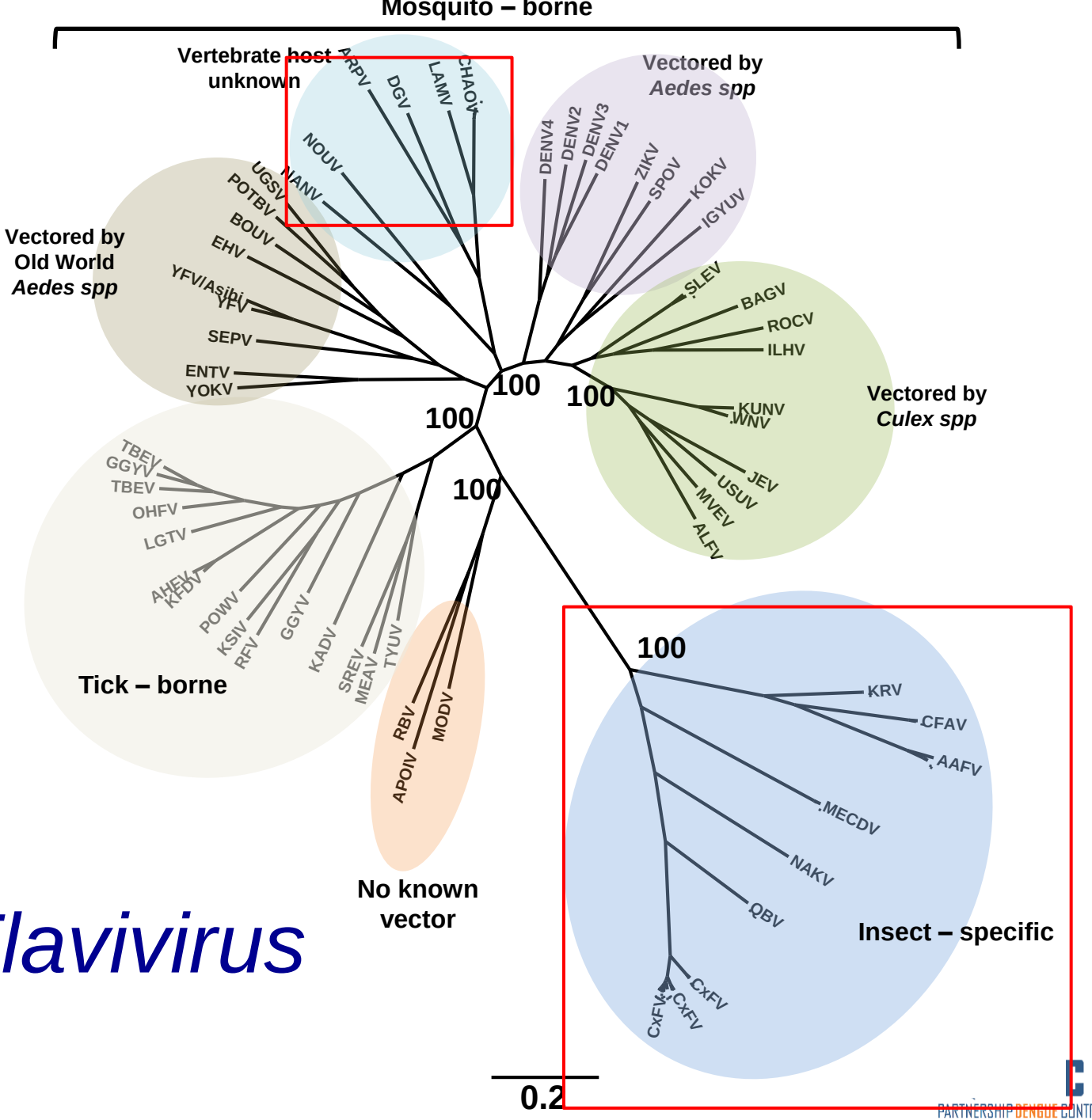
Flaviviruses, An Overview

Outline

- Classification
- Evolution
- Epidemiology
- Examples

Family Flaviviridae

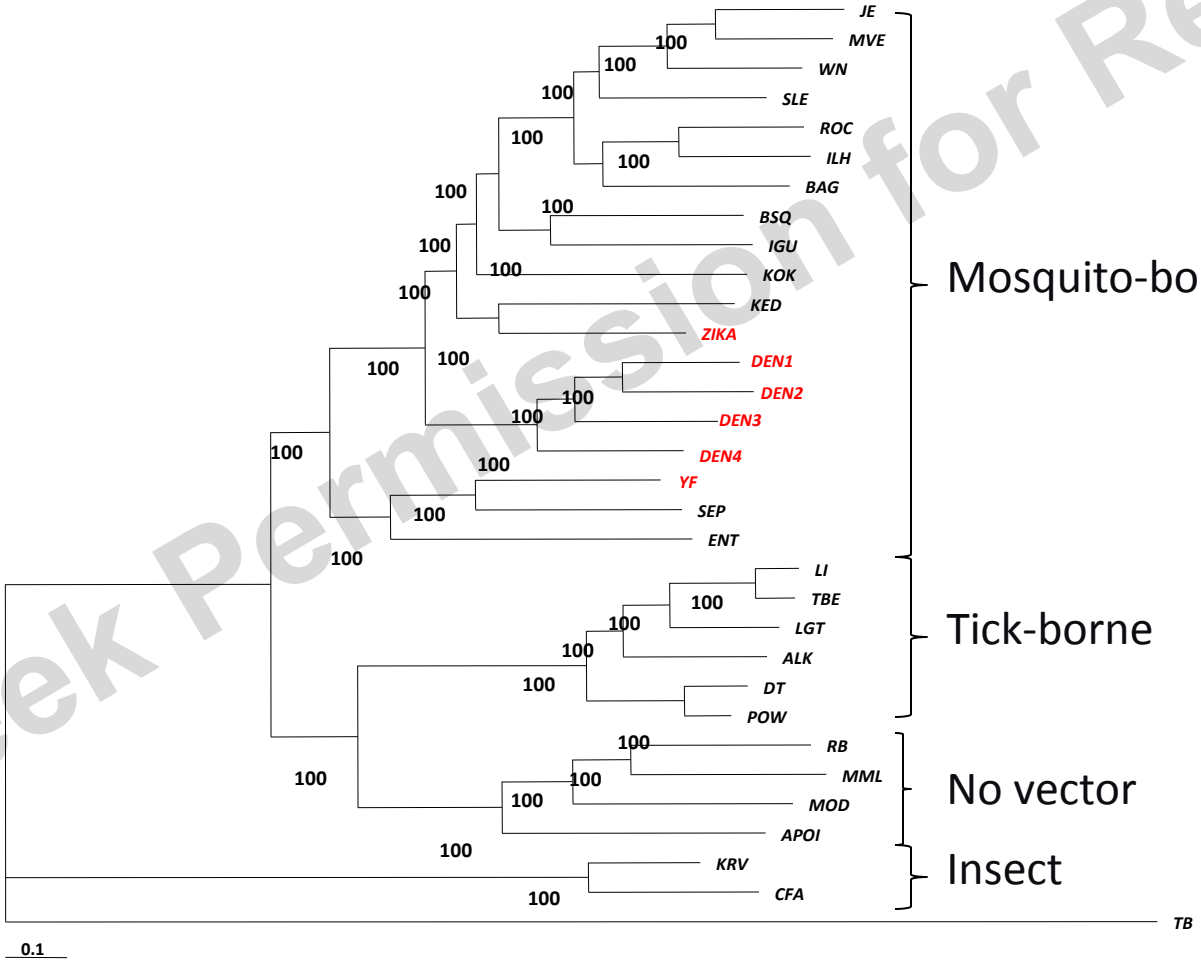




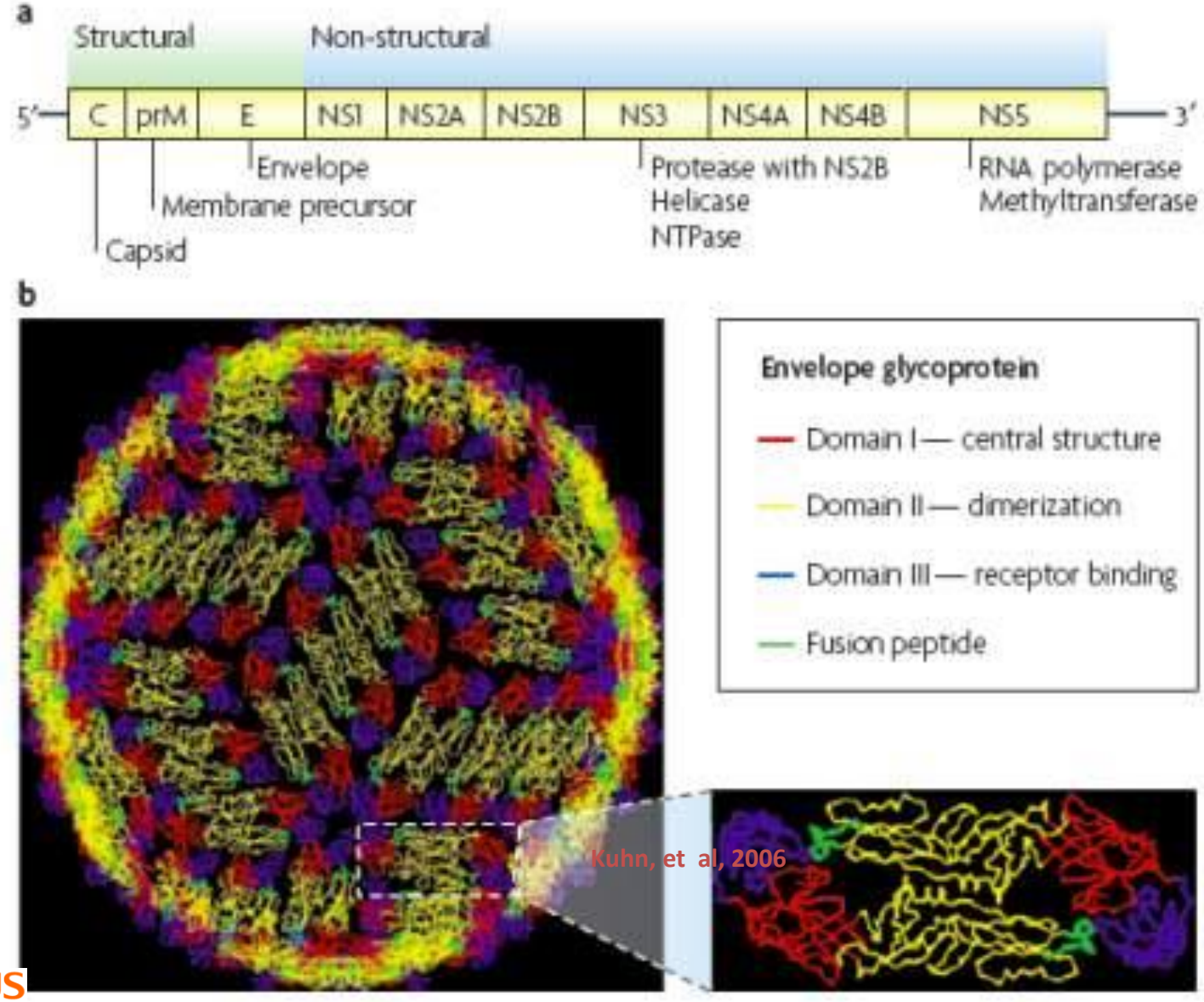
Genus *Flavivirus*

Flavivirus Phylogeny

Nonstructural gene

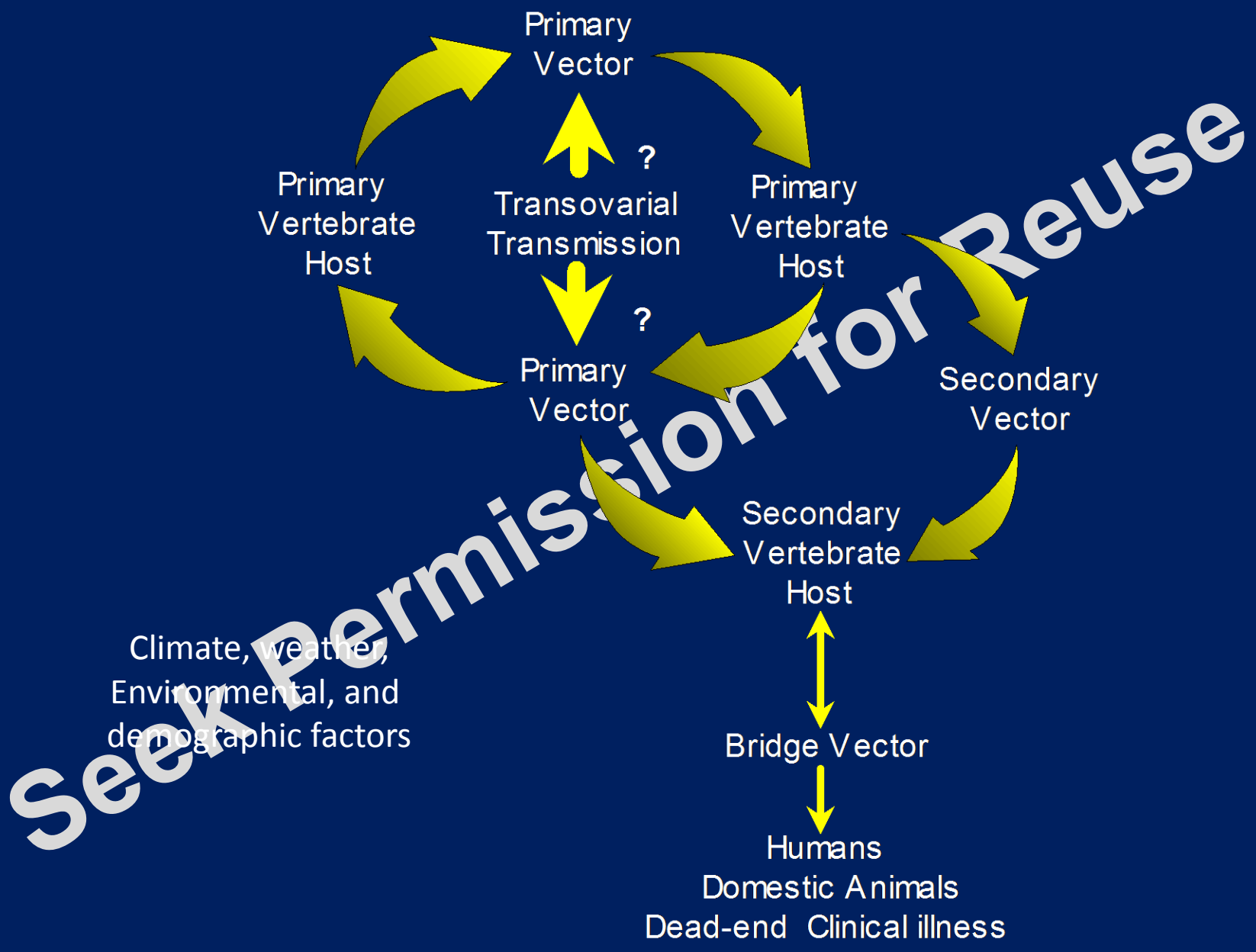


Family: ***Flaviviridae***
Genus: ***Flavivirus***



Principal Clinical Syndromes Caused by Flaviviruses

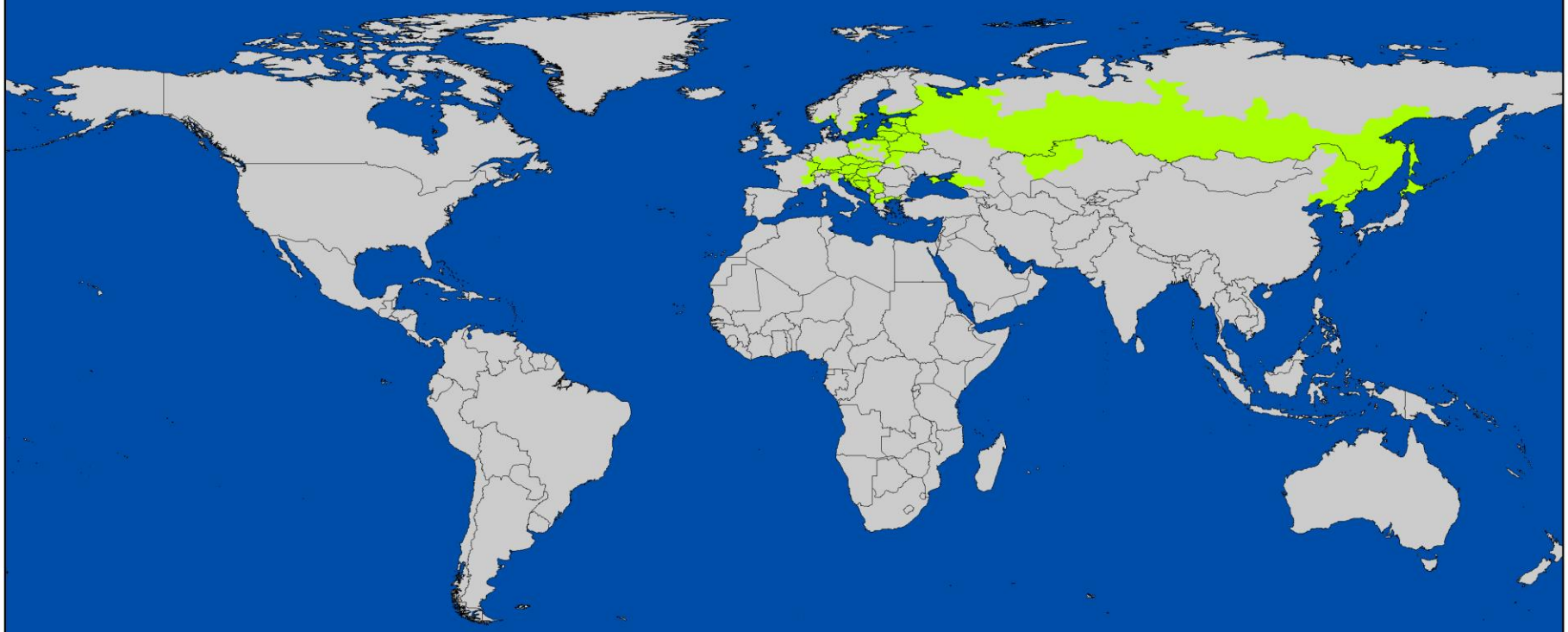
- Systemic Febrile Illness
- Hemorrhagic Fever
- Meningoencephalitis



Tick-Borne Encephalitis Flavivirus

- Vertebrate Hosts:
  - Rodents
- Habitat Associations:
  - Hardwood Forests
- Enzootic Vectors:
  - Ixodes ricinis
  - Ixodes persulcatus

Approximate Global Distribution of Tick Borne Encephalitis, by State/Province, 2005*

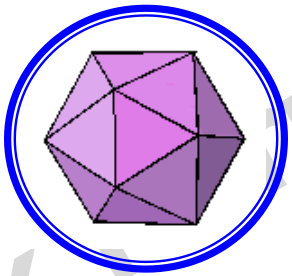


*Modified from Nuttall PA, Labuda M. Tick-Borne Encephalitis. In: Goodman JL, Dennis DT, Sonenshine DE, eds. *Tick-Borne Diseases of Humans*. Washington, DC: ASM Press; 2005.

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

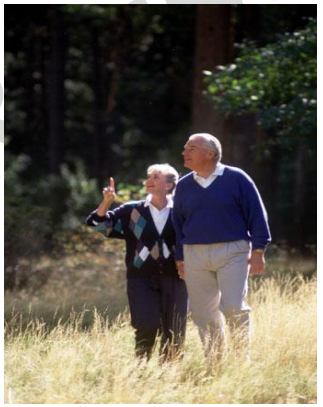
West Nile Virus:
Basic Transmission Cycle

Enzootic (Maintenance/Amplification)



Amplifying hosts

Epidemic



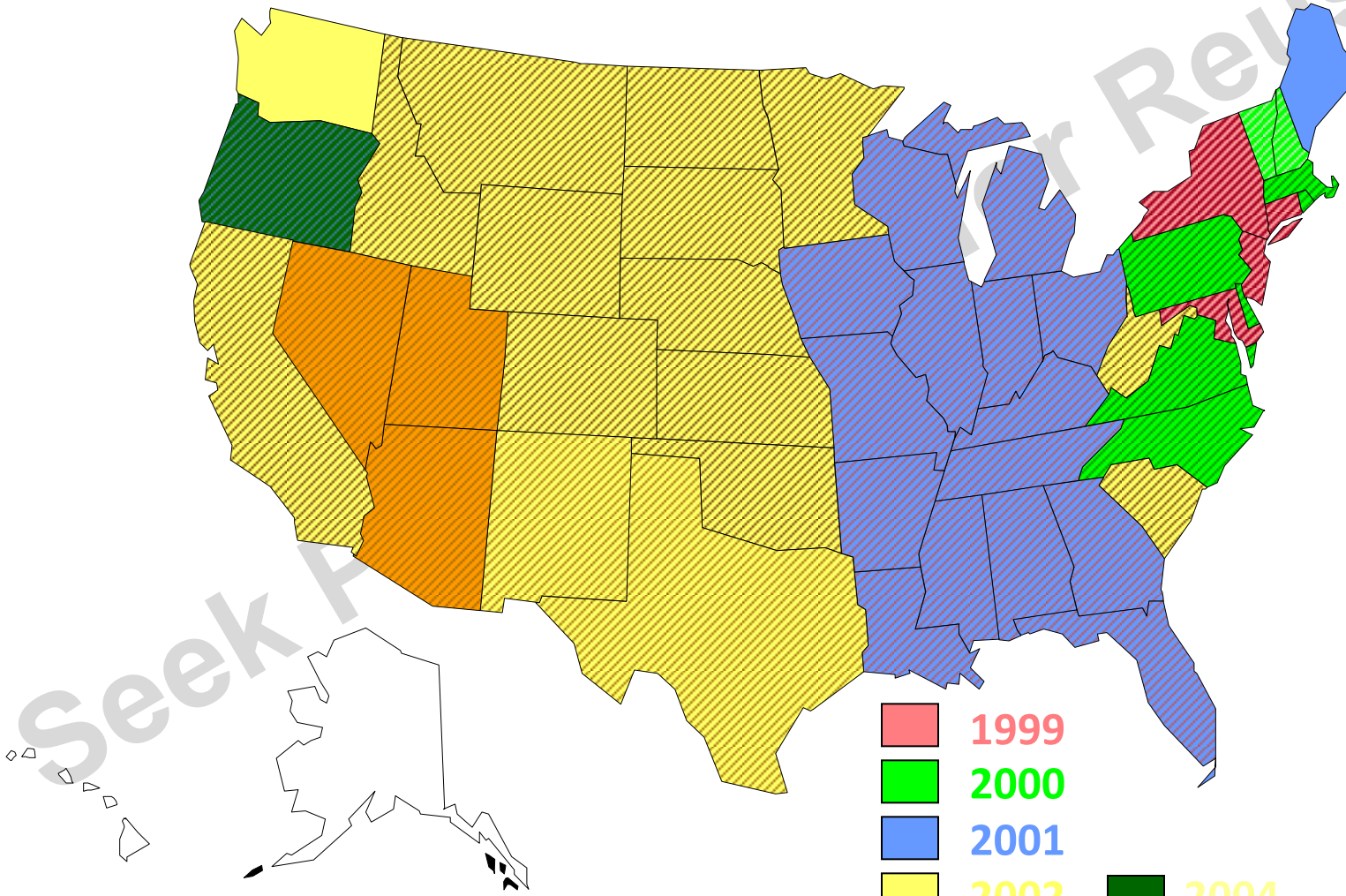
Incidental hosts?

Epizootic

Epidemic/Epizootic West Nile Virus

Adapted from Gubler, 2007

Reported WNV Activity, by State 1999-2004*



* Reported as of 1/31/2005

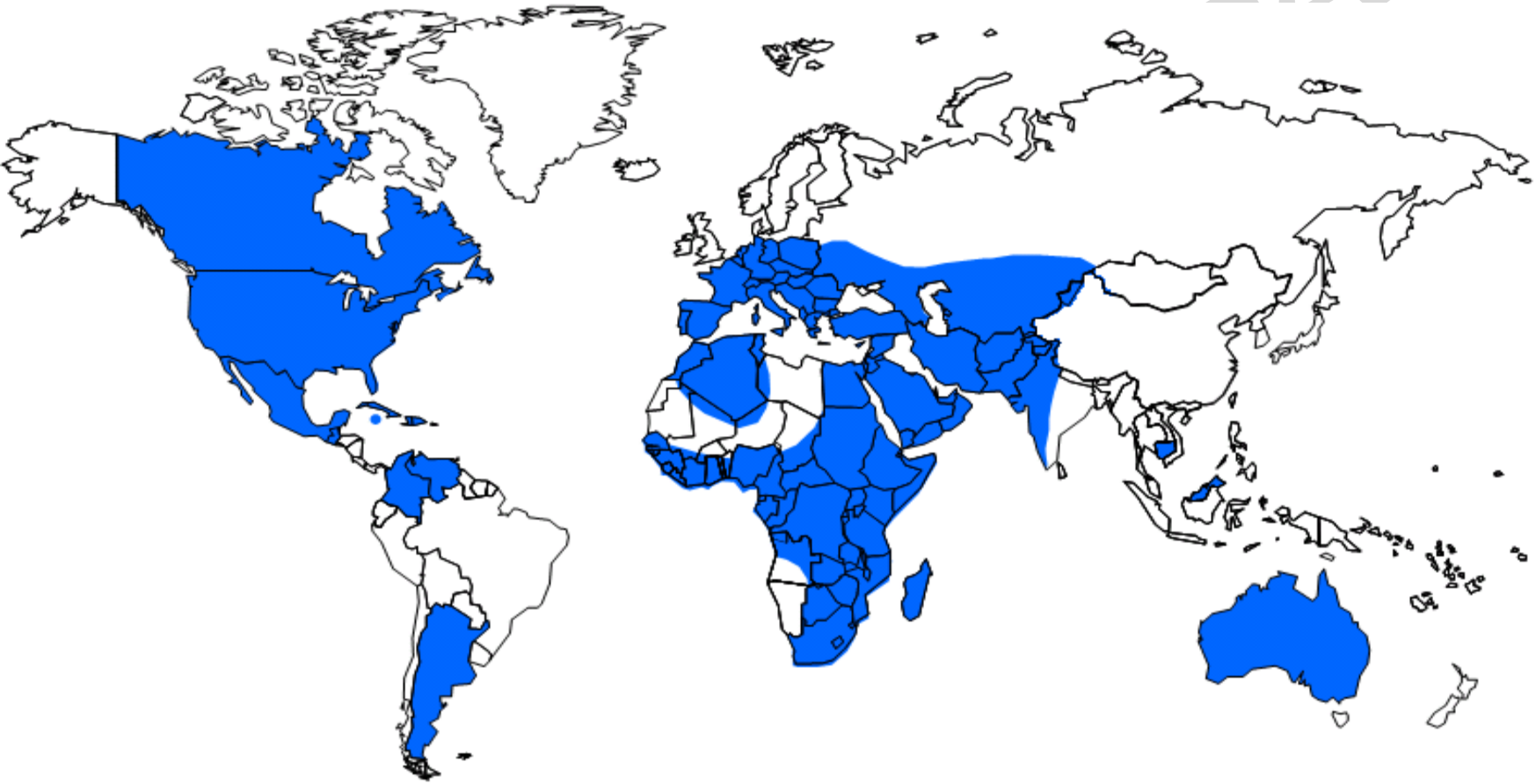
Epidemic/Epizootic West Nile Virus

1937

1950-75

1994 - 2007

Current Approximate West Nile Virus Distribution



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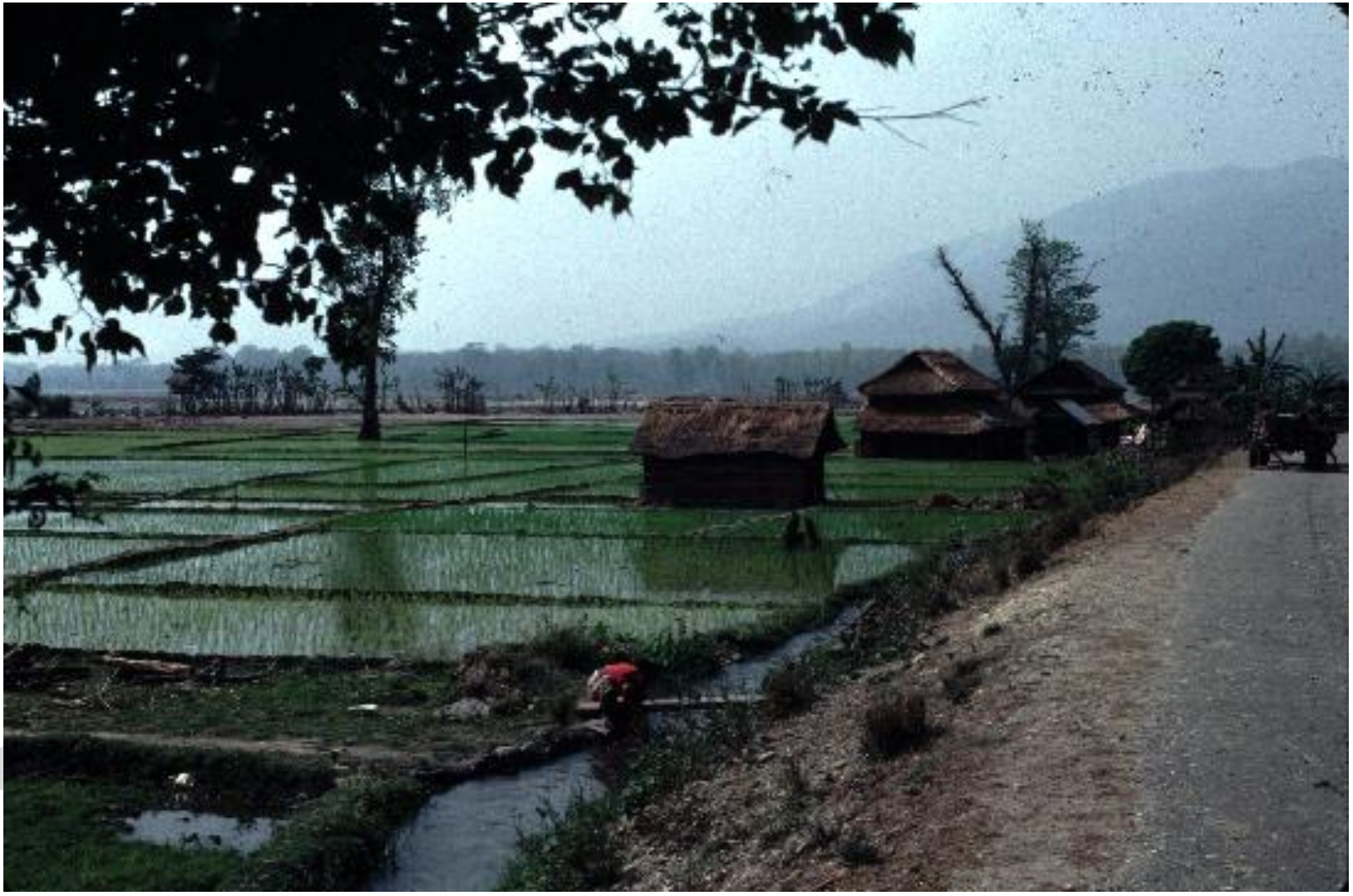


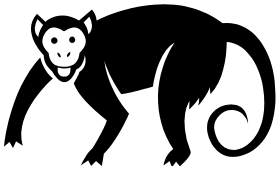
Expanding Distribution of Japanese Encephalitis

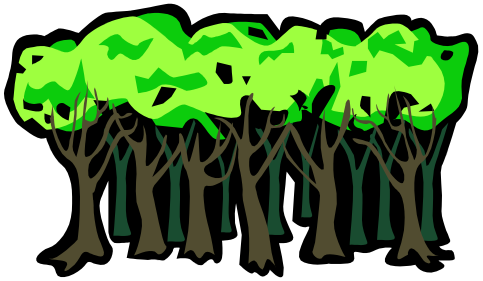
Geographic Distribution of Japanese Encephalitis Virus

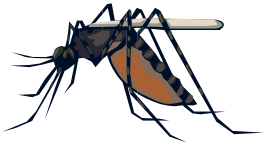
Arboviral Diseases Known to be Transmitted by Aedes (Stegomyia) Species Mosquitoes

- Dengue
- Yellow Fever
- Zika
- Chikungunya
- Epidemic Polyarthritis

Tropical Rainforests of Asia &Africa



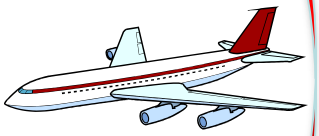


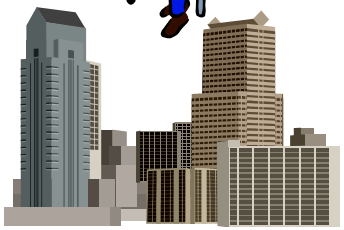


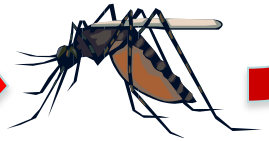
Aedes spp.

No known barriers to initial host range changes

Ae. aegypti aegypti
Ae. albopictus





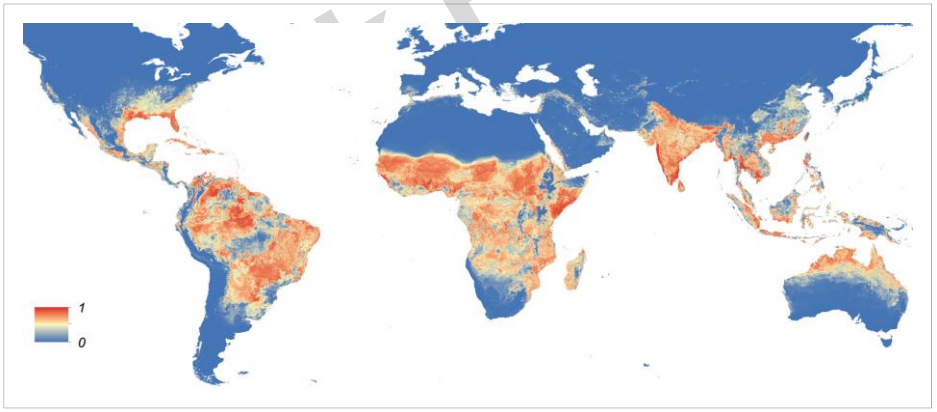


Adapted from TSETSARKIN, K. A., CHEN, R., SHERMAN, M. B. & WEAVER, S. C. 2011. *Curr Opin Virol,* 1, 310-317.

Urban Flavivirus Vectors

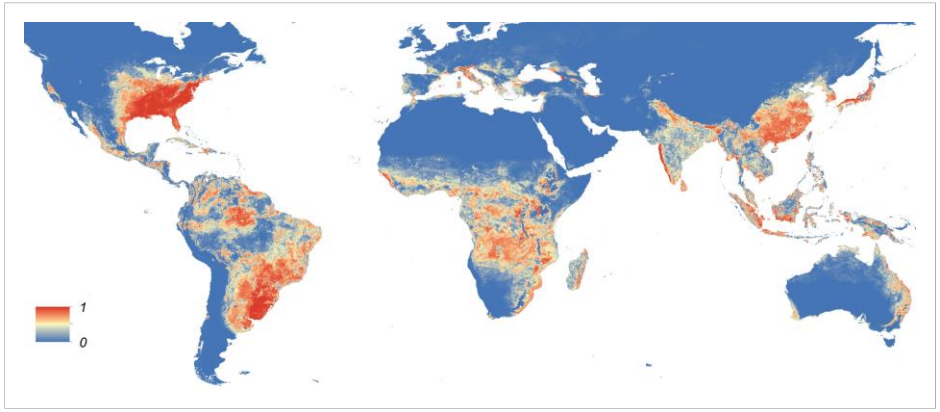
Ae. aegypti

Originated in sub-Saharan Africa, spread throughout the tropics centuries ago



Ae. albopictus

Originated in Asia, spread to the Americas, Africa and Europe beginning in 1980s



Kraemer, M.U., et al., 2015. The global distribution of the arbovirus vectors *Aedes aegypti* and *Ae. albopictus*. Elife 4.

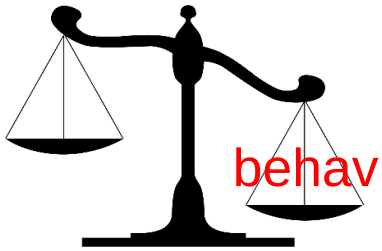
Flavivirus Endemic/Epidemic Vectors

Aedes aegypti aegypti

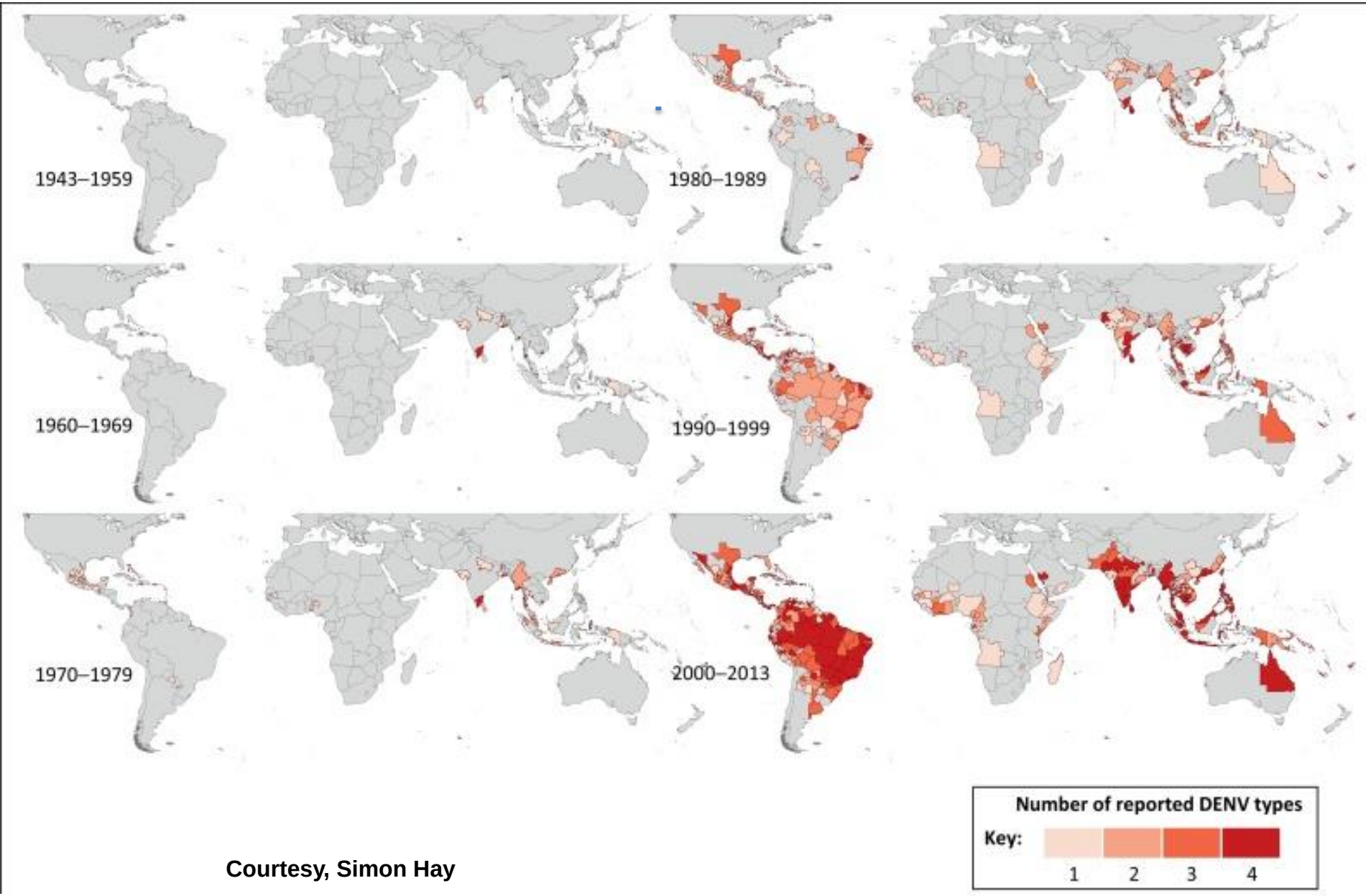
- Tropical and subtropical
- Feeds almost exclusively on humans
- Takes multiple bloodmeals within a gonotrophic cycle (0.76-0.63 blood meals per day) for both egg production and energetic needs
- Exploits artificial water containers in or near houses as larval habitats
- Adult females found mostly inside houses
- Feeds during the daytime

Aedes albopictus

- Tropics and temperate regions
- Feeds opportunistically
- Usually takes a single bloodmeal within a gonotrophic cycle
- Uses artificial and natural larval habitats
- Varied levels of anthrophily and endophily
- Feeds during the daytime

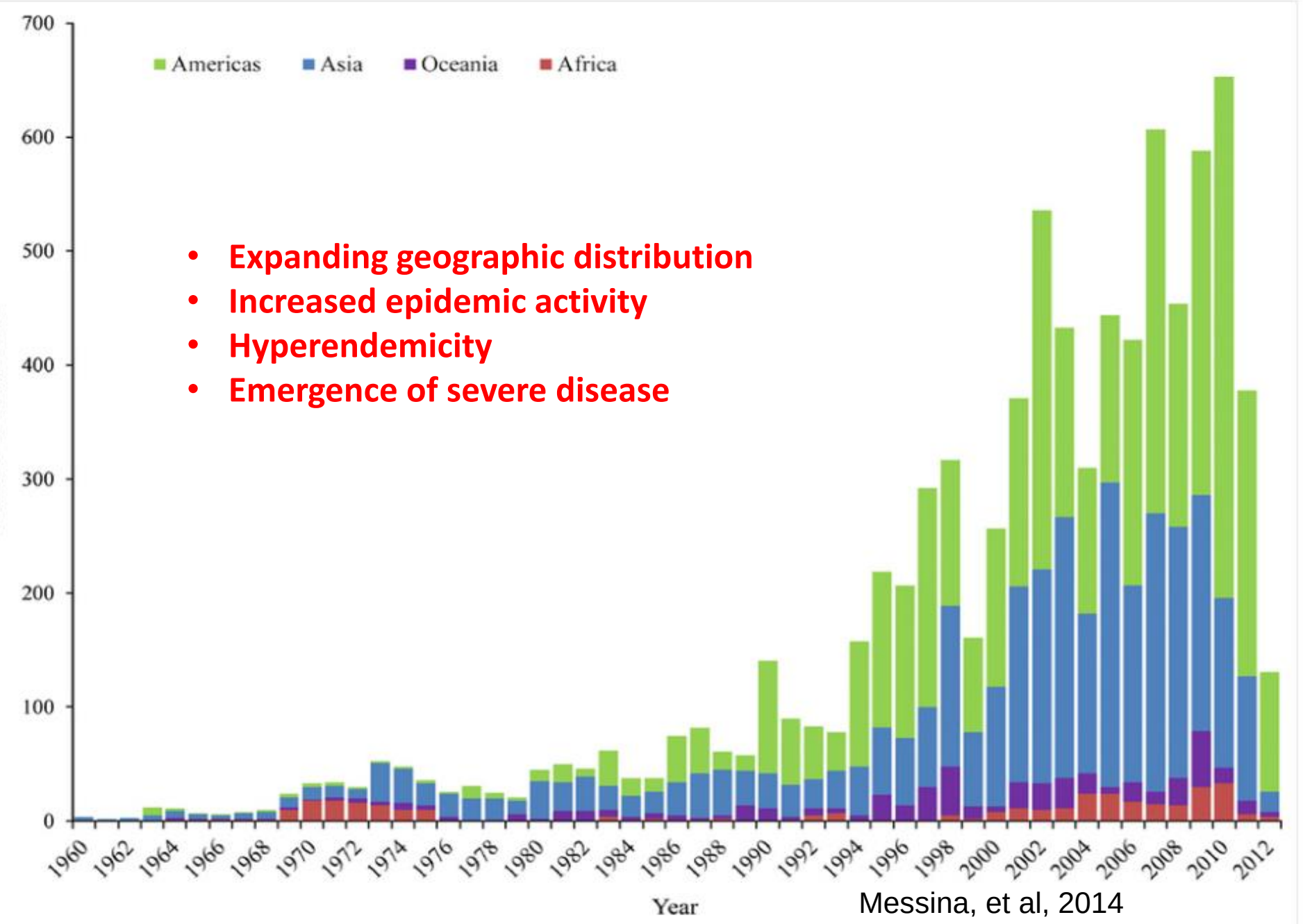


Global Spread of Dengue Viruses



Courtesy, Simon Hay

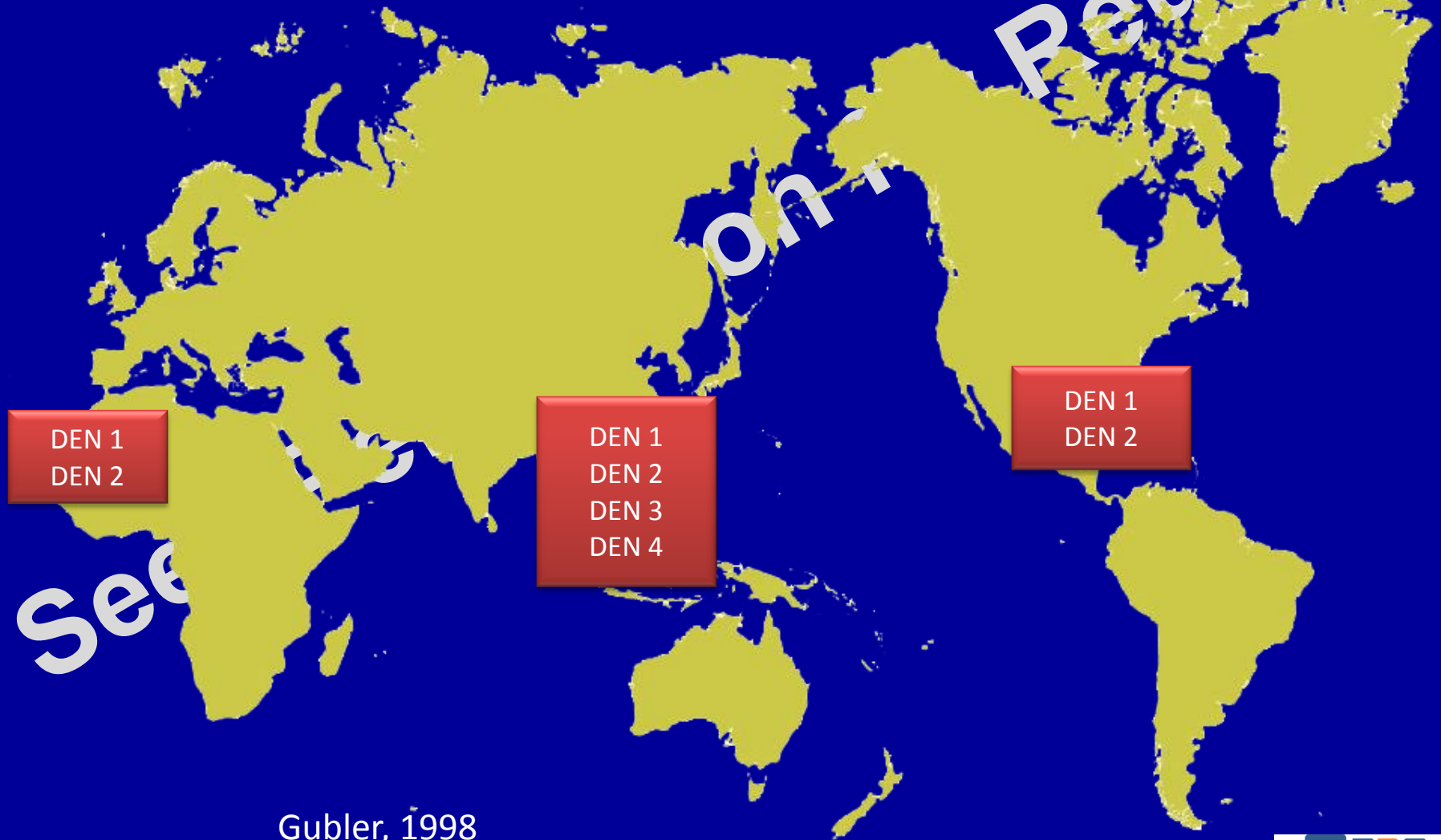
The Changing Epidemiology of Dengue



- **Expanding geographic distribution**
- **Increased epidemic activity**
- **Hyperendemicity**
- **Emergence of severe disease**

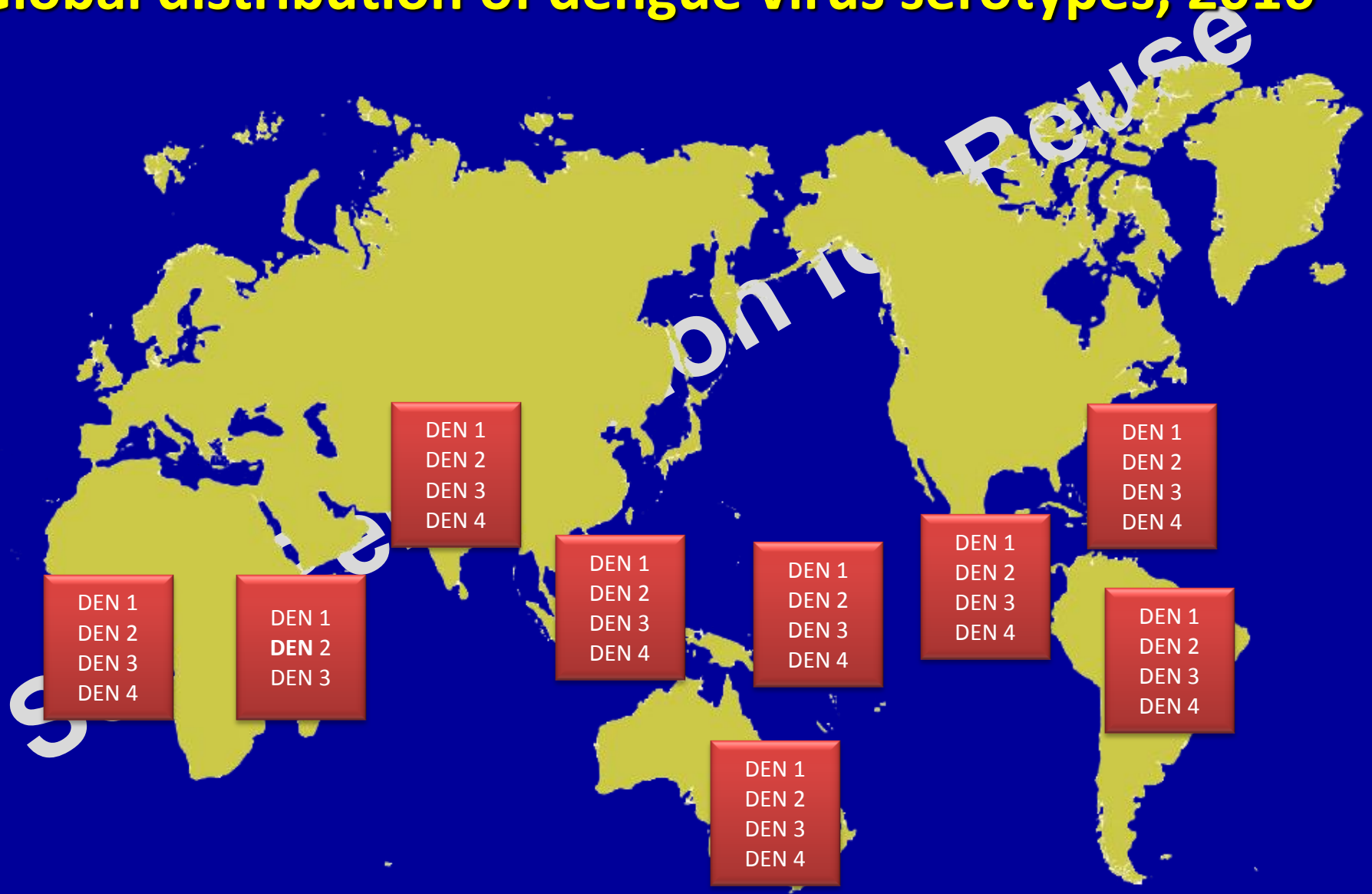
Messina, et al, 2014

Global distribution of dengue virus serotypes, 1970



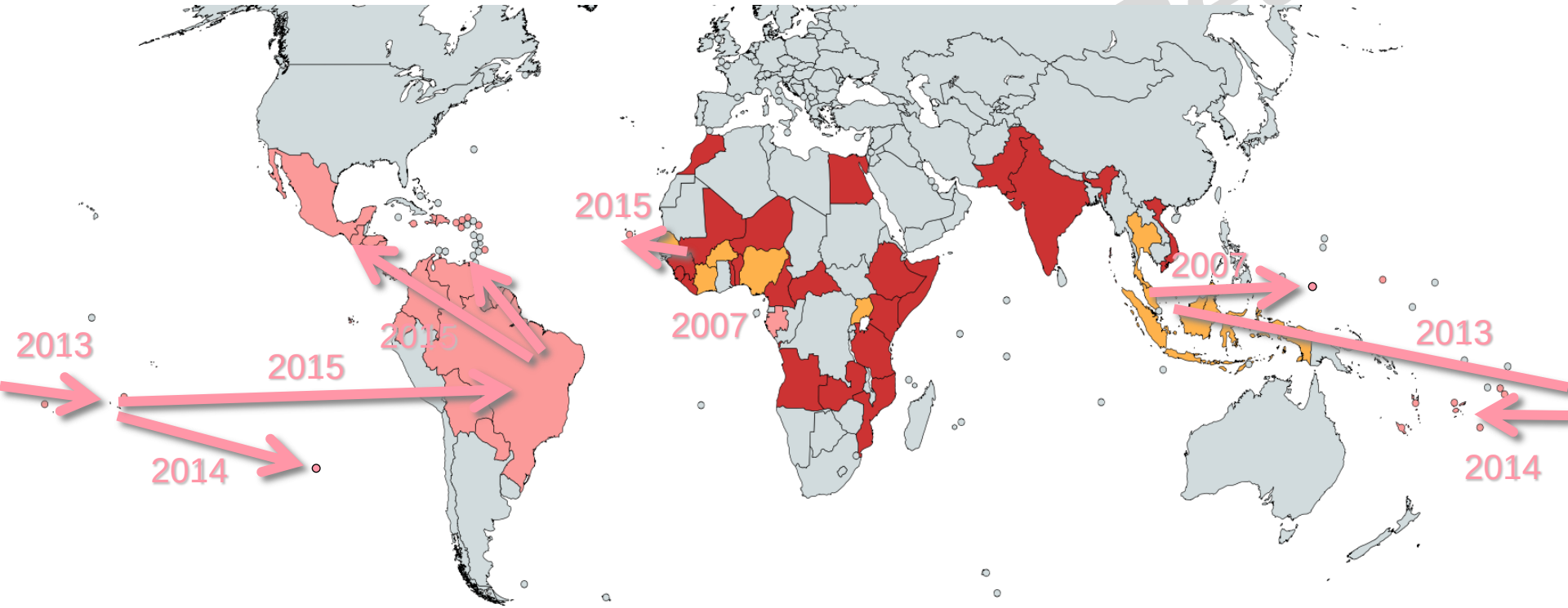
Gubler, 1998

Global distribution of dengue virus serotypes, 2016



Adapted from Gubler, 1998

Spread of Zika Virus Epidemics Since 2007



Outbreaks

Serologic evidence

Virus detection or confirmed human case

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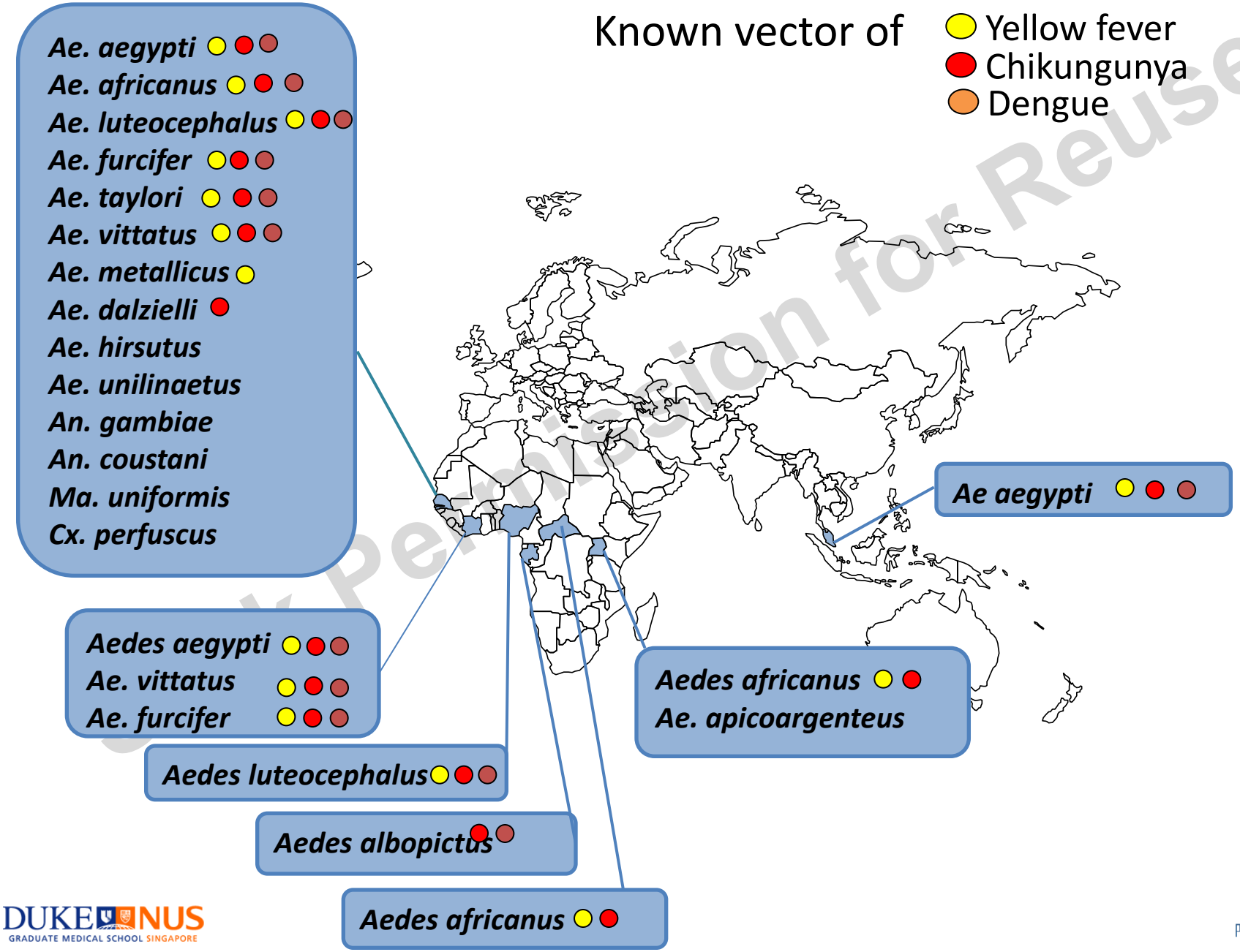
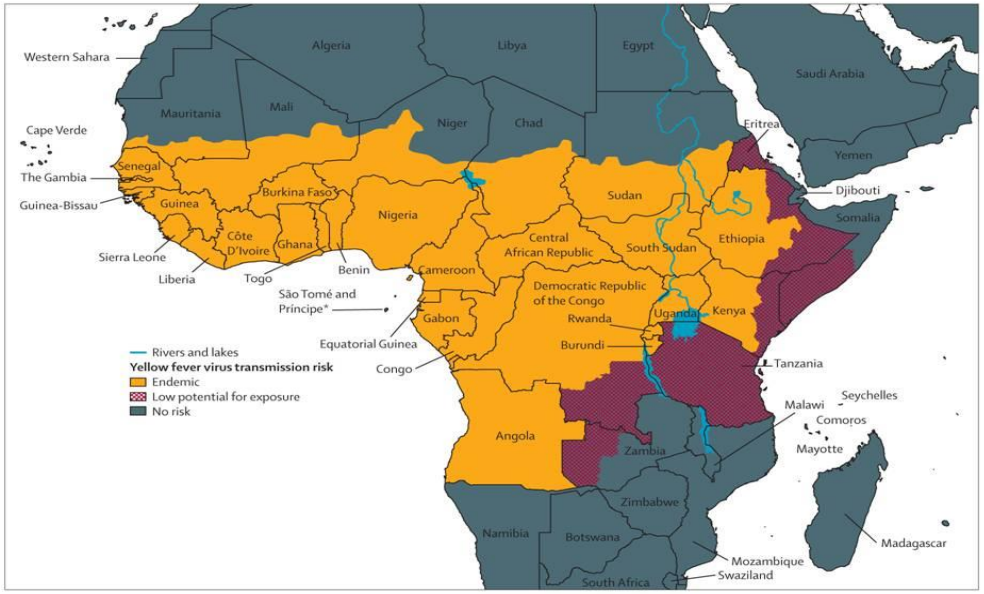
Isolations of Zika virus from mosquito species



Global Distribution of Yellow Fever

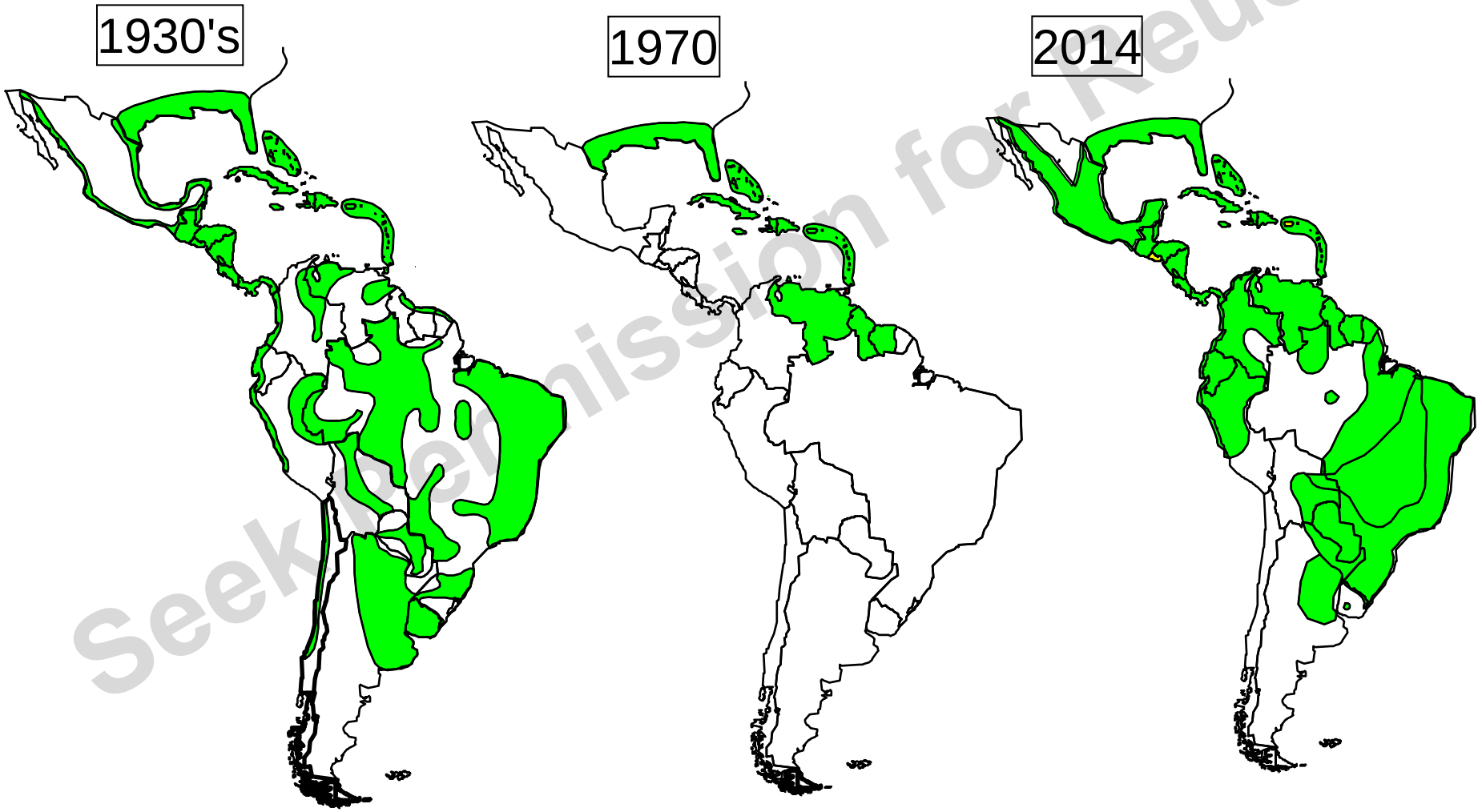


Why Hasn't Epidemic Yellow Fever Returned to Urban Centers in South America?

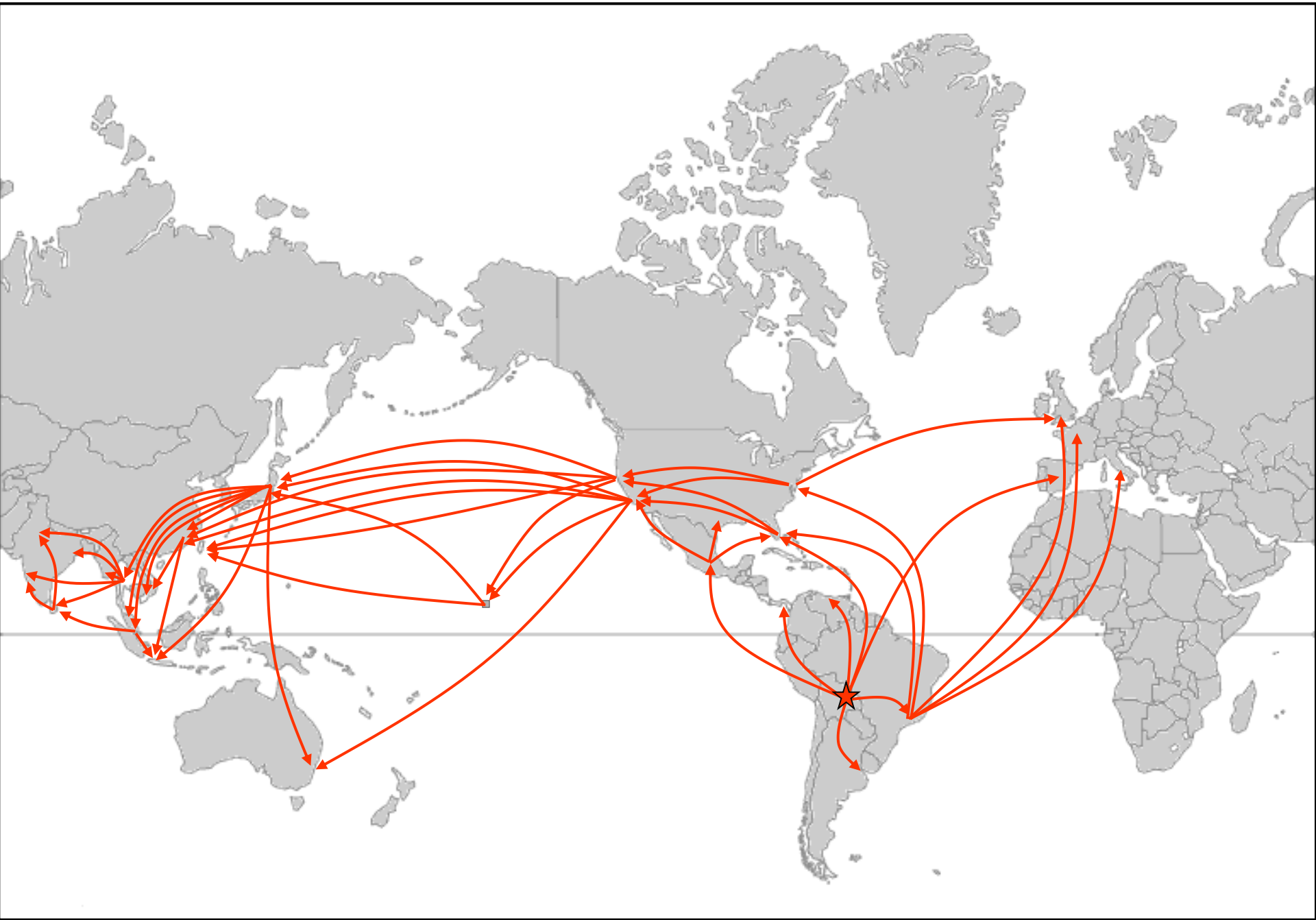
What is the Risk?

- Low herd immunity in humans
- Encroachment of humans on sylvatic cycle
- Human migration
- Reinfestation of urban centers by Ae aegypyi
- Increased Urbanization and air travel
- Aedes albopictus infestation of Latin America

Aedes aegypti Distribution in the Americas



POTENTIAL GLOBAL SPREAD OF URBAN YELLOW FEVER



Why Hasn't Epidemic Yellow Fever Returned to Urban Centers in South America?

Most Important?

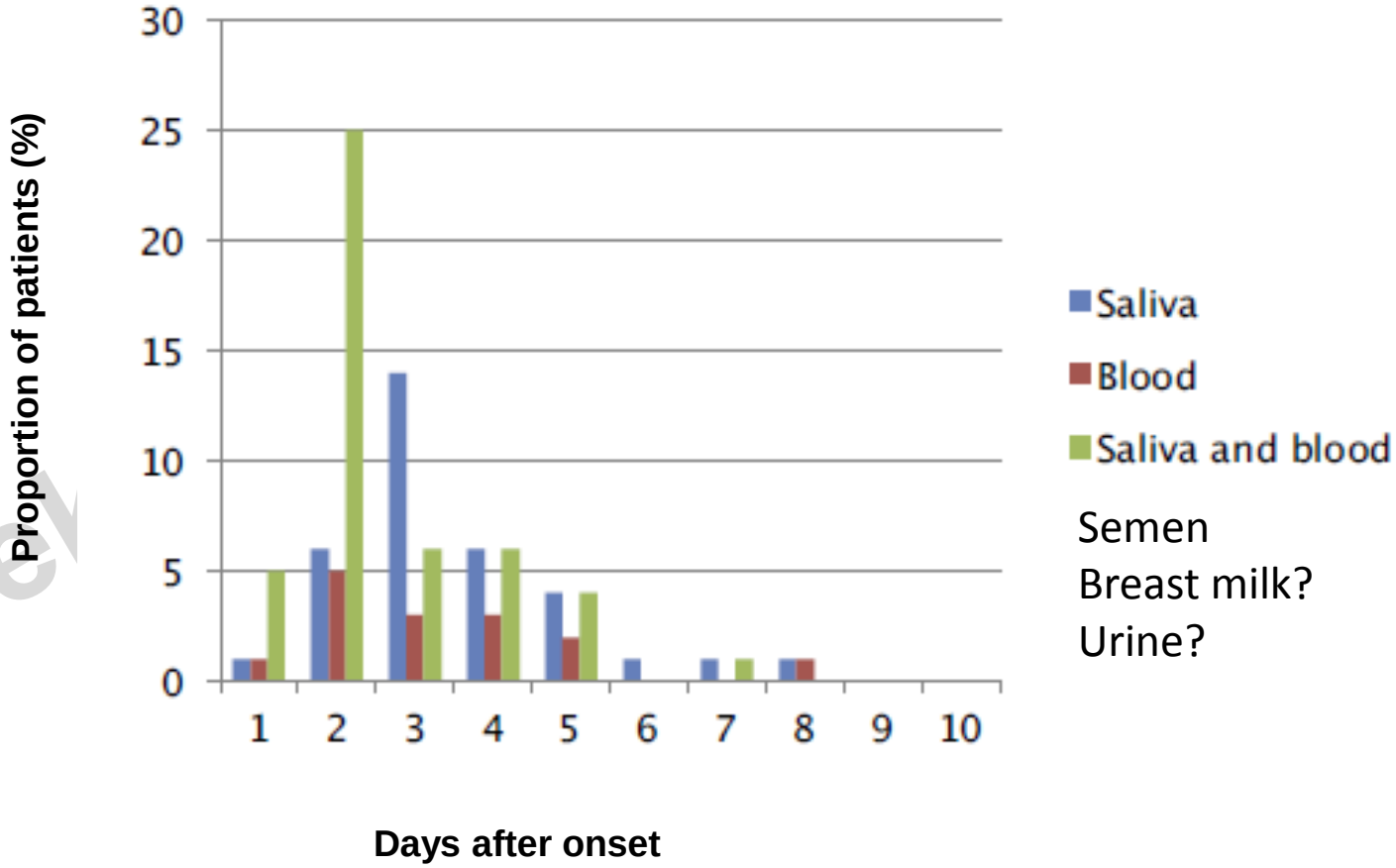
- Barriers of YF immunity in endemic countries
- Cross protective flavivirus immunity
- No YFV lineage adapted to Ae aegypti and human cycle

Novel Modes of West Nile Virus Transmission

- Transfused blood
- Transplanted organs
- Breast milk
- Transplacental transmission
- Percutaneous, occupational exposure
- Conjunctival exposure
- Dialysis?

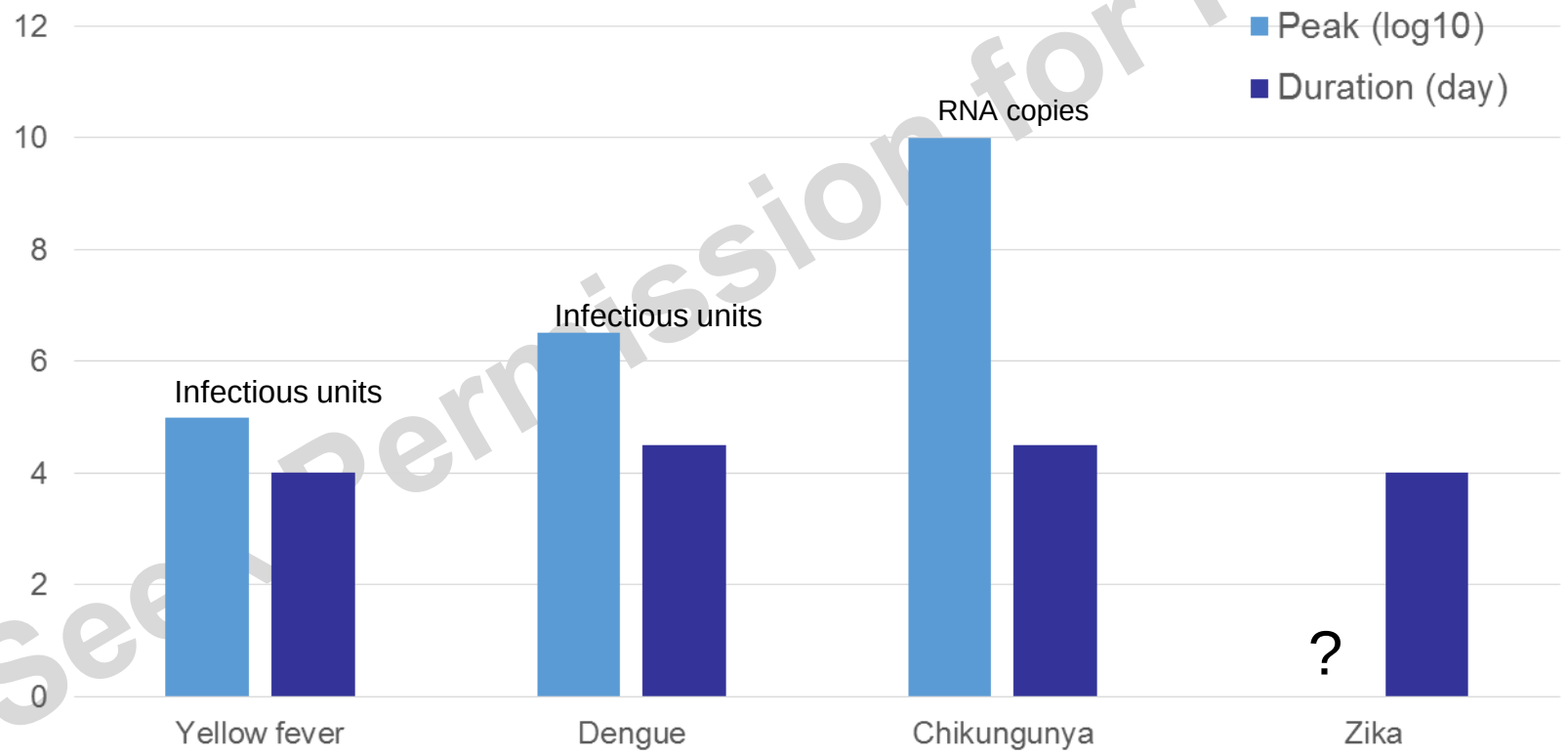
Zika Virus Viremia and Shedding

– RNA detected in saliva for 5-7 days, n=182 patients with Zika symptoms -, Tahiti, 2014 (Musso et al, 2015)



Semen
Breast milk?
Urine?

Viremia Levels and Duration are determinants of Ro



Other Arboviruses with Potential for Urban Emergence