

# **Emerging viruses**

Lecture 22

Biology W3310/4310

Virology

Spring 2016

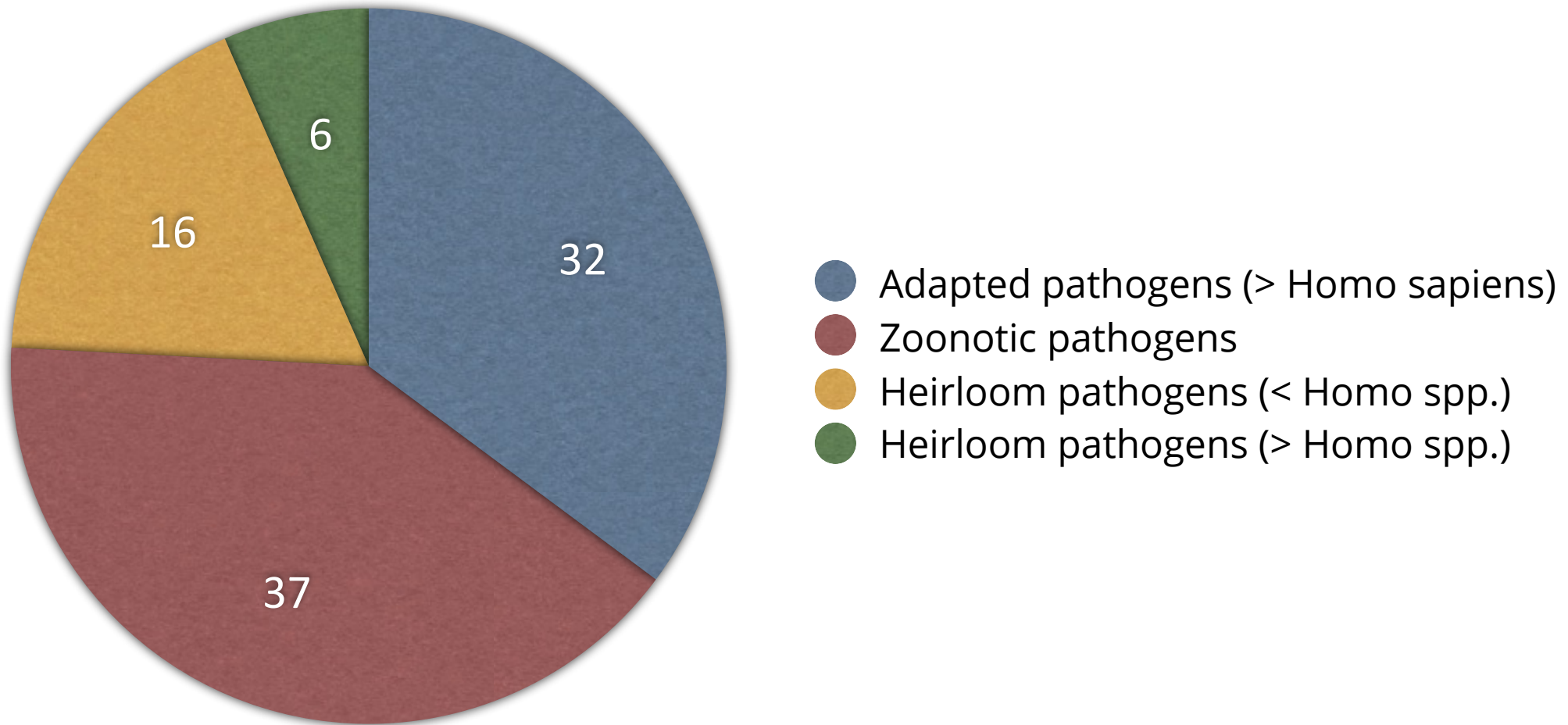
# Emerging viruses

- *Emerging virus* - causative agent of a new or previously unrecognized infection
- The term became popular in 1990s, but emerging viruses are not new
- Since the rise of agriculture - 11,000 years ago - new infectious agents have invaded human populations because they can be sustained by numbers that were unknown before agriculture and commerce

# Emerging viruses

- Expanded host range with an increase in disease not previously obvious
- Transmission of a virus from a wild or domesticated animal to humans - *zoonosis*
- Cross-species infection may establish a new virus in the population (SIV moving from chimps to humans)
- Often cross-species infection cannot be sustained (e.g. Ebola and Marburg from bats to humans)

# Human - animal interface



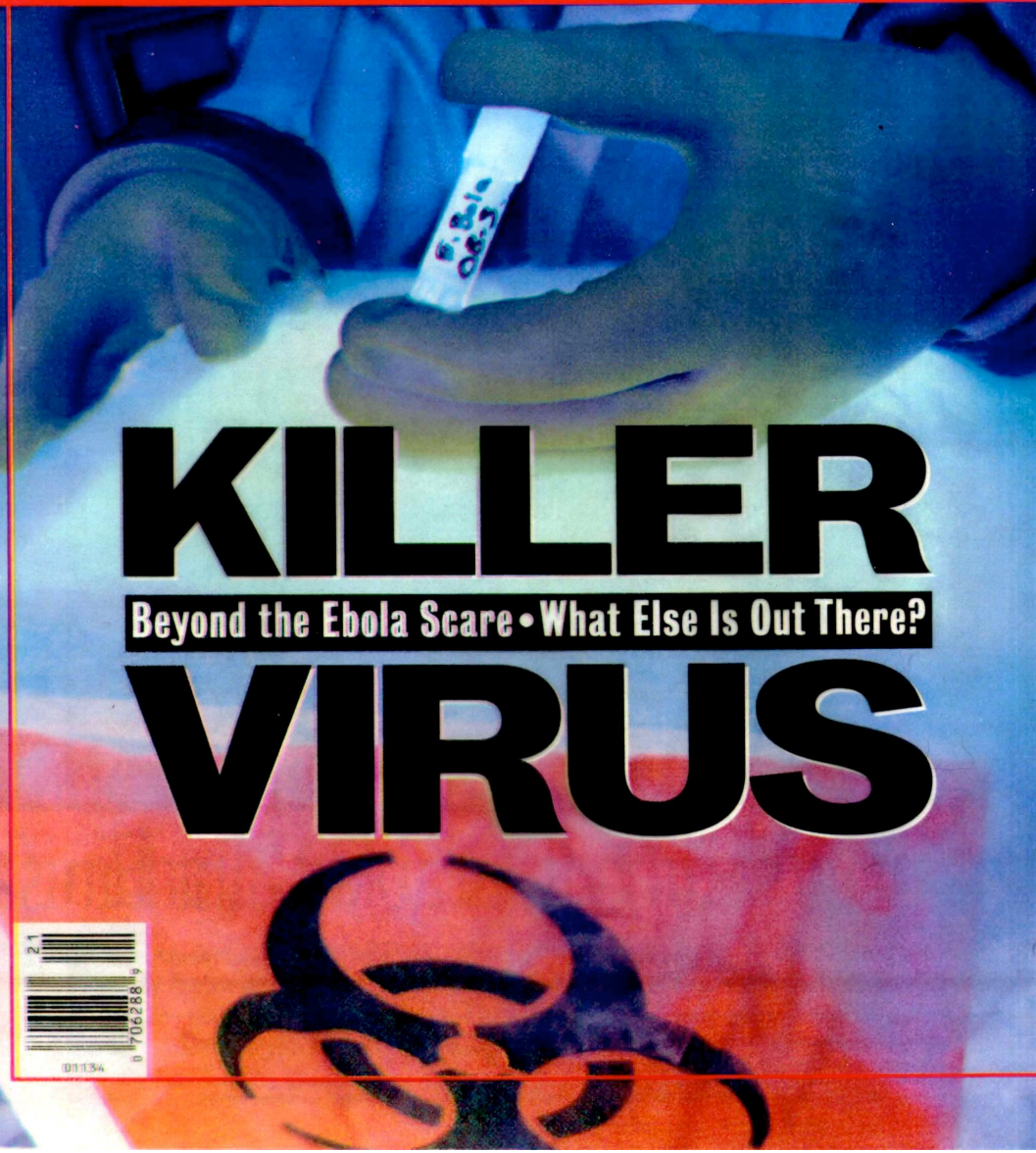
Viruses belonging to # of genera



CALIFORNIA DREAMING: PETE WILSON'S CHALLENGE

# Newsweek

May 22, 1995 : \$2.95



## KILLER Beyond the Ebola Scare • What Else Is Out There? VIRUS



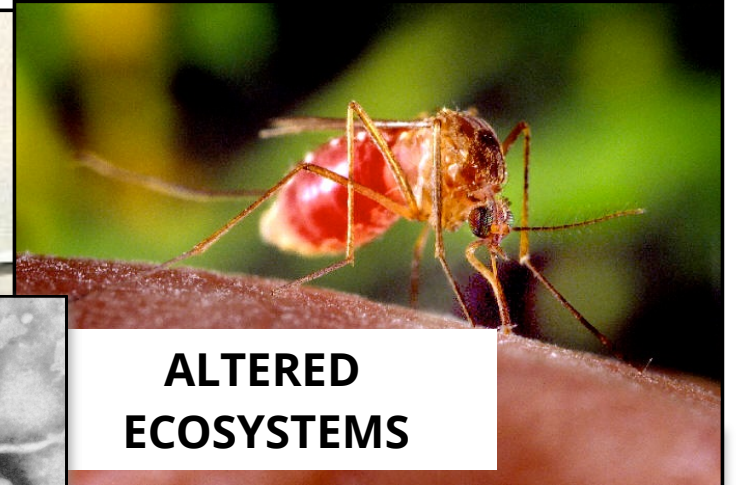


# Convergent forces of disease emergence

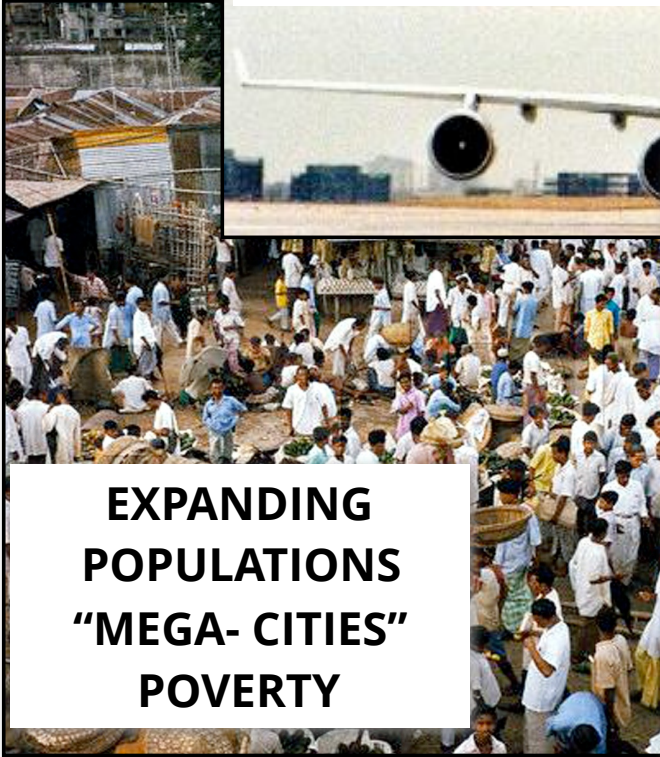
**GLOBALIZATION  
RAPID AIR TRAVEL**



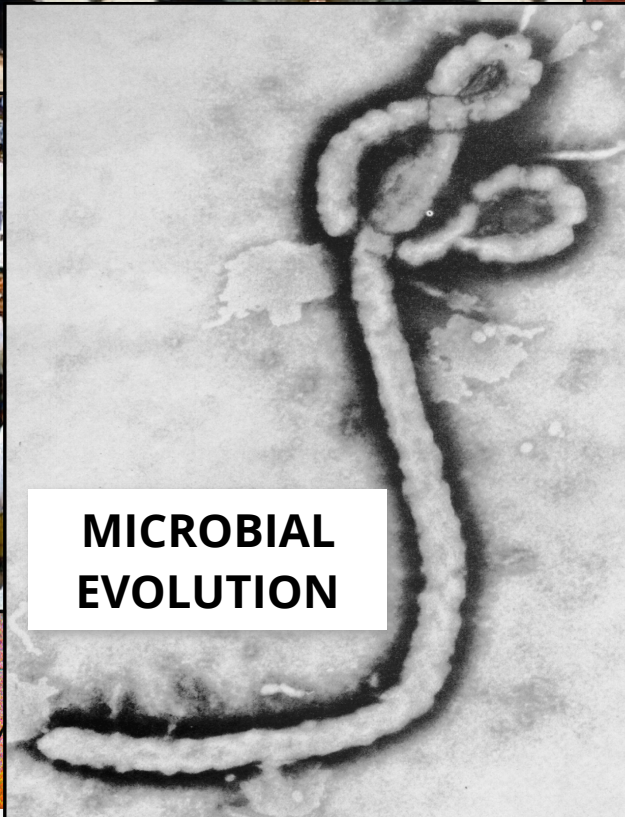
**ALTERED  
ECOSYSTEMS**



**EXPANDING  
POPULATIONS  
"MEGA- CITIES"  
POVERTY**



**MICROBIAL  
EVOLUTION**



**DEFORESTATION**

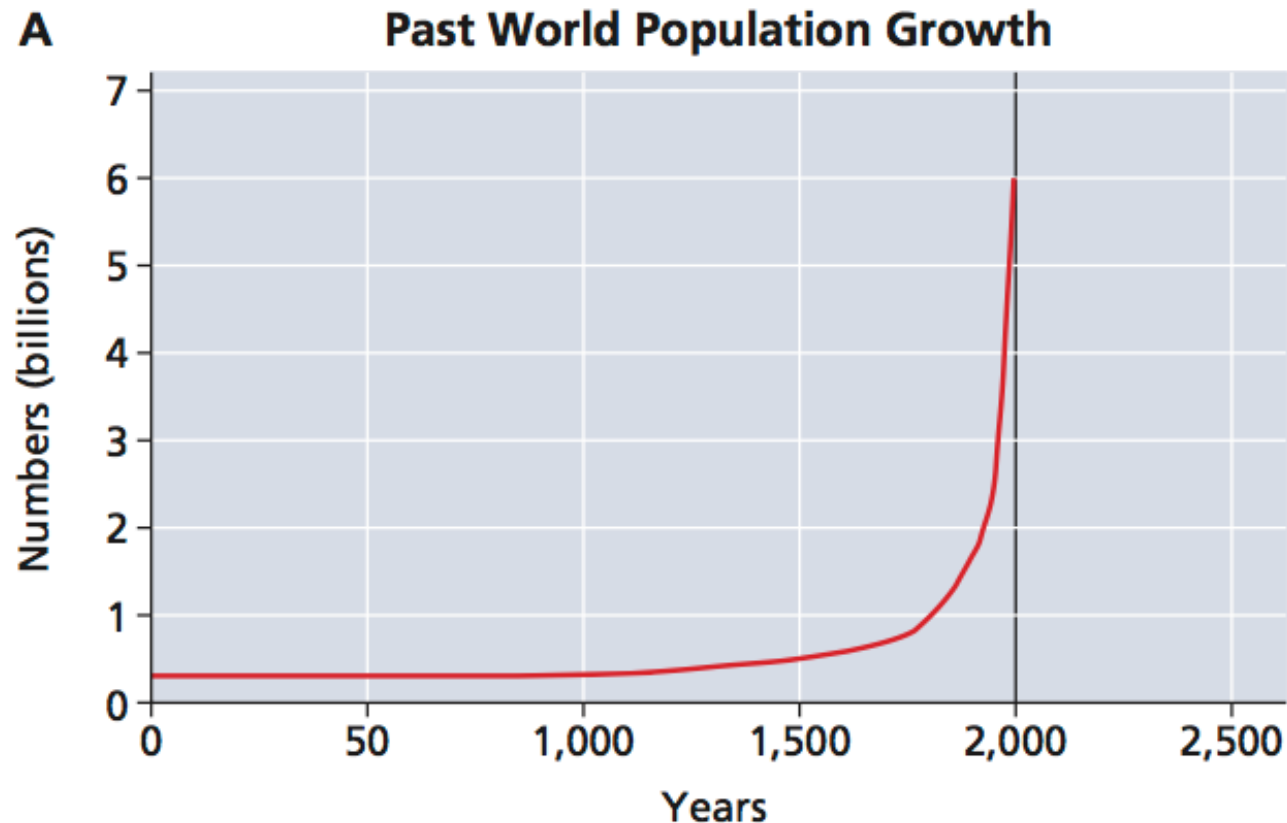


**ENVIRONMENTAL CHANGES**



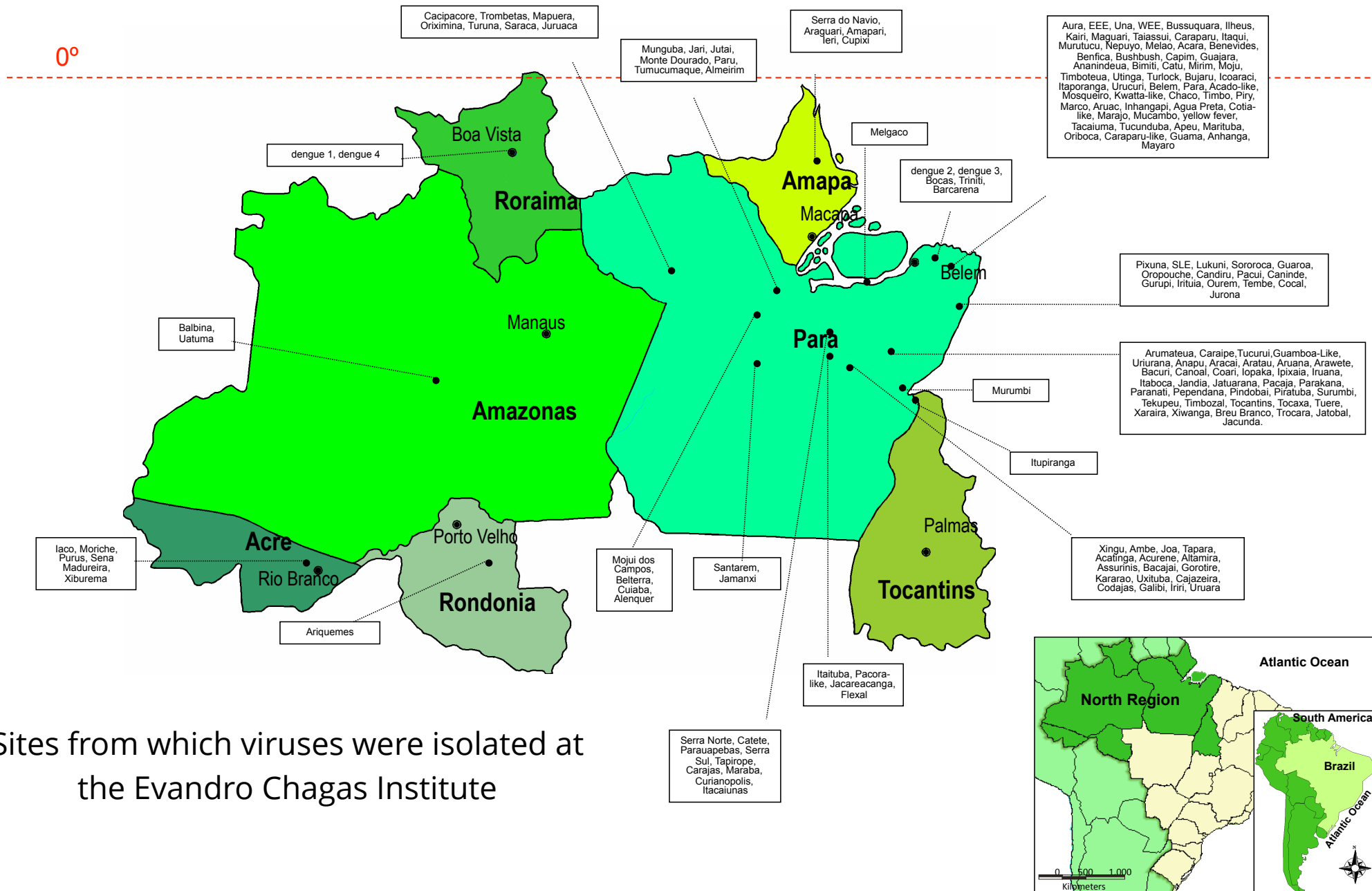
# Over-riding factors driving the emergence of infectious diseases of humans and animals:

*Human population growth and incredible change occurring in all ecosystems brought about by human occupation of almost every corner of the planet*



# The Amazon North Region of Brazil

*Home to 183 Arthropod-borne and Other Vertebrate Viruses*



Sites from which viruses were isolated at the Evandro Chagas Institute

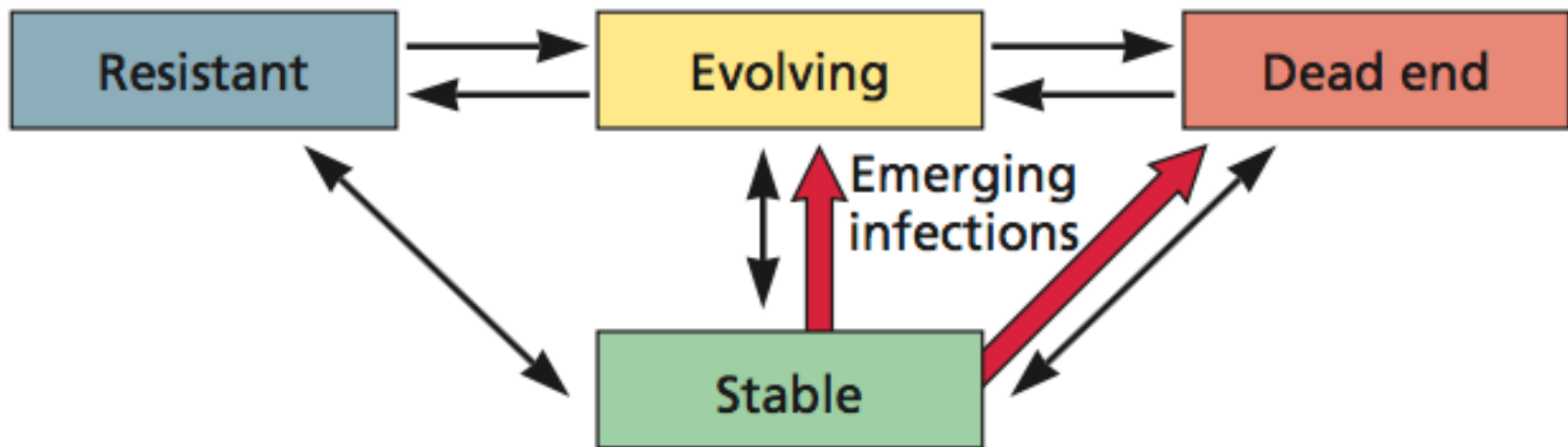


Virus	Family	Drivers of Emergence
Dengue virus	<i>Flaviviridae</i>	Urban population density, mosquito breeding
Ebolavirus	<i>Filoviridae</i>	Human contact with natural host; bushmeat
Hantaan virus	<i>Bunyaviridae</i>	Agriculture: human/rodent contact
Hendra virus	<i>Paramyxoviridae</i>	Bats to horses to stable workers
HIV	<i>Retroviridae</i>	Bushmeat trade
Influenza virus	<i>Orthomyxoviridae</i>	Pig/bird agriculture
Junin virus	<i>Arenaviridae</i>	Agriculture: human/rodent contact
Nipah virus	<i>Paramyxoviridae</i>	Bats to pigs to humans
Machupo virus	<i>Arenaviridae</i>	Agriculture: human/rodent contact
Rift Valley virus	<i>Bunyaviridae</i>	Dams, irrigation
Sin Nombre virus	<i>Bunyaviridae</i>	Weather, human/rodent contact
West Nile virus	<i>Flaviviridae</i>	Mosquito

# Roles of Evolution

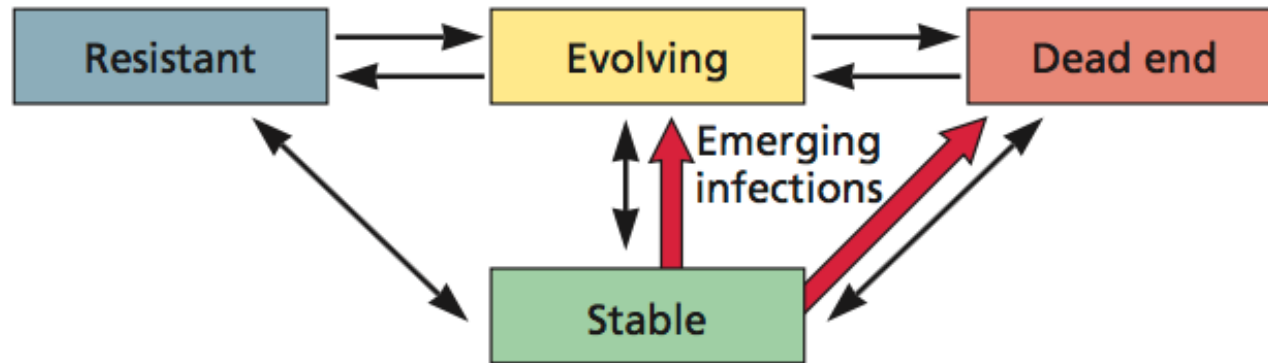
- Leads to the biodiversity of pathogens existing in nature (*quasispecies*)
- Adaptation to new hosts and environments (through variation and selection)

# The general interactions of hosts and viruses



- Stable: maintains virus in ecosystem
- Evolving: passage of virus to naive population
- Dead-end: one way to different species
- Resistant host: infection blocked

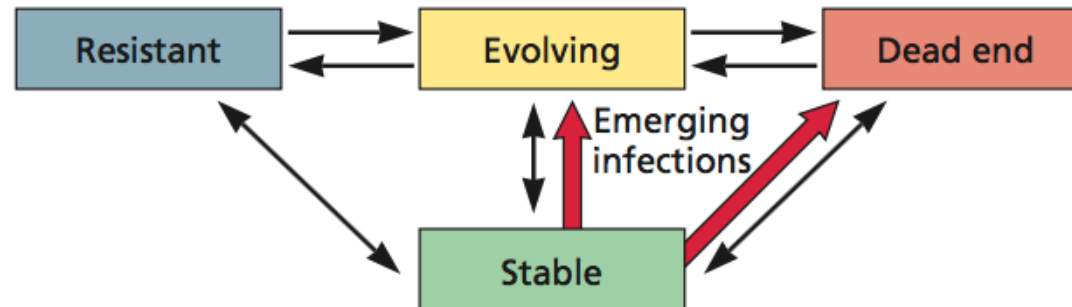
# Stable host-virus interactions



- Both participants survive and multiply
- Some are effectively permanent
  - *Humans are sole natural host for measles virus, herpes simplex virus, HCMV, smallpox*
- May include infection of more than one species
  - *Influenza A virus, flaviviruses, togaviruses*

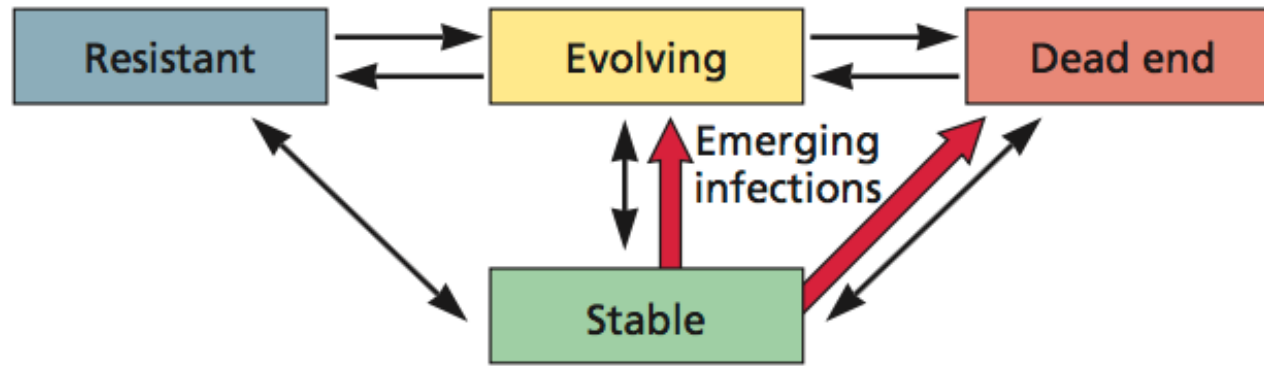


# Evolving host-virus relationship



- Hallmarks are instability and unpredictability
- Outcome of infection may range from benign to death
  - Introduction of smallpox and measles to natives of Americas by Old World colonists and slave traders
  - Introduction of West Nile virus into Western Hemisphere, 1999
- Introduction of rabbits into Australia

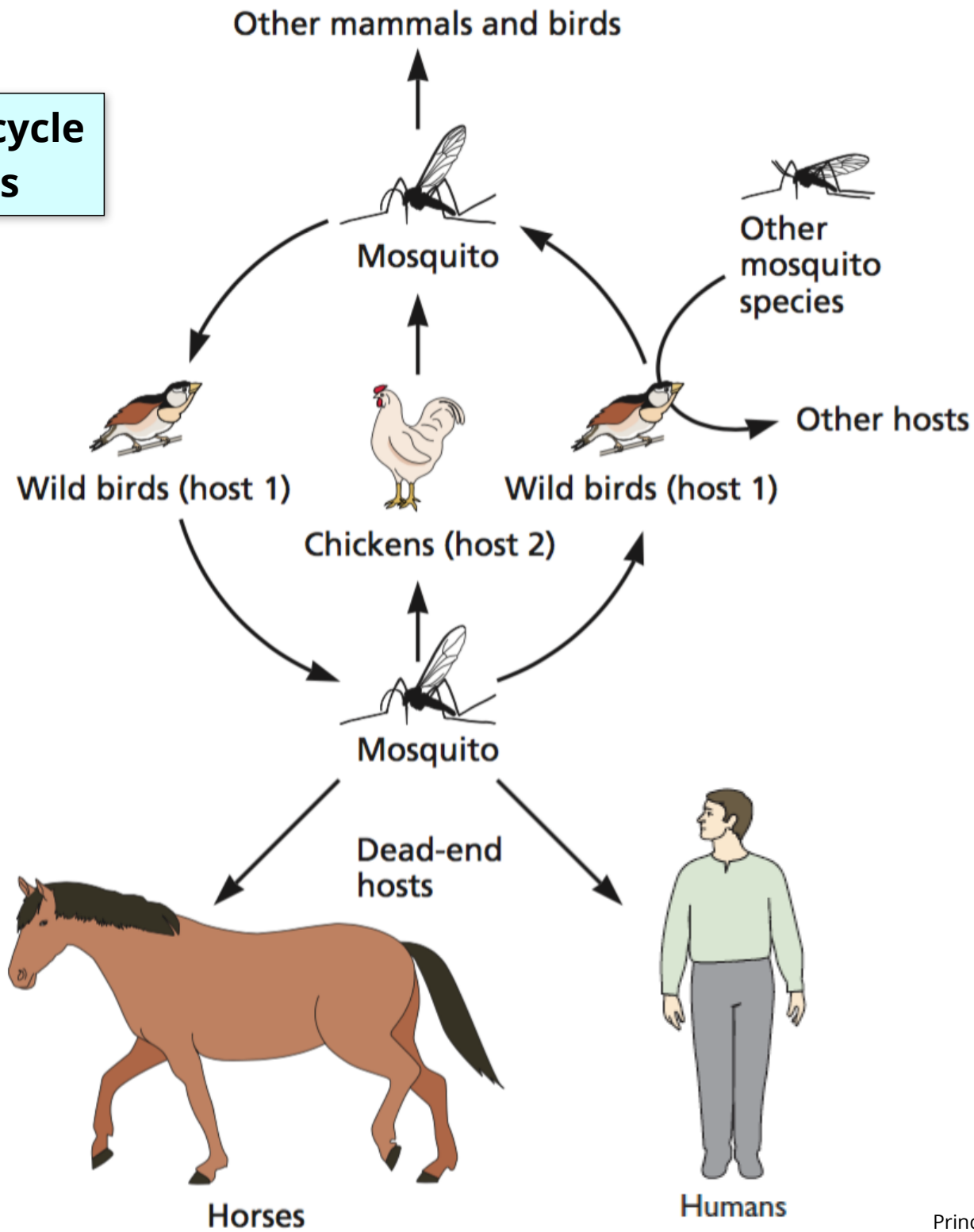
# Dead-end interaction



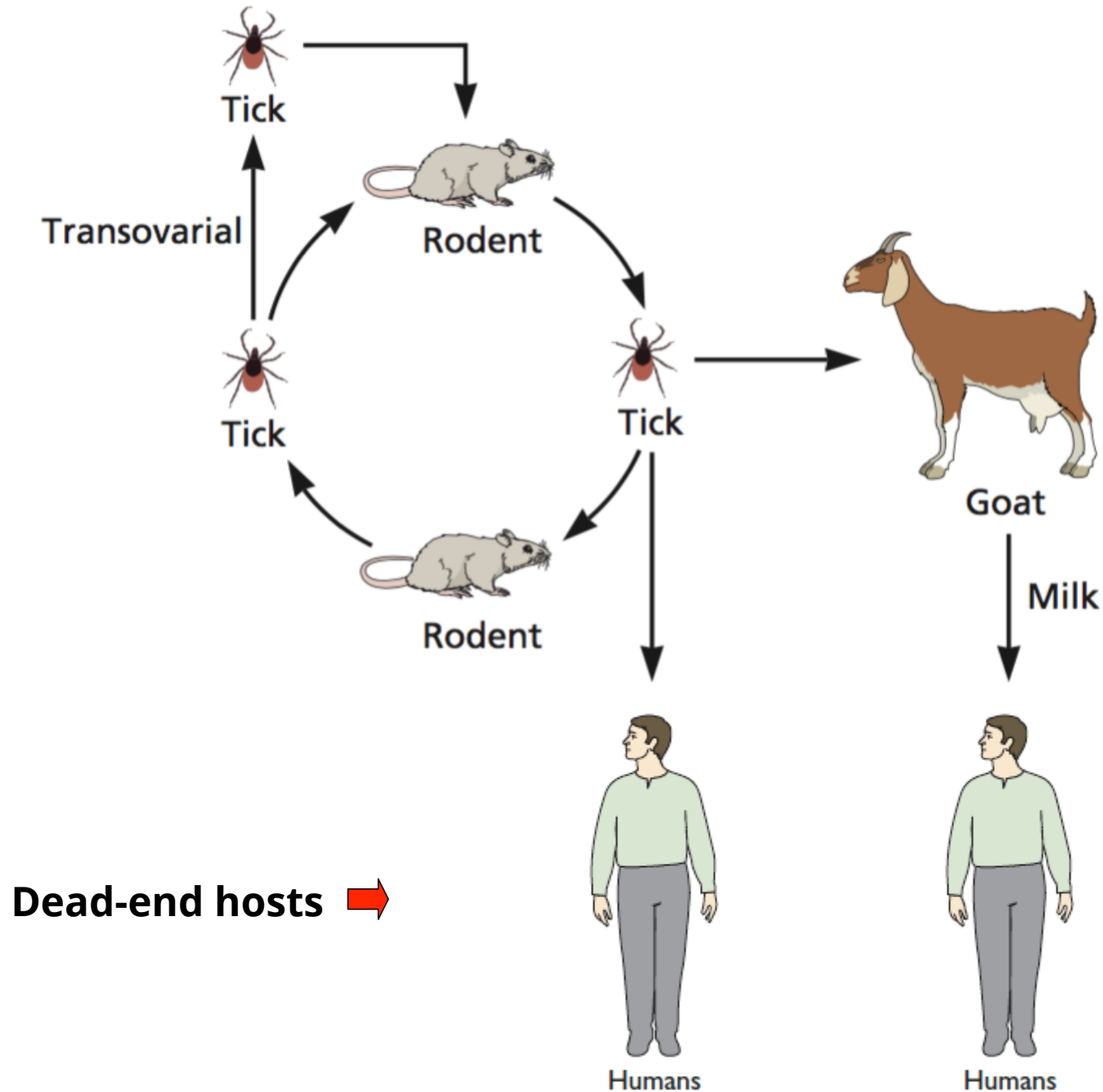
- Frequent outcome of cross-species infection
- Ebolavirus: humans, chimps, gorillas
- New infected host may not transmit the infection to others of the same species (H5N1)
- Contribute little to the spread of a natural infection

## The complex life cycle of an arbovirus

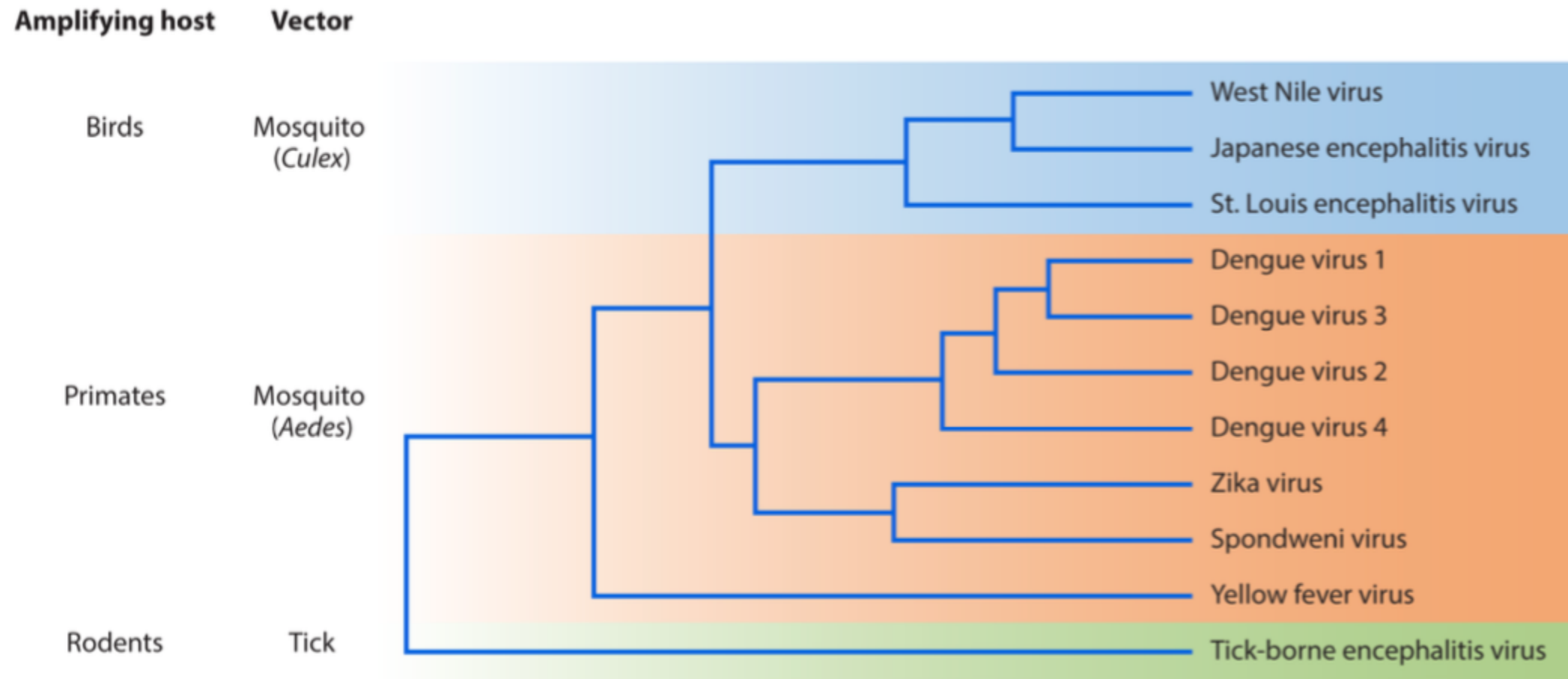
Stable host-virus interactions



# Rodents and insect vectors move European tick-borne encephalitis virus among many hosts



# Flaviviruses: Human pathogens

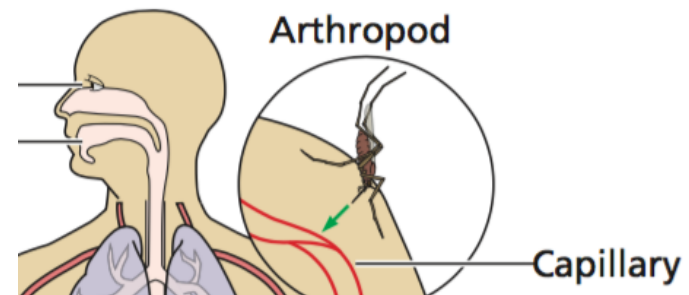
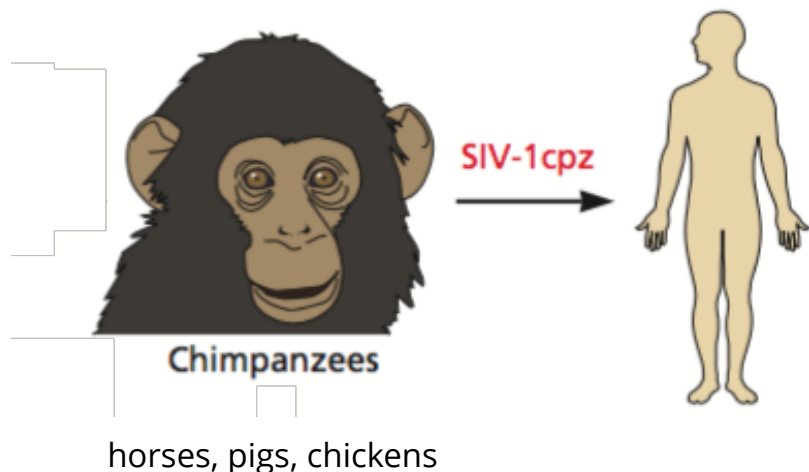


# Emerging infections: Two steps

- Introduction
- Establishment and dissemination

# Encountering new hosts

- Rare chance encounters of viruses with new hosts may never be detected
- Single-host infections are not transmitted among humans for many reasons



# Expanding viral niches

- Successful encounters require access to susceptible and permissive cells
- Population density and health are important factors
- Virus populations will endure in nature only because of *serial infections* (a chain of transmission)



# Human are constantly providing new ways to meet viruses



Dams and water impoundments

Irrigation

Massive deforestation

Rerouting of wildlife migration patterns

Wildlife parks

Long distance transport of livestock and birds

Air travel

Uncontrolled urbanization

Day care centers

Hot tubs

Air conditioning

Millions of used tires



Blood transfusion

Xenotransplantation

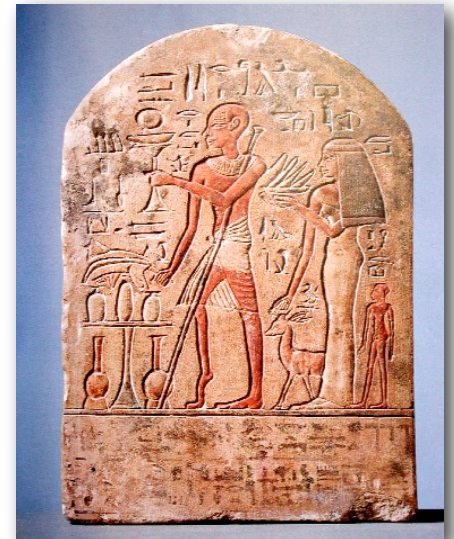
Societal changes with regard to drug abuse and sex

# Diseases of exploration and colonization

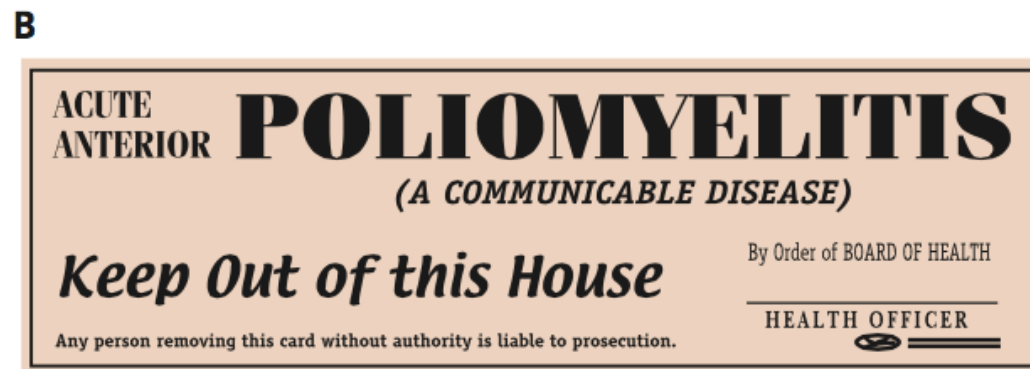
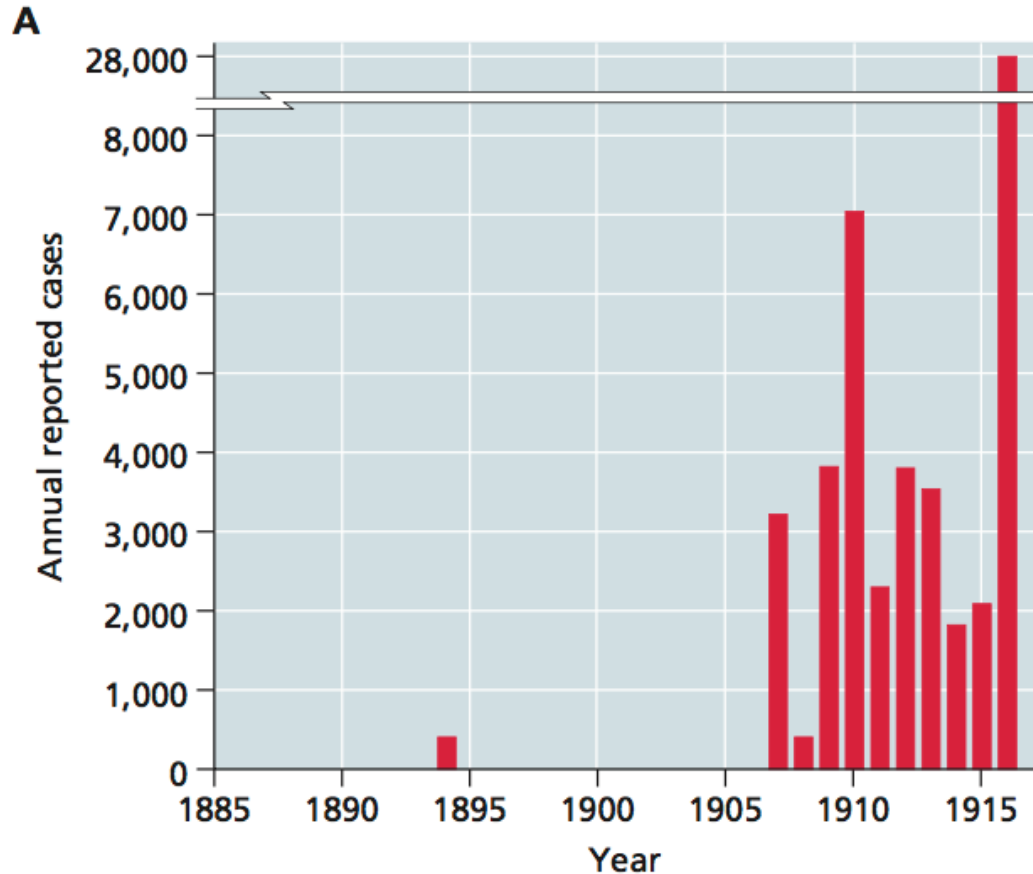
- Explosive epidemic spread may occur when a virus enters a naive population
- Smallpox reached Europe from the Far East in 710 AD, attained epidemic proportions
- Smallpox changed the balance of human populations in the New World - killed 3.5 million Aztecs in 2 years (1520 - spread from Hispaniola), allowing conquest by Cortez

# Changes in human populations and environments

- Emergence of epidemic poliomyelitis in the beginning of the 20th century: improved sanitation delayed transmission
- Known since 4,000 years ago, stable host-virus relationship



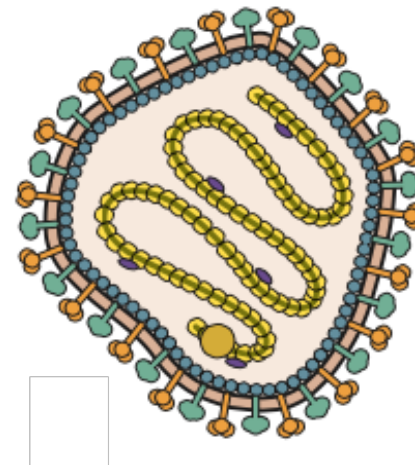
# Poliomyelitis: A disease of modern sanitation





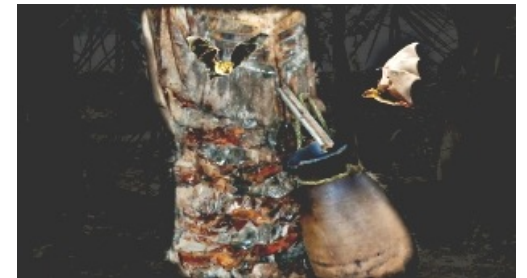
## Bats: a source of zoonotic infections

- Many new paramyxoviruses found in flying foxes since 1995, including Nipah and Hendra viruses
- Cause severe disease in domestic animals (horses and pigs) and are known to infect humans

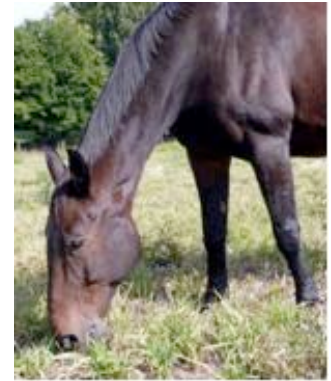


# Nipah virus

- First outbreak Malaysia 1998
  - *Outbreak of respiratory and neurological disease on pig farms*
  - *105 human deaths, 1 million pigs culled*
- Fruit bats excrete virus in urine but are unaffected
- Pig farmers plant mangoes near pigpens
- Pigs spread infection to humans
- Subsequently humans infected by consuming date palm sap contaminated by bats (India, Bangladesh)
- Human to human transmission; infections continue



# Hendra virus

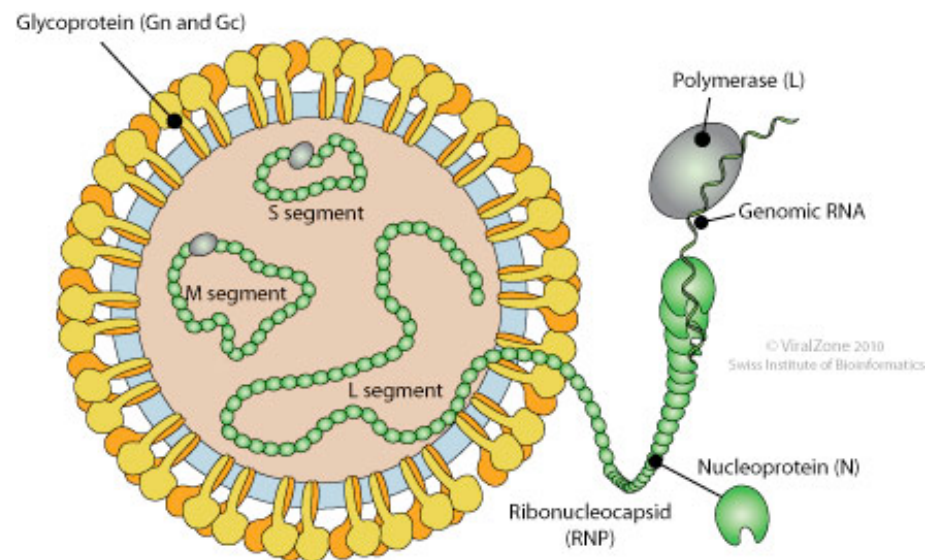


- Discovered in Hendra, Australia, September 1994
  - *Outbreak killed 14 racehorses and a trainer*
- Spread from flying foxes to horses, then to humans
- Horses continue to acquire infection



# Changing climate and animal populations

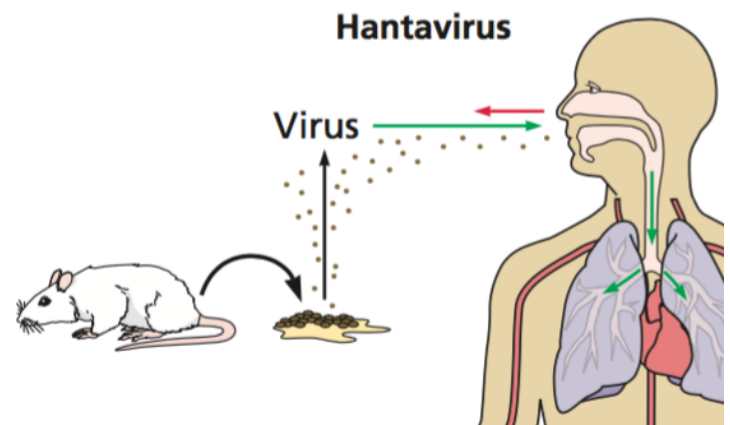
- Hantavirus pulmonary syndrome - first noted in Four Corners area of New Mexico, 1993
- Disease is caused by Sin Nombre virus, endemic in the deer mouse (*Peromyscus maniculatus*, 30% virus positive)
- Originally called Muerto Canyon virus, but residents objected



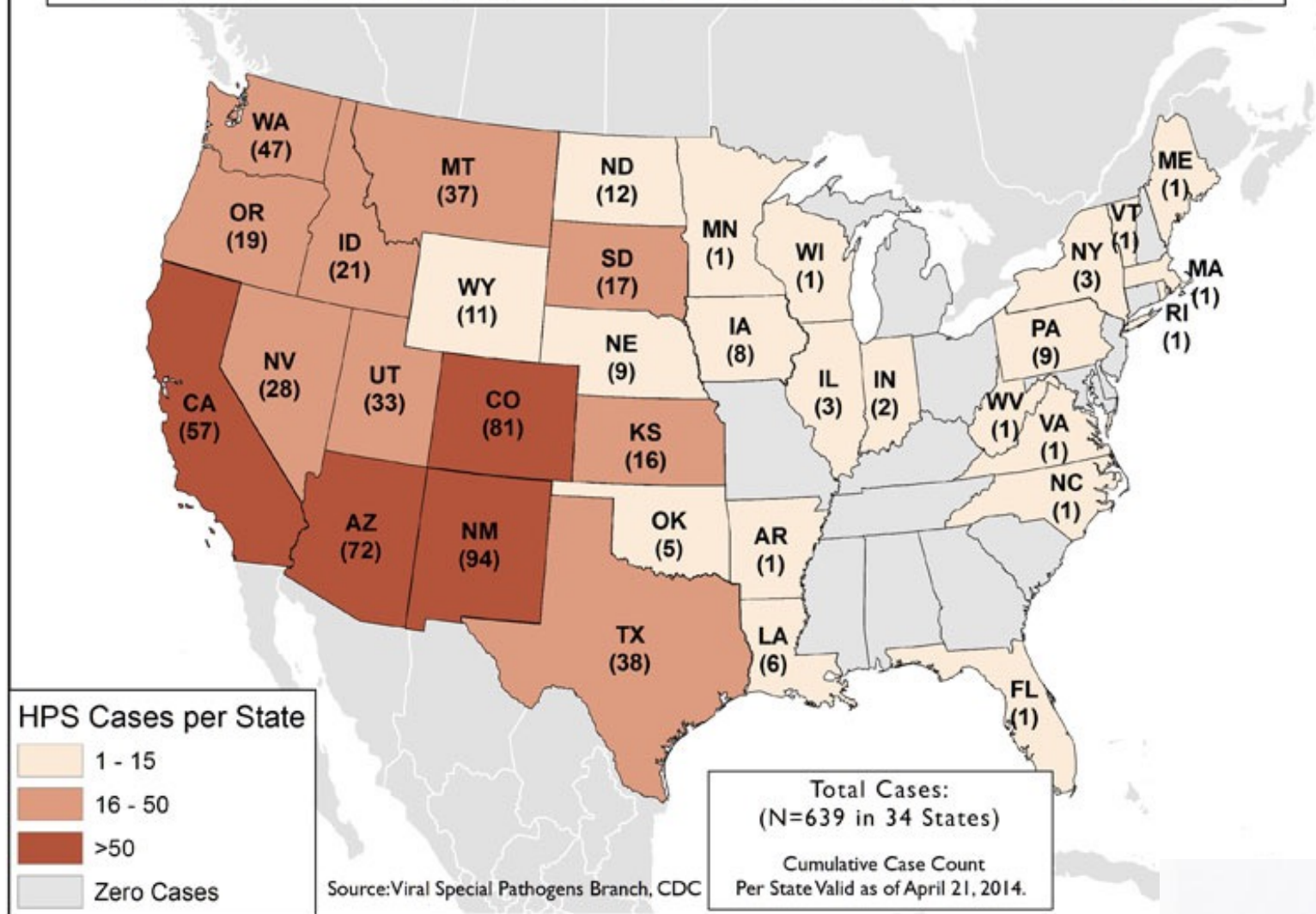


# Changing climate and animal populations

- In 1992-93, abundant rainfall produced a large crop of piñon nuts, food for humans and the deer mouse. Mouse population rose, contact with humans increased.
- Virus is excreted in mouse feces; contaminated blankets or dust from floors provided opportunities for human infection
- Humans not the natural host for Sin Nombre virus, human disease is rare
- Not new - earliest known case 1959



# Hantavirus Pulmonary Syndrome (HPS) Cases, by State of Reporting

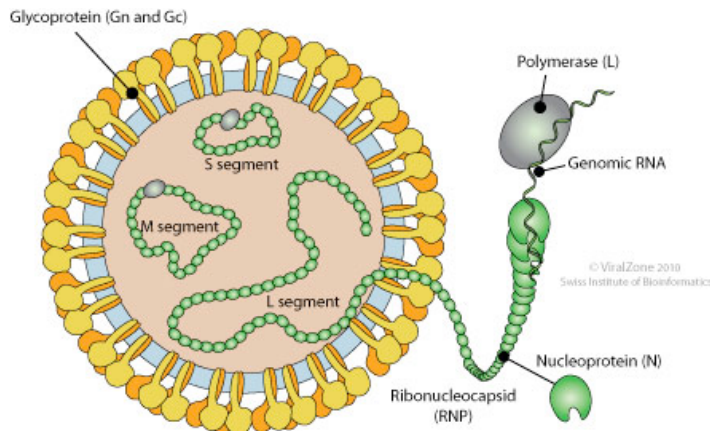


Deer mouse, white-footed mouse, rice rat, cotton rat

# Heartland virus disease



- 2012 - new phlebovirus identified in two farmers in Missouri
- Six subsequent cases identified, tick vector?
- How long had it been infecting people?



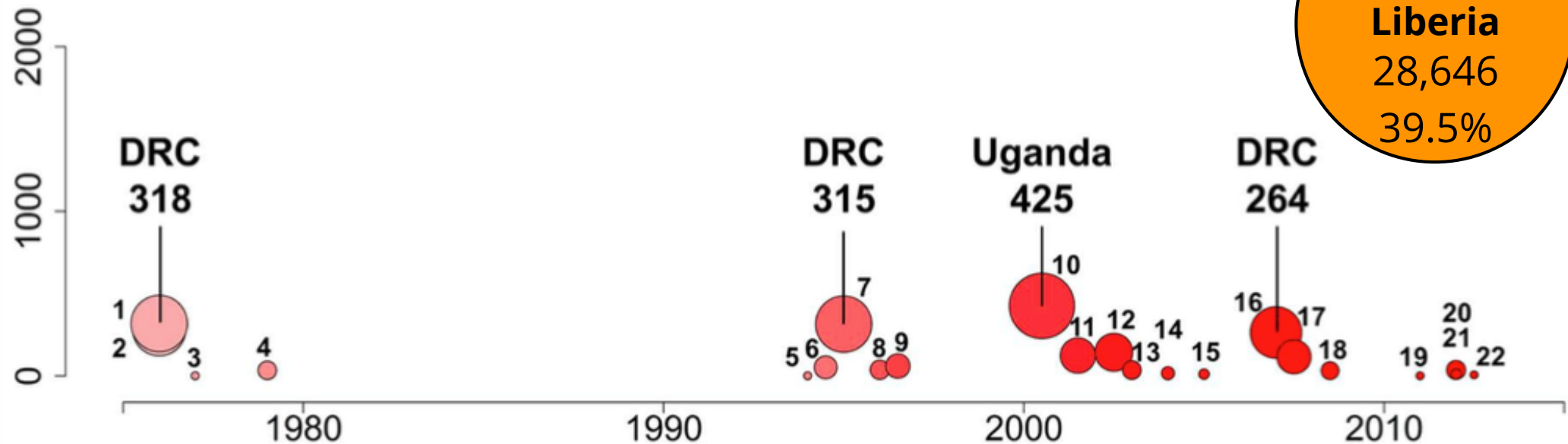
# Ebola hemorrhagic fever

- Simultaneous outbreaks in 1976 in DRC (318, 88%) and Sudan (284, 53%)
- Sudan index case: cotton factory workers
- Spread by use of contaminated needles, among family members
- Named after small river in northwestern DRC



# Outbreaks of Ebolavirus disease

**A**





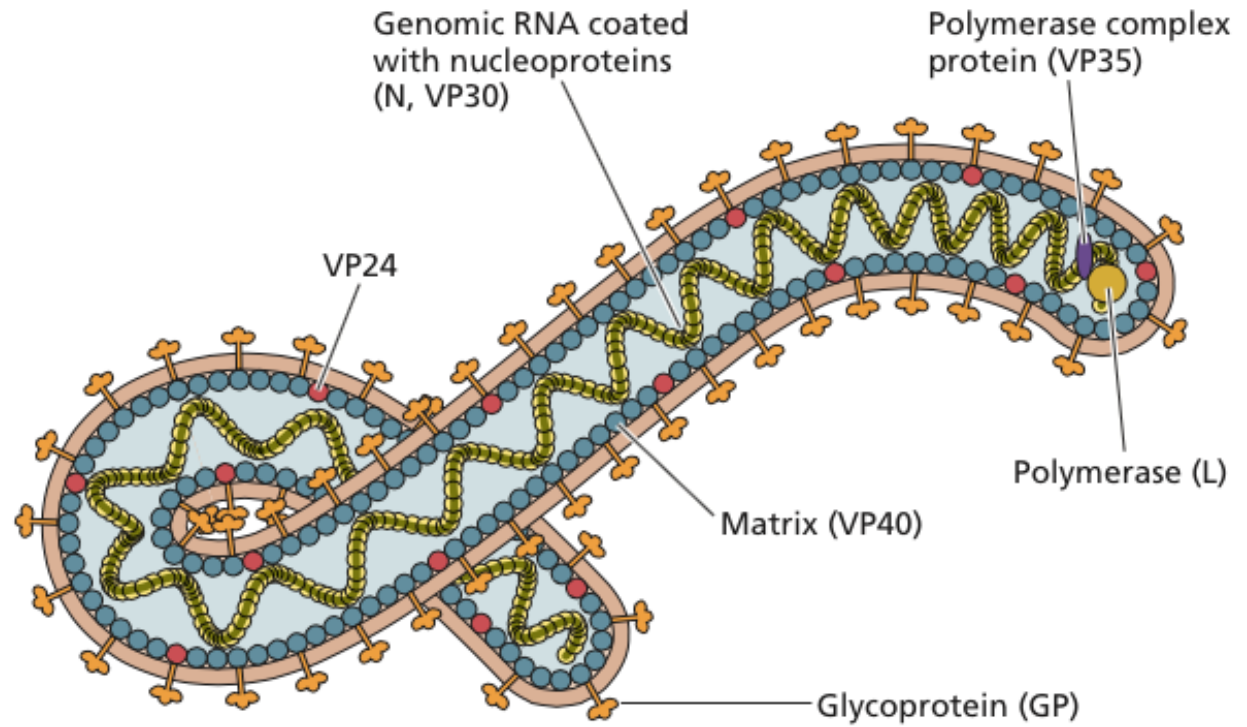
# Biosafety level 4 (BSL-4)

- High mortality
- Person to person transmission
- No approved vaccine or antiviral

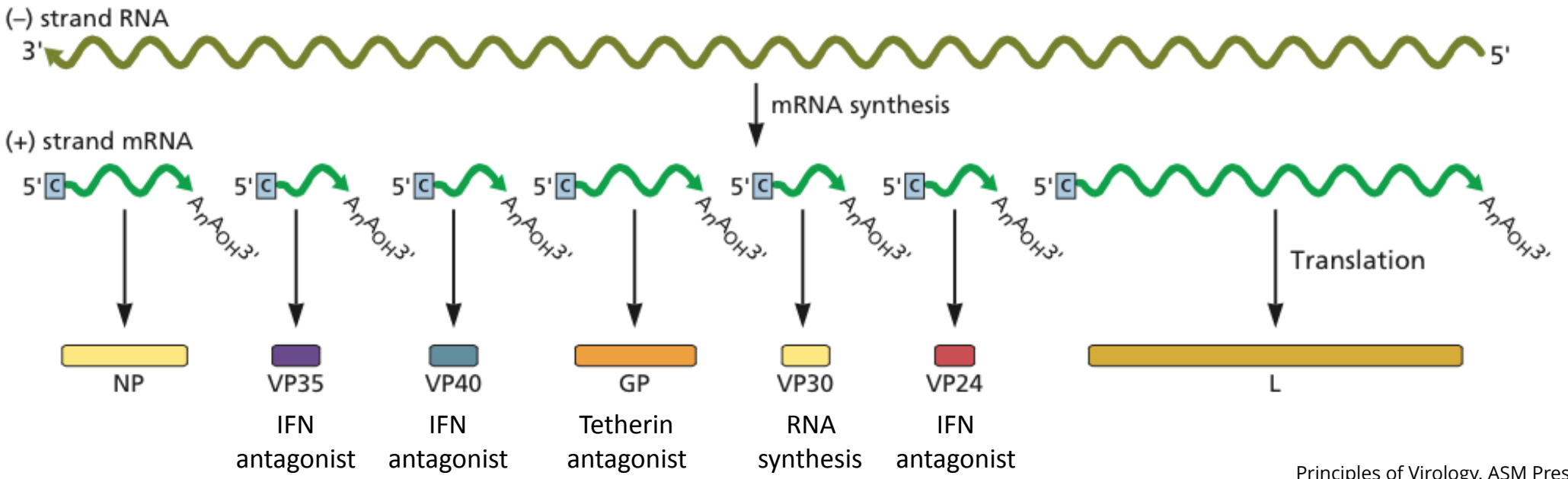


Threading the NEIDL <https://youtu.be/tqAjkjGq8Ug>

A



B



# How are humans infected?

- A classic zoonosis
- Index case: contact with animal carcass\*  
(bushmeat)
- Transmitted to other humans by close contact  
with infected fluids
- Chains of human infections short
- $R_0 = 2$

\*not always identified

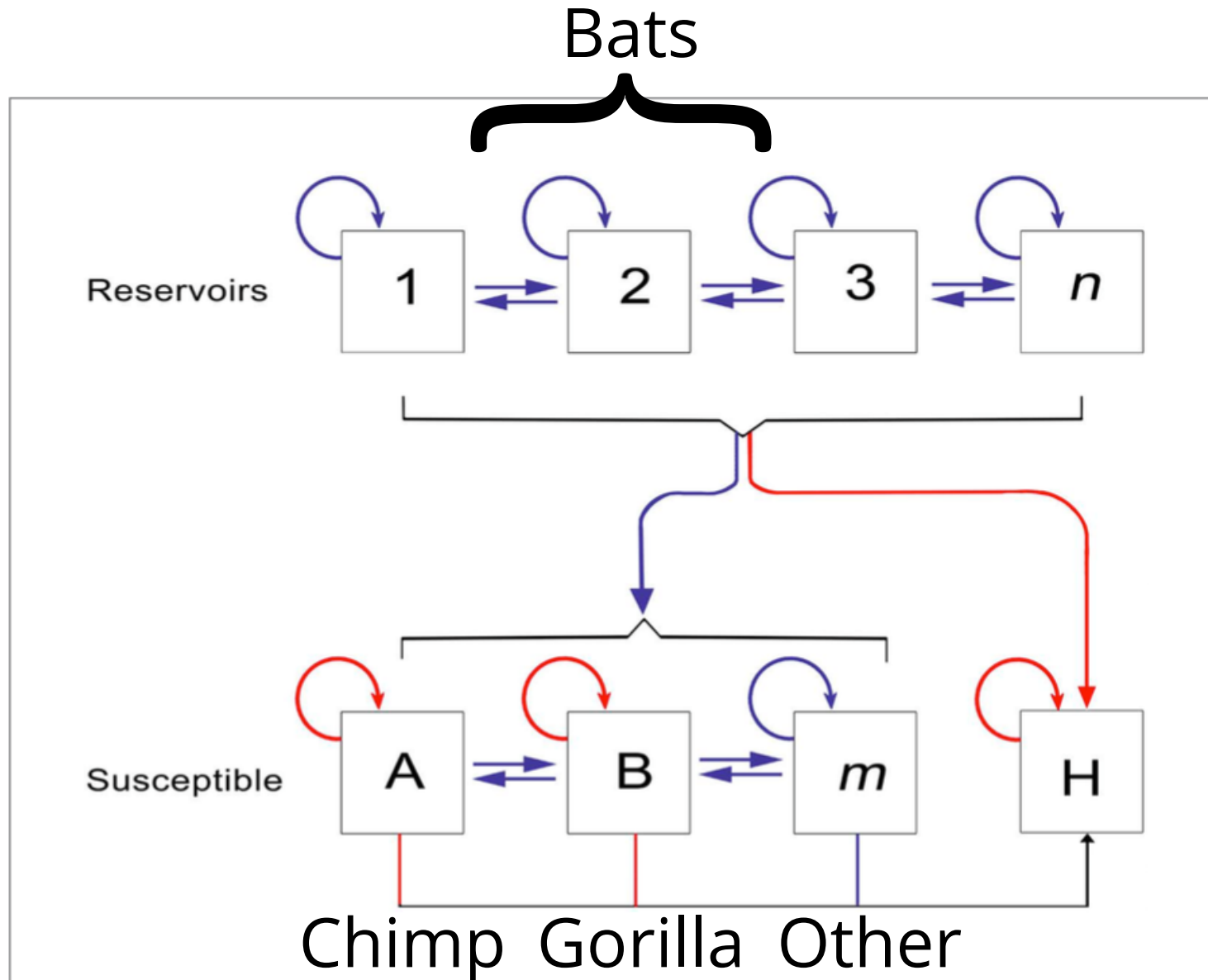


# Filovirus ecology



- Marburg virus has been isolated from cave-dwelling fruit bat (*Rousettus aegyptiacus*)
- Zaire Ebolavirus RNA, antibodies found in three tree-roosting bats (but not infectious virus)
- Humans, gorillas, chimpanzees are dead-end hosts

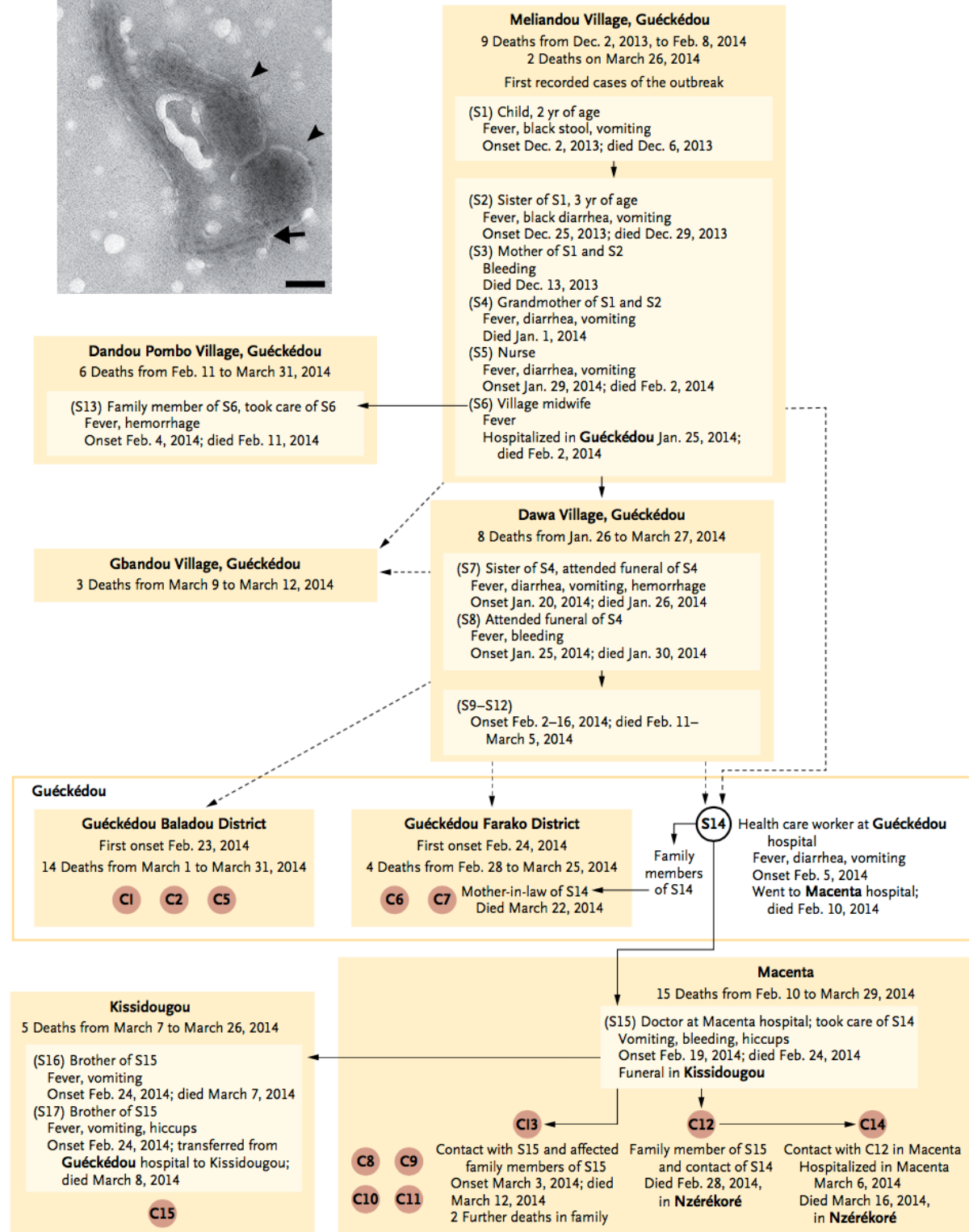
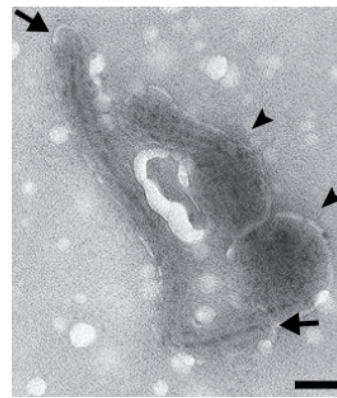
# What is the origin of Ebolaviruses?



# Ebolavirus outbreak examples

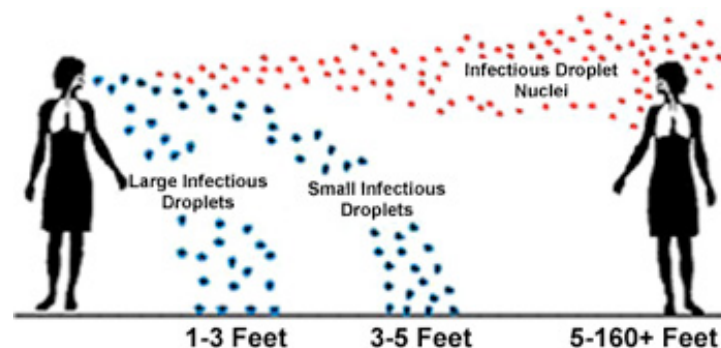
- **Gabon, 1996 (Zaire ebolavirus, 37 cases)** A chimpanzee found dead in the forest was eaten by people hunting for food. Eighteen people who were involved in butchering the animal became ill. Ten other cases occurred in their family members.
- **Gabon, 1996-97 (Zaire ebolavirus, 60 cases)** The index case was a hunter who lived in a forest camp. A dead chimpanzee found in the forest at the time was infected with Ebola virus.

# Ebolavirus emergence in Guinea



# Human-human transmission

- Contact with infected blood or body fluids (urine, saliva, sweat, feces, vomit, breast milk, semen) from someone who is sick or has died
- Contact with contaminated objects (needles, syringes)
- Not by insects, water, food, or aerosol



# Host entry

- Mucosal surfaces
- Breaks or abrasions in skin
- Parenteral (e.g. contaminated needles)
- Virus detected in skin, body fluids, nasal secretions, blood, semen

# Ebolavirus disease: Clinical features

- Incubation period 2-21 days (not contagious)
- Early symptoms: fever, headache, muscle pain, diarrhea, vomiting, stomach pain
- Peak illness: rash, hemorrhage, convulsions, severe metabolic disturbances, diffuse coagulopathy

# **Clinical features: Multisystem involvement**

- Systemic (prostration)
- Gastrointestinal (anorexia, nausea, vomiting, abdominal pain, diarrhea)
- Respiratory (chest pain, shortness of breath, cough)
- Vascular (conjunctival injection, postural hypotension, edema)
- Neurological (headache, confusion, coma)



# Pathogenesis

- Extensive necrosis in parenchymal cells of many organs (liver, spleen, kidney, gonads)
- Broad cell tropism: Monocytes, macrophages, dendritic cells, endothelial cells, fibroblasts, hepatocytes, adrenal cortical cells, epithelial cells
- Elevation of liver enzymes, shock (adrenal)
- Massive lymphocyte death but not infected

# Immunopathogenesis

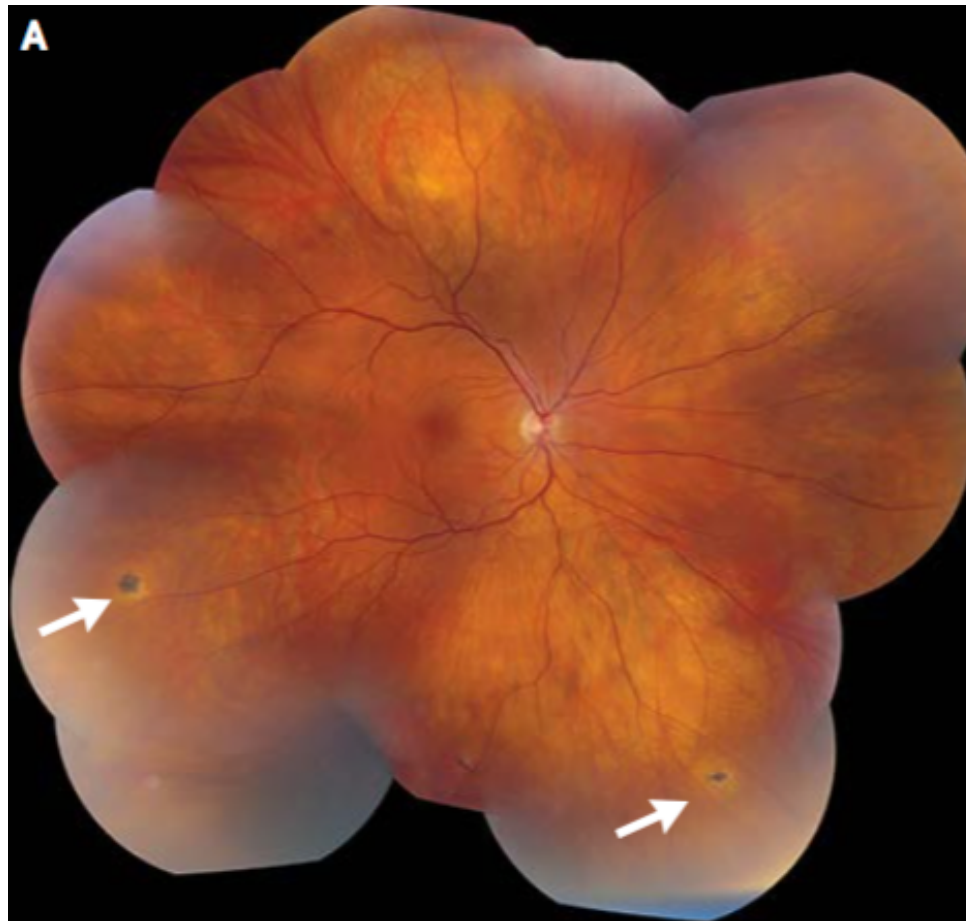
- Many inflammatory mediators produced, especially by infection/activation of monocytes/macrophages
- Imbalanced cytokine production => disease
- Impairment of vascular and coagulation systems

# Case fatality ratio

- 30-90% case fatality ratio in Africa
- Inapparent infections?
- The effect of treatment

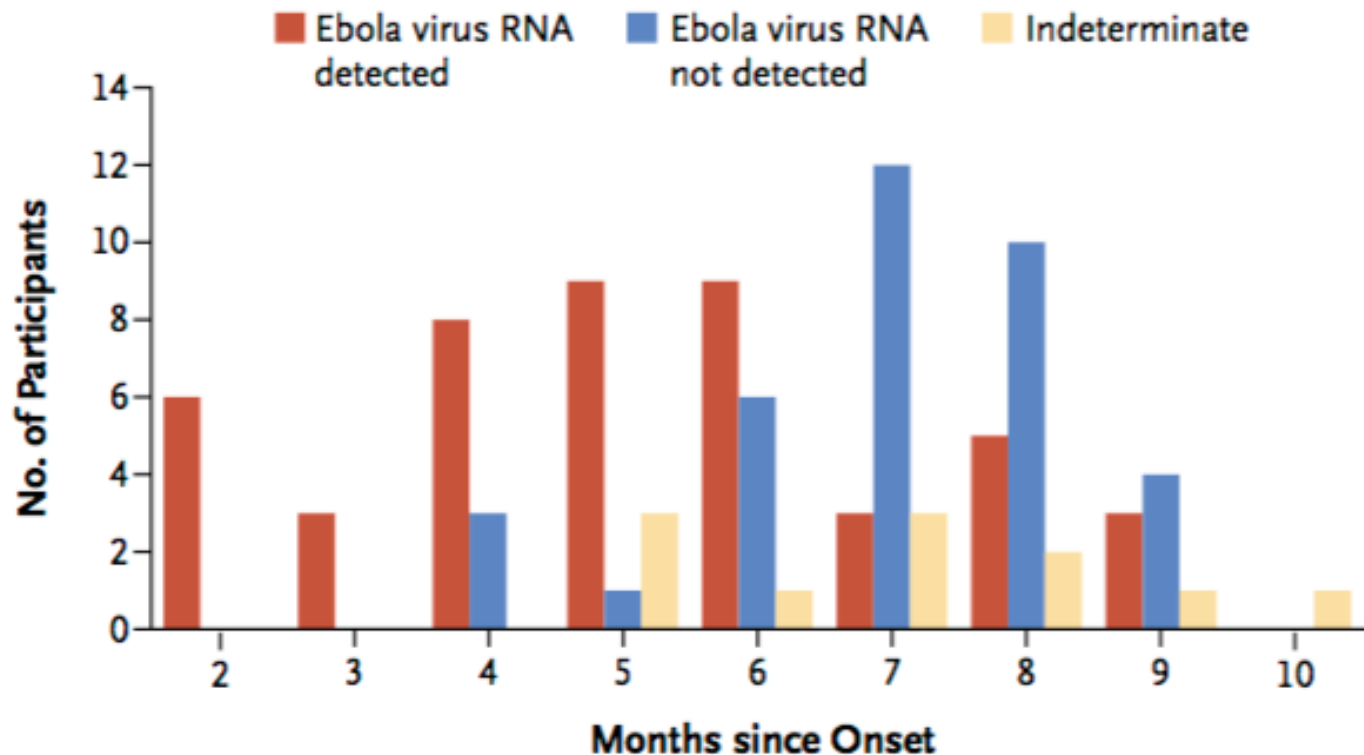
# An acute infection?

*Persistence of Ebolavirus in ocular fluid during convalescence  
9 weeks after clearance of viremia*



# An acute infection?

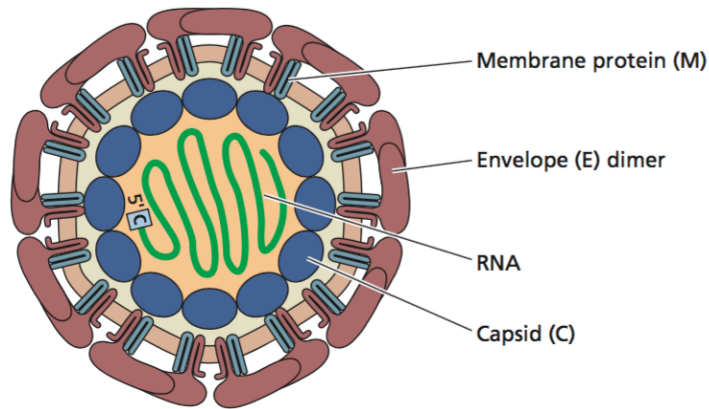
*Evidence of sexual transmission*  
*Presence of viral genome in semen*



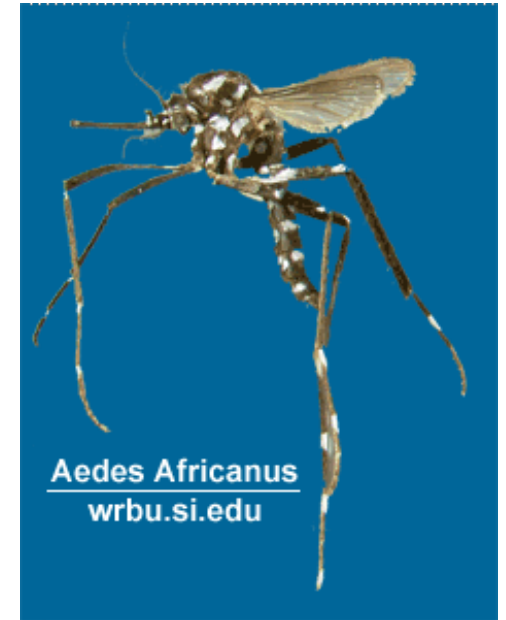
46/93 men (49%)

# What have we learned?

- Every infectious disease is a global problem
- Ebolavirus vaccines have been ready for clinical trials for some time
- What other viruses should we be preparing for?



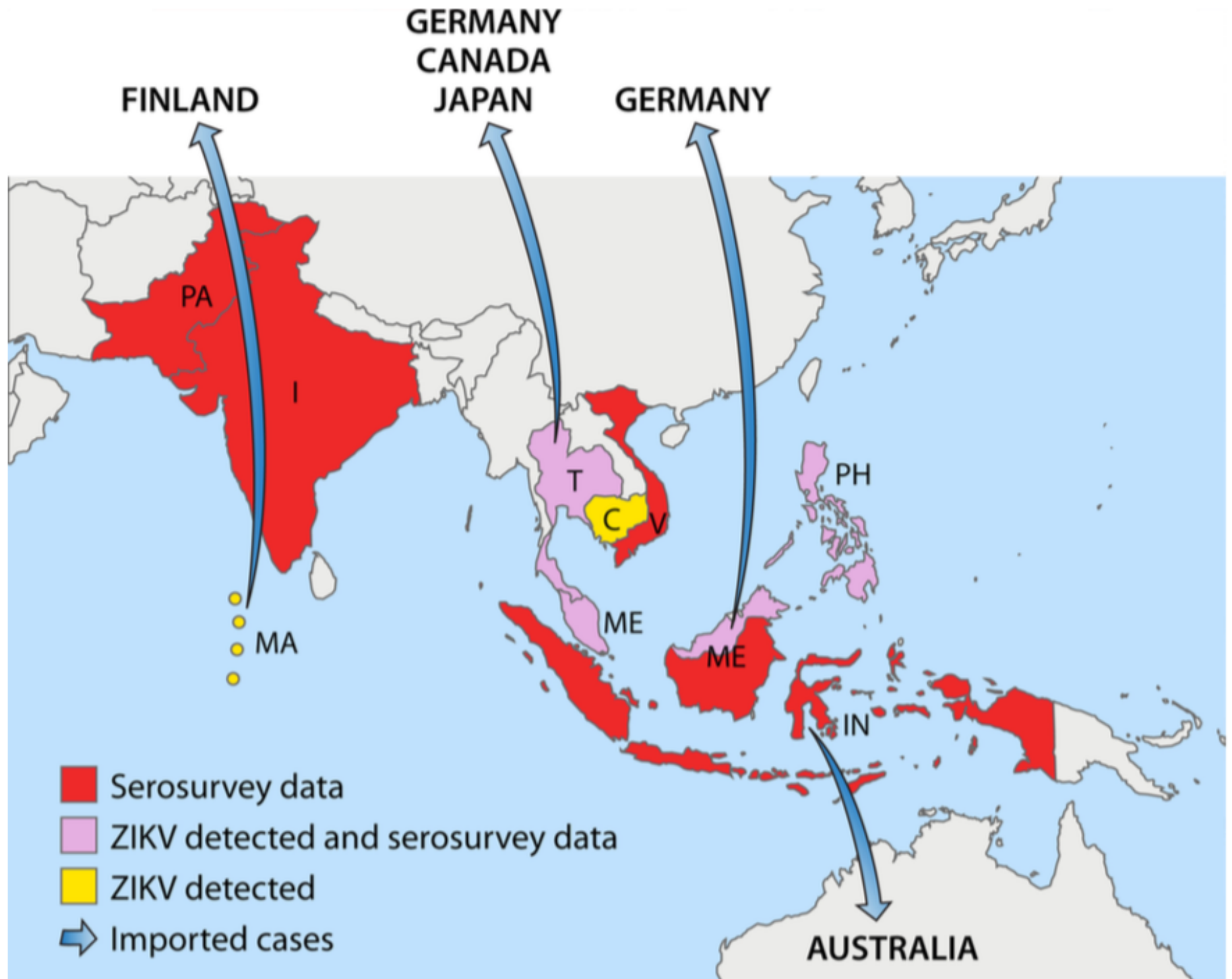
# Zika virus



- 1947, Zika Forest, Uganda
- Isolated from *A. africanus*
- Virus isolated from humans, Nigeria, 1954
- Serological detection throughout Africa, Asia but no outbreaks
- <20 cases over next 50 years



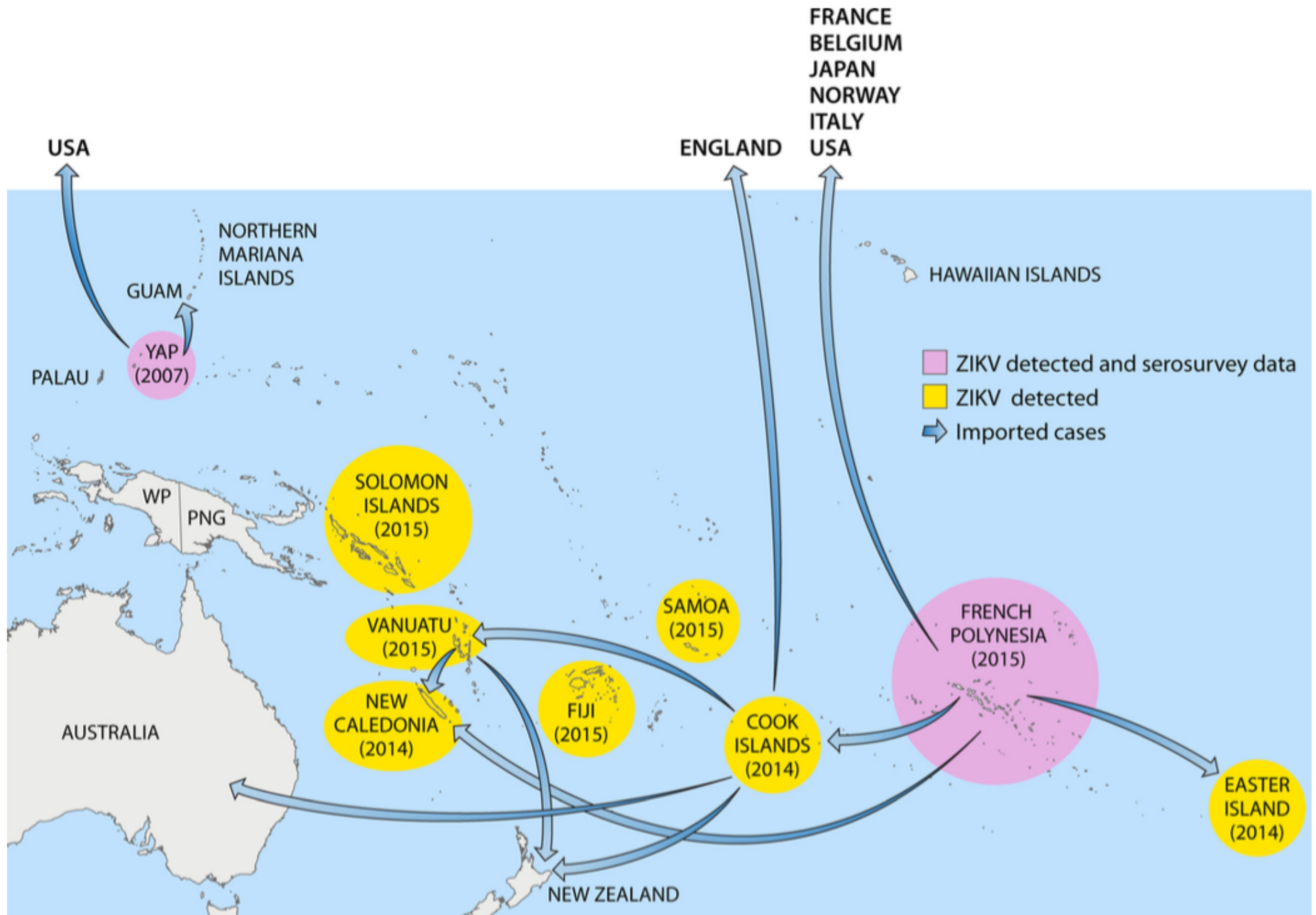




# Zika virus

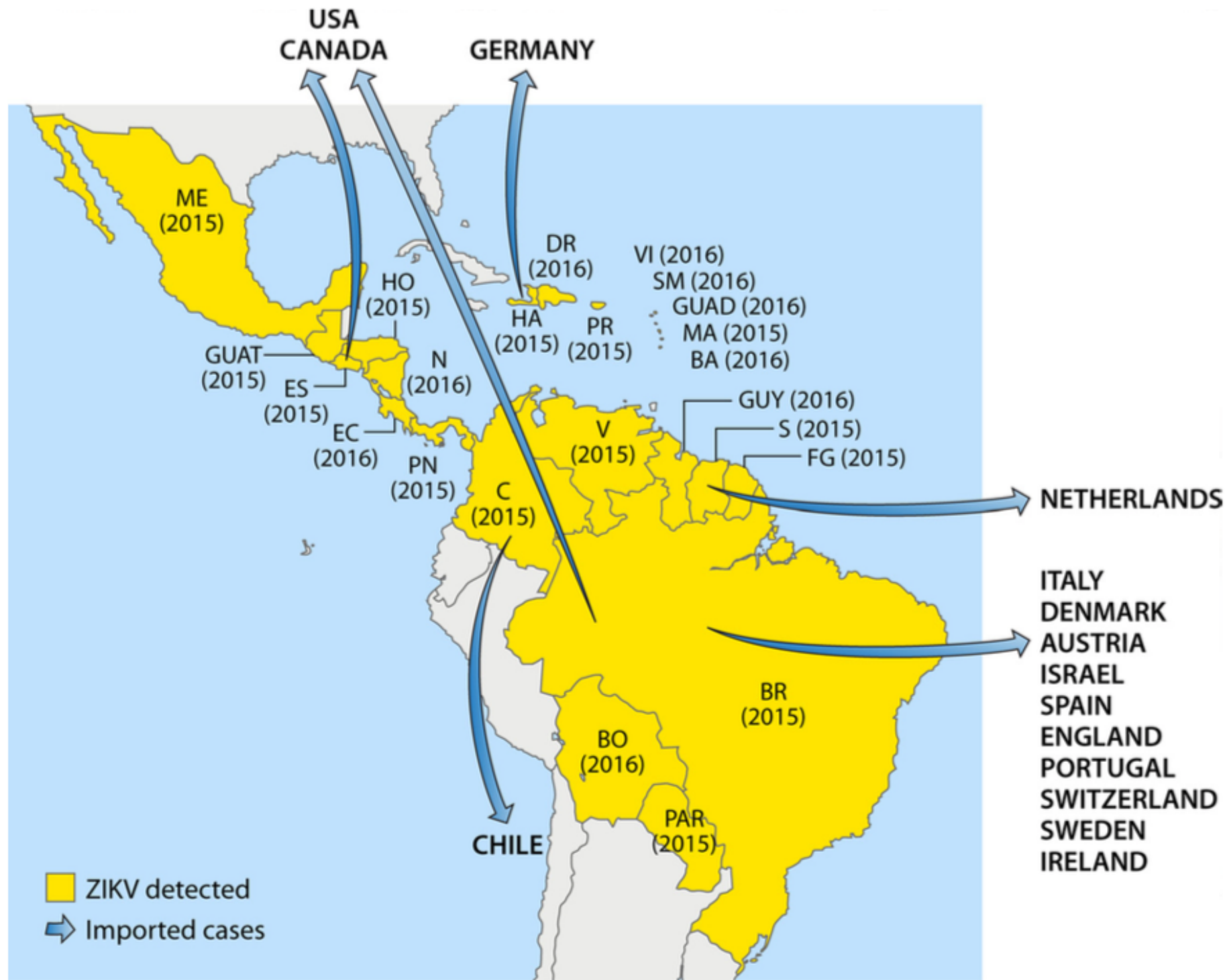
- 2007 outbreak on Yap Island (5,005/6,892 residents) first outside Africa, Asia
- 2013 outbreak French Polynesia (30,000, 11% of population)
- 2014 New Caledonia (1,400, 0.8%), Cook Islands (905), Easter Island (50)
- 2015 Vanuatu, Solomon Islands, Samoa, Fiji

# Zika virus in the Pacific

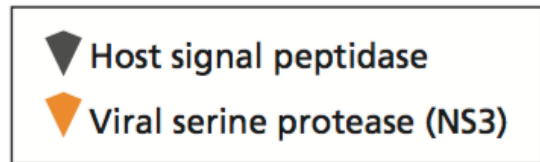
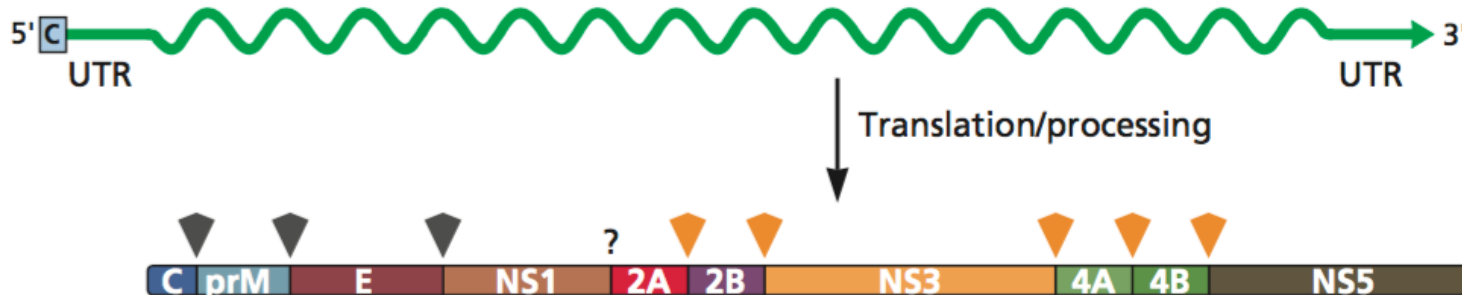
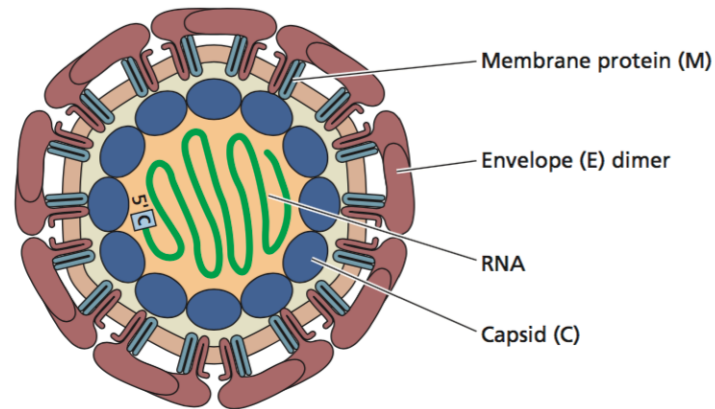


# Zika virus in the Americas

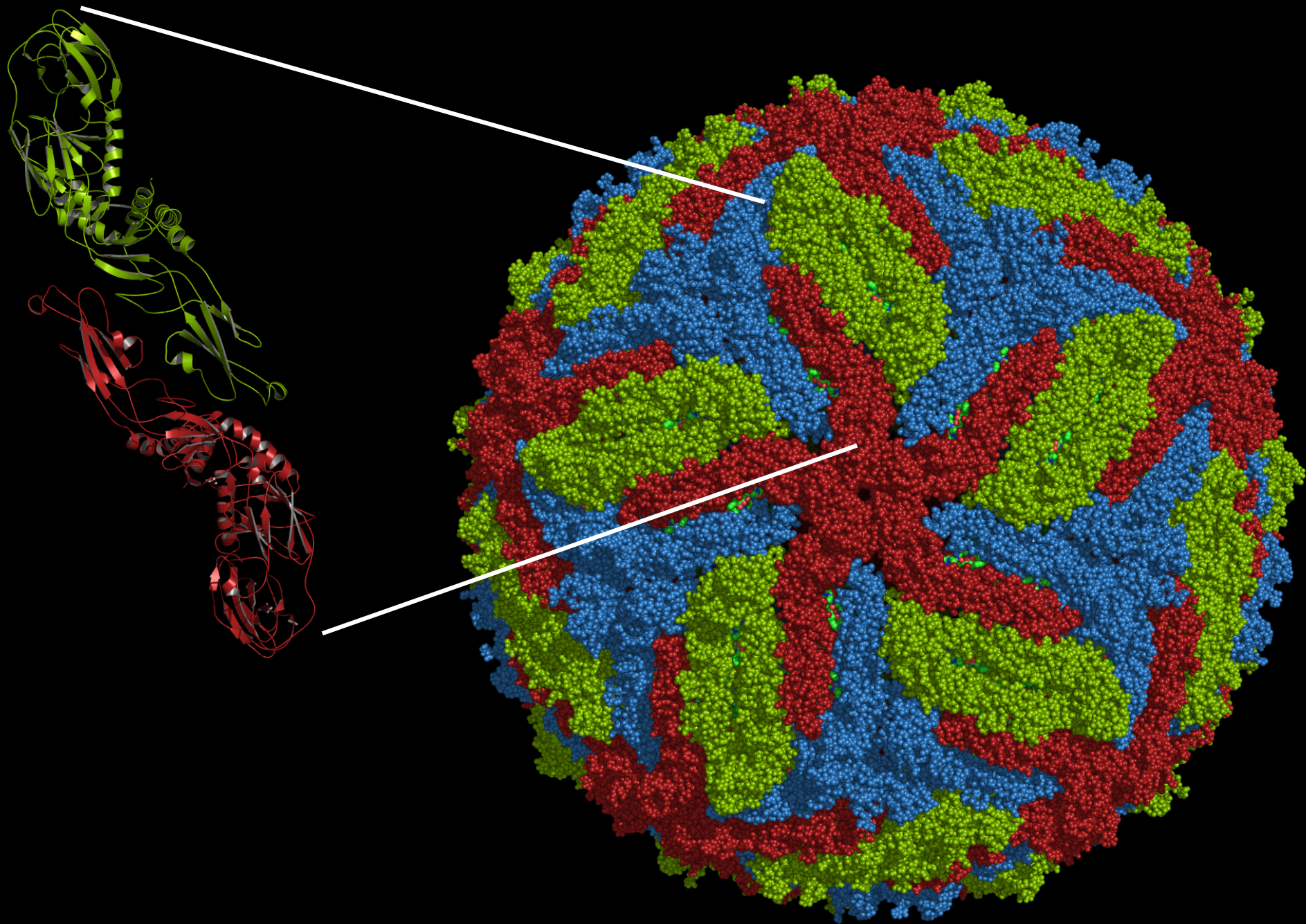
- First cases in Americas Brazil, 2015, Asian genotype
- Introduction correlates with increase in air travel from endemic areas
- Predicted 4 million cases, end of 2016
- Has now spread extensively (52 countries)



# Zika virus

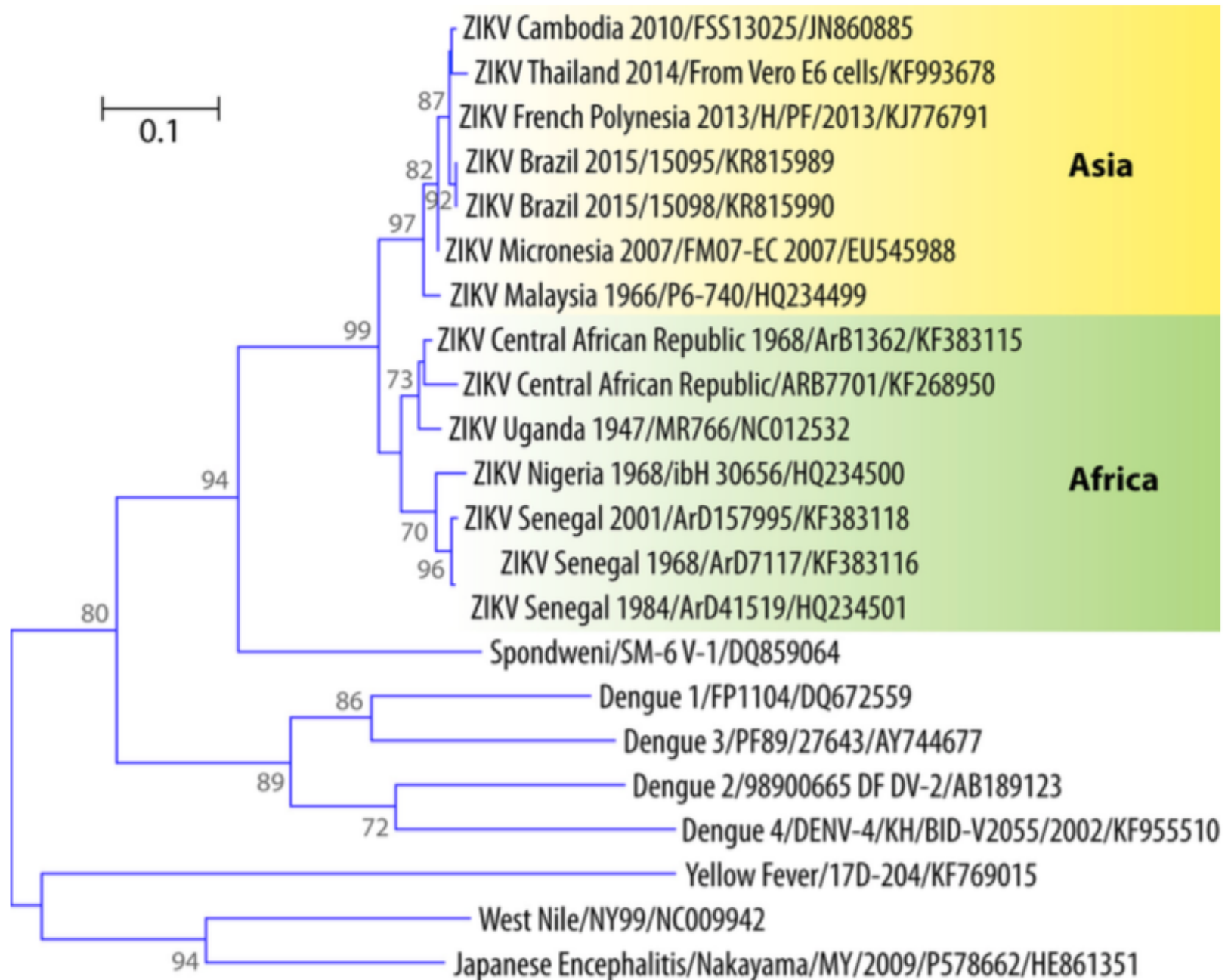






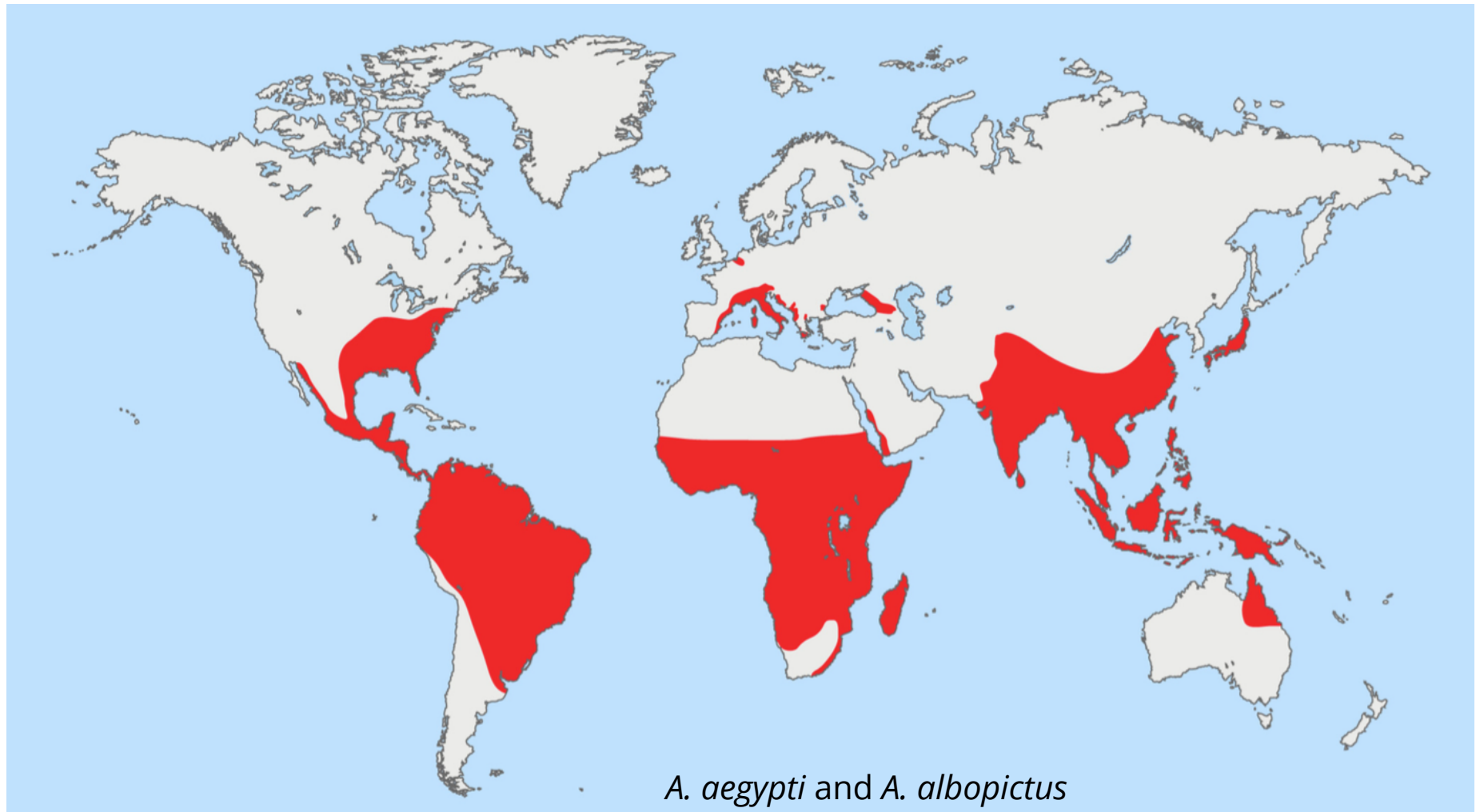


# Zika virus - Asian and African lineages



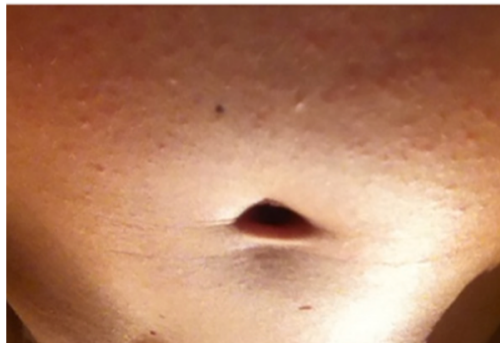
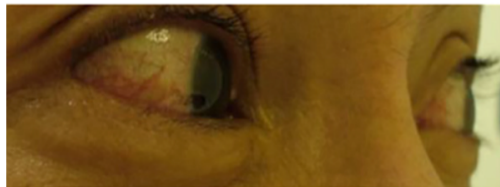
# Zika virus

- Vector: *Aedes* spp
- Reservoir - primates (Old World & humans)



# Zika virus

- Disease: rash, fever, joint pain, conjunctivitis, headache (similar to dengue, chikungunya)
- Incubation period 2-10 days
- 1 in 5 develop symptoms; 5 day course
- Fatalities rare



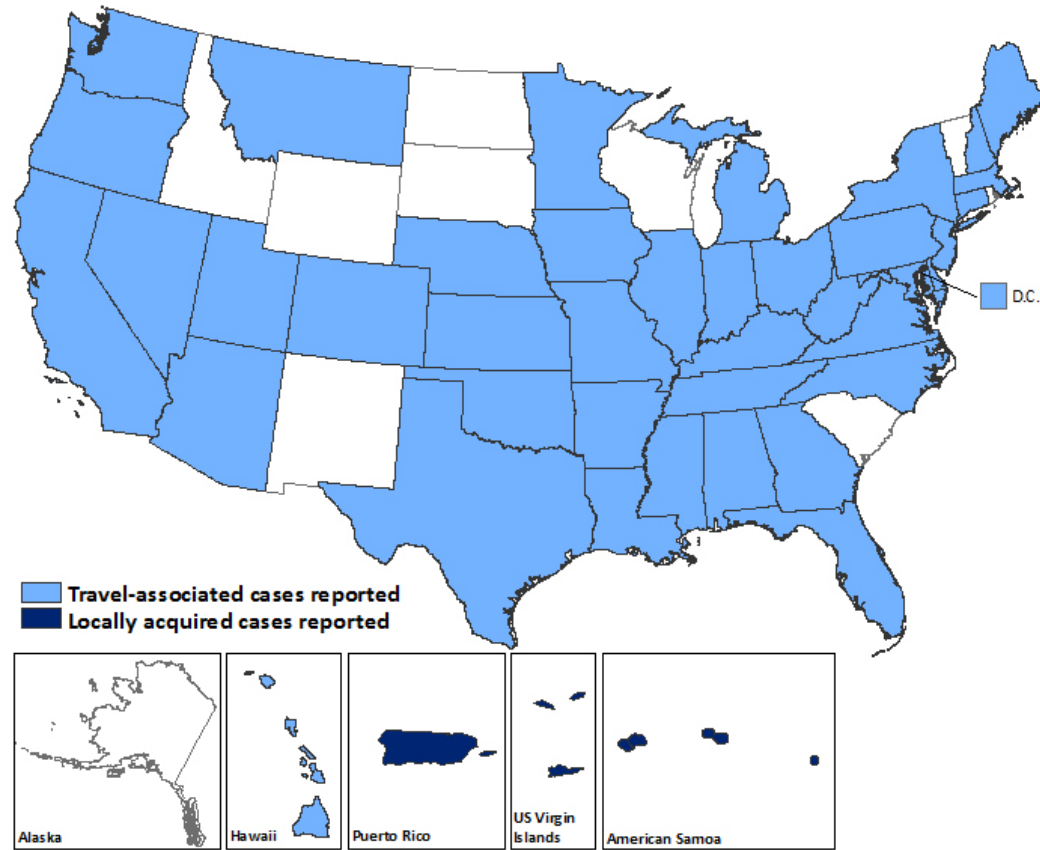
# Zika virus shedding

- Semen
- Urine (PCR) - up to 30 days after symptom onset
- Saliva (more frequently than in blood)
- Blood
- Breast milk
- Except for blood, unknown how virus reaches these sites

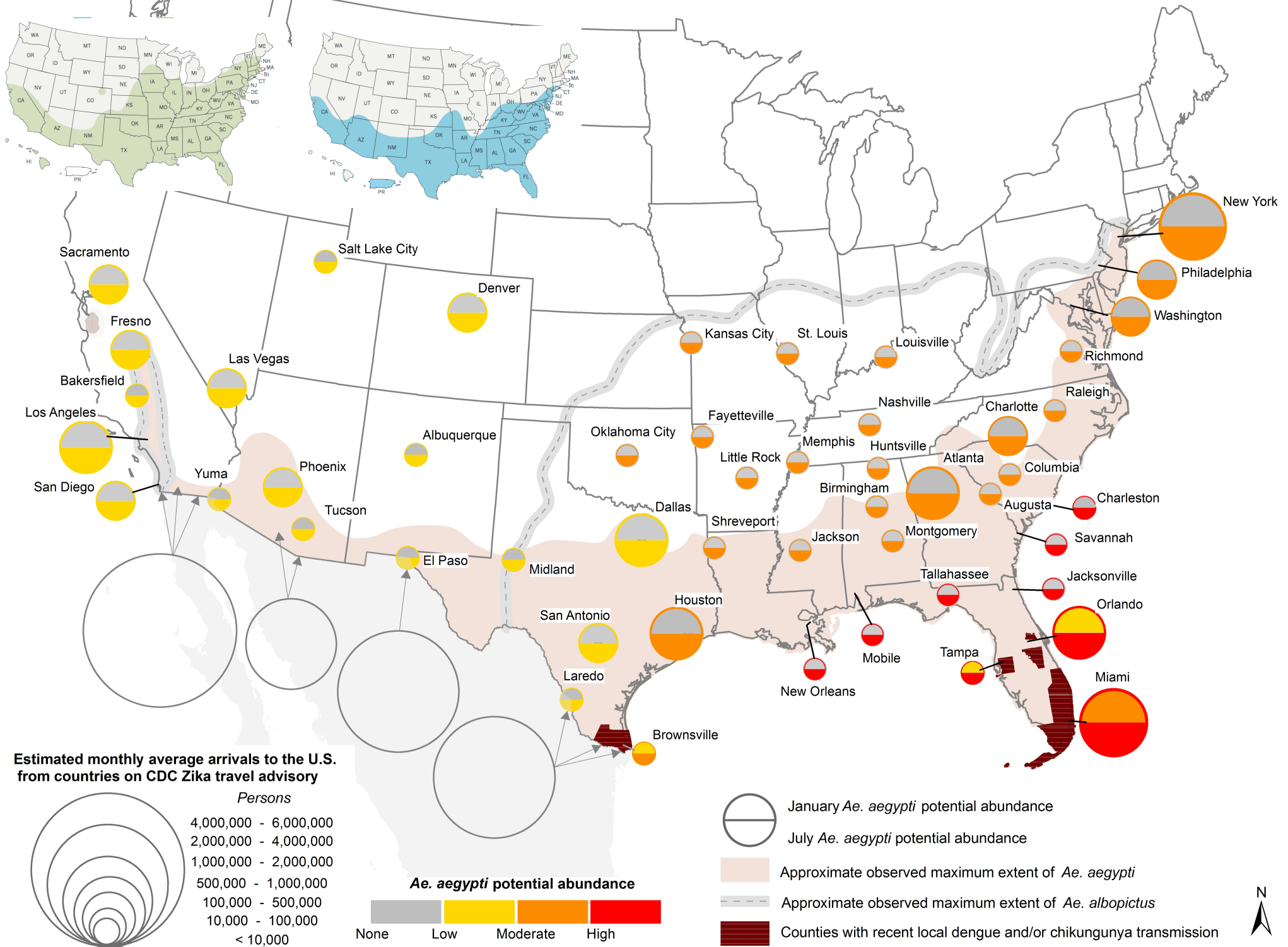
# **Zika possible sexual transmission**

- CDC claims 7 sexually transmitted infections in US (of 358 travel-related), M-F and 1 M-M
- Transmission by close person-person contact not ruled out - e.g. saliva, urine
- Unlikely to be major cause of outbreaks, but CDC advises against pregnant women having unprotected sex with potentially infected partners
- Not known how long virus persists in semen, urine, saliva - need more studies

# Zika virus in the US



- 358 travel-associated cases (31 in pregnant women)
- 0 locally vector-acquired cases
- US territories: 471 locally acquired cases (PR, US VI, American Samoa)





# Zika in the US

- Minimal local US spread of dengue virus and chikungunya virus, vectored by *Aedes* (FL, TX)
- 1793 yellow fever epidemic, Philadelphia
- Screens, A/C, population density
- West Nile spread across US in 1999 - different mosquito (*Culex* sp), bird reservoir

SPECIAL REPORT

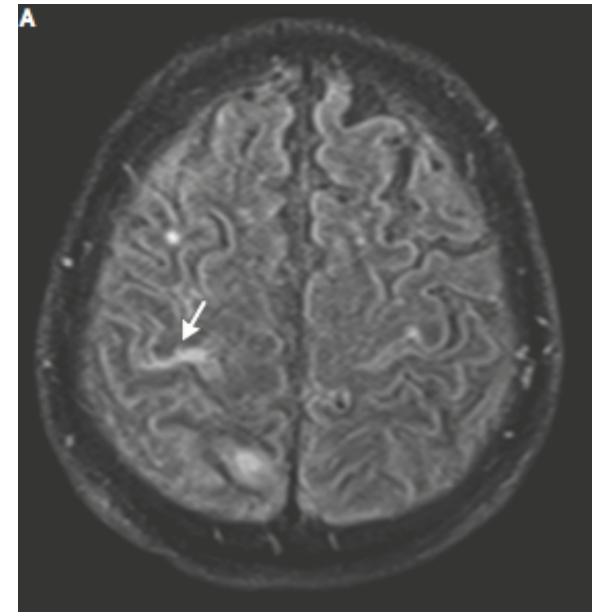
# **Zika Virus and Birth Defects — Reviewing the Evidence for Causality**

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

“On the basis of this review, we conclude that a causal relationship exists between prenatal Zika virus infection and microcephaly and other serious brain anomalies.”

# Other conditions associated with Zika virus infection

- Guillain-Barré Syndrome (post-infection autoimmune neuropathy; weakness, paralysis, death)
- Acute myelitis (virus in CSF)
- Meningoencephalitis (virus in CSF)



# How common are host range jumps?

- Dead end: Very common
- Those that produce sustaining transmission: Rare
- Can we predict them? No
- But we can know what is out there, and react (preparedness)