



# VIROLOGY LIVE

WITH VINCENT RACANIELLO

## Emerging viruses

Session 22

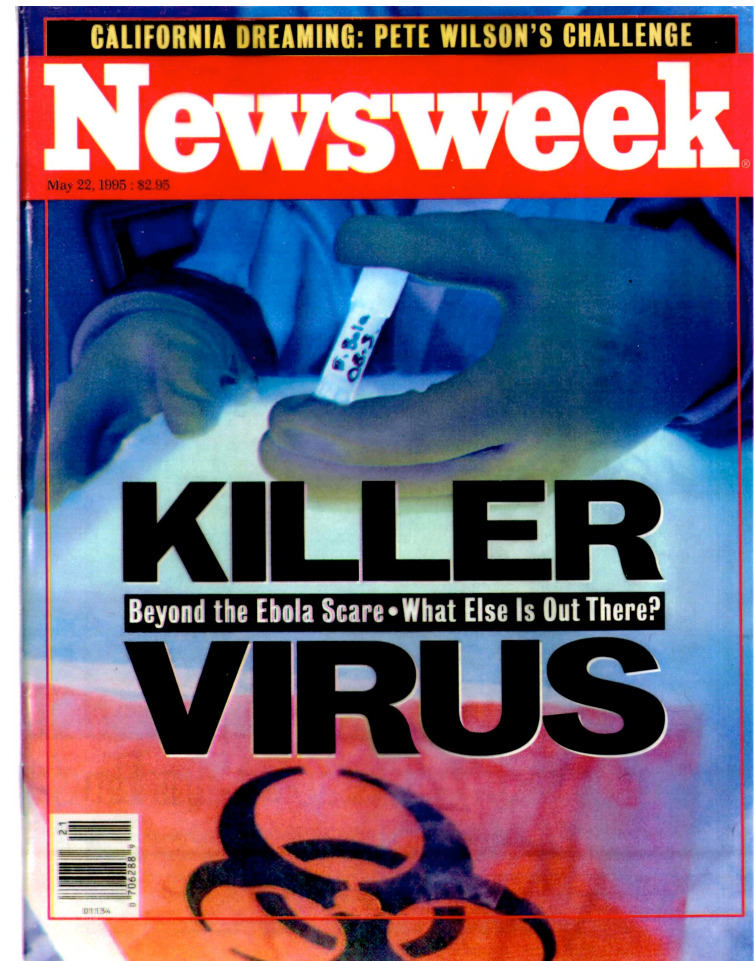
Virology Live

Fall 2021

*Nothing endures but change*  
HERACLITUS

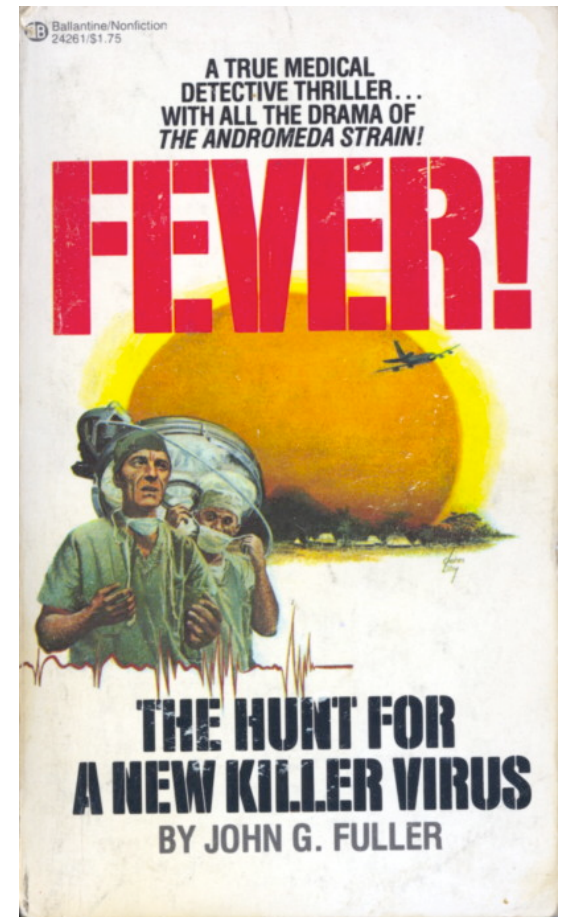
## Emerging viruses

- *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
- Only recently have we become good at detecting emerging viruses

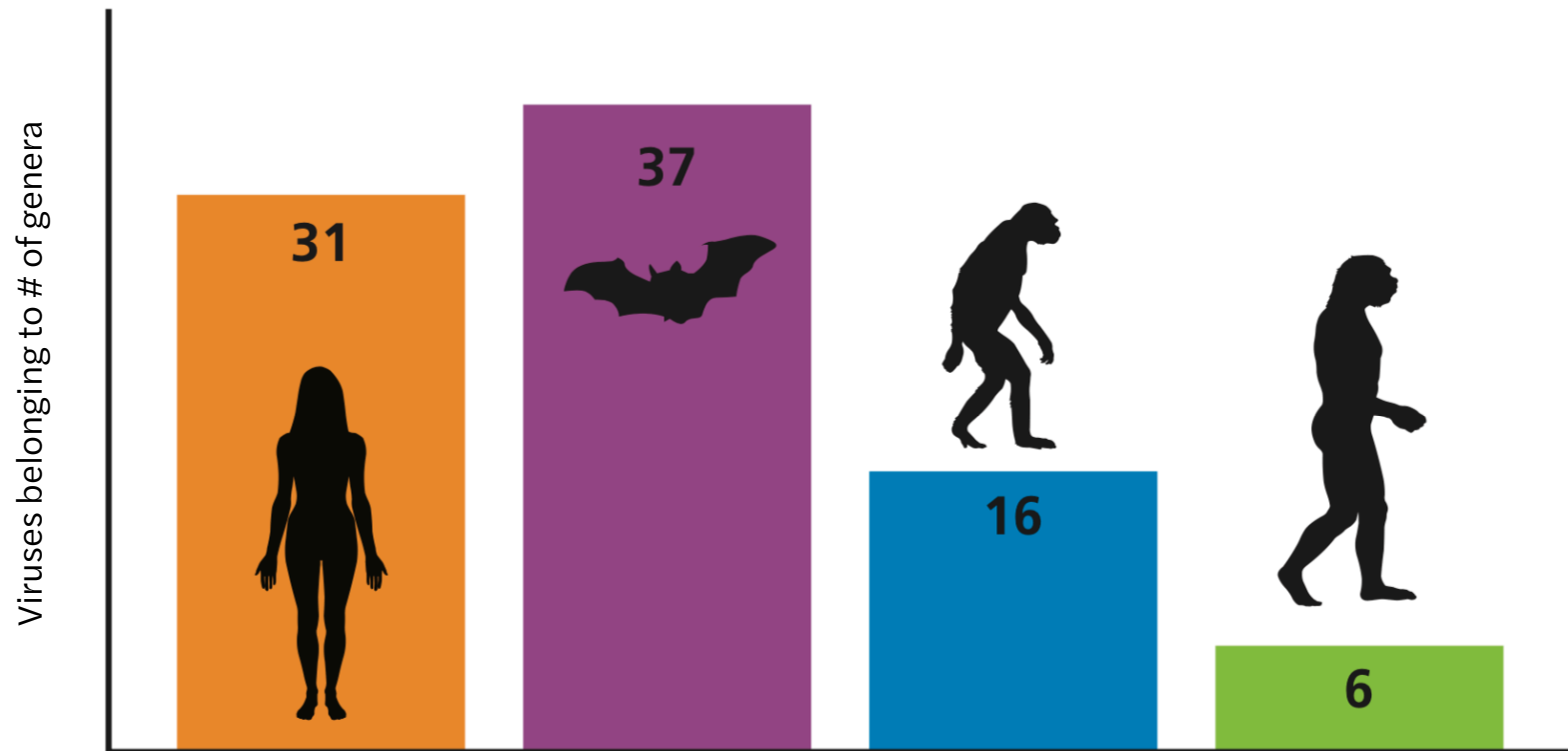


## Emerging viruses

- 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, SARS-CoV-2)
- Often cross-species infection cannot be sustained (e.g. Ebolavirus from bats to humans, MERS-CoV from camels to humans)



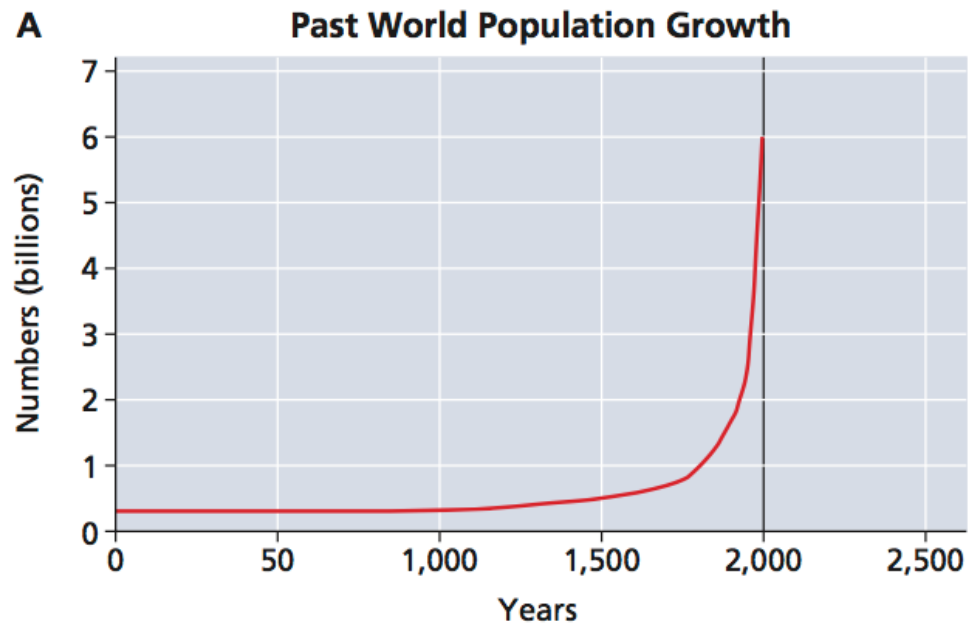
# Ancestral origins of human pathogens





# 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*



# Ecological and anthropogenic activities that promote virus emergence

*Human continuously devise new ways to encounter viruses*



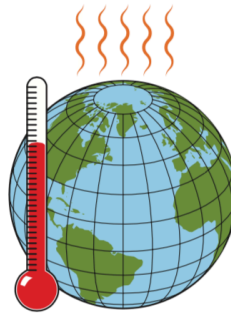
Dams and water impoundments  
Irrigation  
Massive deforestation  
Rerouting of wildlife migration patterns  
Wildlife parks  
Long-distance transport of livestock and birds



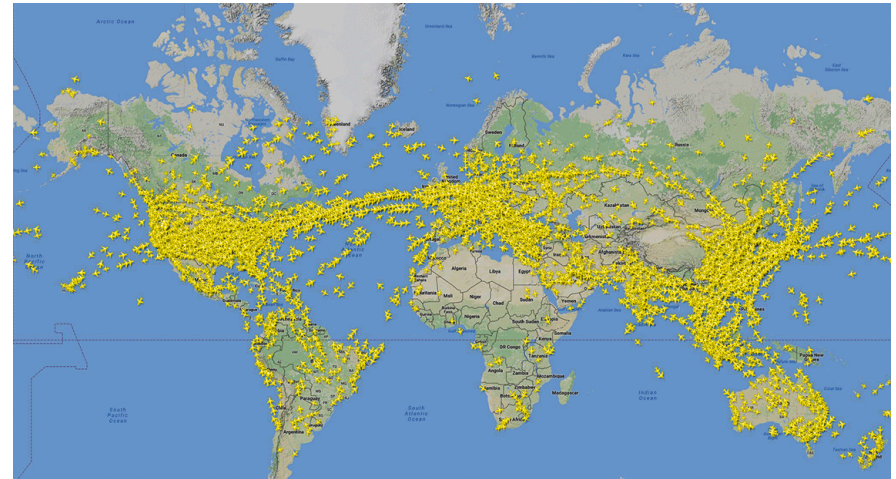
Blood transfusion  
Xenotransplantation  
Societal changes with regard to drug abuse and sex



Air travel  
Uncontrolled urbanization  
Day care centers  
Hot tubs  
Air conditioning  
Millions of used tires

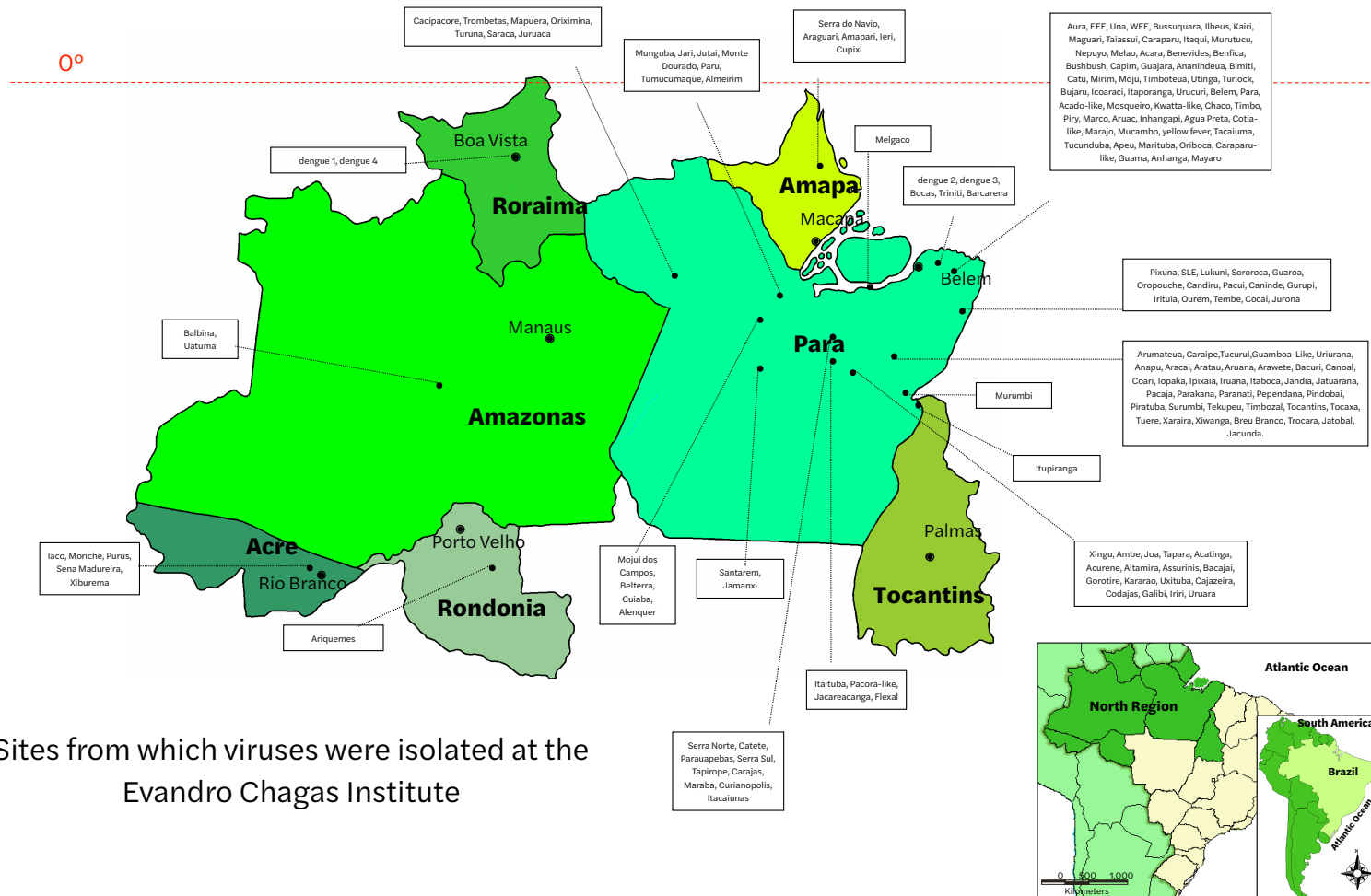


Climate change  
Natural disasters









# The Amazon North Region of Brazil

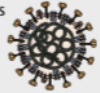





*Home to 183 Arthropod-borne and Other Vertebrate Viruses*



Sites from which viruses were isolated at the  
Evandro Chagas Institute

# Factors that led to emergence of new viruses

Virus	Family	Factors leading to emergence
Dengue virus 	<i>Flaviviridae</i>	Urban population density; open water storage favoring mosquito breeding (e.g., millions of used tires)
Ebola virus 	<i>Filoviridae</i>	
Hantaan virus 	<i>Bunyaviridae</i>	
Hendra virus 	<i>Paramyxoviridae</i>	
Human immunodeficiency virus type 1 	<i>Retroviridae</i>	
Influenza virus 	<i>Orthomyxoviridae</i>	

Virus	Family	Factors leading to emergence
Middle East respiratory syndrome (MERS) Coronavirus 	<i>Coronaviridae</i>	Camel husbandry, contact with humans
Nipah virus 	<i>Paramyxoviridae</i>	
Severe acute respiratory syndrome (SARS) coronavirus 	<i>Coronaviridae</i>	Open-air meat markets
Sin Nombre virus 	<i>Hantaviridae</i>	
West Nile virus 	<i>Flaviviridae</i>	Mosquito transmission from bird reservoir; global travel
Zika virus 	<i>Flaviviridae</i>	

SARS-CoV-2

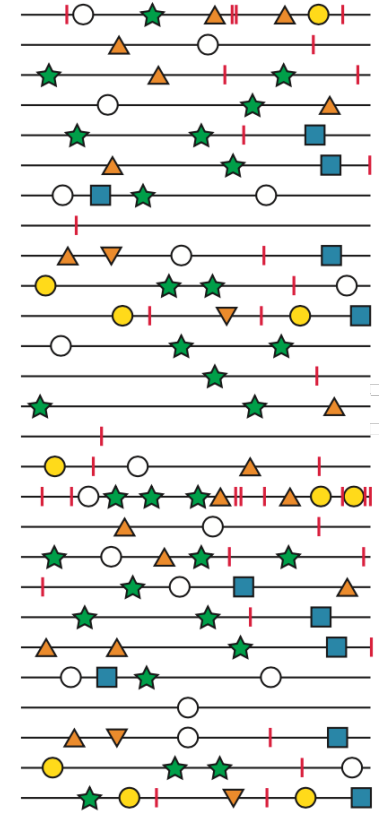
*Coronaviridae*

Open-air meat markets?

# Roles of Evolution



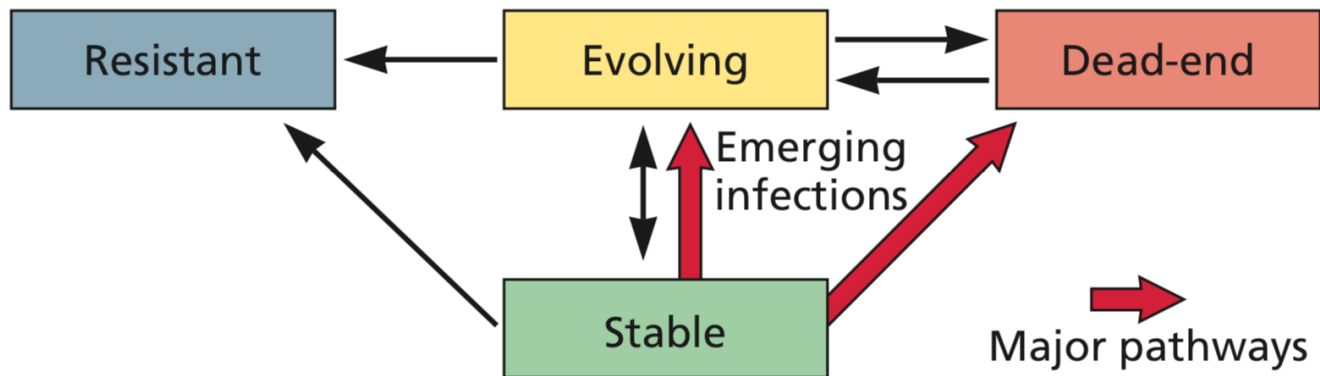
- Leads to the biodiversity of pathogens existing in nature (*quasispecies*)
- Adaptation to new hosts and environments (through variation and selection)



**Question break**

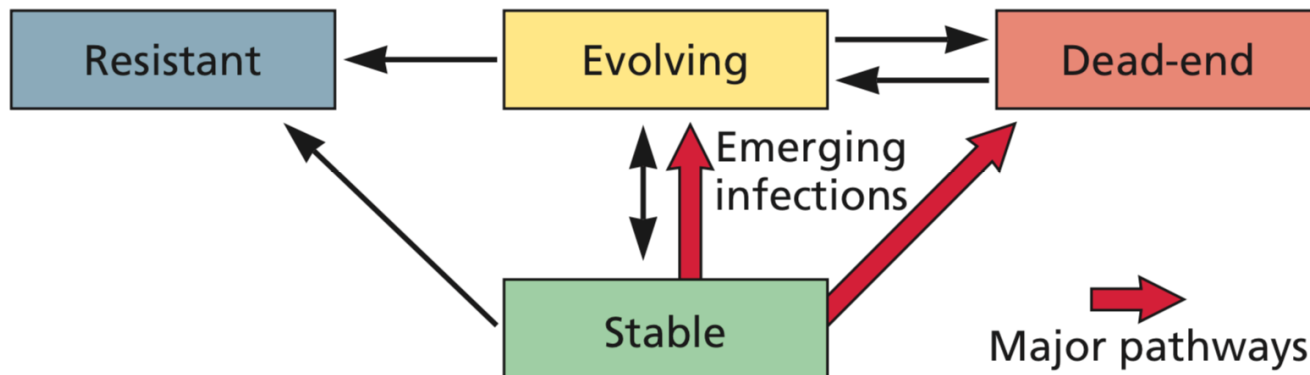


# General categories of interactions between hosts and viruses



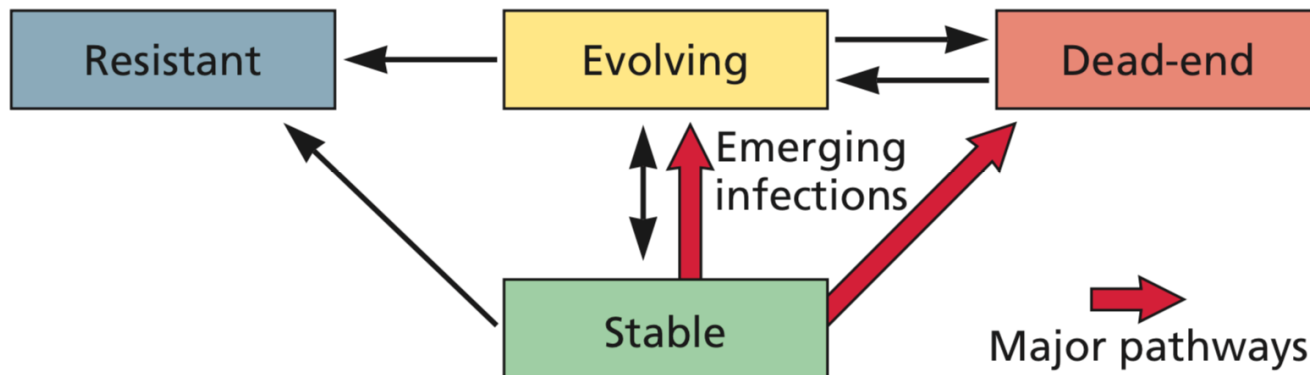
- Stable: maintains virus in ecosystem
- Evolving: passage of virus to naive population (same or different host)
- Dead-end: one way passage to different species
- Resistant host: infection blocked

## Stable host-virus interactions



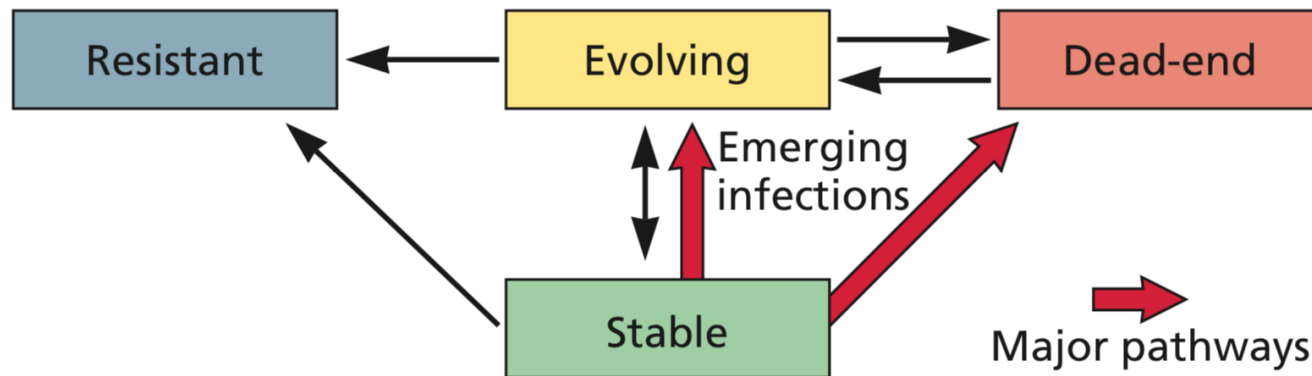
- Both participants survive and multiply
- Some are effectively permanent
  - *Humans are sole natural host for measles virus, herpes simplex virus, HCMV, smallpox*
- May include infection of more than one species
  - *Influenza A virus, flaviviruses, togaviruses*

## 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 myxoma virus to eliminate rabbits into Australia

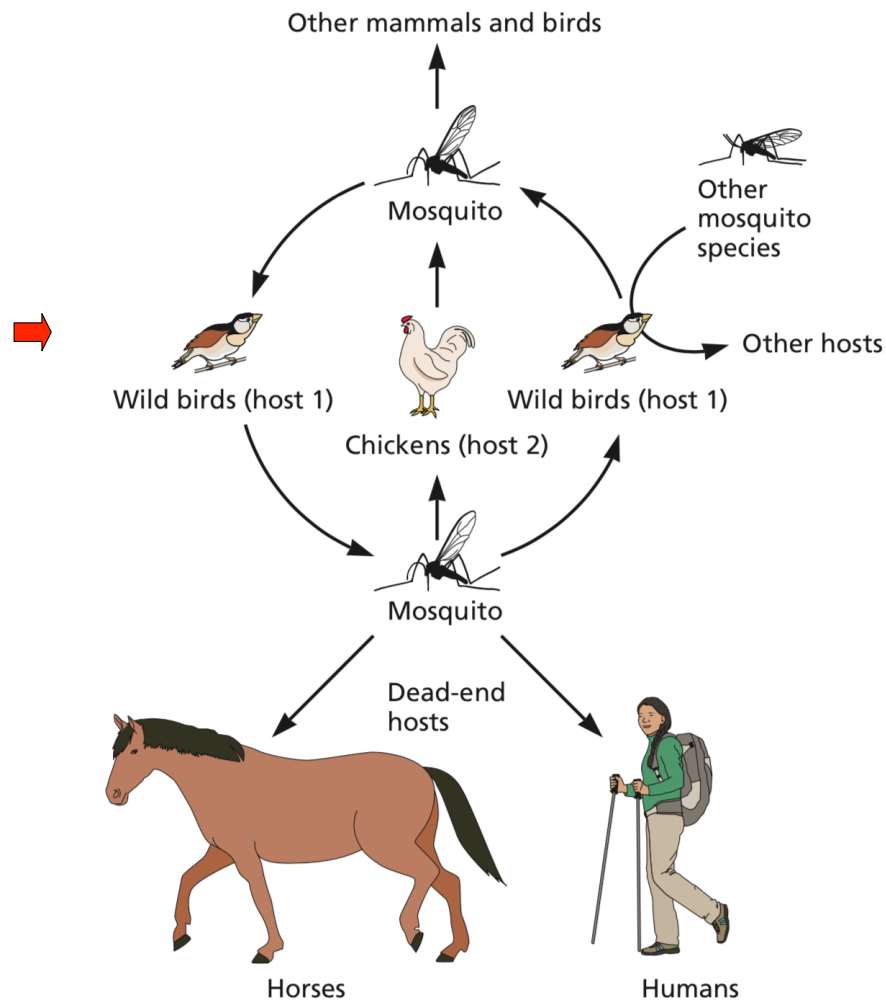
## Dead-end interaction



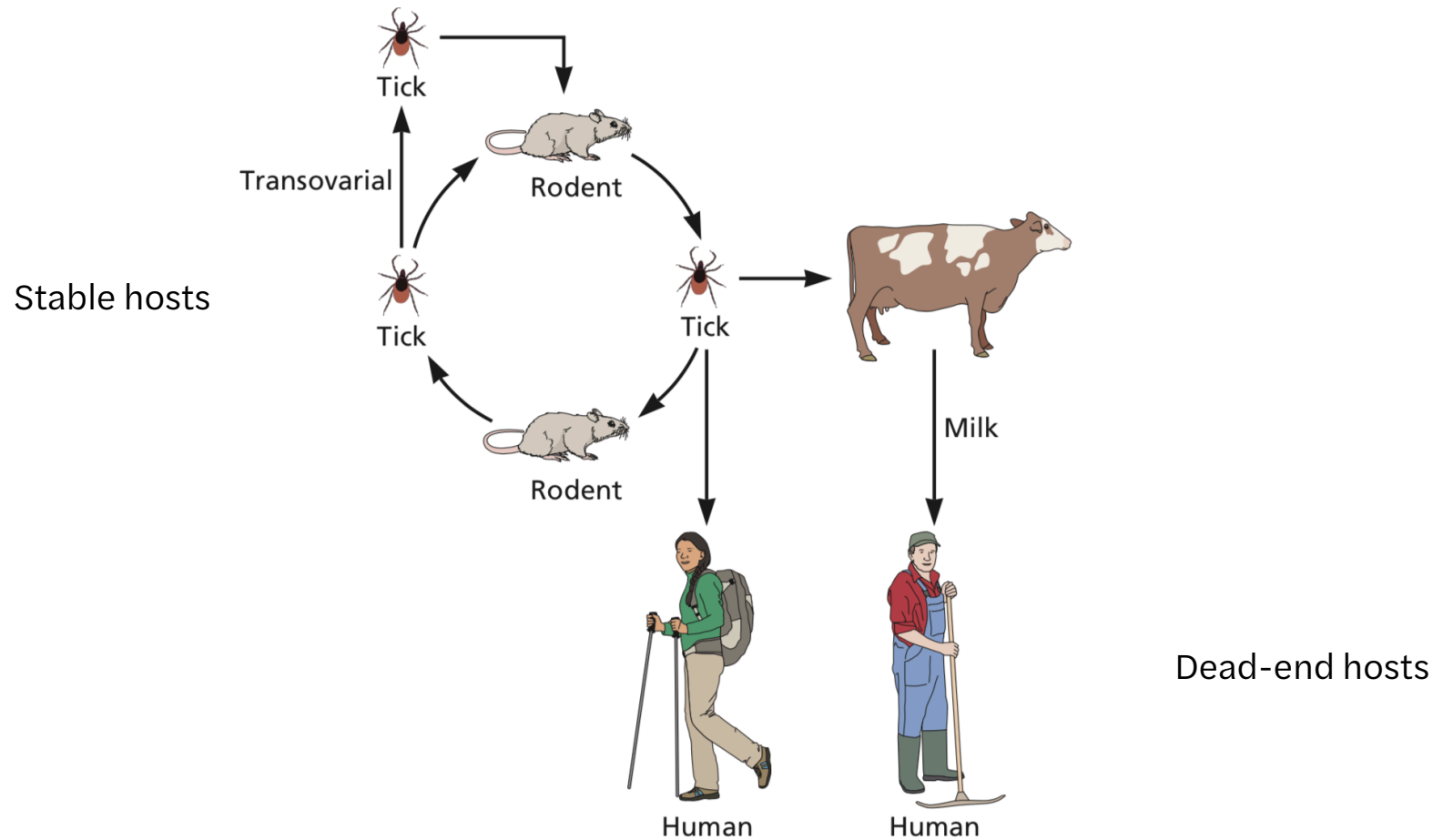
- Frequent outcome of cross-species infection
- No sustained transmission from new infected host to others of the same species
- Ebolavirus: humans, chimps, gorillas
- Influenza H5N1 virus
- Contribute little to the spread of the natural infection

# Examples of stable and dead-end host-virus relationships

Stable host-virus interactions



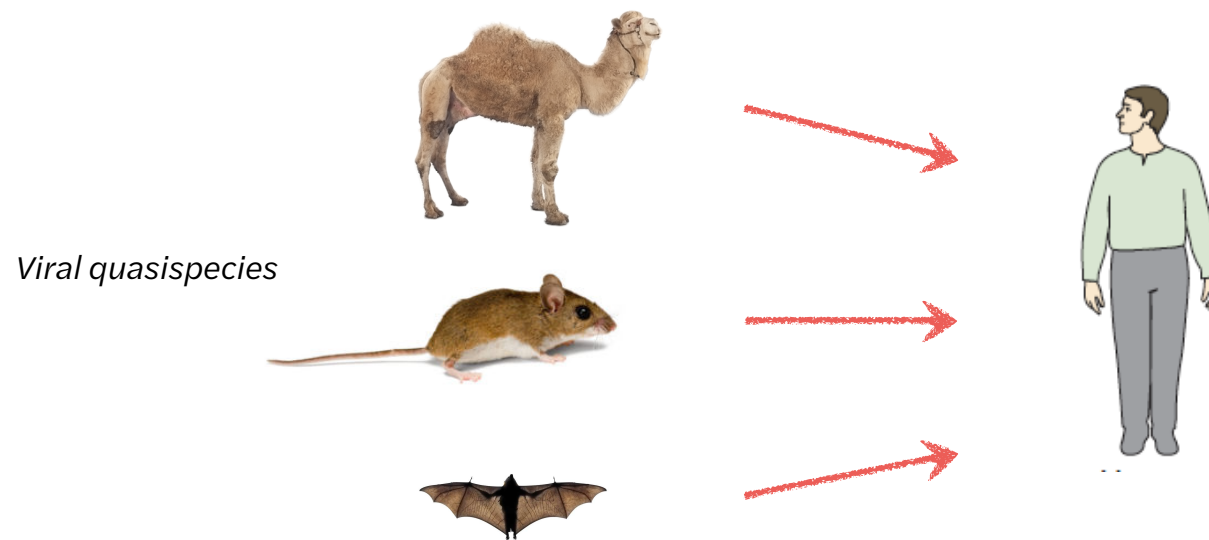
# Stable and dead-end relationships: tick-borne encephalitis virus





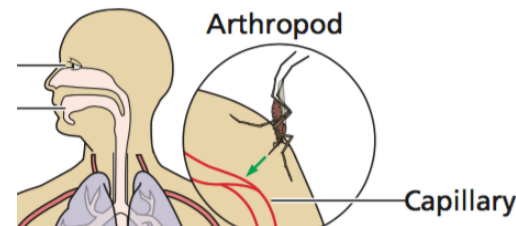
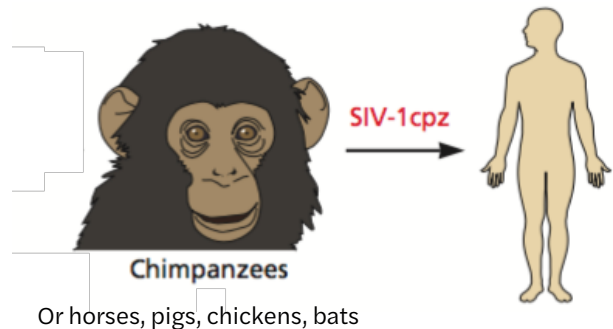
# Emerging infections: Two steps

- Encounter
- Establishment and dissemination



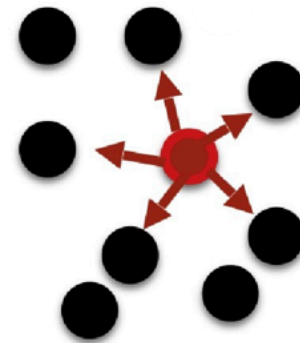
## Encountering new hosts

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

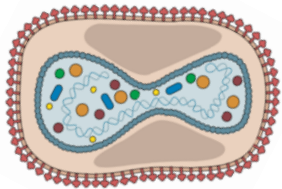


## Expanding viral niches

- 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)

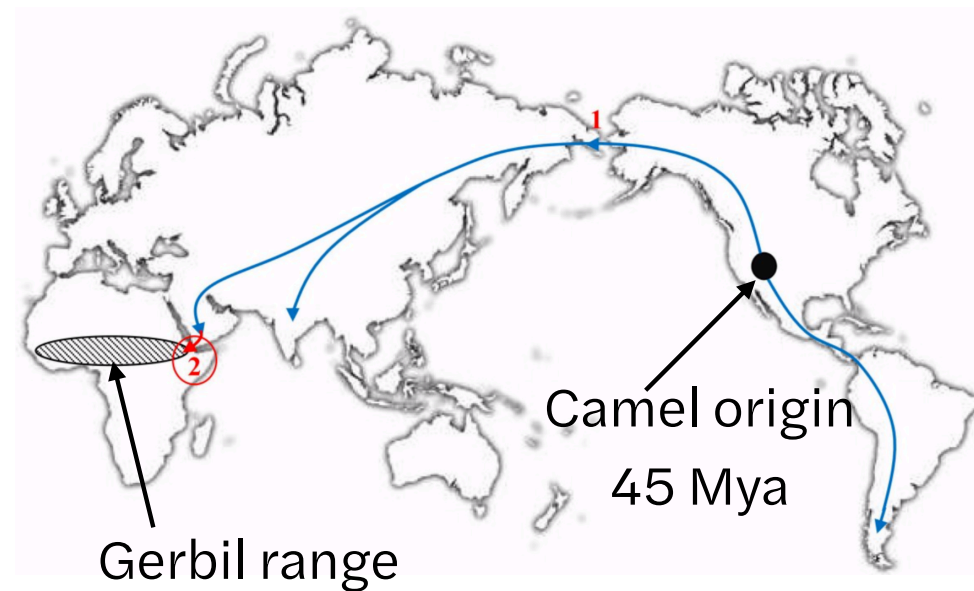


**Question break**



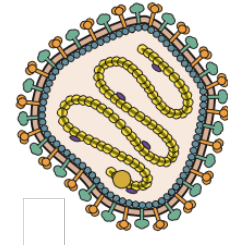
## Origins of smallpox virus

- Phylogenetic analysis of related viruses and their hosts suggests emergence 3000-4000 years ago in East Africa, transmitted from camels
- Camels were introduced to Africa 3500-4500 years ago
- Camels likely infected with a smallpox virus ancestor from gerbils





## Origins of measles virus

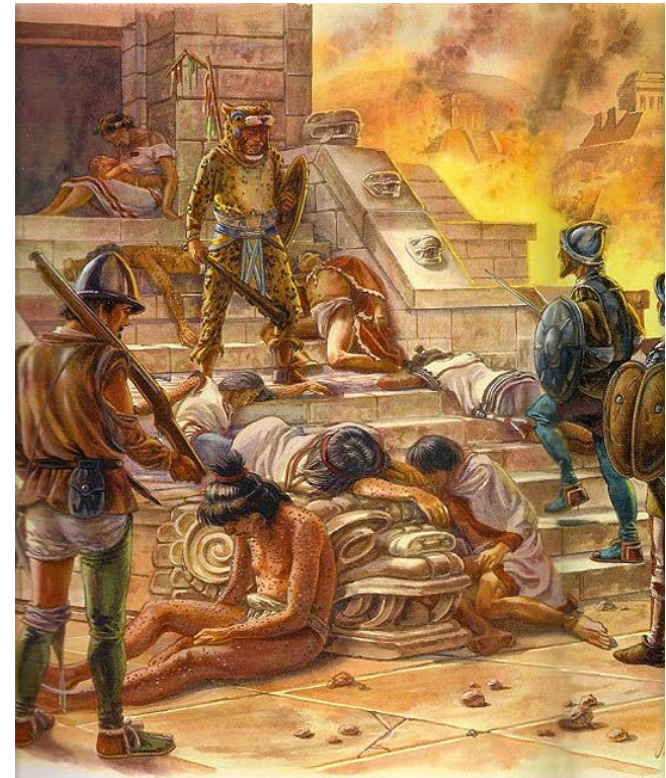


- Measles virus is closely related to rinderpest virus, a bovine pathogen
- Probably evolved from an ancestral rinderpest virus when humans first began to domesticate cattle (11th-12th centuries, 1000-1200)
- Established in the Middle East when human populations began to congregate in cities (MV maintenance requires populations of 250,000-500,000)
- Spread around the world by colonization and migration, reaching Americas in 16th century and destroying native Americans

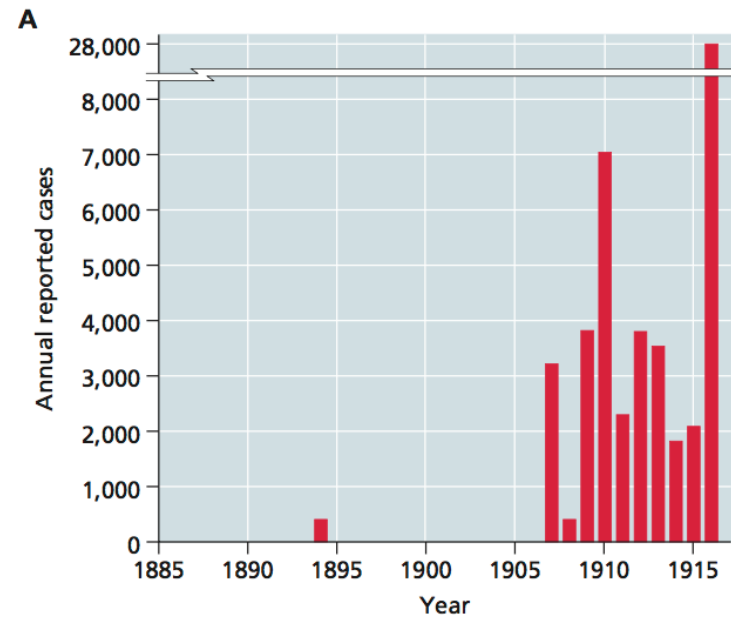


## Diseases of exploration and colonization

- 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
- Known since 4,000 years ago, sporadic cases, stable host-virus relationship

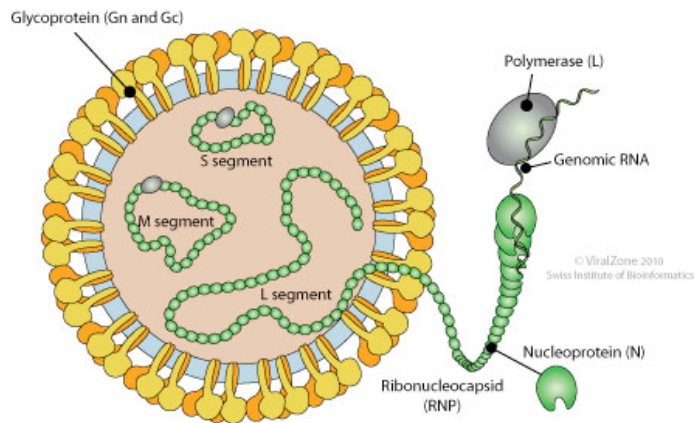
## **Poliomyelitis: A disease of modern sanitation**

- Pre-1900, poliovirus circulated freely and infected most shortly after birth
- Maternal antibodies prevented paralysis
- Improved sanitation delayed infection until later in life = epidemic poliomyelitis
- Had there been genome sequencing in 1908, would the emergence of epidemic polio been blamed on mutation?



# Changing climate and animal populations

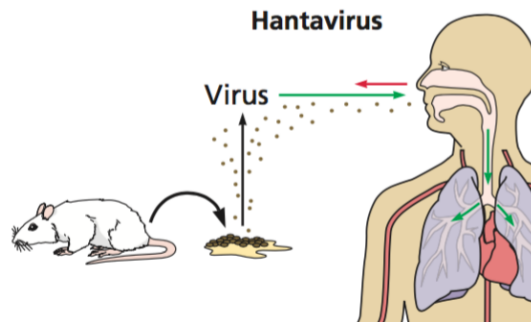
- Hantavirus pulmonary syndrome - first noted in Four Corners area of New Mexico, 1993
- Disease is caused by Sin Nombre virus, endemic in the deer mouse (*Peromyscus maniculatus*, 30% virus positive)
- Originally called Muerto Canyon virus, but residents objected



*Bunyaviridae*

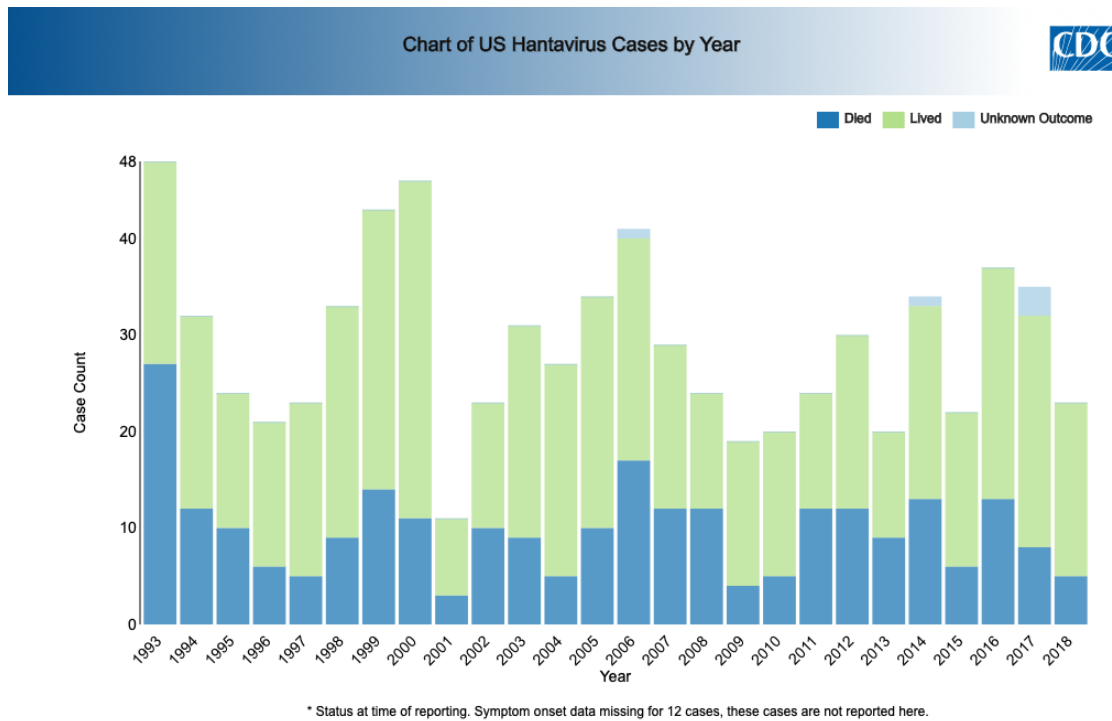
## Changing climate and animal populations

- 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



# HPS by State, January 2018

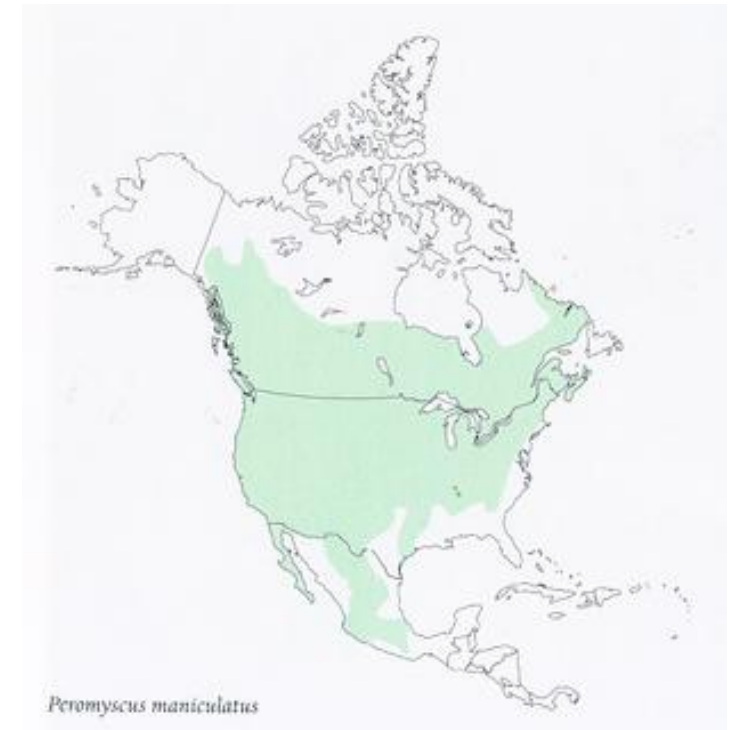
## n=728



<https://www.cdc.gov/hantavirus/surveillance/index.html>

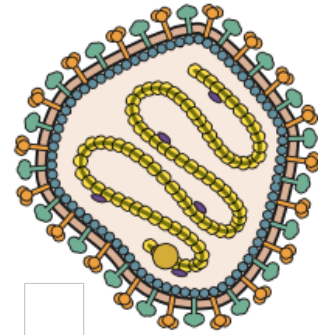
Deer mouse, white-footed mouse, rice rat, cotton rat

## Range of *P. maniculatus*





# 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 infect humans

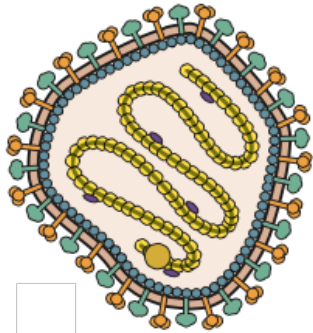
## ARTICLE

Received 14 Sep 2011 | Accepted 19 Mar 2012 | Published 24 Apr 2012 | Updated 23 Jan 2014

DOI: 10.1038/ncomms1796

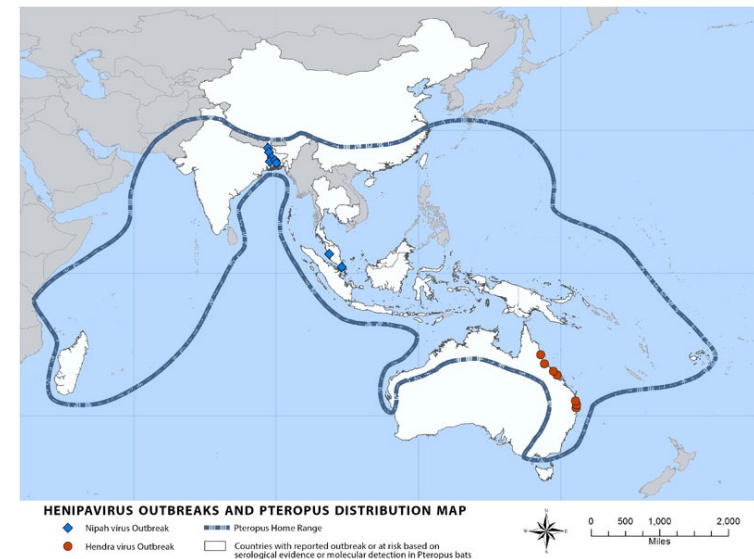
## Bats host major mammalian paramyxoviruses

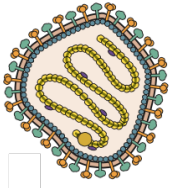
66 new paramyxoviruses from 119 bat and rodent species



## Hendra virus

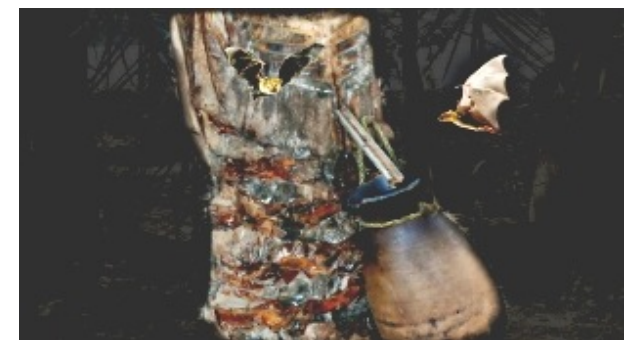
- Discovered in Hendra, Australia, September 1994
  - *Outbreak killed 14 racehorses and a trainer*
- Spread from flying foxes to horses, then to humans
- Horses continue to acquire infection
- Vaccine for horses: One World health

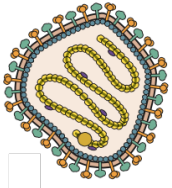




# Nipah virus

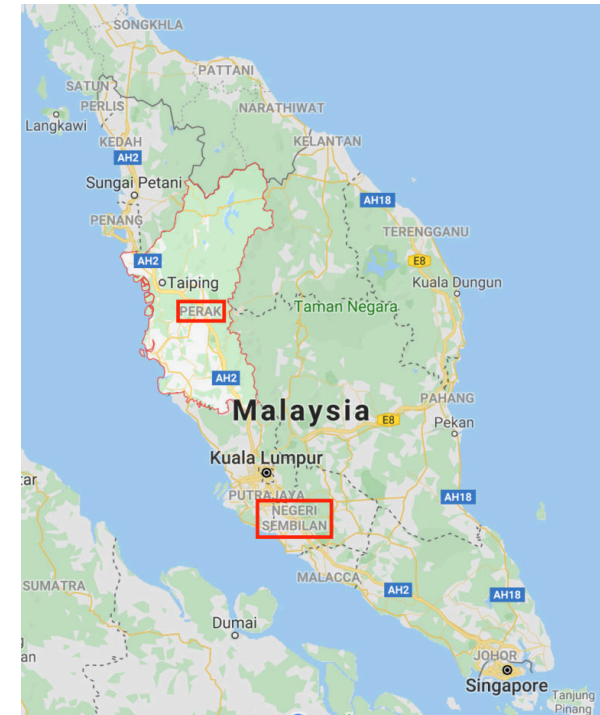
- First outbreak Malaysia 1998
  - *Outbreak of respiratory and neurological disease on pig farms*
  - *105 human deaths, 1 million pigs culled*
- Fruit bats are unaffected, excrete virus in urine
- Pigs spread infection to humans
- Subsequently humans infected by consuming date palm sap contaminated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





## Factors leading to Nipah virus emergence

- Reservoir: Fruit bats (*Pteropus vampyrus*)
- 1970s-1990s Deforestation for pulpwood and industrial plantations reduced fruit bat habitat
- Haze from slash-and-burn blanketed much of Southeast Asia in months before outbreak
- Exacerbated by drought driven by severe 1997-98 El Niño Southern Oscillation
- Acute reduction in availability of flowering and fruiting forest trees for foraging flying foxes
- Encroachment of flying foxes into cultivated fruit orchards
- Location of open piggeries in fruit orchards

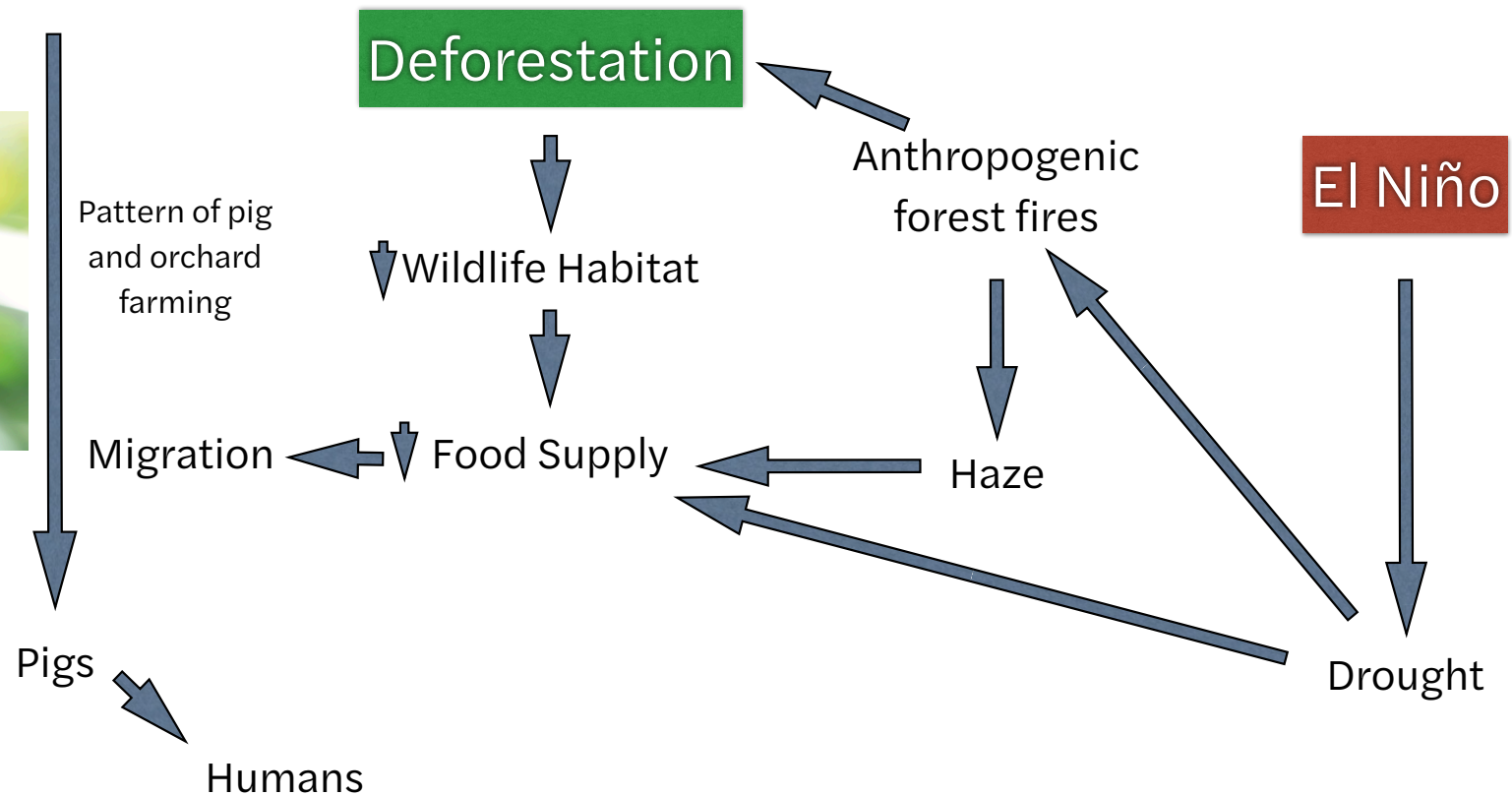


# Web of Nipah virus emergence

Natural Reservoir Hosts of Nipah Virus

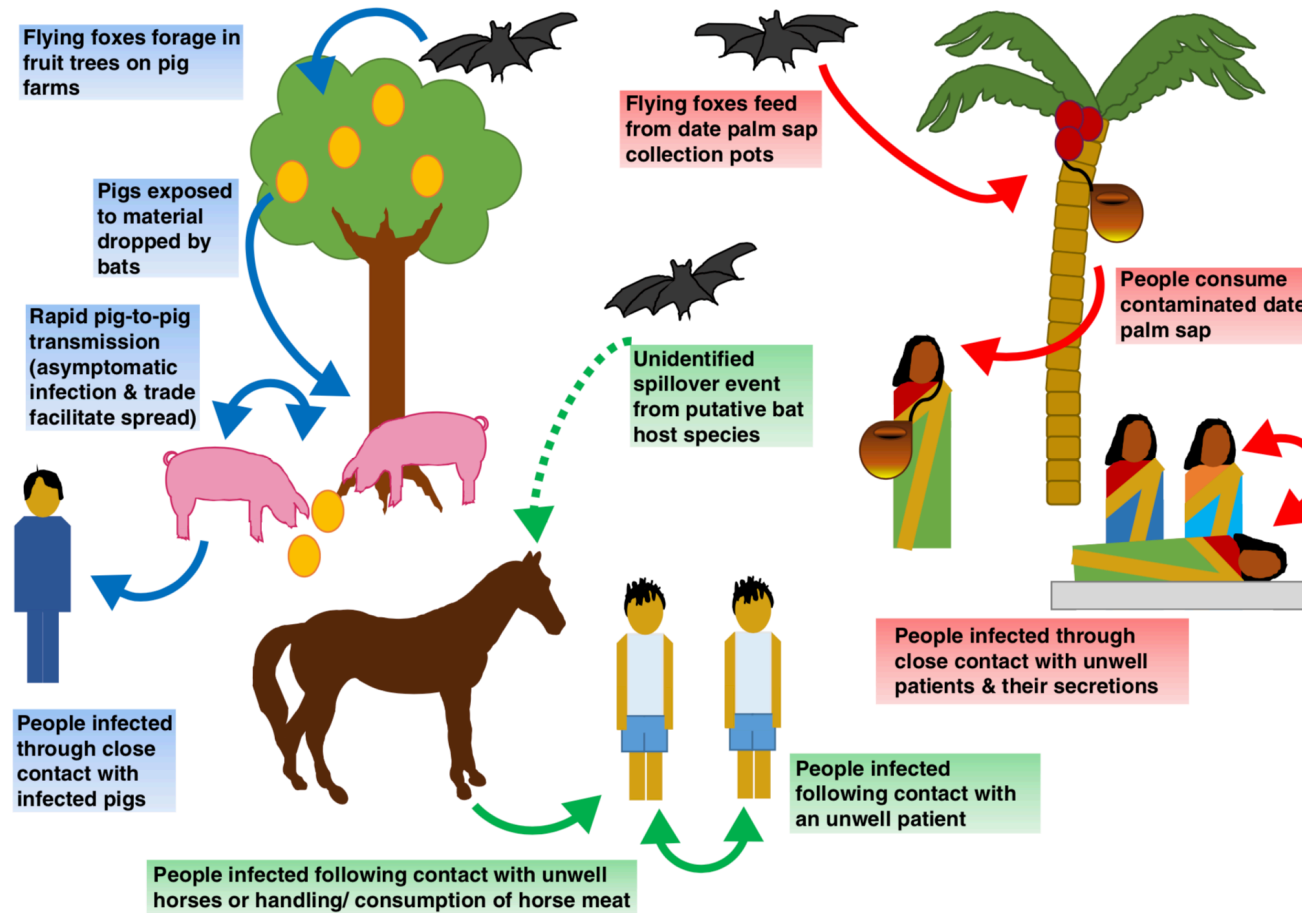


*P. vampyrus*

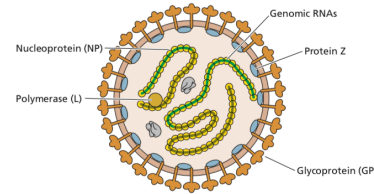




# Ecology of Nipah virus spillovers



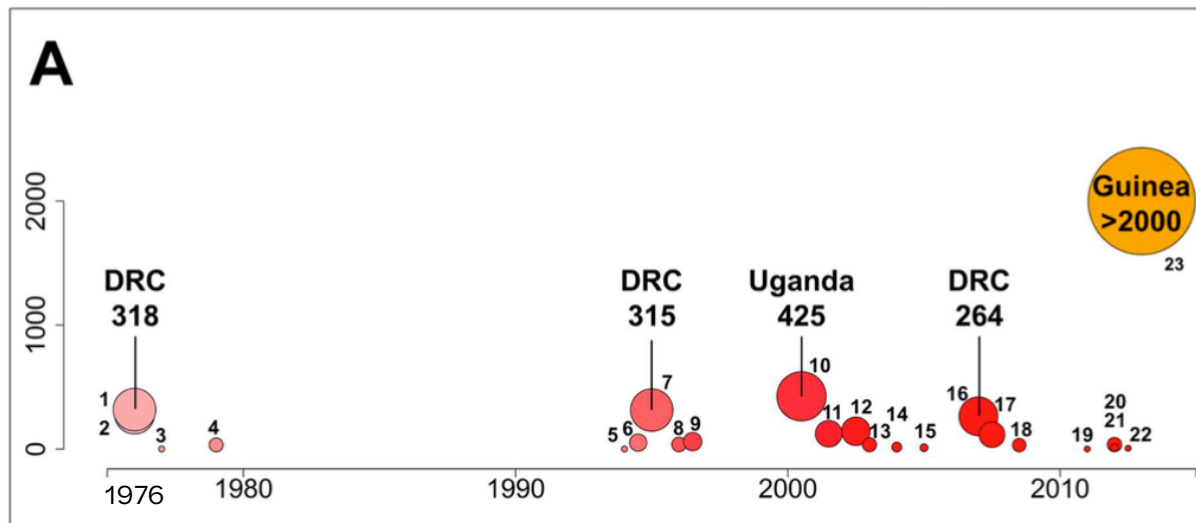
# Argentine hemorrhagic fever, Junin virus



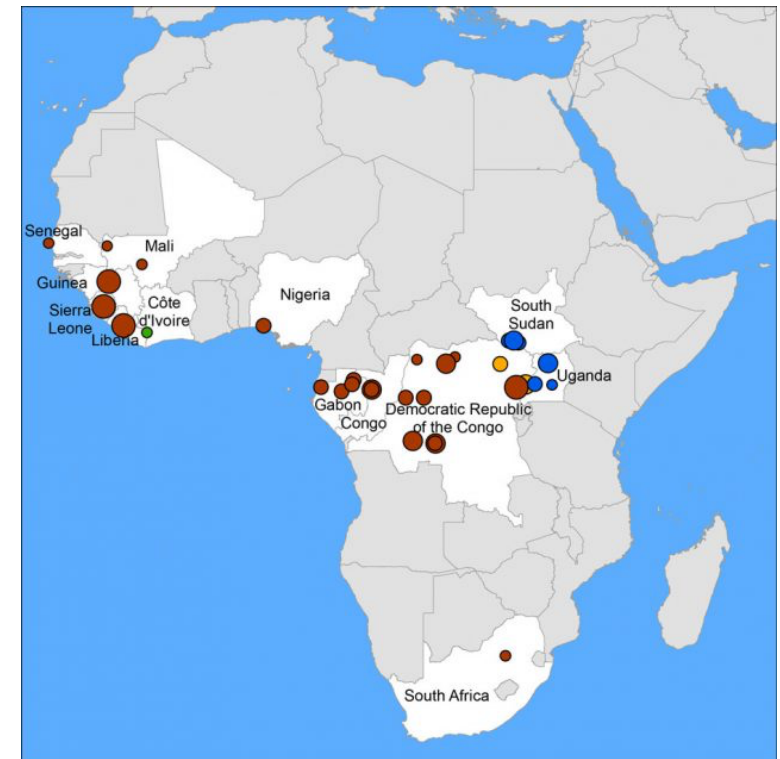
- Use of herbicides to control weeds and convert the Argentine pampa to land for growth of maize
- A new shade-tolerant grass grew in shadow of maize
- This grass led to emergence of new dominant mouse, *Calomys musculus*, reservoir of Junin virus
- Argentine hemorrhagic fever first described in 1953, virus isolated 1958

# Outbreaks of Ebolavirus disease

*Each outbreak represents a new zoonotic spillover*



Pigott et al. eLife 2014;3:e04395. DOI: 10.7554/eLife.04395



## Species

- Zaire ebolavirus
- Sudan ebolavirus
- Tai Forest ebolavirus
- Bundibugyo ebolavirus

## Number of Cases

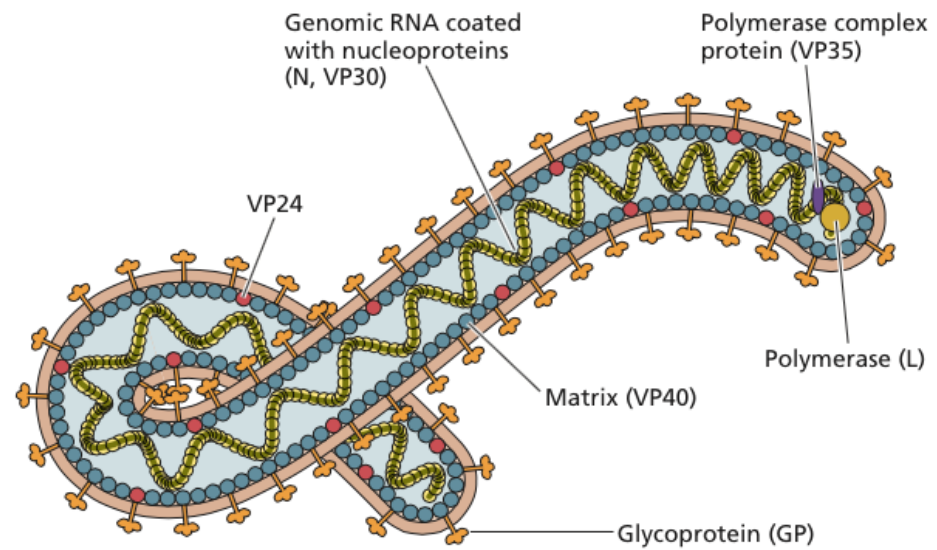
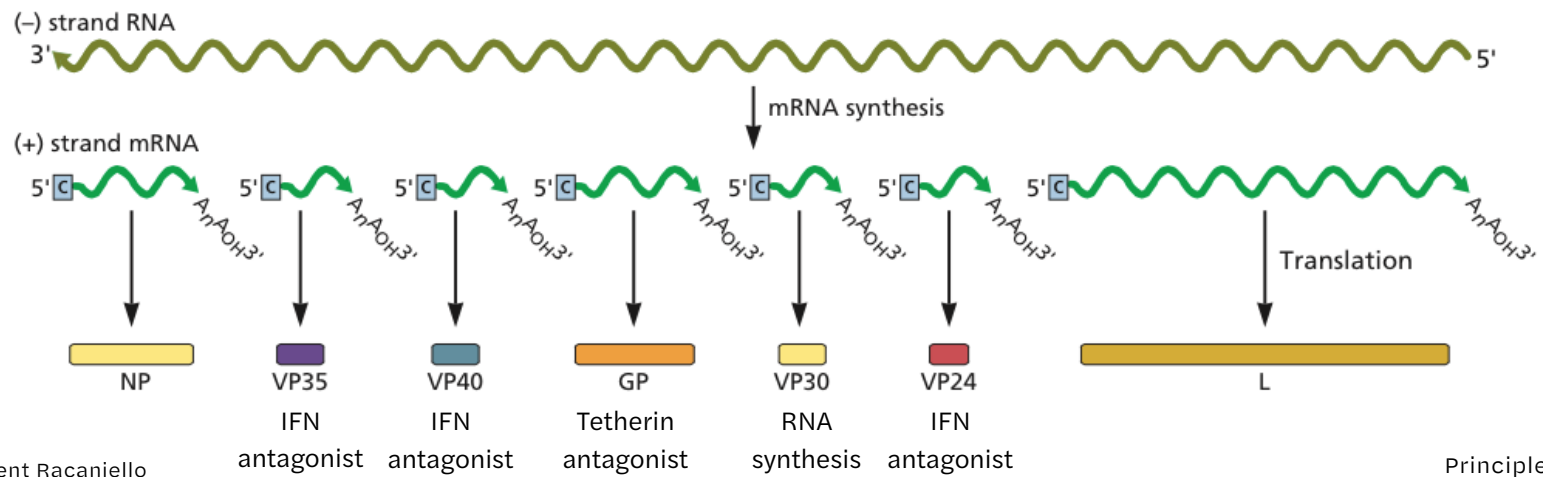
- 1 - 10
- 11 - 100
- 101 - 425
- Greater than 425



0 250 500 1,000 Miles

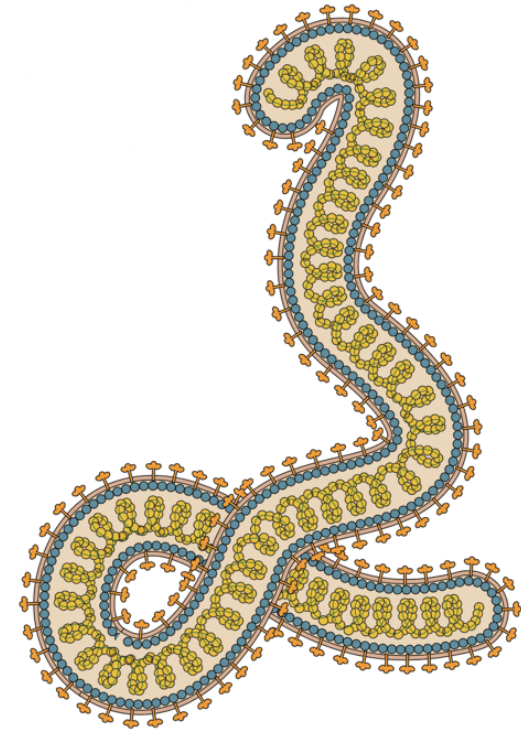
<https://www.cdc.gov/vhf/ebola/history/distribution-map.html>



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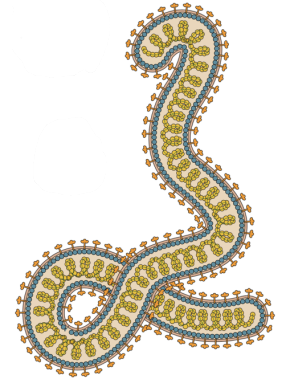
## How are humans infected?

- 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

# Ebolavirus outbreak examples

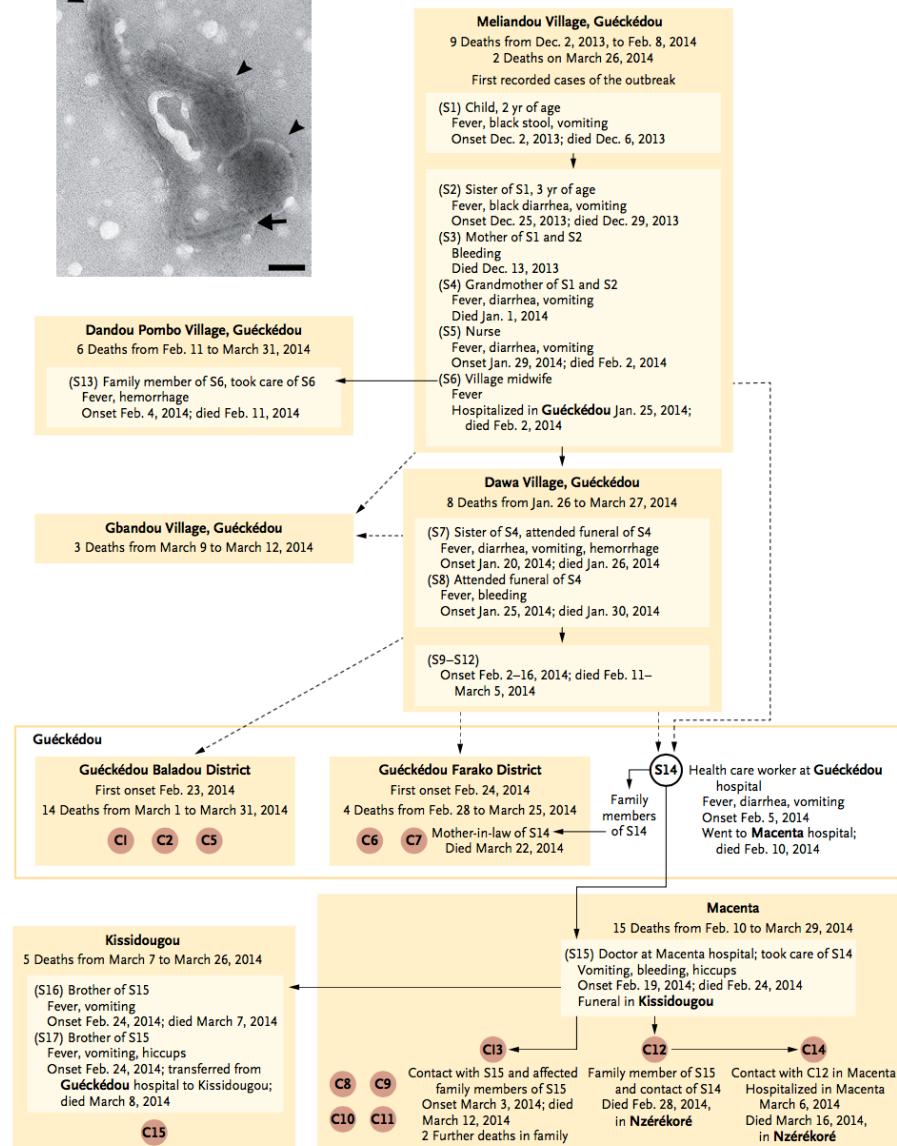
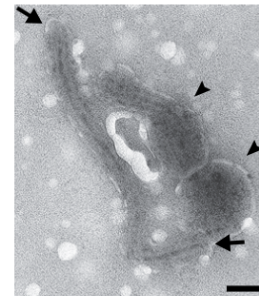


- Gabon, 1996 (Zaire ebolavirus, 37 cases) A chimpanzee found dead in the forest was eaten by people hunting for food. Eighteen people who were involved in butchering the animal became ill. Ten other cases occurred in their family members.
- Gabon, 1996-97 (Zaire ebolavirus, 60 cases) The index case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



N Engl J Med 2014; 371:1418-1425

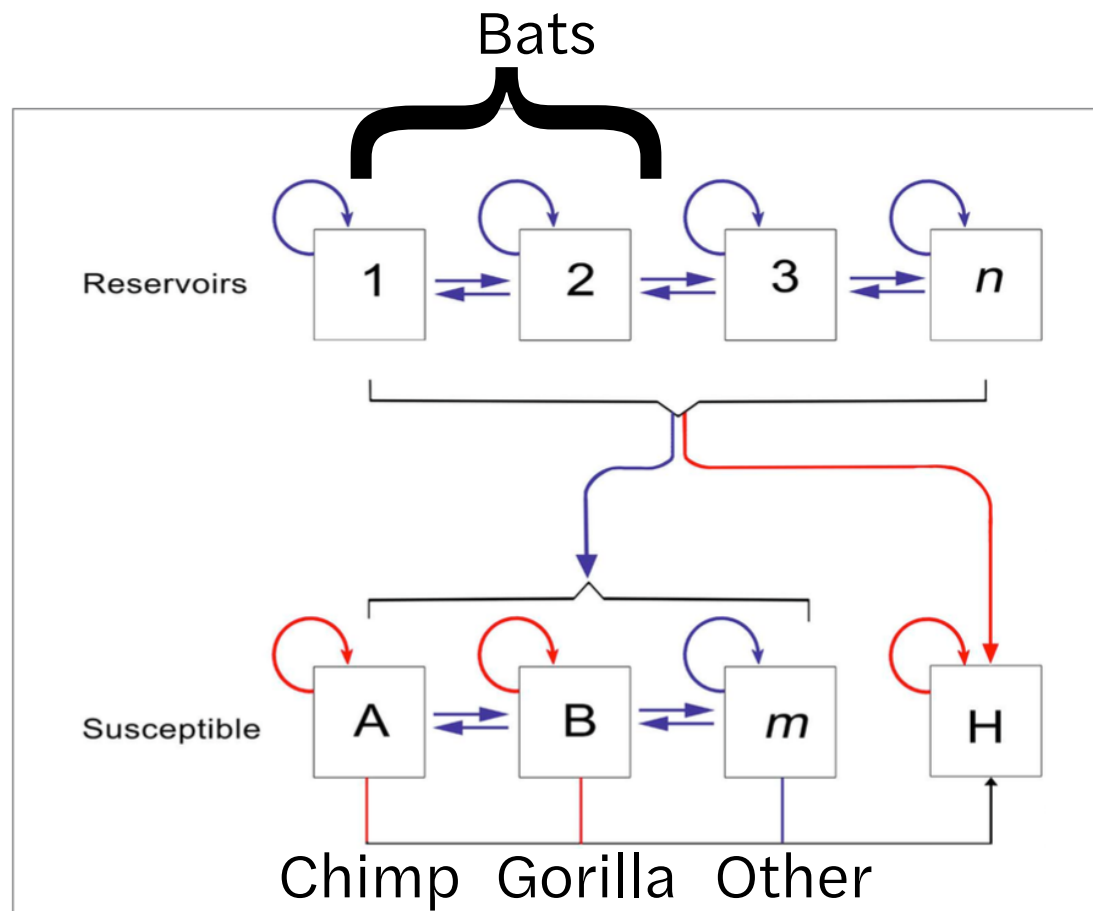


## Filovirus ecology



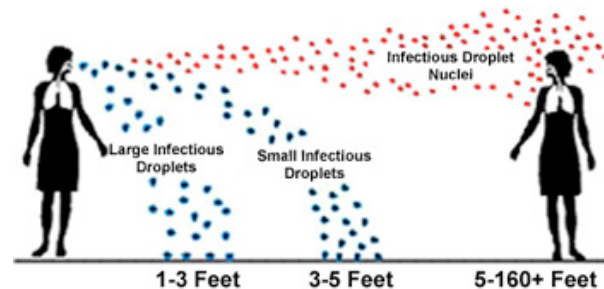
- Marburg virus has been isolated from cave-dwelling fruit bat (*Rousettus aegyptiacus*)
- Zaire Ebolavirus RNA, antibodies found in three tree-roosting bats (but not infectious virus)
- Humans, gorillas, chimpanzees are dead-end hosts

# What is the origin of Ebolaviruses?



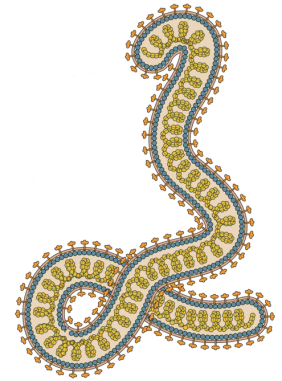
## Human-human transmission

- 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



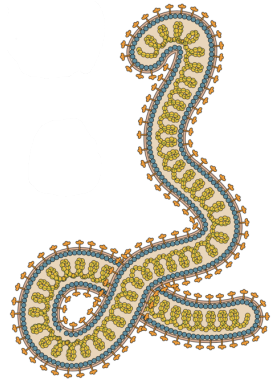
## Host entry

- Mucosal surfaces
- Breaks or abrasions in skin
- Parenteral (e.g. contaminated needles)
- Virus detected in skin, body fluids, nasal secretions, blood, semen
- Incubation period 2-21 days (not contagious)





## 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)
- 30-90% case fatality ratio in Africa

**Question break**

# SARS - Rise and fall of a zoonotic infection

PNEUMONIA - CHINA (GUANGDONG): RFI

\*\*\*\*\*

A ProMED-mail post

<<http://www.promedmail.org>>

ProMED-mail is a program of the International Society for Infectious Diseases <<http://www.isid.org>>

[1]

Date: 10 Feb 2003

From: Stephen O. Cunnion, MD, PhD, MPH <[cunnion@erols.com](mailto:cunnion@erols.com)>

This morning I received this e-mail and then searched your archives and found nothing that pertained to it. Does anyone know anything about this problem?

"Have you heard of an epidemic in Guangzhou? An acquaintance of mine from a teacher's chat room lives there and reports that the hospitals there have been closed and people are dying."

--

Stephen O. Cunnion, MD, PhD, MPH

International Consultants in Health, Inc

Member ASTM&H, ISTM

## SARS (severe acute respiratory syndrome)

- Outbreak of severe atypical pneumonia, unknown etiology, Guangdong Province, China, Nov 2002
  - *305 cases, 5 deaths*
- Incubation period 2-10 days
- Illness begins with prodrome of fever
  - *Chills, headache, malaise, myalgia*
- Next phase: dry cough, shortness of breath
- 10-20% may require mechanical ventilation



# SARS

- A Chinese doctor who treated first patients traveled to Hong Kong on 21 February 2003, stayed on ninth floor of Metropole Hotel
- He died in hospital 22 February
- Infection spread to 10 people in hotel, who flew to Singapore, Vietnam, Canada, US before symptoms evident
- Infection spread to 8000 people in 29 countries, 10% mortality



Life is exciting

*Hong Kong will take  
Your breath away.*



Hong Kong doesn't do things by halves. The first thing that grabs your attention is the forest of skyscrapers towering over the harbour. The second is the sheer energy of the place. Step onto any street and you'll be swept away in a wave of excitement, sound and colour. From the dragon boat races in summer to the Chinese New Year fireworks, from morning tai chi to late night dancing. Whenever you go and whatever you do in Hong Kong, one thing's for certain. You'll never be bored.

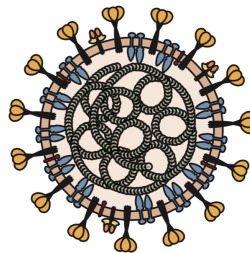
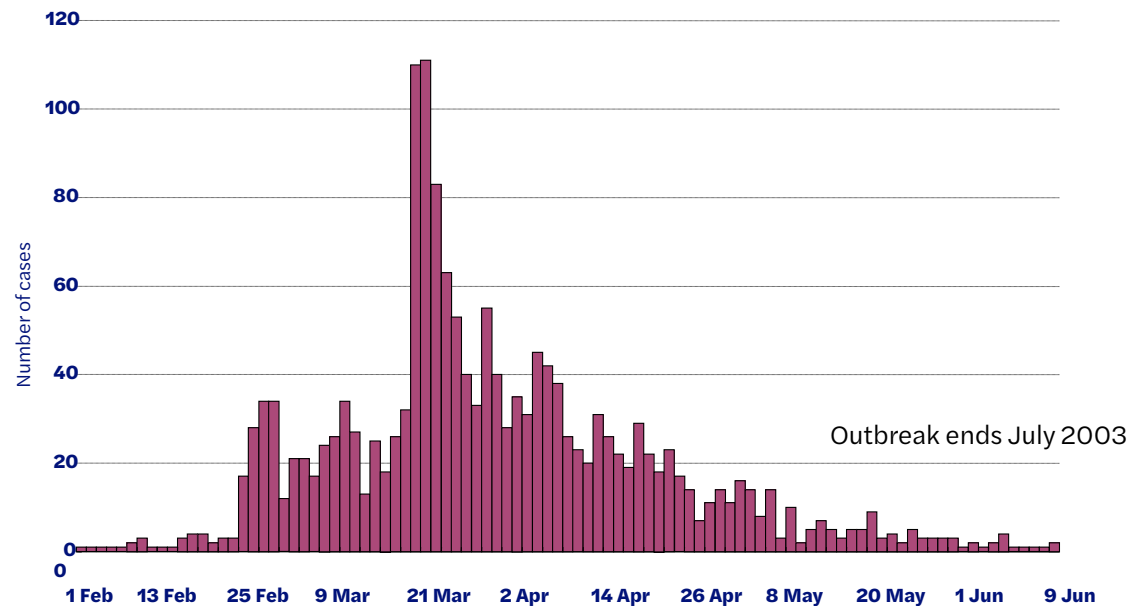
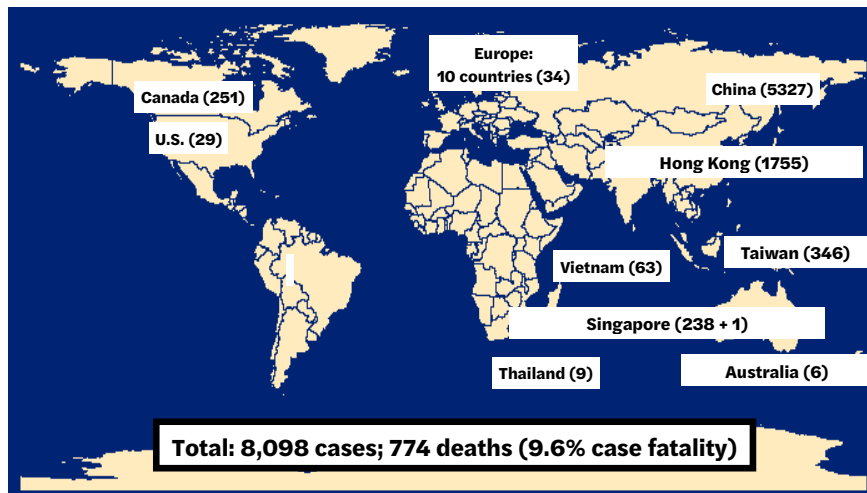
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# Probable SARS Cases Worldwide Reported to WHO as of Sept. 26, 2003



## Origin of SARS-CoV

- Human sera collected before SARS outbreak do not contain antibodies to SARS-CoV
- Early Guangdong SARS cases were in handlers of animals for the exotic food market
- Animal traders had significantly higher prevalence of anti-SARS-CoV antibodies than control groups



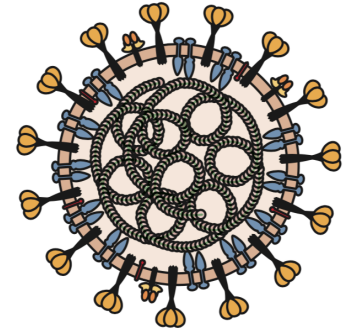
## Origin of SARS-CoV

- Highly diverse SARSr-CoV found in horseshoe bats (*Rhinolophus*) in a cave in Yunnan Province
- All genetic elements needed to form SARS-CoV in this cave
- No SARS cases in Yunnan Province during outbreak
- Direct progenitor of SARS-CoV not identified
- Direct progenitor of SARS-CoV thought to have emerged in bats, then infected civet cats which were then transported to Guangdong markets

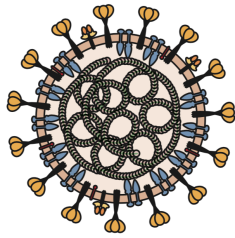




# MERS-CoV



- Index case September 2012: 60 yo male patient, died of pneumonia, renal failure
- Virus recovered, genome sequenced, binds dipeptidyl peptidase 4 receptor
- Closely related to bat coronaviruses
- Not SARS-CoV



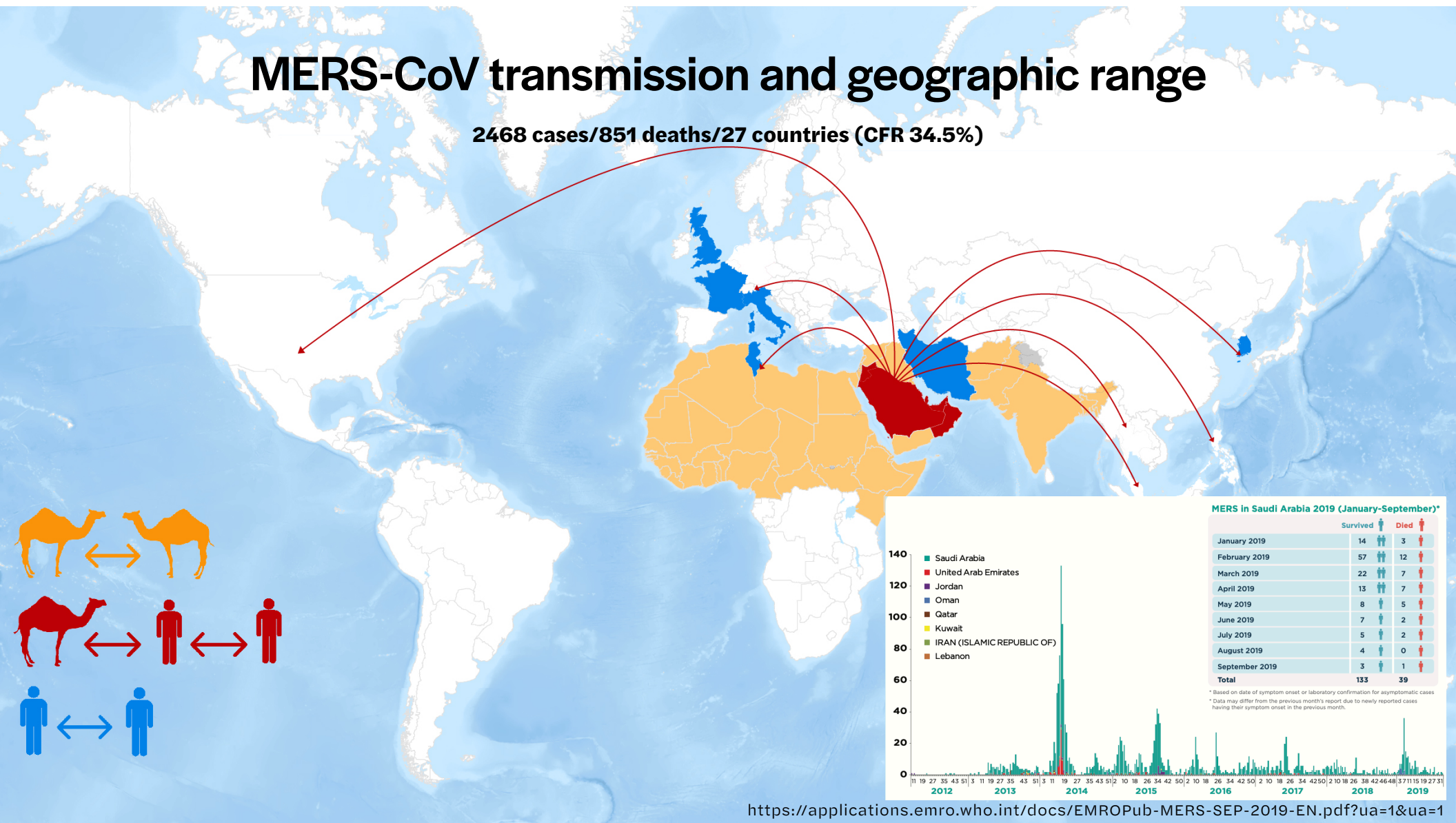
## MERS-CoV



- Spread from dromedary camels (endemic in Middle East and Africa)
- Not all infections have camel source
- How is the virus transmitted to humans? Virus does not transmit well among humans
- Camel vaccine in testing (One Health approach)

# MERS-CoV transmission and geographic range

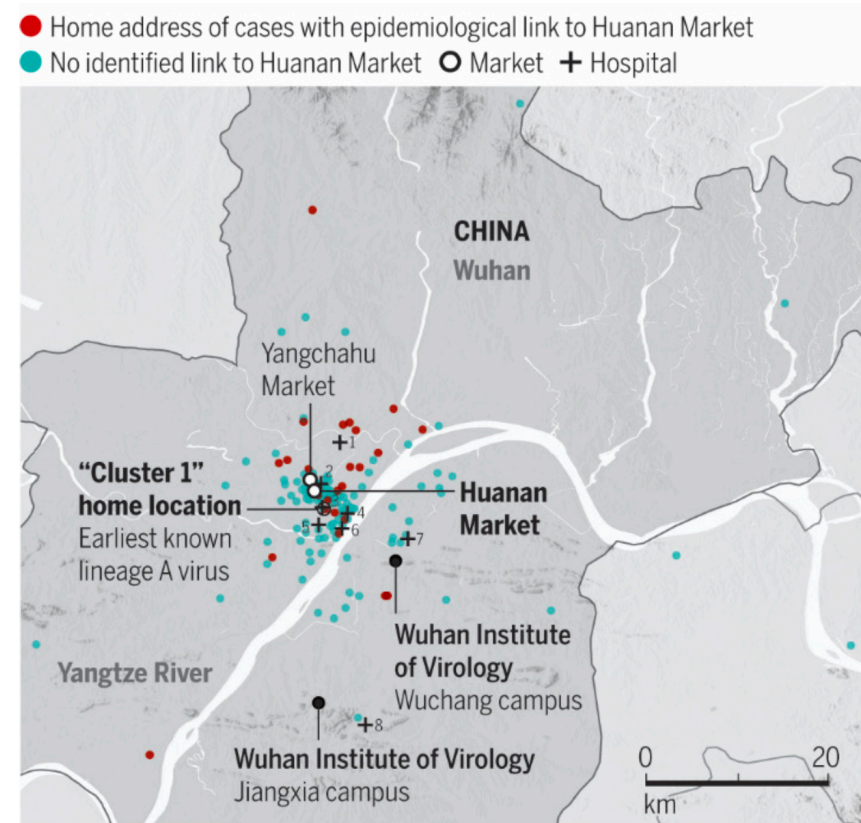
2468 cases/851 deaths/27 countries (CFR 34.5%)

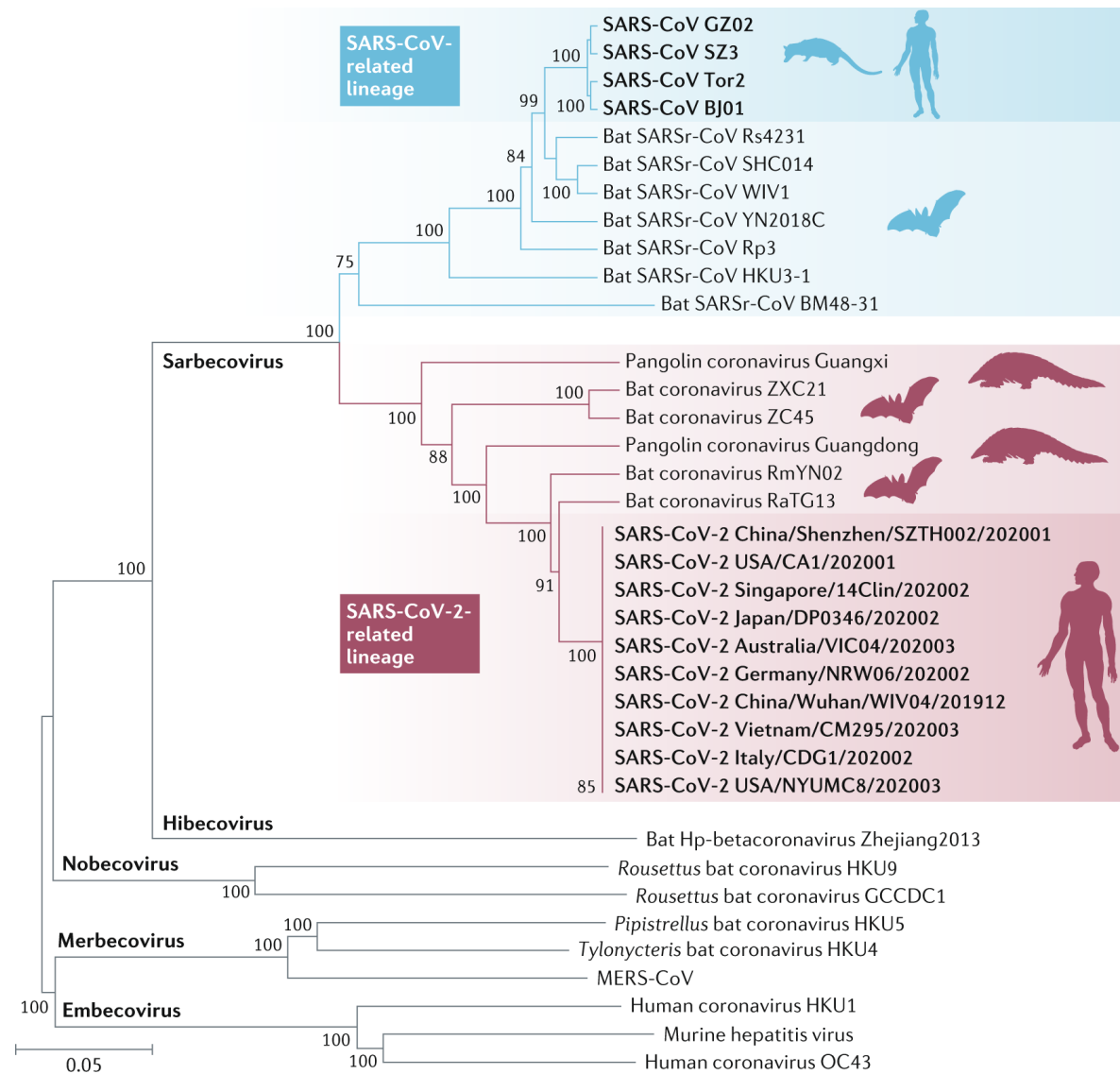


<https://applications.emro.who.int/docs/EMROPub-MERS-SEP-2019-EN.pdf?ua=1&ua=1>

# SARS-CoV-2, third pandemic of the 21st century

- Cluster of pneumonia cases, unknown cause, Wuhan December 2019
- Huanan seafood market suspected as origin, one of several in Wuhan
- As of 12/21: 275,000,000 cases, 5.3 million deaths globally

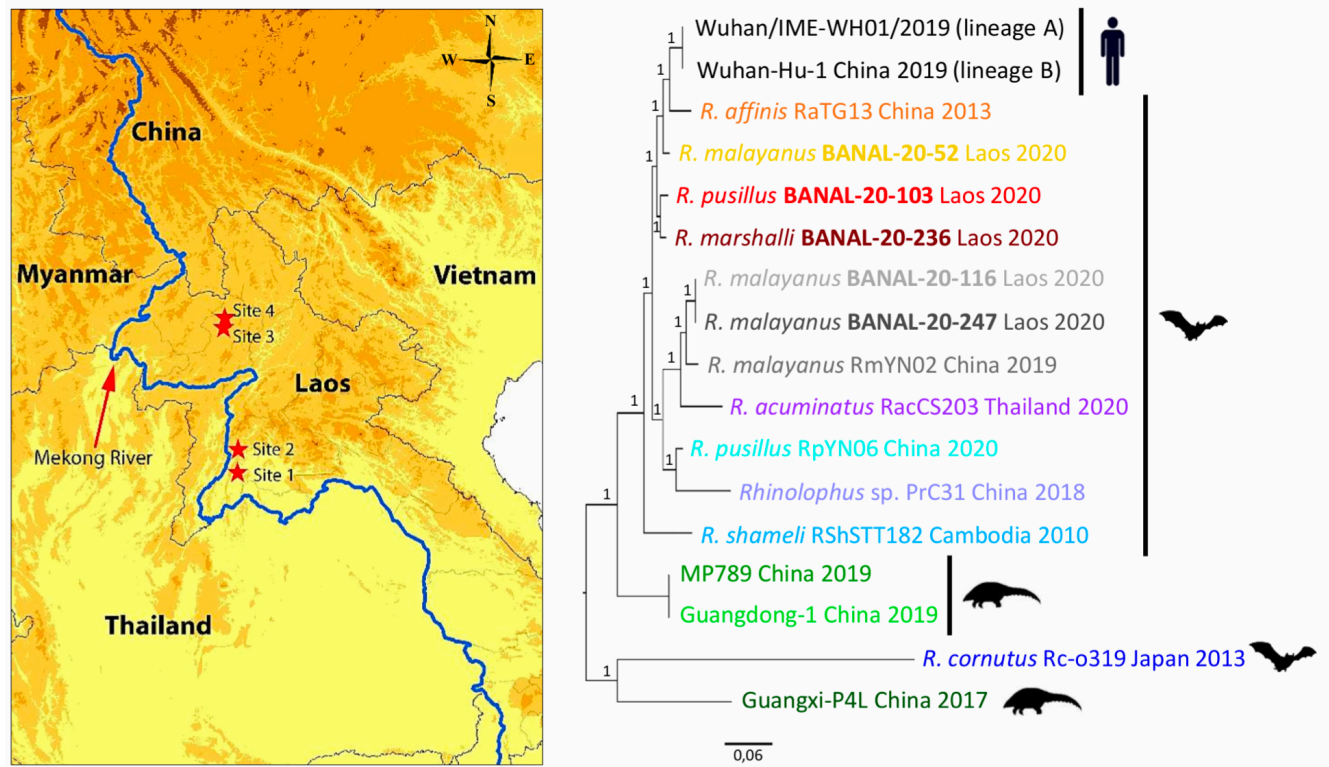


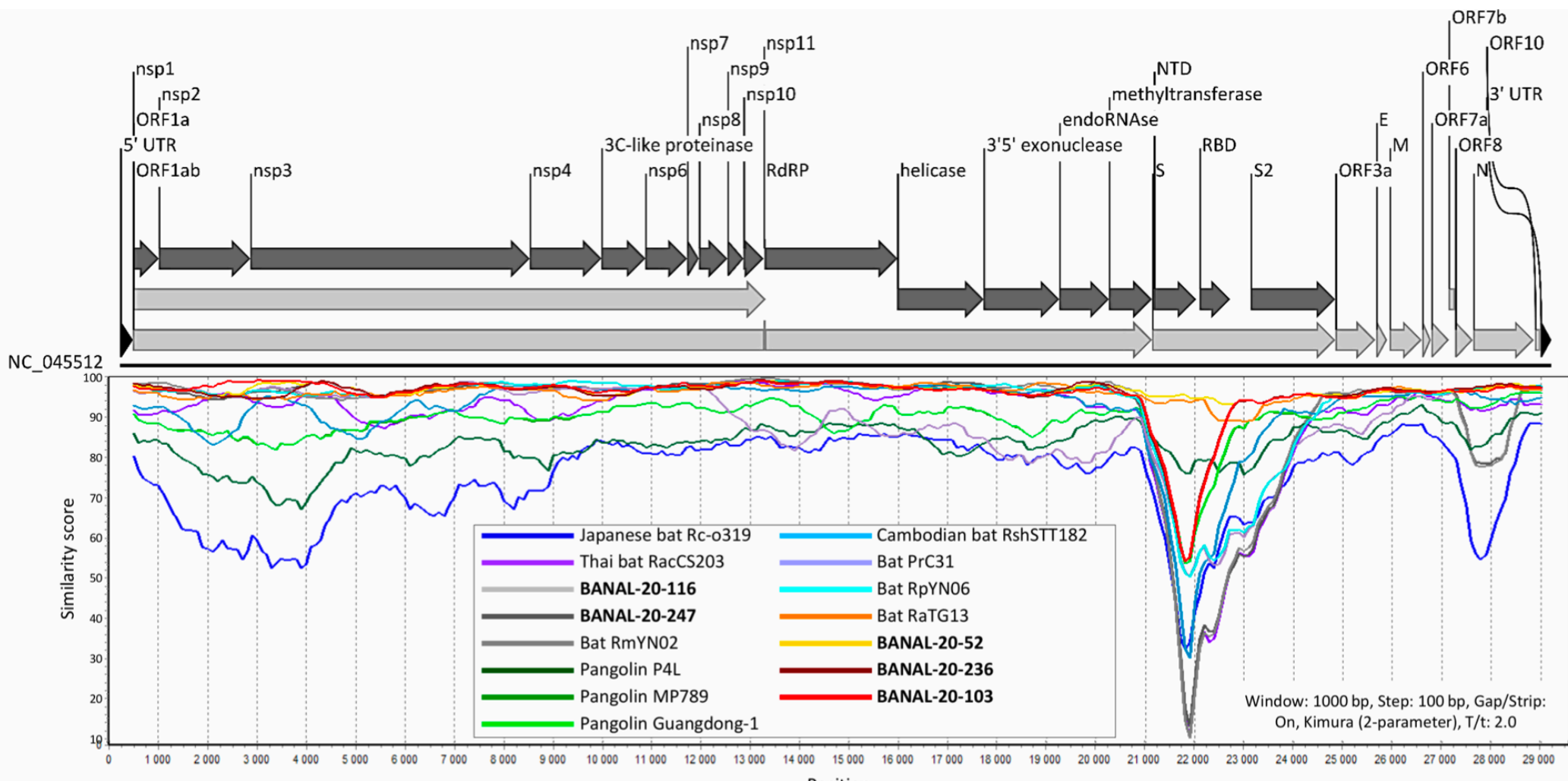


96% nucleotide identity  
with Bat CoV RaTG13

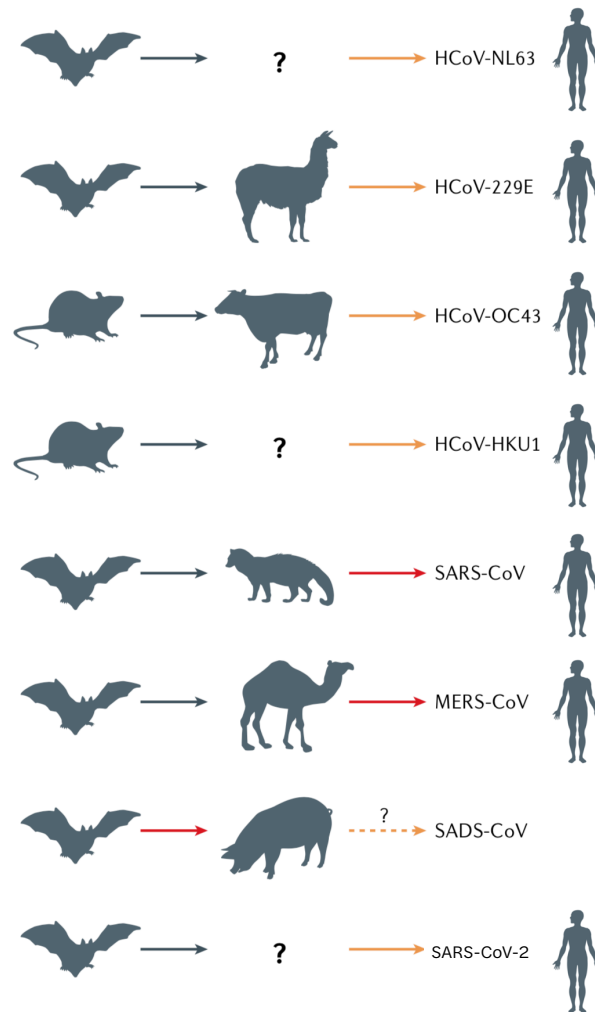


# Coronaviruses with a SARS-CoV-2-like receptor-binding domain allowing ACE2-mediated entry into human cells isolated from bats of Indochinese peninsula

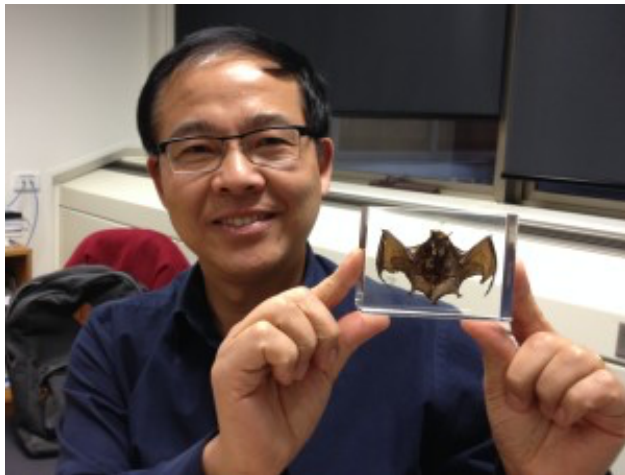




# Origins of human coronaviruses - in Nature, not in a lab







# TWiV 296: The real Batman, Linfa Wang

August 3, 2014

Host: [Vincent Racaniello](#)

Guest: [Linfa Wang](#)

Vincent visits the Australian Animal Health Laboratory in Geelong, Australia and speaks with Linfa about his work on bats and bat viruses.

<https://www.microbe.tv/twiv/twiv-296/>

## Biosafety level 4 (BSL-4)

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



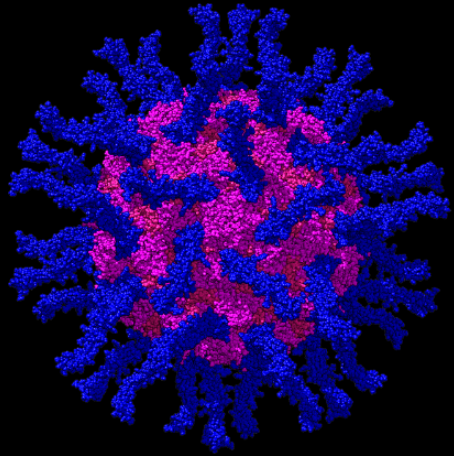
Threading the NEIDL <https://youtu.be/tqAjkjGq8Ug>

# 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)
- We can make pan-CoV antivirals!





# **VIROLOGY LIVE**

**WITH VINCENT RACANIELLO**

**Next time: HIV and AIDS**