

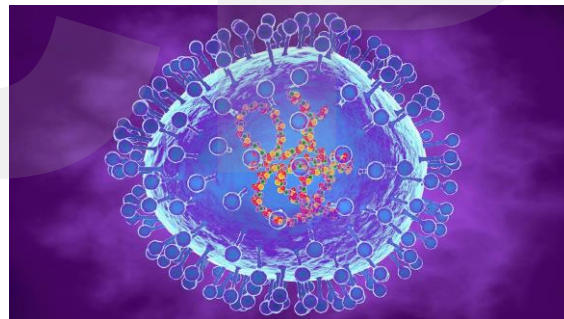


Modern hits and timeless classics: Emerging and re-emerging viruses in 2024



56th Annual Primary Care Review Presentation
14FEB2025

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Disclosures

- Dr. Messer has nothing to disclose

Objectives

- Recognize virology, epidemiology, and origins of viral emergences in 2024
- Describe viral genomic recombination as a driver of virus emergence and re-emergence
- Summarize clinical pearls for each pathogen
- Identify key factors driving viral emergence in 2024

Overview

- Background
 - Emerging, re-emerging, ever-present
 - The central dogma of virology
- Viruses
 - Oropouche virus
 - Avian Influenza
 - Human metapneumovirus
 - Dengue virus

Emerging, Re-emerging and ever-present

- Emerging pathogens/diseases
 - newly appeared in a population
 - have existed but are rapidly increasing in incidence or geographic range.
 - Ebola
 - HIV
 - Sin Nombre virus
 - SARS, MERS, SARS-CoV-2
- Specific factors precipitating disease emergence can often be identified

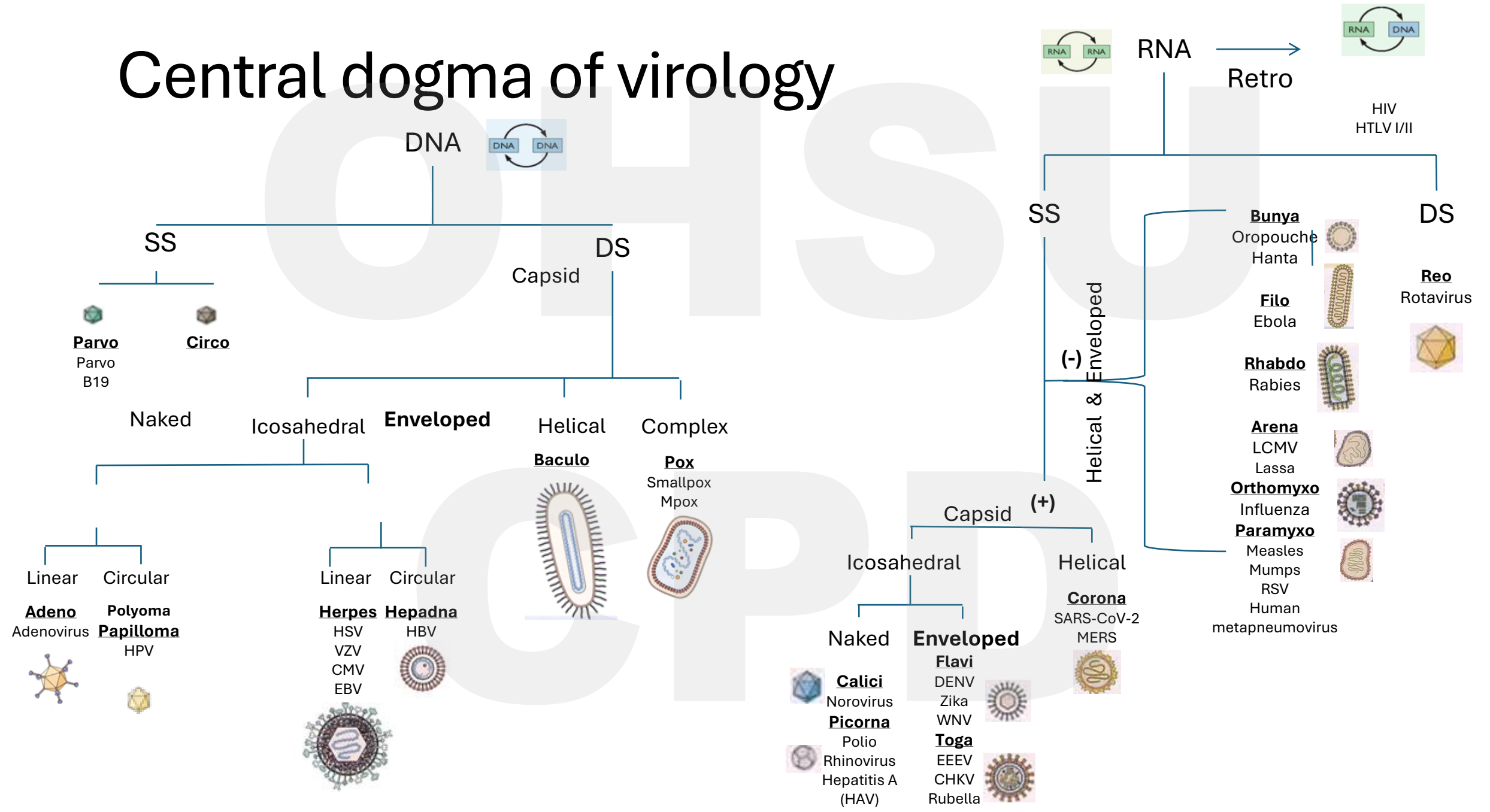
Emerging, Re-emerging and ever-present

- Re-emerging
 - infections that have returned after being mostly controlled.
 - Measles
 - Yellow fever
 - Influenza
 - Malaria
 - Syphilis
 - Gonorrhea
- Specific factors precipitating disease emergence can often be identified

Emerging, Re-emerging and ever-present

- Factors leading to emergence or re-emergence
 - Ecologic changes
 - Global climate change
 - Landscape modification/transformation
 - Deforestation, transition to agriculture, river damming/diversion
 - Agricultural development
 - Industrial farming
 - monoculture
 - Changes in human demographics and behavior
 - Population growth
 - Changes in age structure
 - Conflict
 - Rural-urban migration
 - International travel and commerce –
 - worldwide movement of people and goods
 - Air travel
 - Technology and Industry
 - Microbial evolution
 - Breakdowns in public health measures

Central dogma of virology

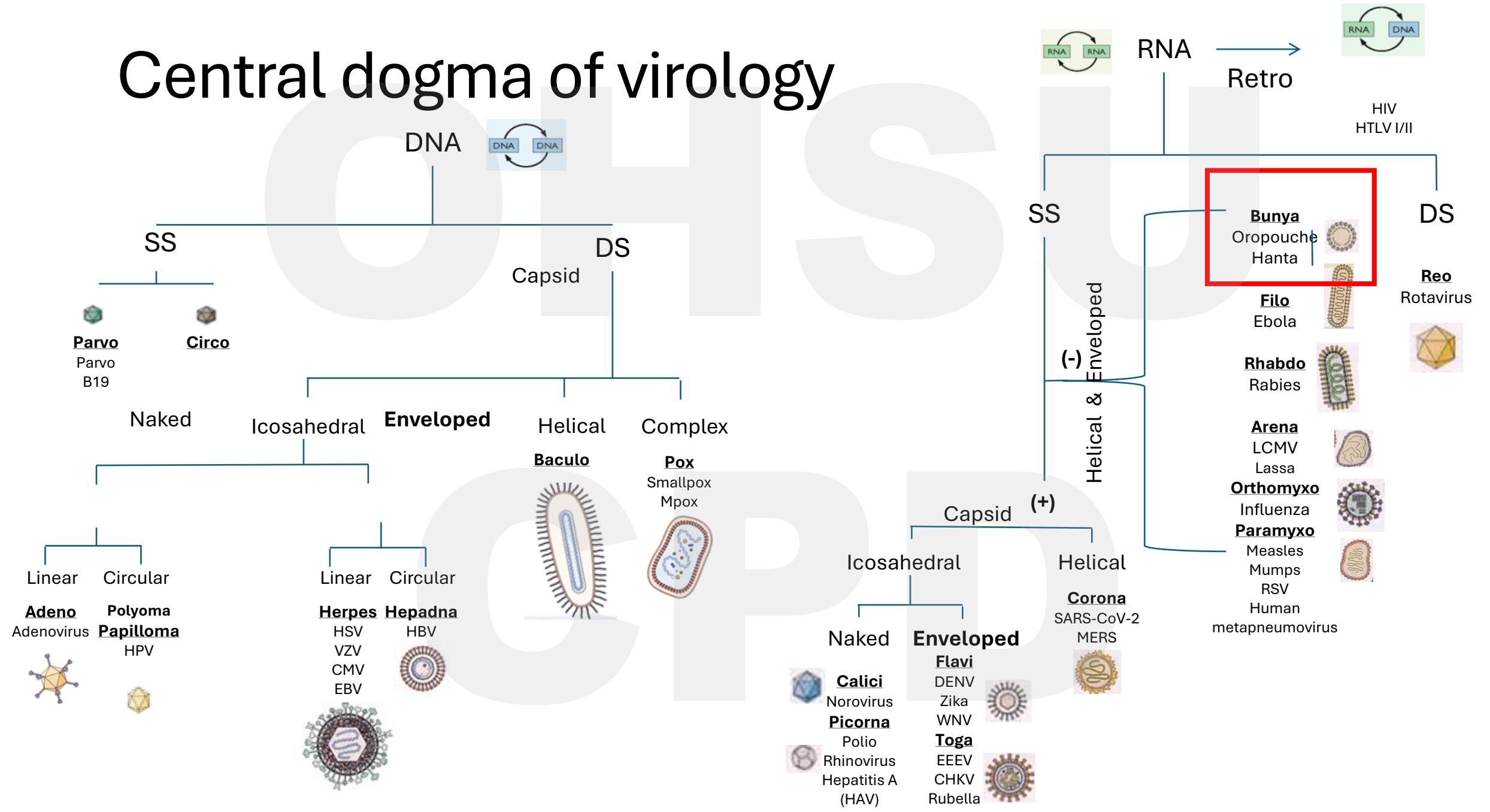


Oropouche virus

OH SU

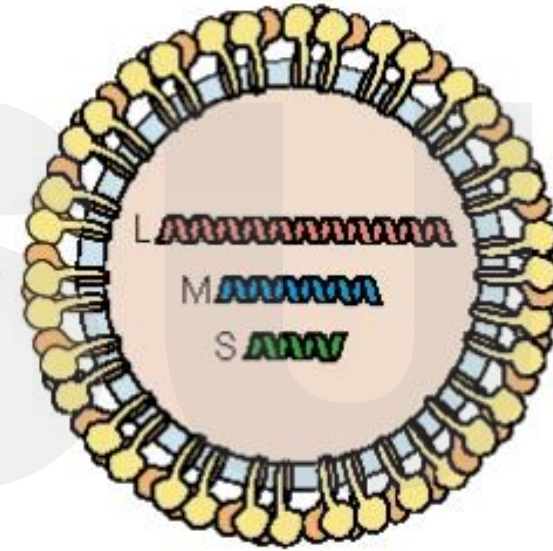
CPD

Central dogma of virology



Oropouche virus

- Enveloped 3 stranded (-) RNA virus



Oropouche virus

- Enveloped 3 stranded (-) RNA virus
- Discovered in 1965 in Trinidad and Tobago (febrile forest worker) near the Oropouche river.
- Historically endemic in the Amazon basin



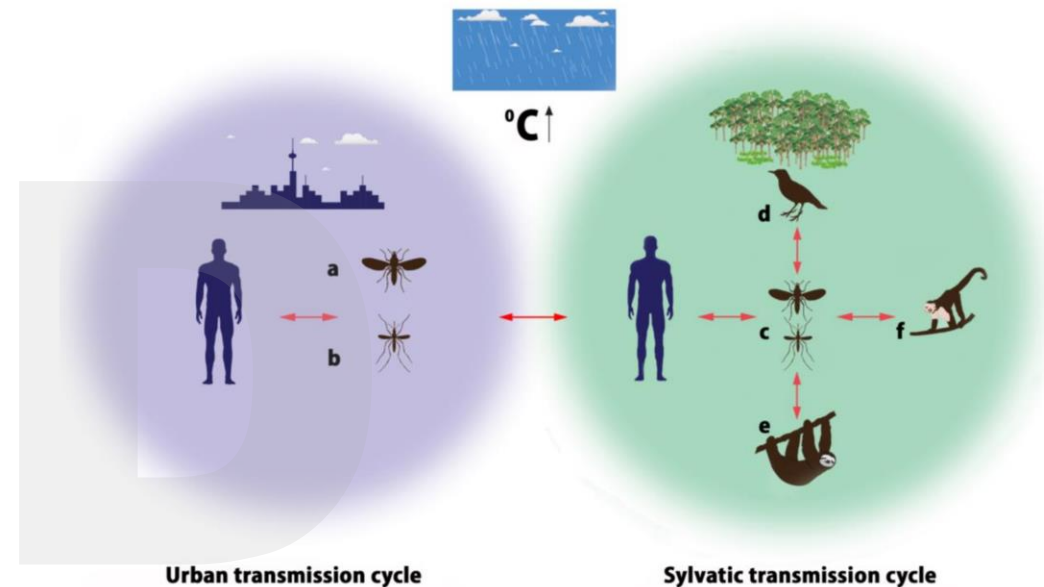
Oropouche virus

- Enveloped 3 stranded (-) RNA virus
- Discovered in 1965 in Trinidad and Tobago (febrile forest worker) near the Oropouche river.
- Historically endemic in the Amazon basin
- “Sloth Fever”



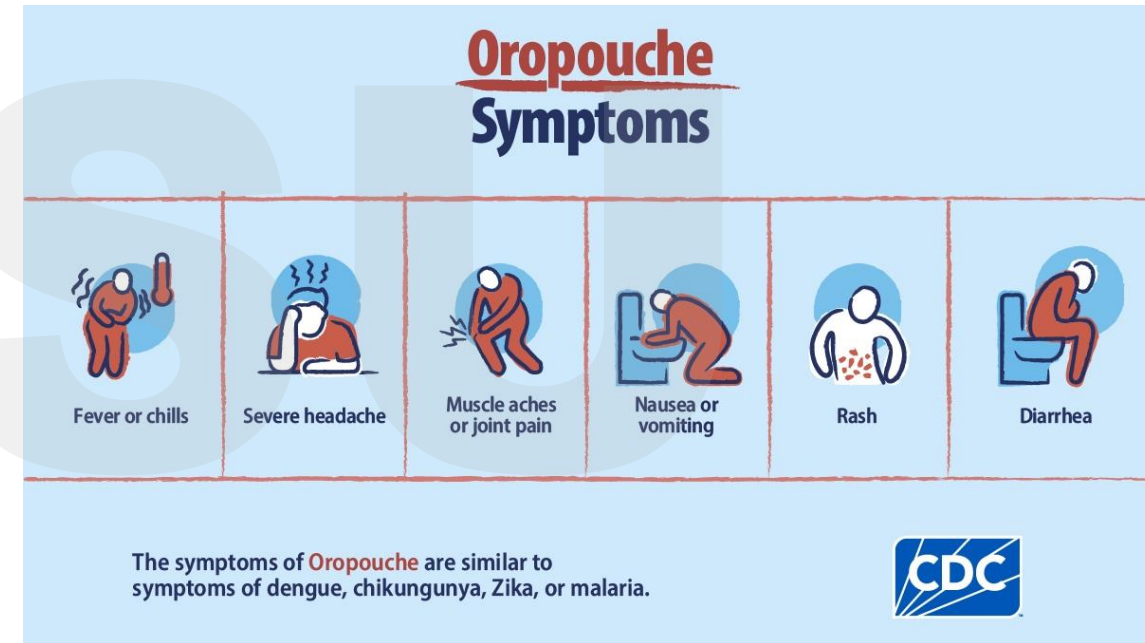
Oropouche virus

- Transmission to humans via biting midges (*Culicoides paraensis*) and possibly some mosquito species.
- Maintained in sylvatic/enzootic transmission cycles between mosquitoes and nonhuman vertebrate hosts (sloths, domestic and wild birds, rodents)



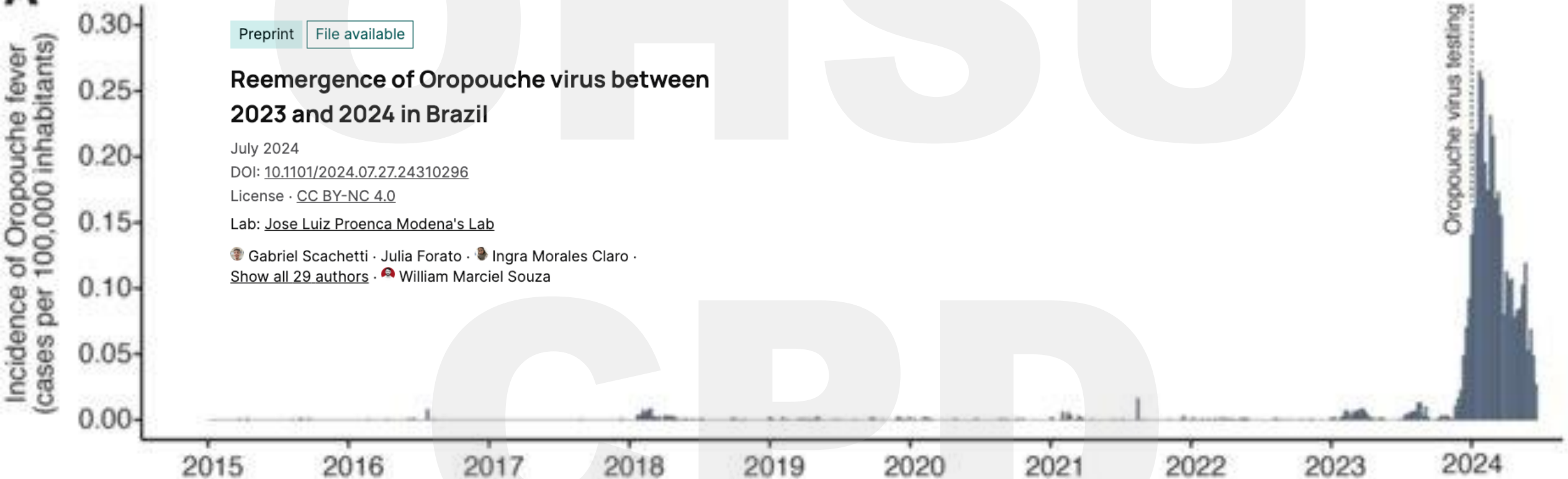
Oropouche virus

- Clinical syndrome
 - 60% infections are symptomatic
 - Incubation 3 to 10 days after insect bite.
 - Symptoms include: Fever, Chills, Headache, Arthralgia, Retro orbital eye pain, Photophobia, Nausea, vomiting, diarrhea
 - Exam findings: fever, maculopapular, rash, conjunctival injection, abdominal pain
 - Lab abnormalities: lymphopenia, leukopenia, elevated CRP.
 - Clinical course self limited, but 70% of patients will experience recurrent symptoms days to weeks after initial defervescence
 - Approx 5% of pts will develop complications include hemorrhagic manifestations and neuroinvasive disease and vertical transmission associated with adverse birth outcomes. There is some evidence of sexual transmission and evidence of post-infectious GBS.
 - Dx and Tx: serology or RT-PCR (CDC, Wadsworth, NY).



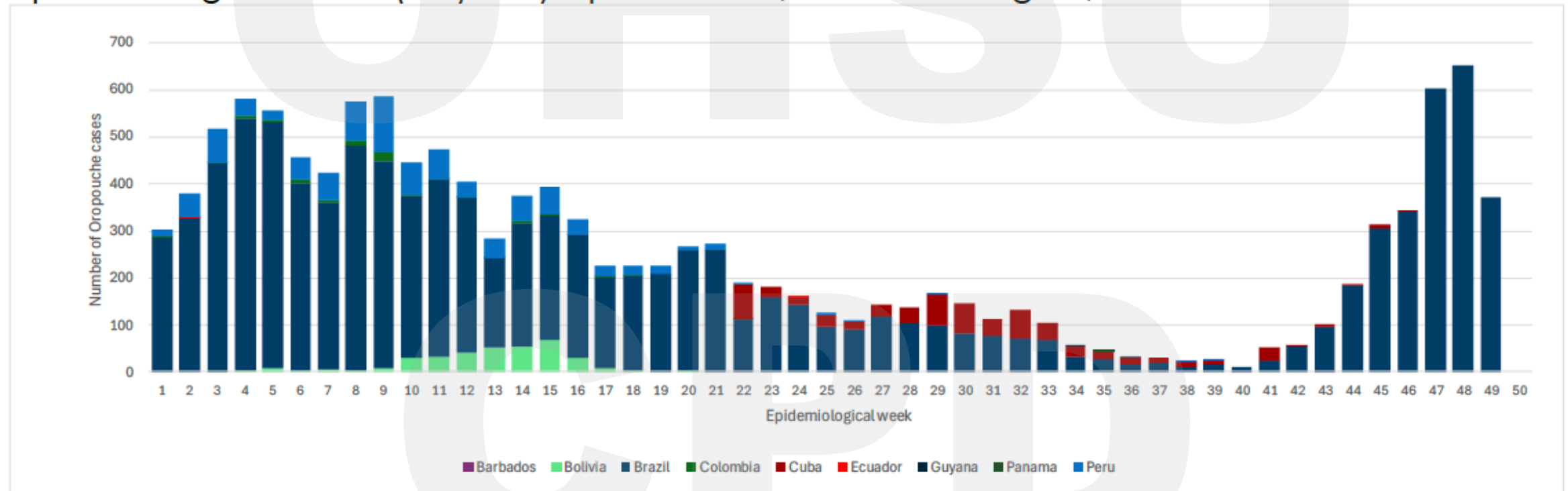
Oropouche virus

A



Oropouche virus

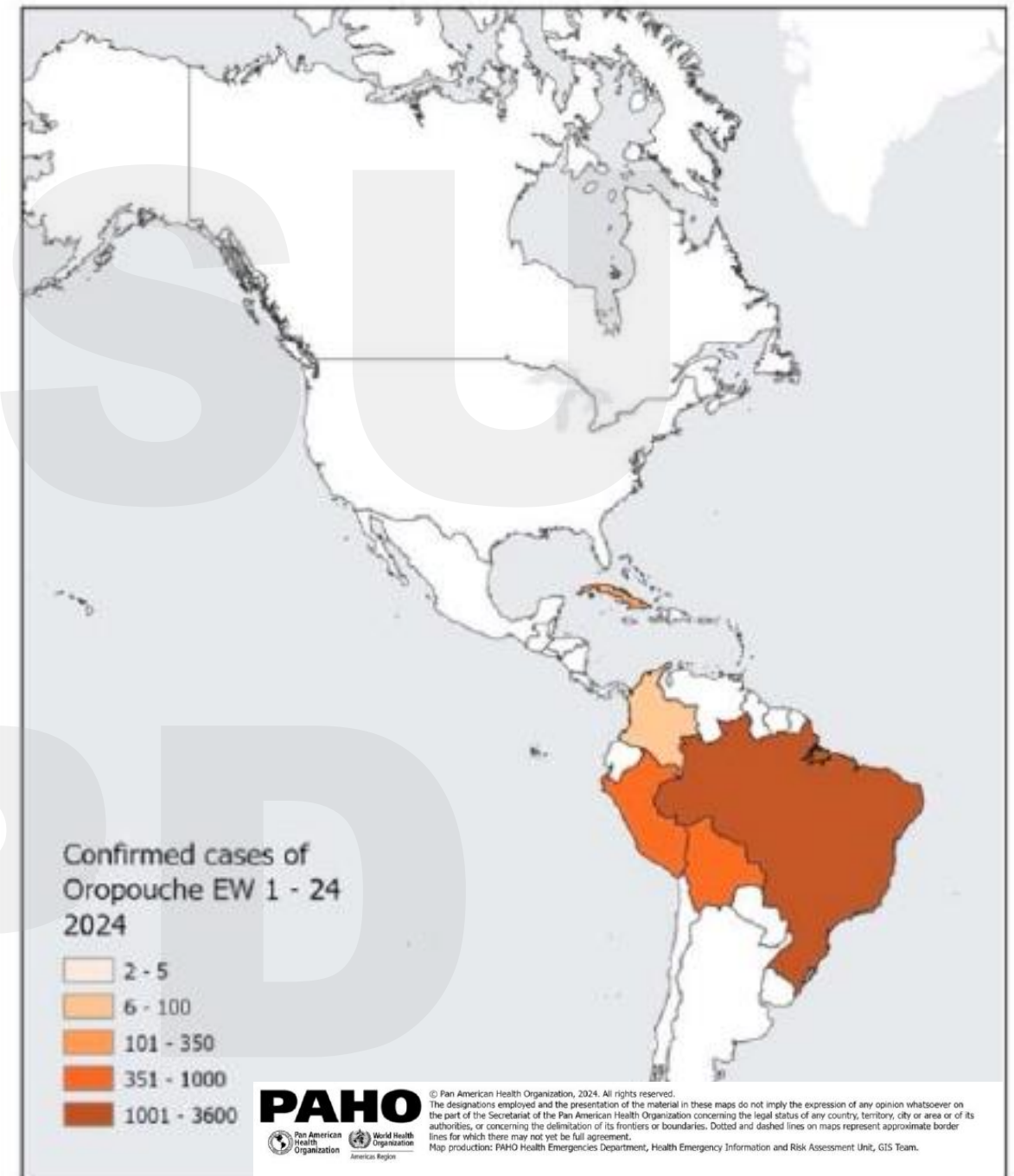
Figure 1. Number of confirmed autochthonous cases of Oropouche by country and epidemiological week (EW) of symptom onset, Americas Region, 2024



Source: Adapted from data provided by the respective countries and reproduced by PAHO/WHO (1-6, 8-11, 14, 16, 17).

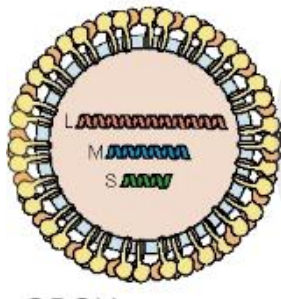
Oropouche virus

- "Emerged" in 2024 with local or "autochthonous" transmission in:
 - Barbados, 2 cases
 - Bolivia, 356
 - Brazil, 10,940, two deaths
 - Columbia, 74
 - Cuba, 603
 - Ecuador, 2
 - Guyana, 2
 - Cayman Islands, 1
 - Panama, 1
 - Peru, 936
- Imported cases
 - Canada, 2
 - United States, 94
 - Europe, 30



Oropouche virus

- Emergence associated with a genetic reassortment between strains from Eastern Amazonia and strains from Peru, Columbia and Ecuador



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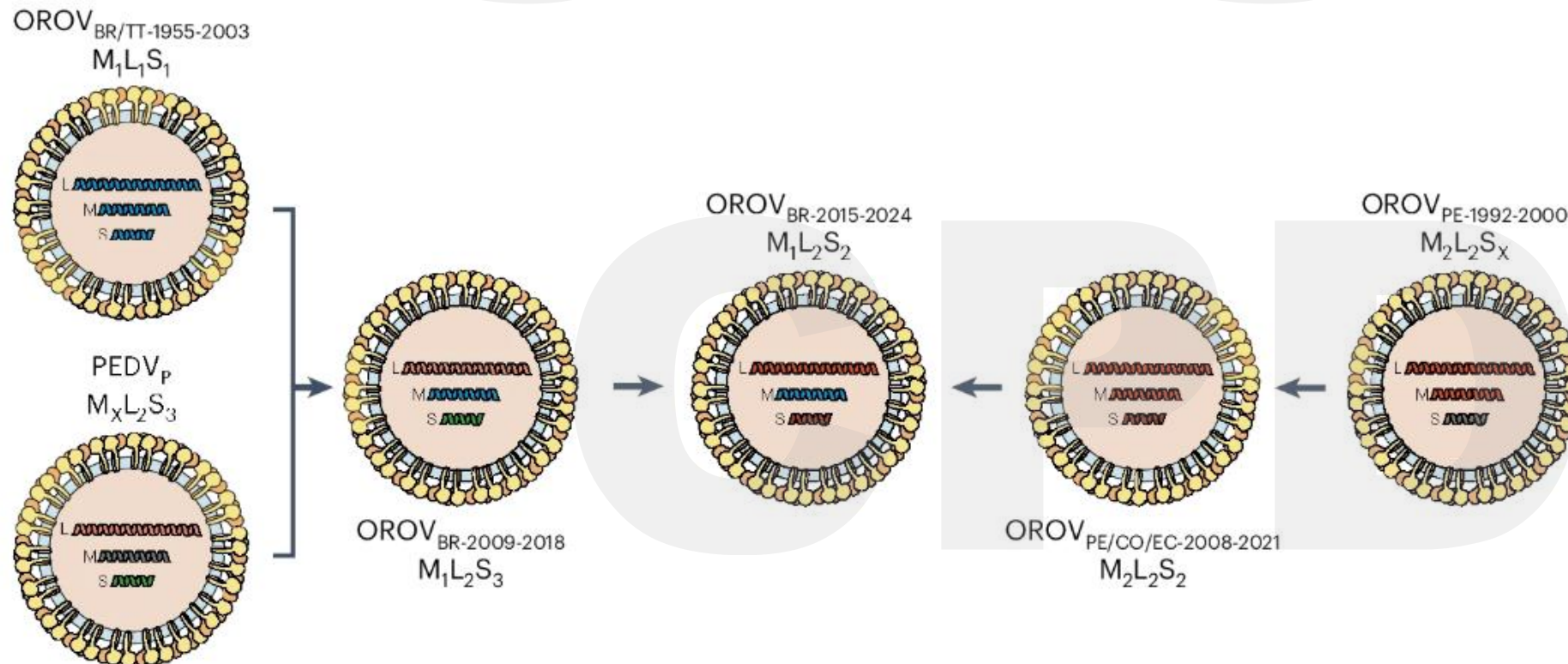
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Article | Published: 18 September 2024

Human outbreaks of a novel reassortant Oropouche virus in the Brazilian Amazon region

Oropouche virus

- Emergence associated with a genetic reassortment between strains from Eastern Amazonia and strains from Peru, Columbia and Ecuador



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Human outbreaks of a novel reassortant Oropouche virus in the Brazilian Amazon region

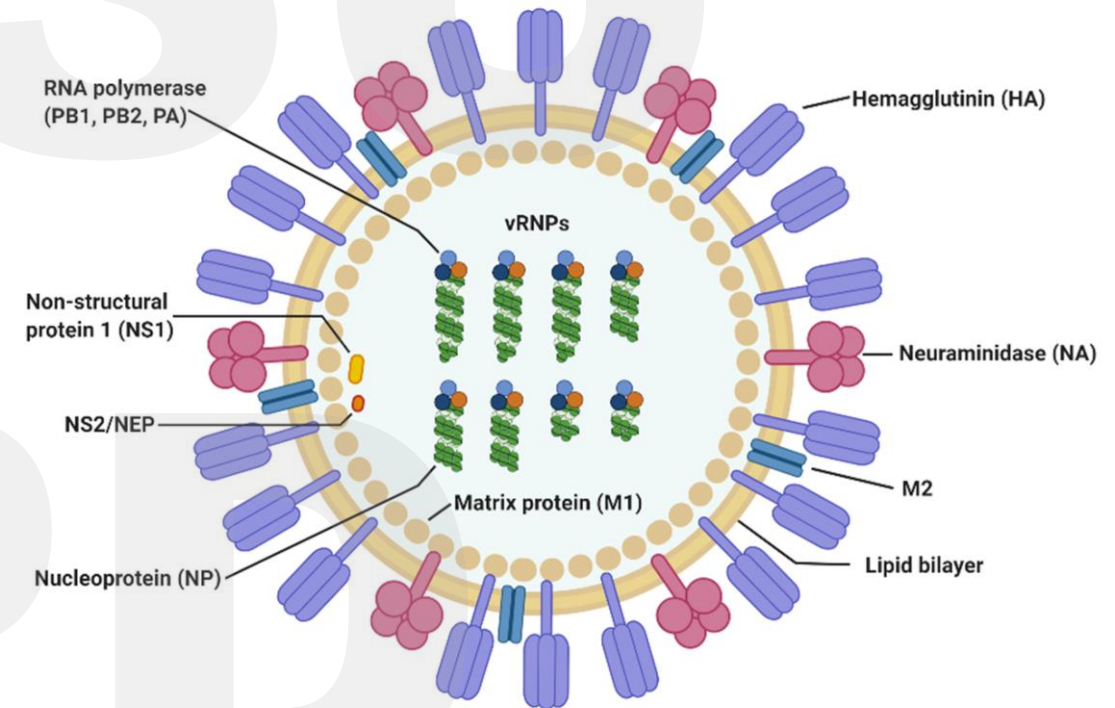
Oropouche virus

- Clinical pearls
 - Suspect in travelers with fever 0–2 weeks from return from outbreak areas.
 - Always rule out dengue (see below).
 - In confirmed cases:
 - 70% will experience current symptoms
 - Be aware of the risk of vertical transmission and pregnant patients.
 - Complications are more likely in pregnant patients, older patients, patients with underlying immunity, suppression, hypertension, diabetes, cardiovascular disease
 - Reportable disease.
 - Pre-travel advise pregnant women of potential risk, take measures for the insect bites.

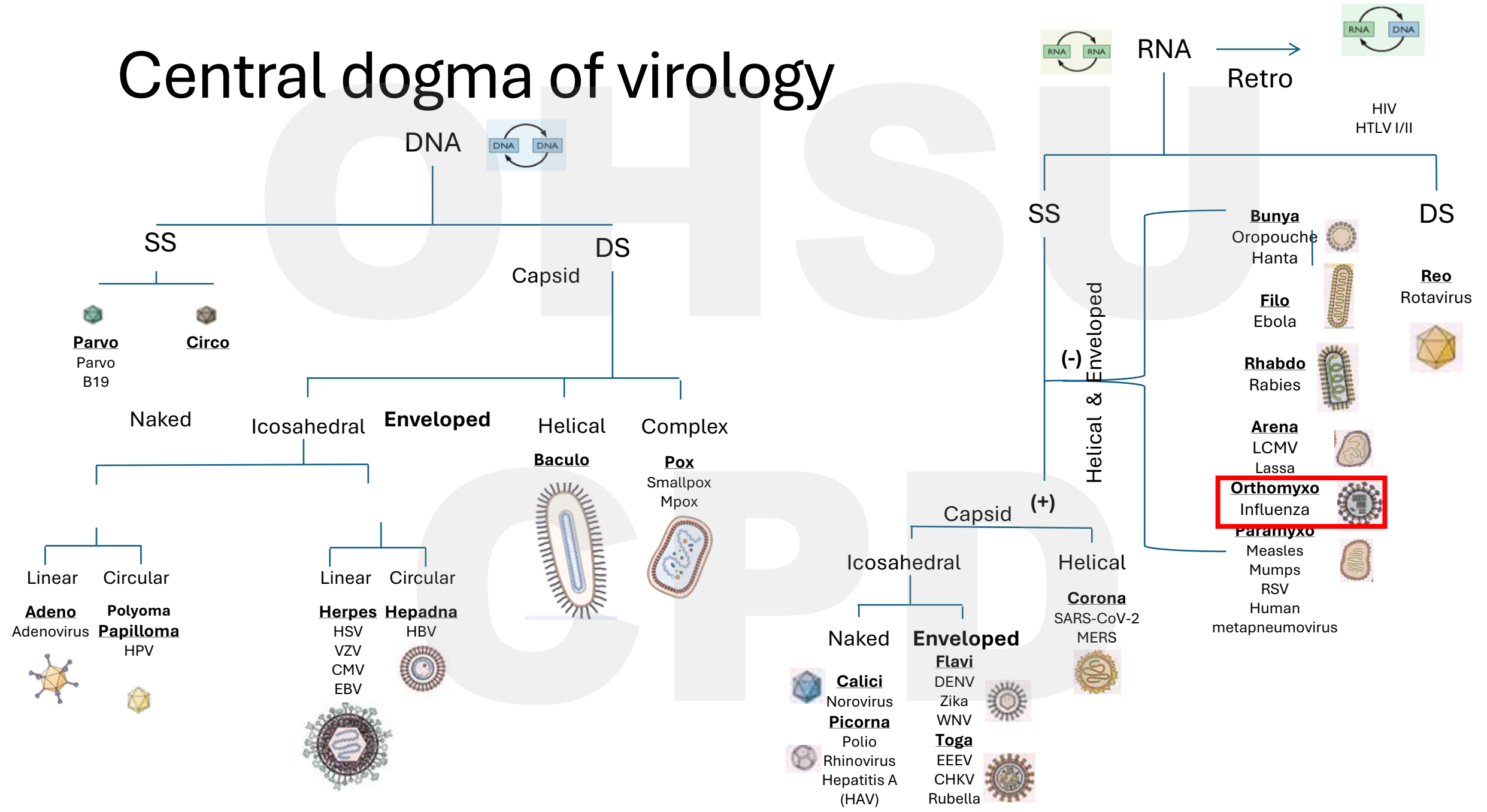


H5N1 avian influenza

- Enveloped, 8 segmented gene (-) RNA virus, *Orthomyxoviridae*

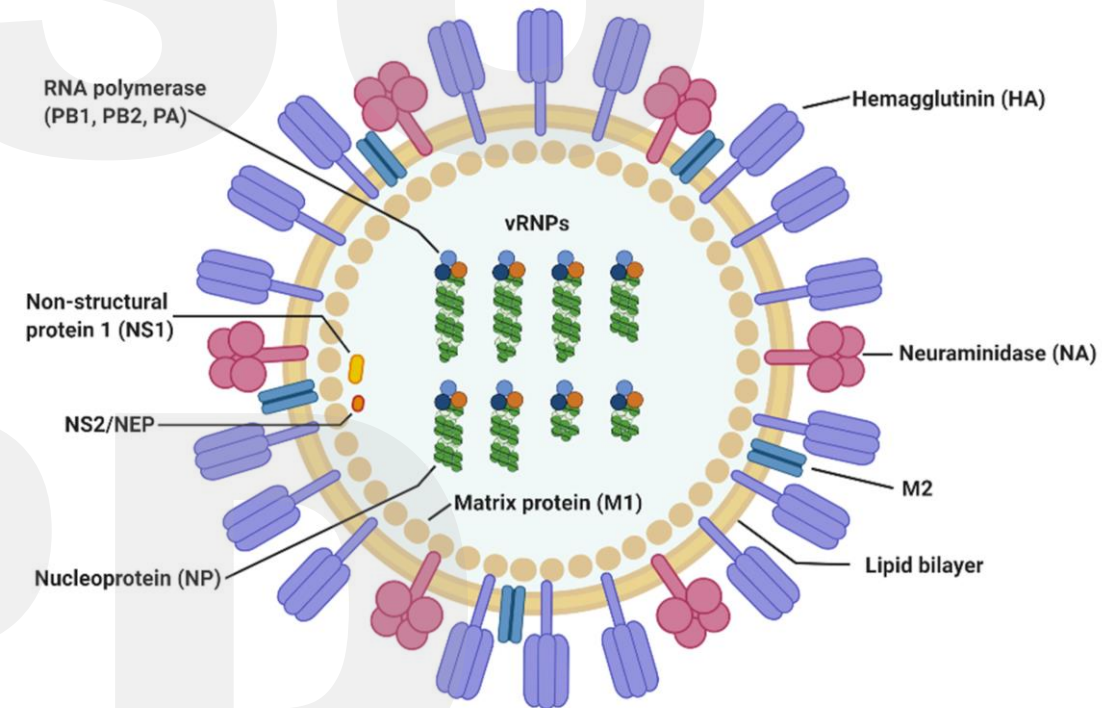


Central dogma of virology



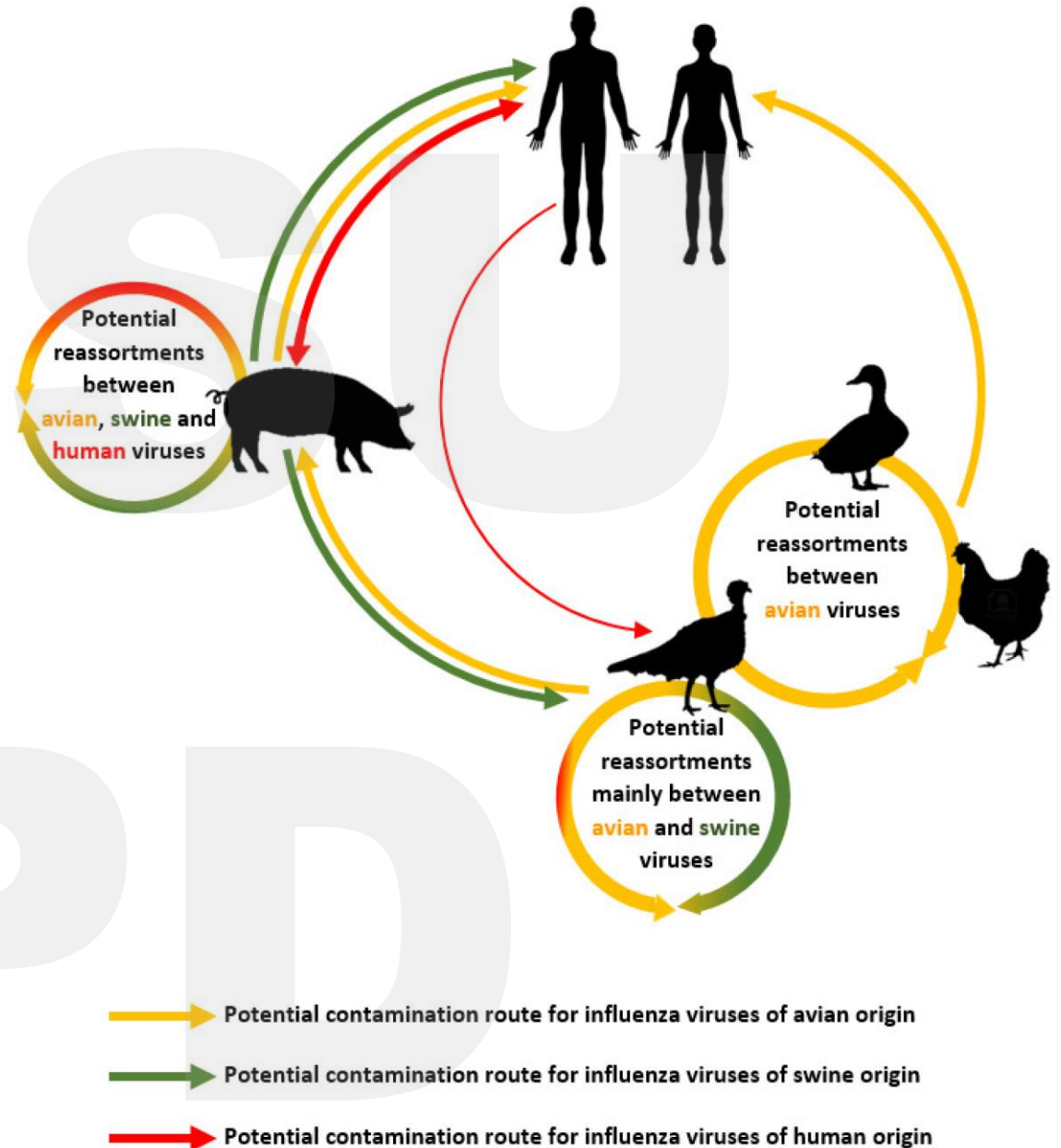
H5N1 avian influenza

- Enveloped, 8 segmented gene (-) RNA virus
 - Hemagglutinin (H, 16)
 - Neuraminidase (N, 9)
 - H5N1



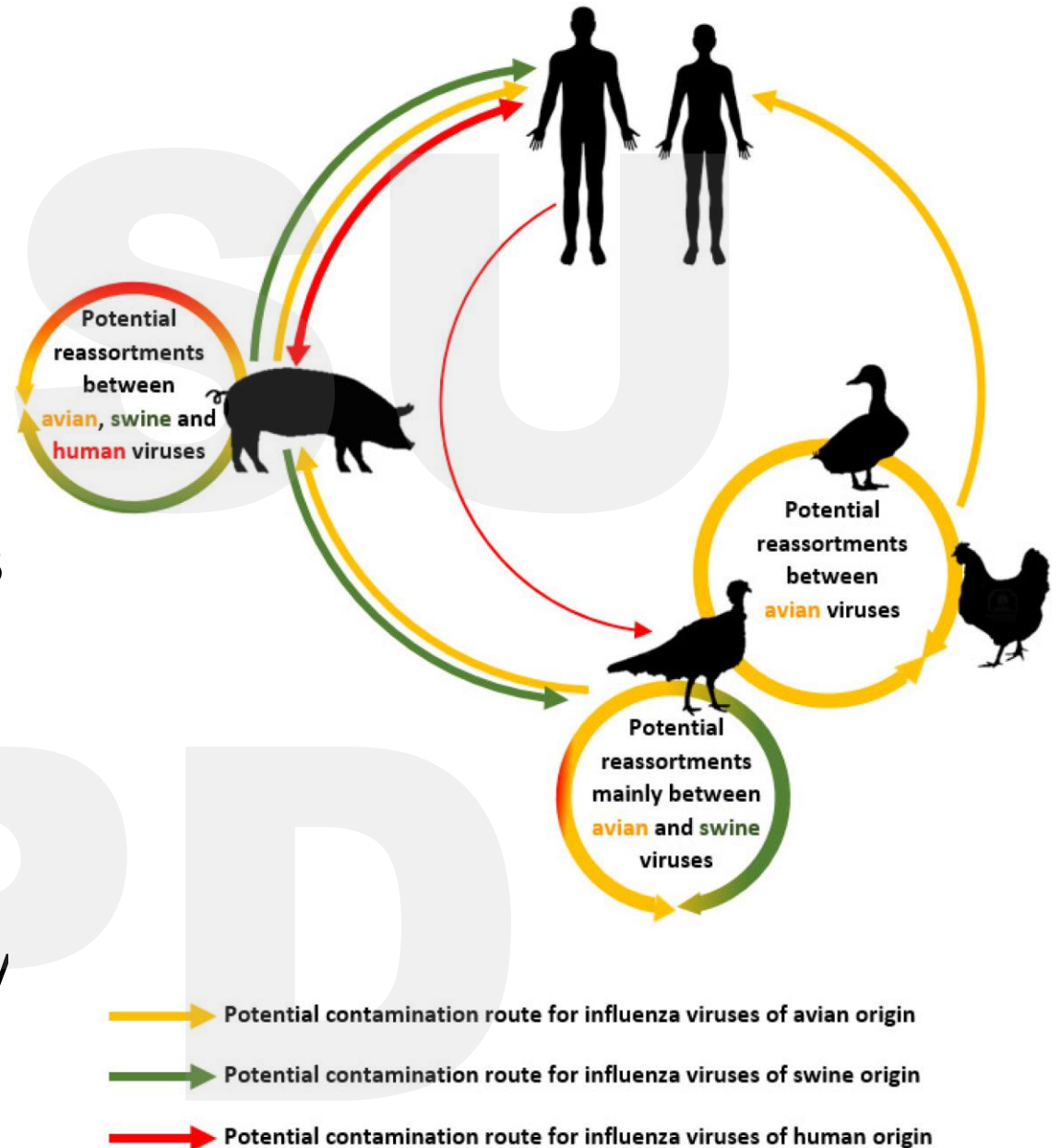
H5N1 avian influenza

- Enveloped, 8 segmented gene (-) RNA virus
 - Hemagglutinin (H, 16)
 - Neuraminidase (N, 9)
 - H5N1
- 3 key hosts facilitate genetic reassortment
 - Humans
 - Avian
 - pigs

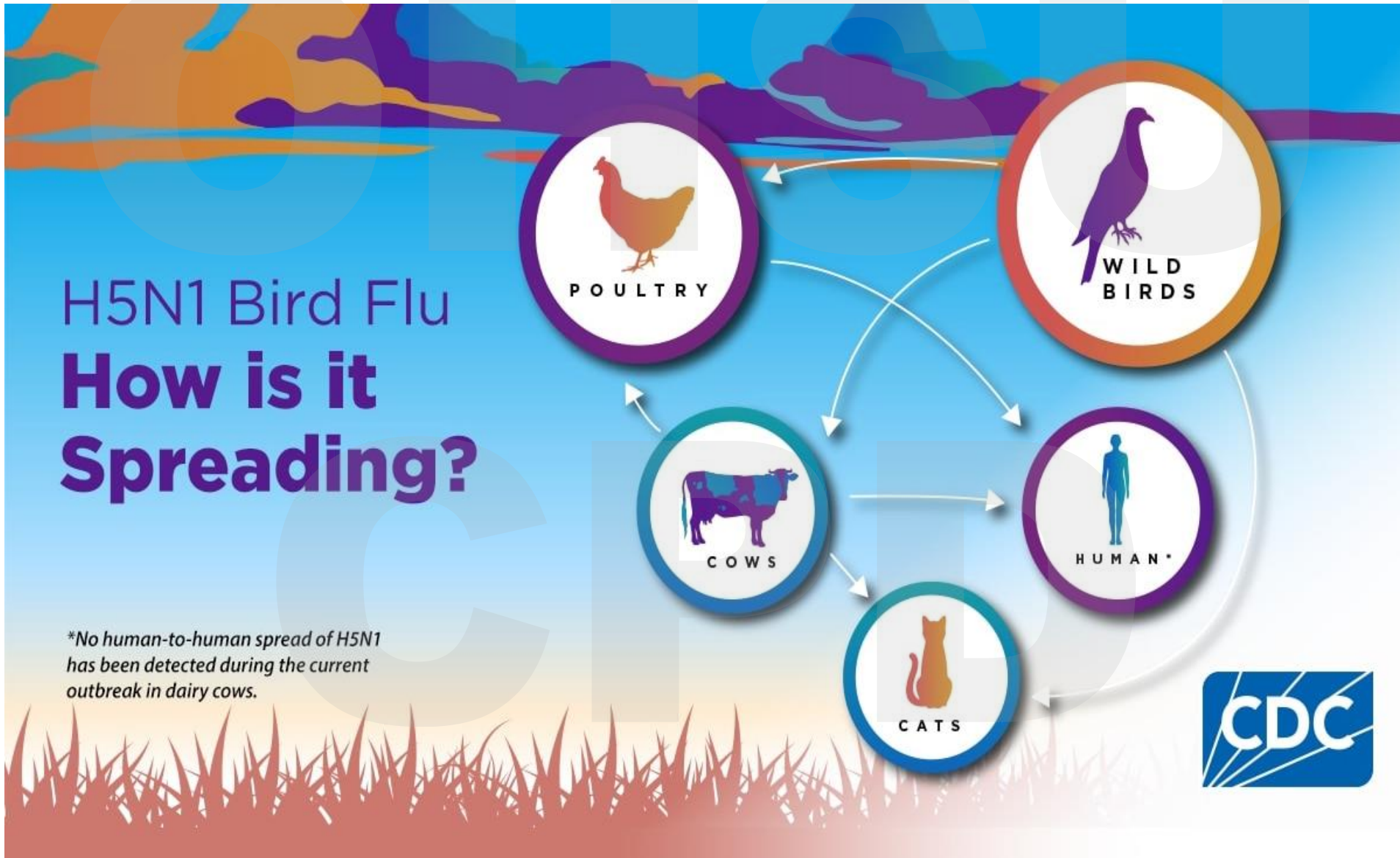


H5N1 avian influenza

- Serotype combination first detected in the 1950's in Asia.
- H5N1 viruses evolved
 - 1997 Hong Kong H5N1 outbreak, 18 human cases, six deaths
 - Re-emerged 2003-2006, then H1N1 happened
- Current clade 2.3.4.4b infects wild* and domestic birds, domestic cattle, and occasionally humans.

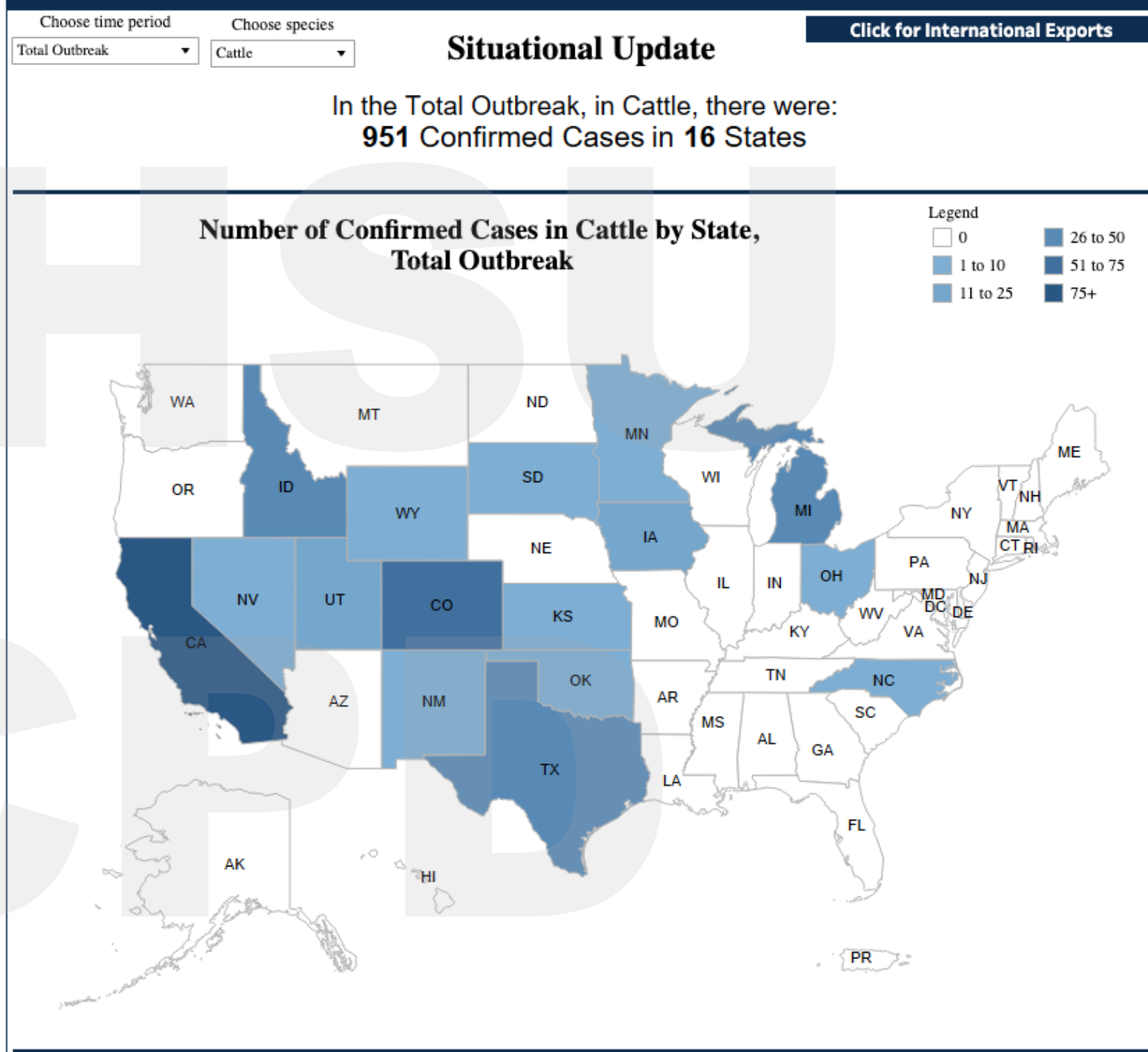


H5N1 avian influenza



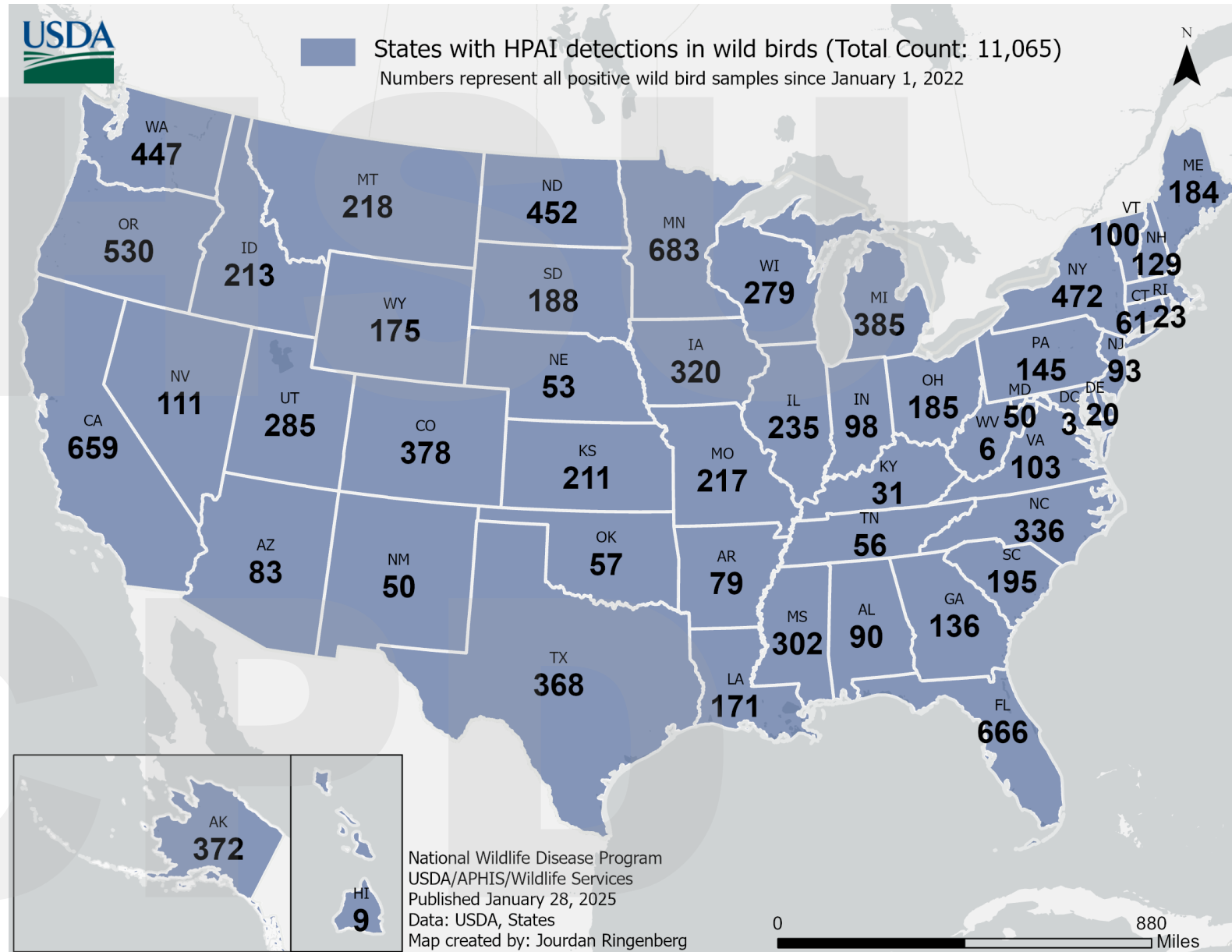
H5N1 avian influenza

- Multi-state cattle outbreaks



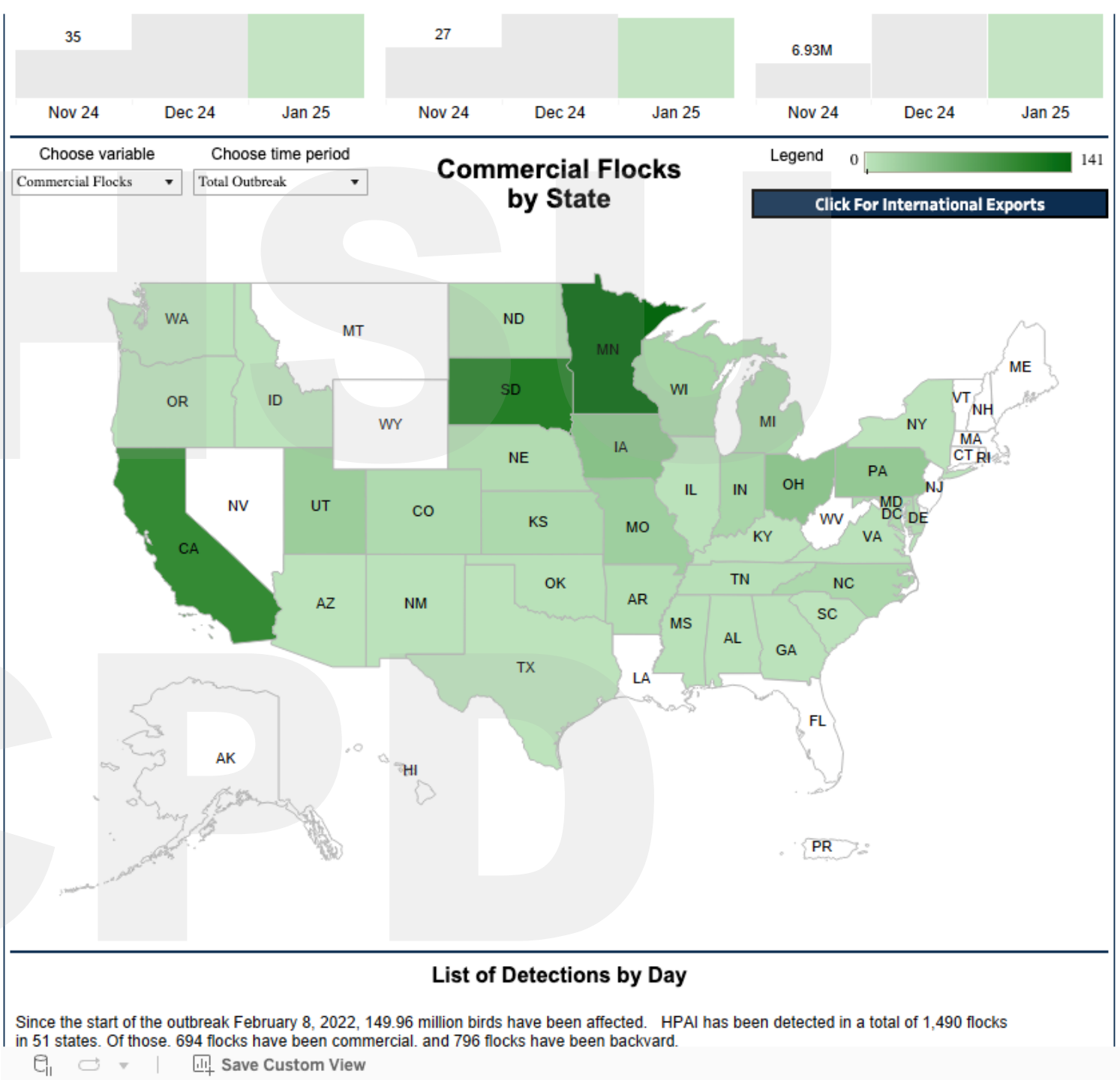
H5N1 avian influenza

- Multi-state cattle outbreaks
- Widespread wild-bird infection



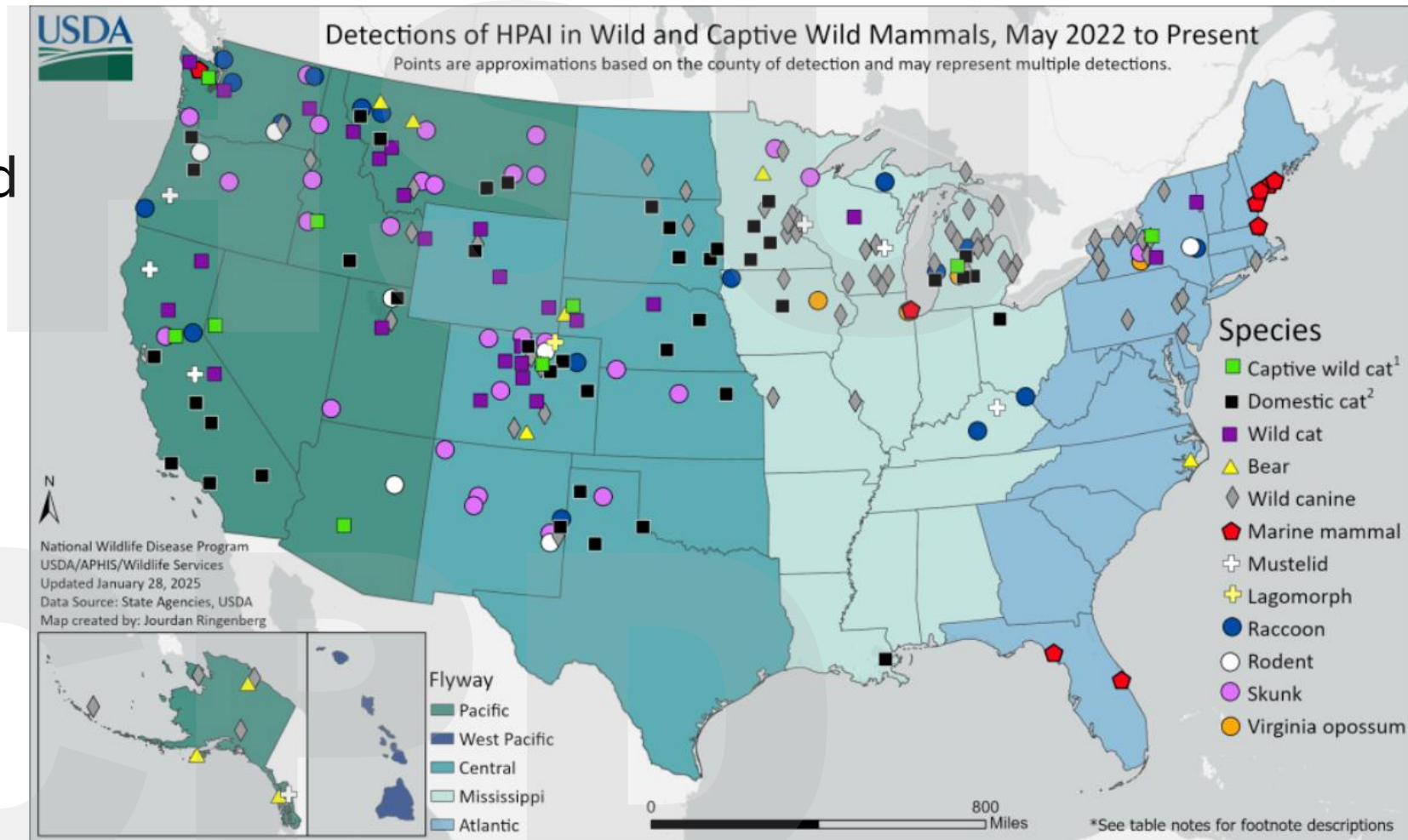
H5N1 avian influenza

- Multi-state cattle outbreaks
- Widespread wild-bird infection
- Widespread domestic flock infection
 - Commercial
 - Backyard



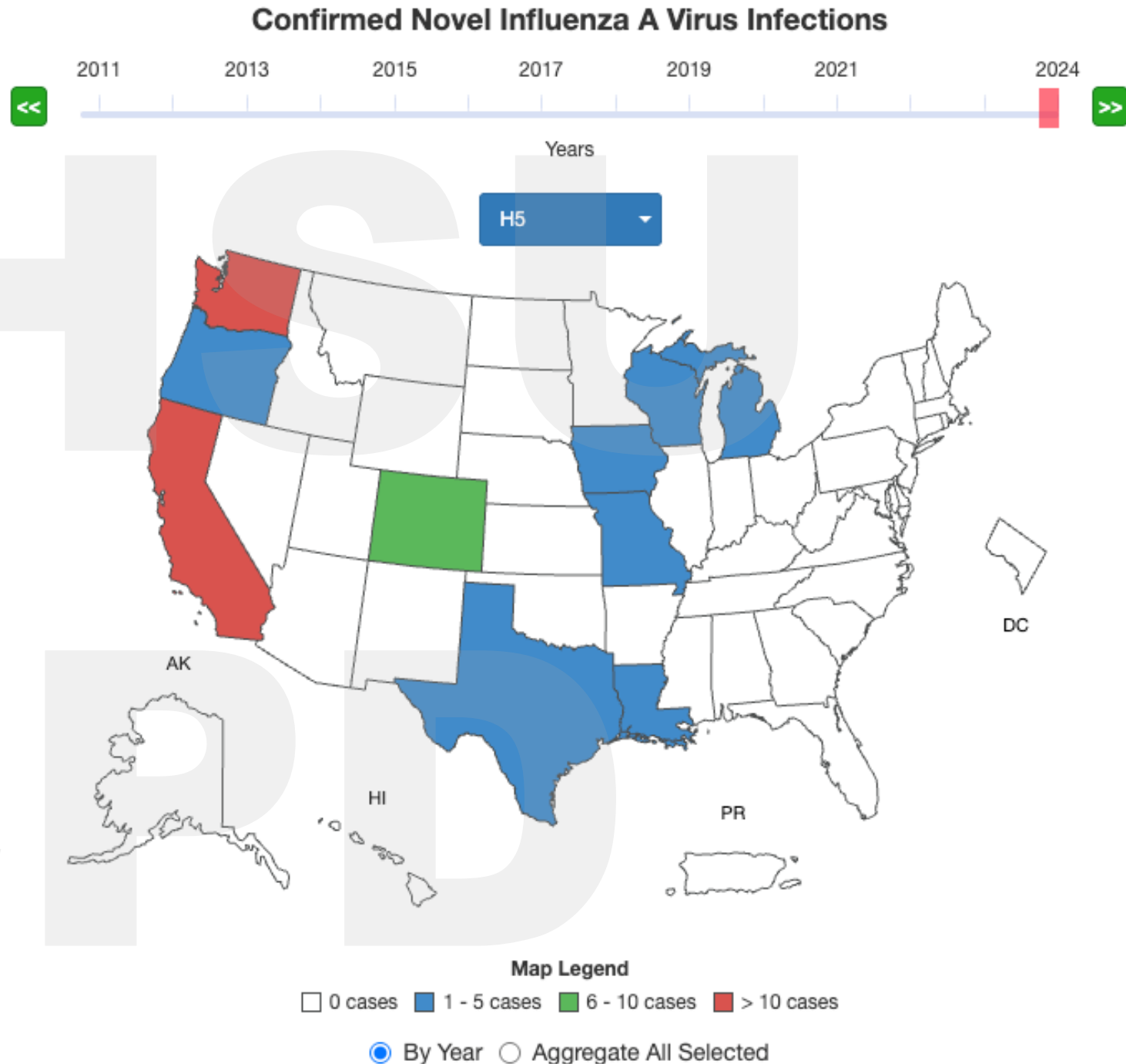
H5N1 avian influenza

- Widespread wild and captive mammals
- A major driver of virus persistence
 - Cannot cull wild-animal flocks or herds
- Migratory birds suspected to play a key role virus movement



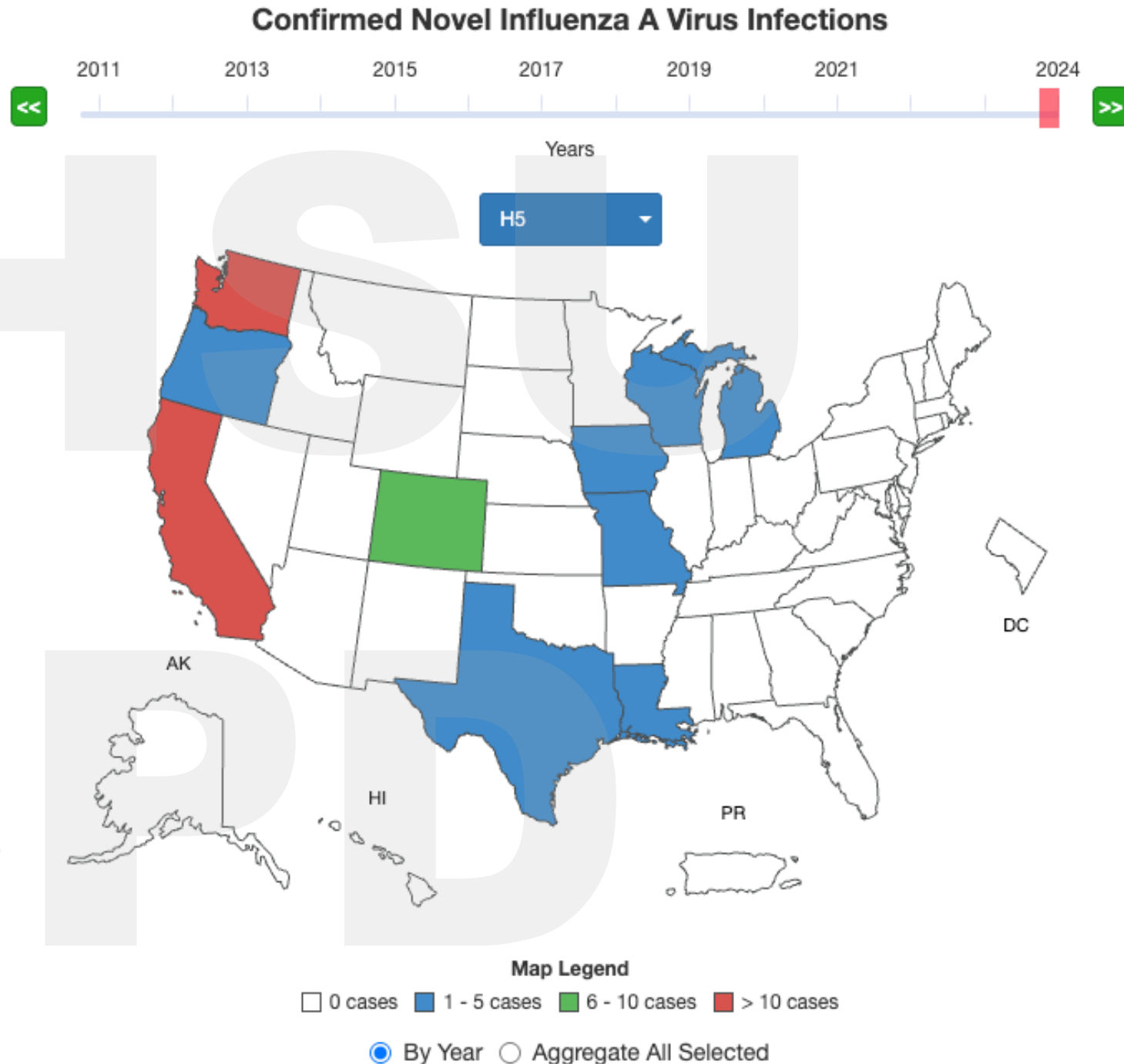
H5N1 avian influenza

- Widespread wild and captive mammals
- 67 confirmed human cases, 1 death



H5N1 avian influenza

- Widespread wild and captive mammals
- 67 confirmed human cases, 1 death
- By comparison, 343 +tive seasonal cases in Portland Metro area the first week of Jan, 2025



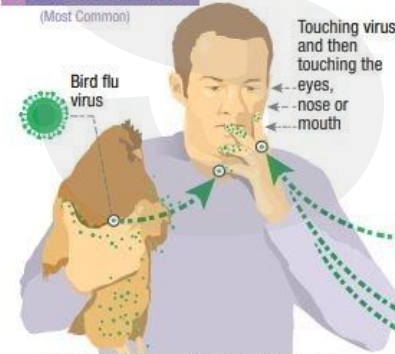
H5N1 avian influenza

- Clinical pearls
 - Major risk factors are interactions with:
 - Dairy cows,
 - Poultry (commercial, backyard)
 - Wild birds
 - Airborne precautions for suspected cases
 - Conjunctivitis is a predominant symptom
 - Neither Cepheid nor Biofire panels detect H5 avian influenza
 - Seasonal flu vaccine not effective
 - Oseltamivir is effective
 - No human to human transmission has been documented

How Infected Backyard Poultry Could Spread Bird Flu to People

Human Infections with Bird Flu Viruses Rare But Possible

1 Direct Contact (Most Common)

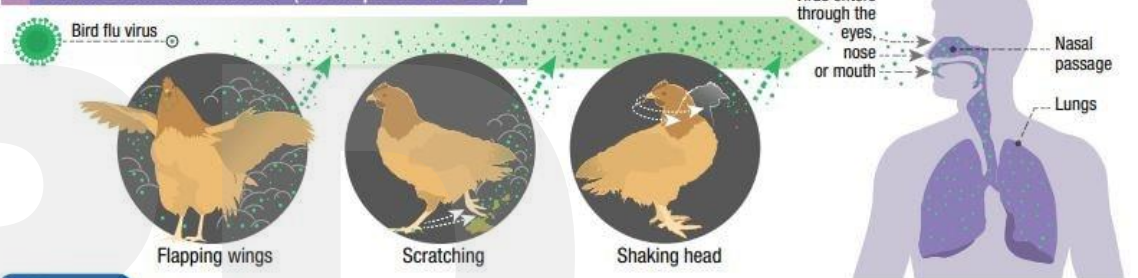


Infection can occur without touching poultry.

2 Contaminated Surfaces



3 Bird Flu Virus in the Air (in Droplets or Dust)



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

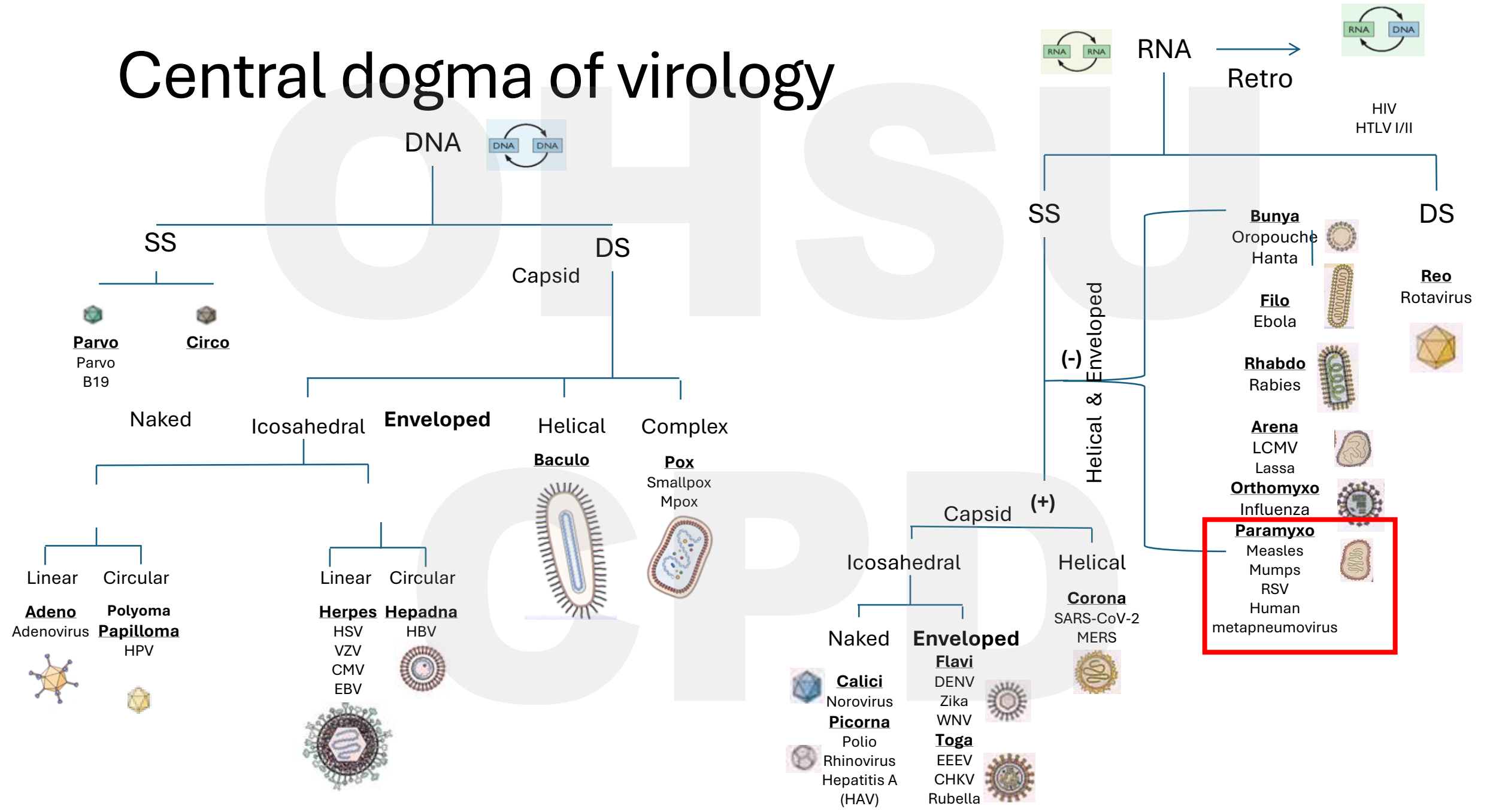
www.cdc.gov/flu/avianflu/avian-in-humans.htm

CS201152

Human metapneumovirus

- Single stranded (-) RNA virus,
Paramyxoviridae

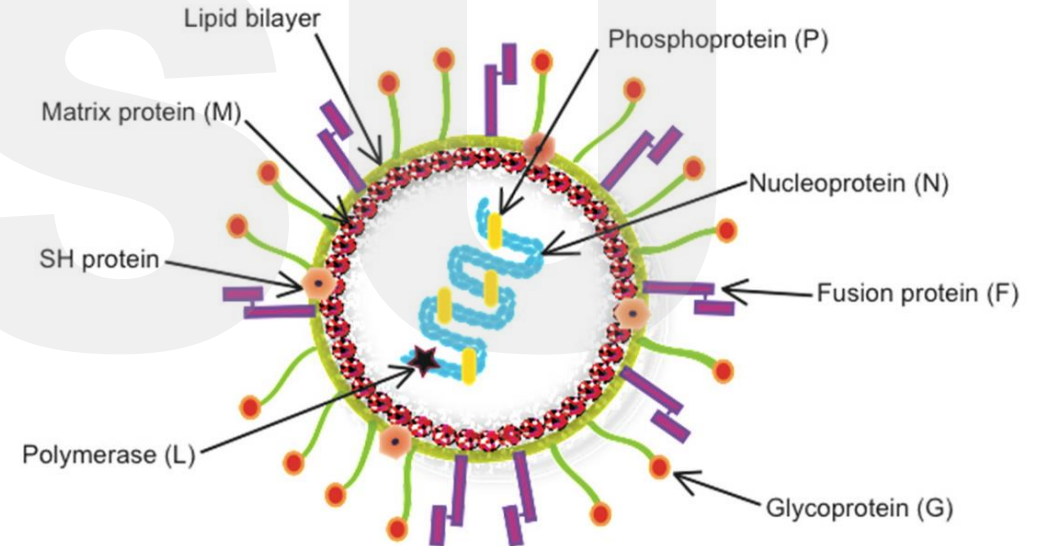
Central dogma of virology



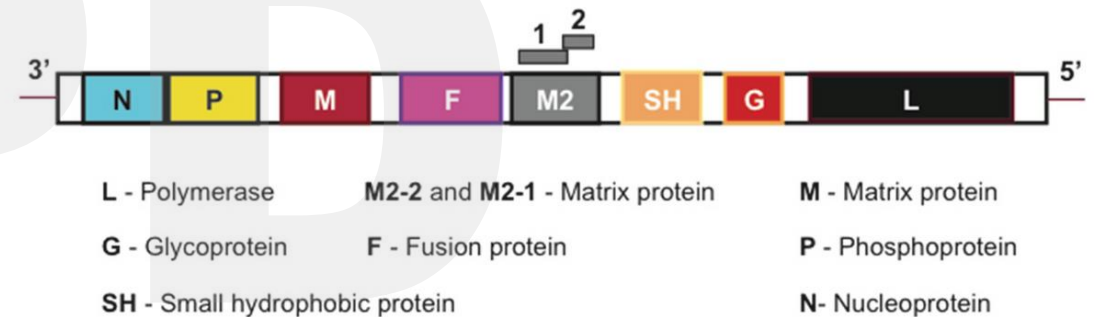
Human metapneumovirus

- Single stranded (-) RNA virus, *Paramyxoviridae*

a. Model structure of hMPV



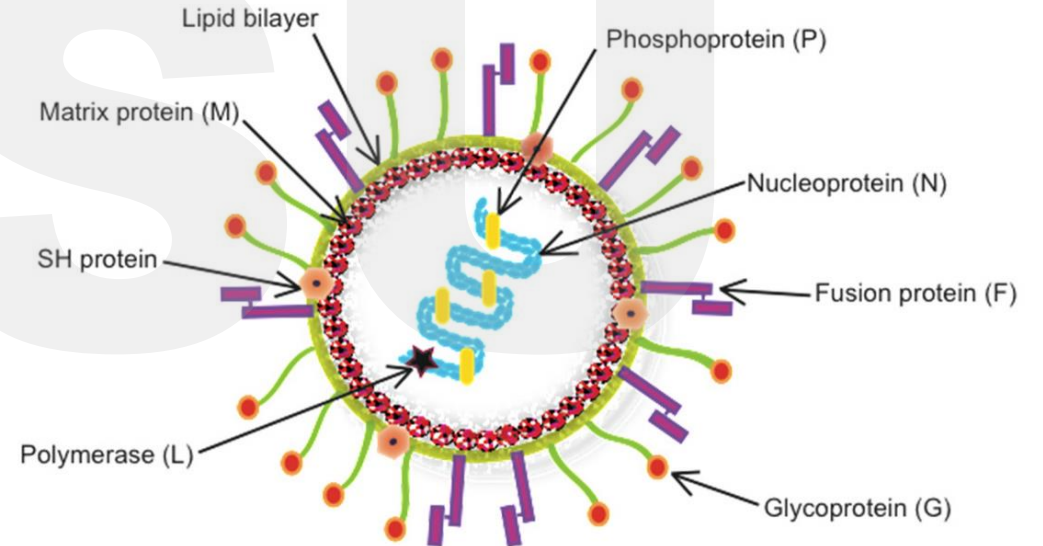
b. Proteins encoded by hMPV genome



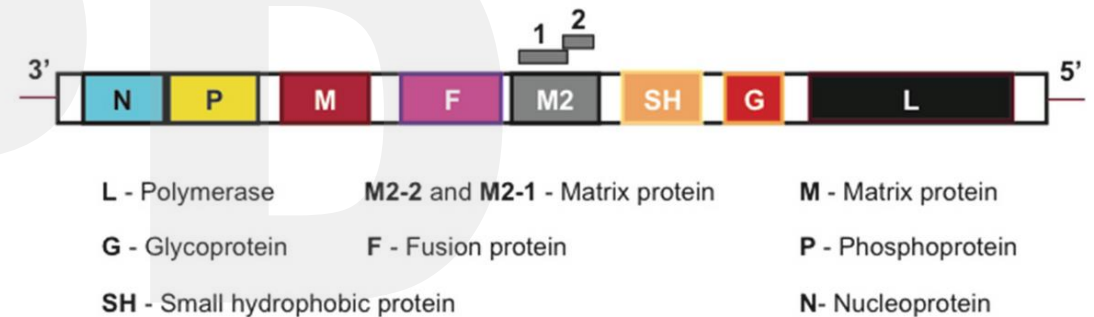
Human metapneumovirus

- Single stranded (-) RNA virus, *Paramyxoviridae*
- “Emerging” infection discovered in 2001 in the Netherlands
 - Likely circulating for decades before detection
- URI and LRI, PNA
- Strong seasonality, less common than SARS-CoV-2 or influenza viruses.

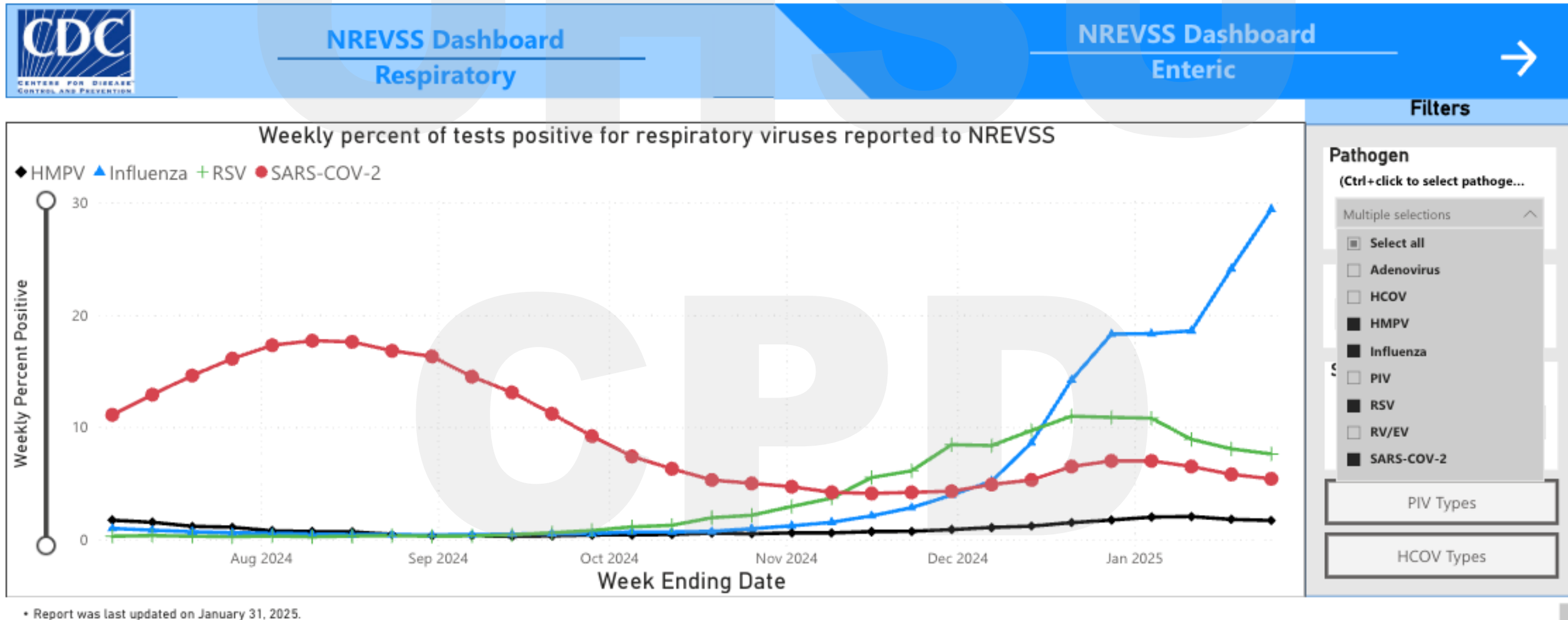
a. Model structure of hMPV



b. Proteins encoded by hMPV genome



Human metapneumovirus



Human metapneumovirus

Observational Study > Clin Microbiol Infect. 2021 Jan;27(1):127.e1-127.e6.

doi: 10.1016/j.cmi.2020.04.005. Epub 2020 Apr 10.

Characteristics of human metapneumovirus infection in adults hospitalized for community-acquired influenza-like illness in France, 2012–2018: a retrospective observational study

7.e6

127.e5

Table 2

Sociodemographic, clinical characteristics and outcome of hospitalized patients infected with human metapneumovirus, compared with respiratory syncytial virus and influenza virus infected patients, 2012–2018

	hMPV+ (n = 90)	Influenza+ (n = 908)	p	RSV+ (n = 129)	p
Outcome					
At least one complication during the hospital stay, n (%)	56/90 (62%)	473/908 (52%)	0.07	85/129 (66%)	0.58
Pneumonia, n (%)	32/89 (36%)	257/904 (28%)	0.14	50/128 (39%)	0.64
Respiratory failure, n (%)	32/89 (36%)	254/904 (28%)	0.12	47/128 (37%)	0.91
Acute heart failure, n (%)	22/89 (25%)	114/903 (13%)	0.002	21/128 (16%)	0.13
Acute respiratory distress syndrome, n (%)	8/89 (9%)	83/904 (9%)	0.95	15/128 (12%)	0.52
Median length of stay, days (IQR)	7 (4–13)	6 (3–10)	0.06	7 (5–14)	0.50
ICU admission after hospitalization in acute care, n (%)	15/90 (17%)	155/908 (17%)	0.88	33/128 (26%)	0.20
Death, n (%)	4/90 (4%)	36/906 (4%)	0.78	9/129 (7%)	0.44

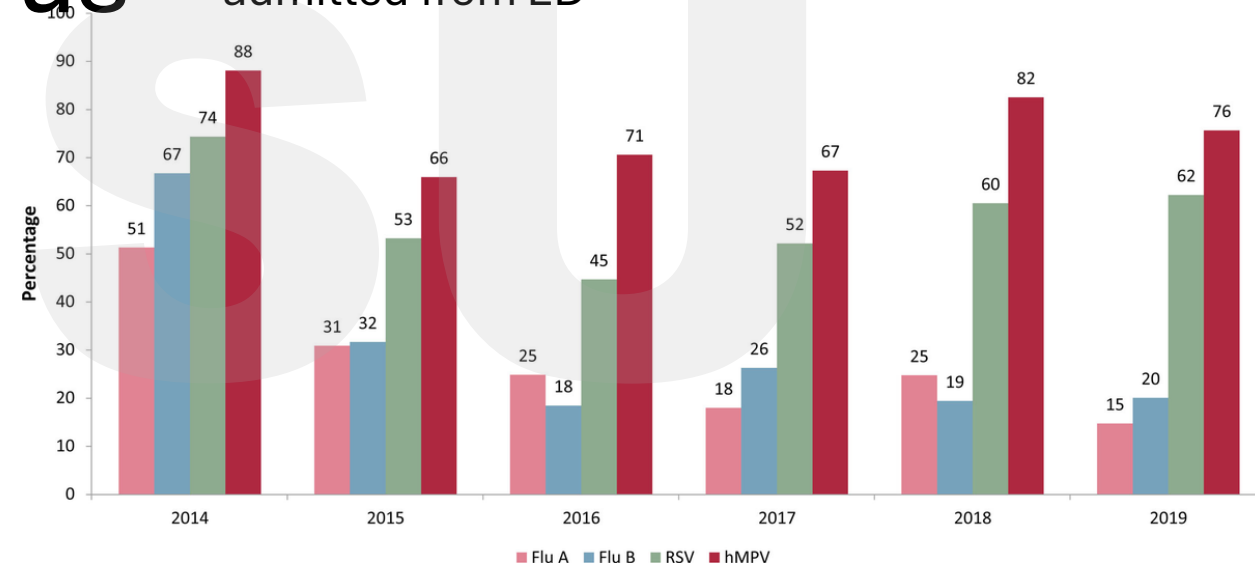
Human metapneumovirus

**Pediatric Infectious Disease
Journal**

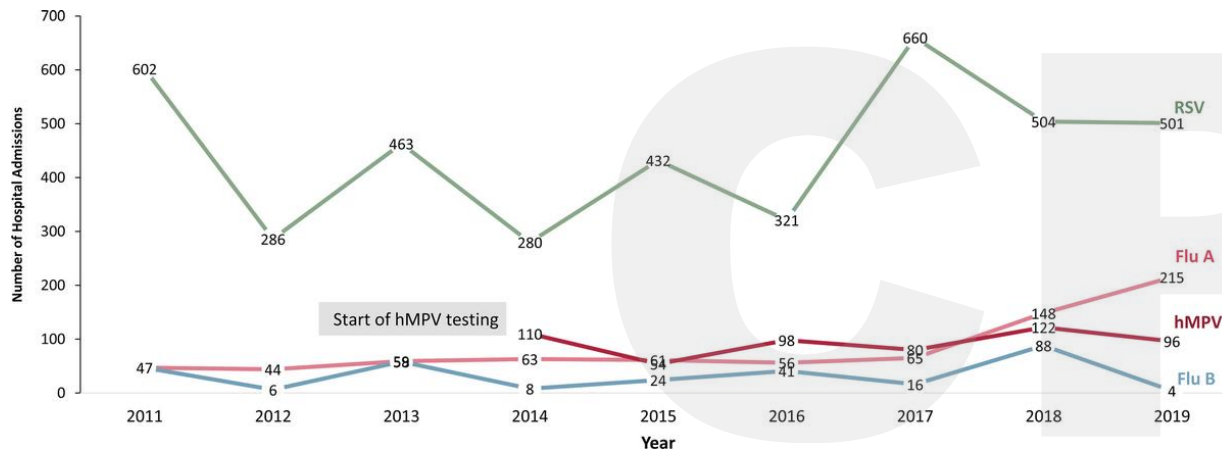
April 2022 , Volume 41 (4), p 284 – 289

Single hospital experience from 2014-2019
Children's Hospital of Orange County, CA

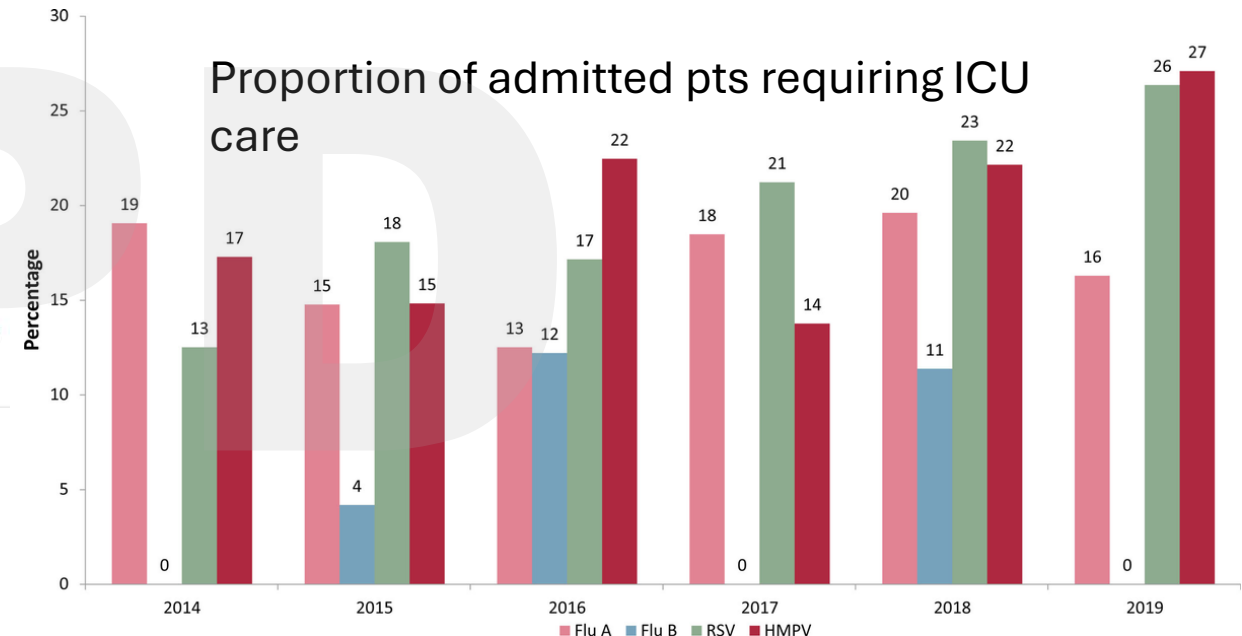
Proportion of test positive pts
admitted from ED



Admissions per virus, 2014-2019

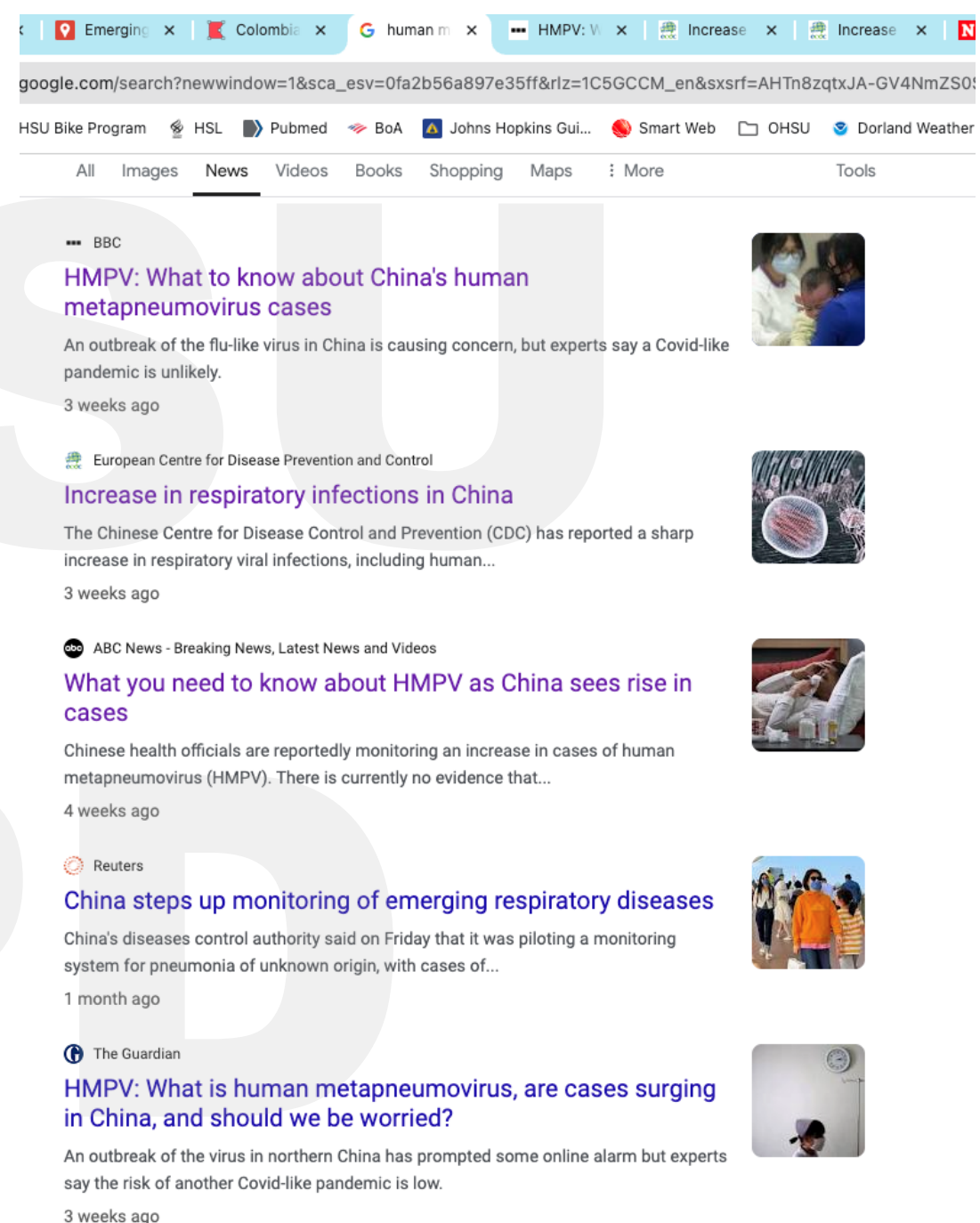


Proportion of admitted pts requiring ICU
care



Human metapneumovirus

- Single stranded (-) RNA virus, *Paramyxoviridae*
- “Emerging” infection, discovered in 2001 in the Netherlands
 - Likely circulating for decades before detection
- URI and LRI, PNA
- Strong seasonality, less common than SARS-CoV-2 or influenza viruses.



The screenshot shows a Google search results page for the query 'human metapneumovirus'. The browser tabs at the top include 'Emerging', 'Colombia', 'human m', 'HMPV: V', 'Increase', and 'Increase'. The search bar shows the query 'human metapneumovirus' and the URL 'google.com/search?newwindow=1&sca_esv=0fa2b56a897e35ff&rlz=1C5GCCM_en&sxsrf=AHn8zqtJA-GV4NmZS0...'. The search results are displayed under the 'News' tab, showing four articles from BBC, European Centre for Disease Prevention and Control, ABC News, and Reuters. Each article includes a title, a brief description, and a timestamp. To the right of each article is a small thumbnail image.

... BBC
HMPV: What to know about China's human metapneumovirus cases
An outbreak of the flu-like virus in China is causing concern, but experts say a Covid-like pandemic is unlikely.
3 weeks ago

European Centre for Disease Prevention and Control
Increase in respiratory infections in China
The Chinese Centre for Disease Control and Prevention (CDC) has reported a sharp increase in respiratory viral infections, including human...
3 weeks ago

ABC News - Breaking News, Latest News and Videos
What you need to know about HMPV as China sees rise in cases
Chinese health officials are reportedly monitoring an increase in cases of human metapneumovirus (HMPV). There is currently no evidence that...
4 weeks ago

Reuters
China steps up monitoring of emerging respiratory diseases
China's diseases control authority said on Friday that it was piloting a monitoring system for pneumonia of unknown origin, with cases of...
1 month ago

The Guardian
HMPV: What is human metapneumovirus, are cases surging in China, and should we be worried?
An outbreak of the virus in northern China has prompted some online alarm but experts say the risk of another Covid-like pandemic is low.
3 weeks ago



European Centre for Disease Prevention and Control

An agency of the European Union

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< Media centre

Increase in respiratory infections in China

News

8 Jan 2025



Translate this page

The Chinese Centre for Disease Control and Prevention (CDC) has reported a sharp increase in respiratory viral infections, including human metapneumovirus (hMPV) infections, in northern China since December 2024.

Human metapneumovirus regularly circulates in the EU/EEA during colder months. Currently, the surveillance of acute respiratory infections in the EU/EEA shows increased activity of respiratory viruses, particularly influenza, with no unusual or unexpected pattern for this time of year.

Human metapneumovirus can affect all age groups and normally causes mild-to-moderate respiratory illness but sometimes the infection can be severe in young children, older adults, and immunocompromised individuals. In the EU/EEA, hMPV is most active during late winter and spring, often circulating alongside other respiratory viruses. There is no vaccine or specific antiviral treatment available for hMPV.

Based on the current information, the European Centre for Disease Prevention and Control (ECDC) considers that the current epidemiological situation in China reflects a seasonal rise in respiratory infections caused by common respiratory pathogens and does not pose any specific concern for the EU/EEA.

Human metapneumovirus

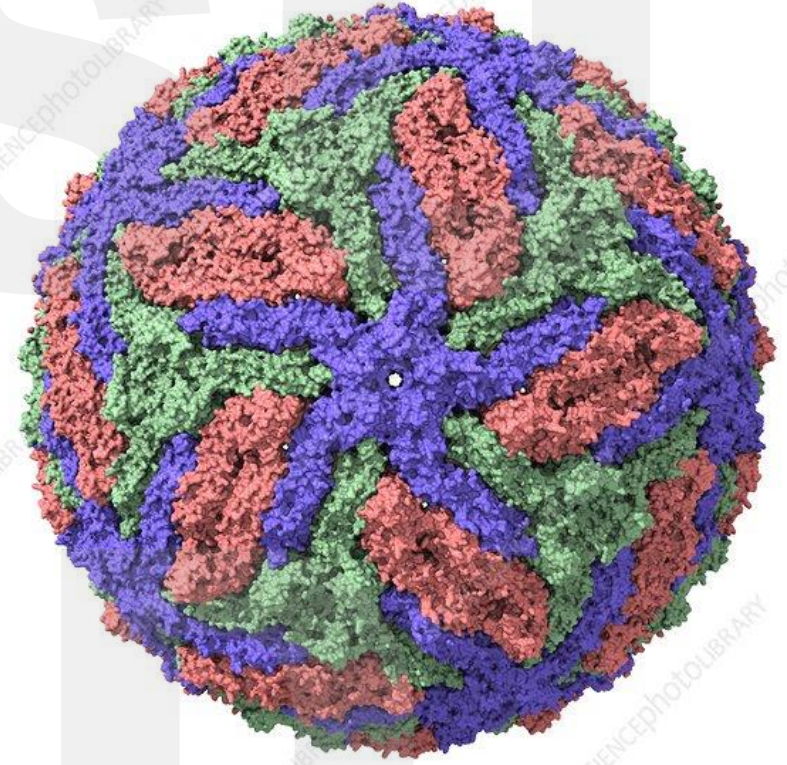
- Clinical pearls
 - Clinical presentations similar to RSV
 - High risk individuals include:
 - Older patients
 - COPD
 - Newborns and infants
 - Can cause severe disease (not just a common cold virus) requiring hospitalization and ICU care.
 - Despite its low incidence, comparable clinical courses and outcomes:
 - Influenza
 - RSV

Human metapneumovirus

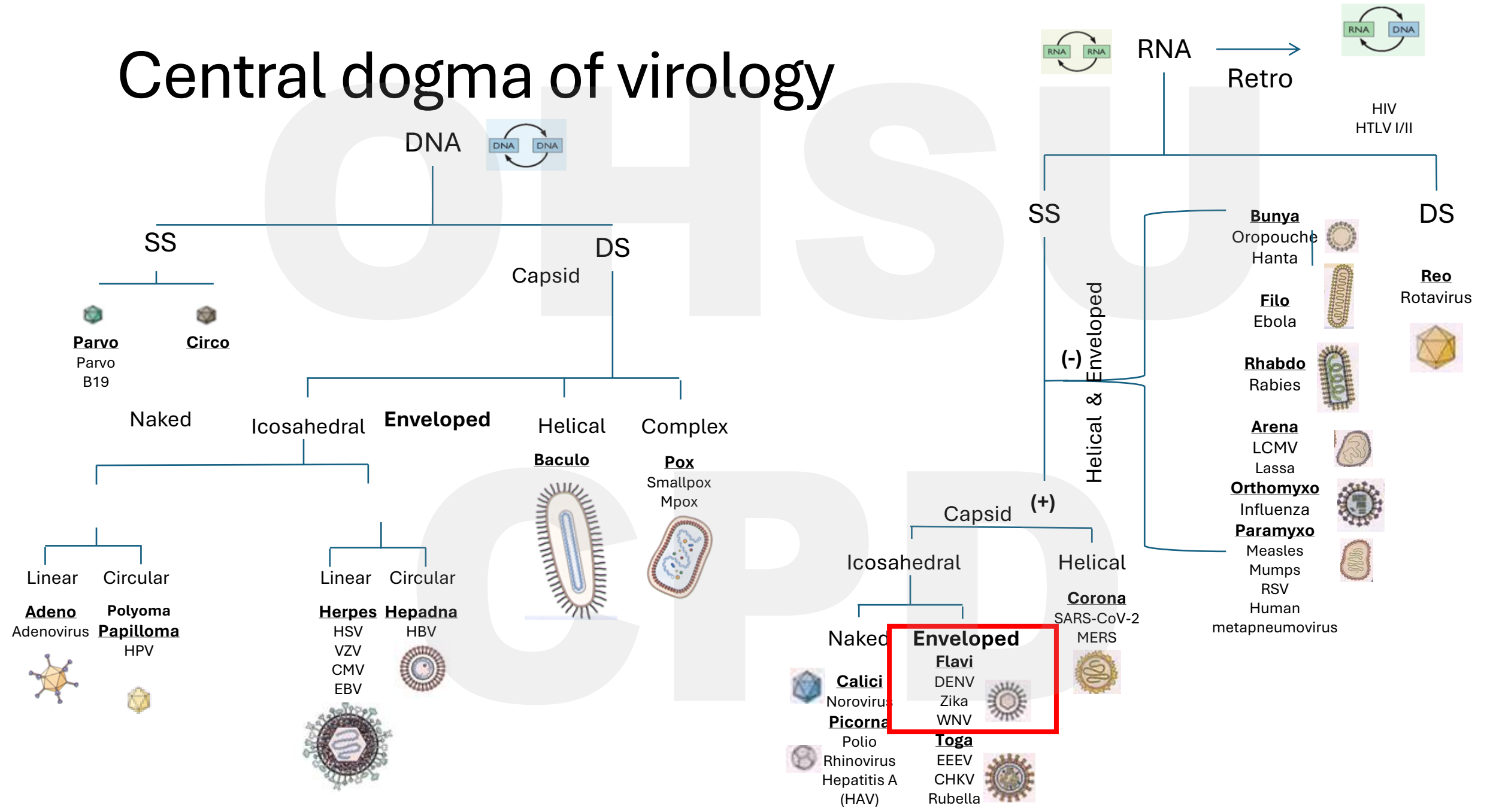
- Single stranded (-) RNA virus, *Paramyxoviridae*
- Discovered in 2001 in the Netherlands
 - Likely circulating for decades before detection
- URI and LRI, PNA
- Strong seasonality, less common than SARS-CoV-2 or influenza viruses.
- Probably not an outbreak
 - Not moved into a new region or population
 - Incidence appears stable
 - Severity of illness appears unchanged

Dengue virus

- Enveloped single stranded (+) RNA virus, Orthoflavivirus



Central dogma of virology



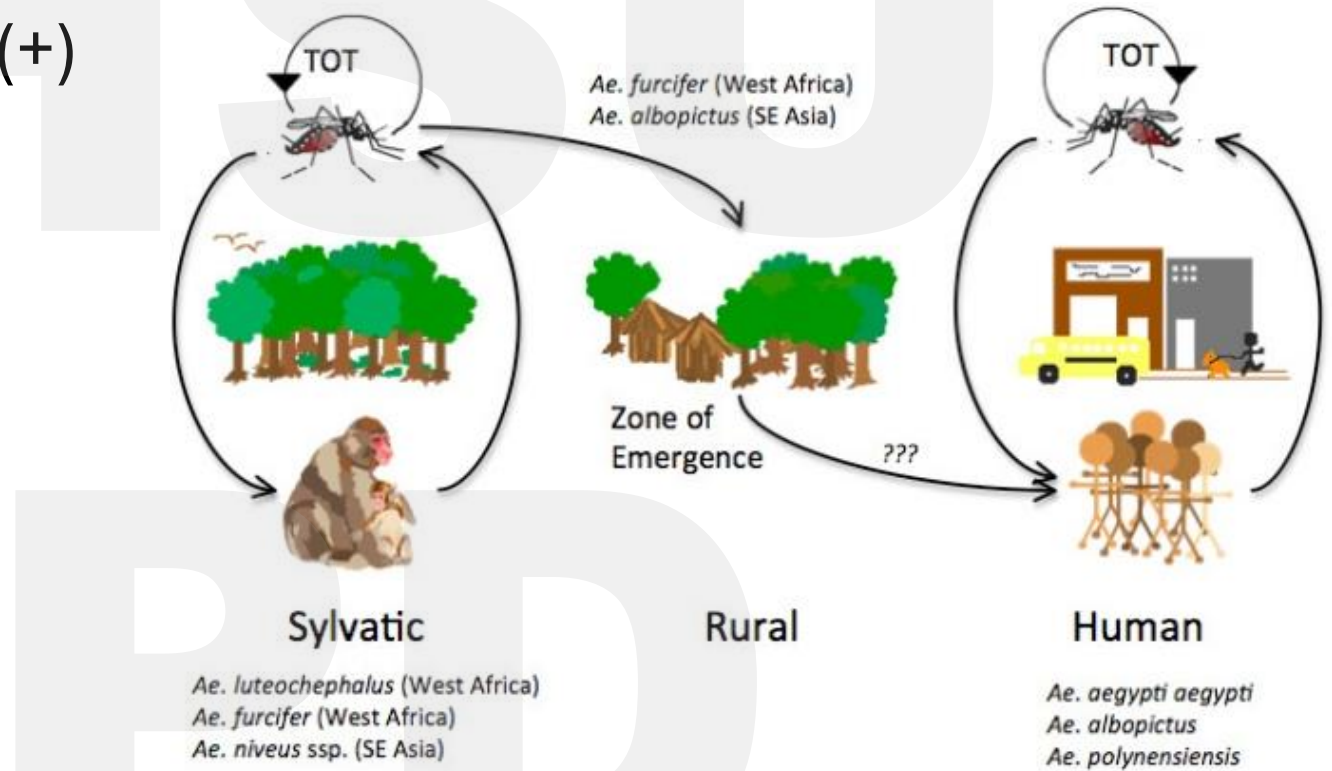
Dengue virus

- Enveloped single stranded (+) RNA virus, Orthoflavivirus
- Four serotypes DENV1-DENV4



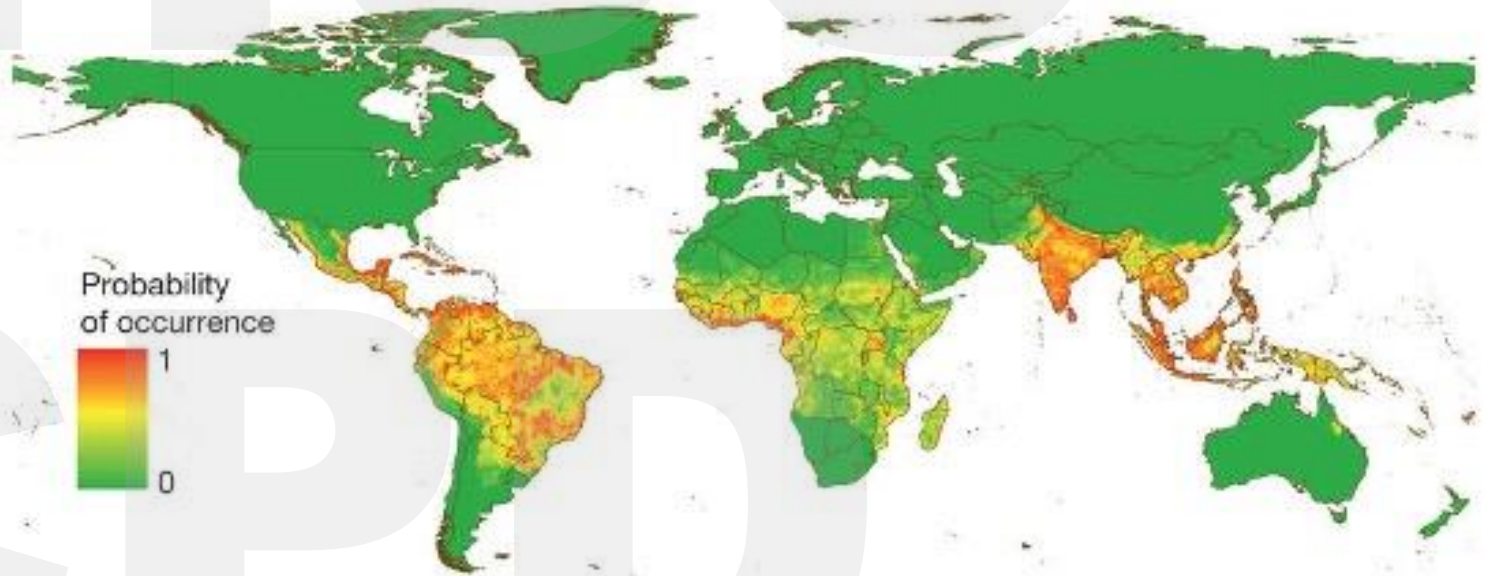
Dengue virus

- Enveloped single stranded (+) RNA virus, Orthoflavivirus
- Four serotypes DENV1-DENV4
- Maintained by human-mosquito transmission



Dengue virus

- Enveloped single stranded (+) RNA virus, Orthoflavivirus
- Four serotypes DENV1-DENV4
- Maintained by human-mosquito transmission
- Occurs throughout the tropics and subtropics



Dengue virus

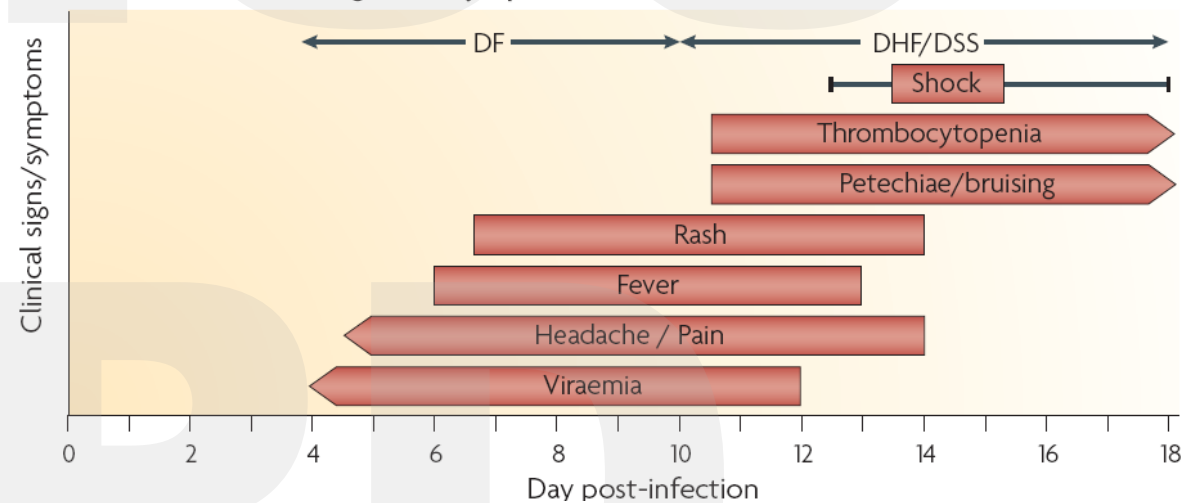
- Febrile illness
 - 20-80% symptomatic
 - Undifferentiated fever
 - Fever with warning signs
 - Severe dengue (prev. dengue hemorrhagic fever, dengue shock syndrome)
- Biphasic illness
- Vaccines are approved but partially effective at best

DENGUE ± WARNING SIGNS

SEVERE DENGUE



d Time course of clinical signs and symptoms

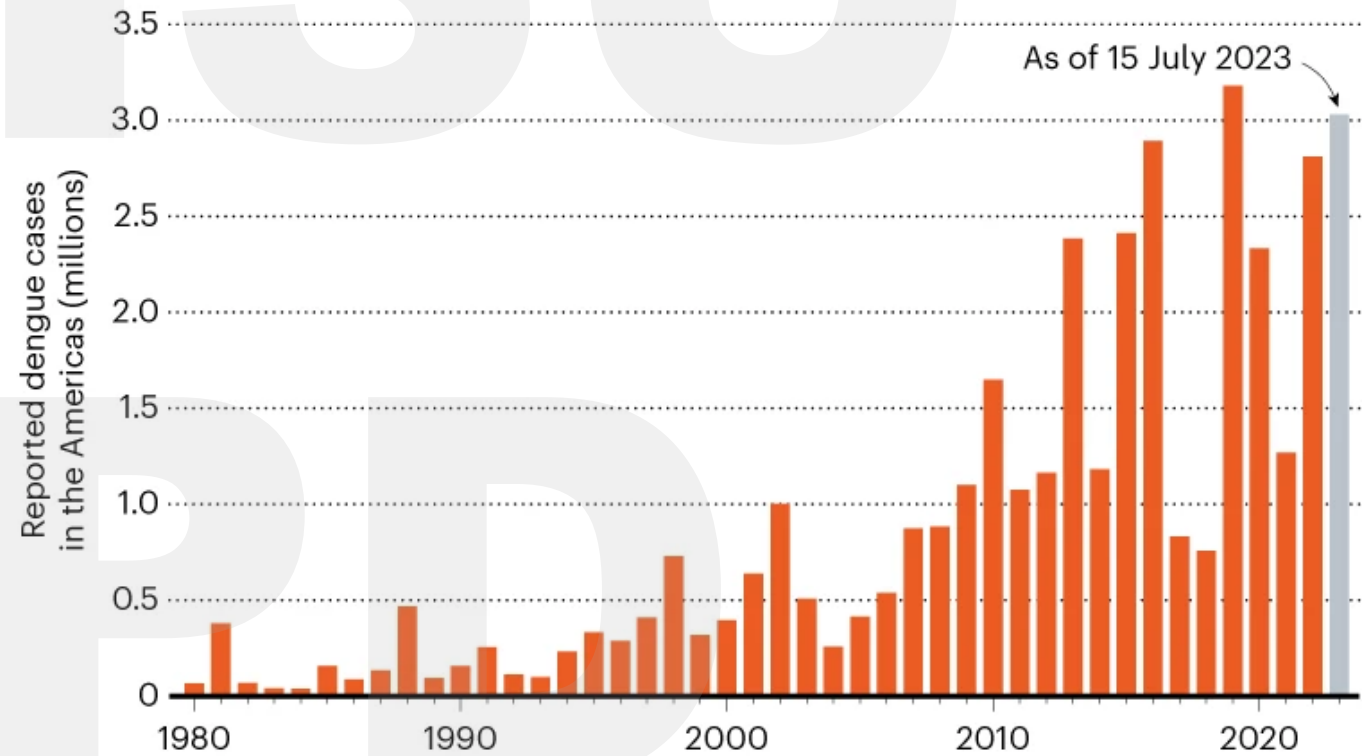


Dengue virus

- Dengue virus has been “re-emerging” since the 1970s

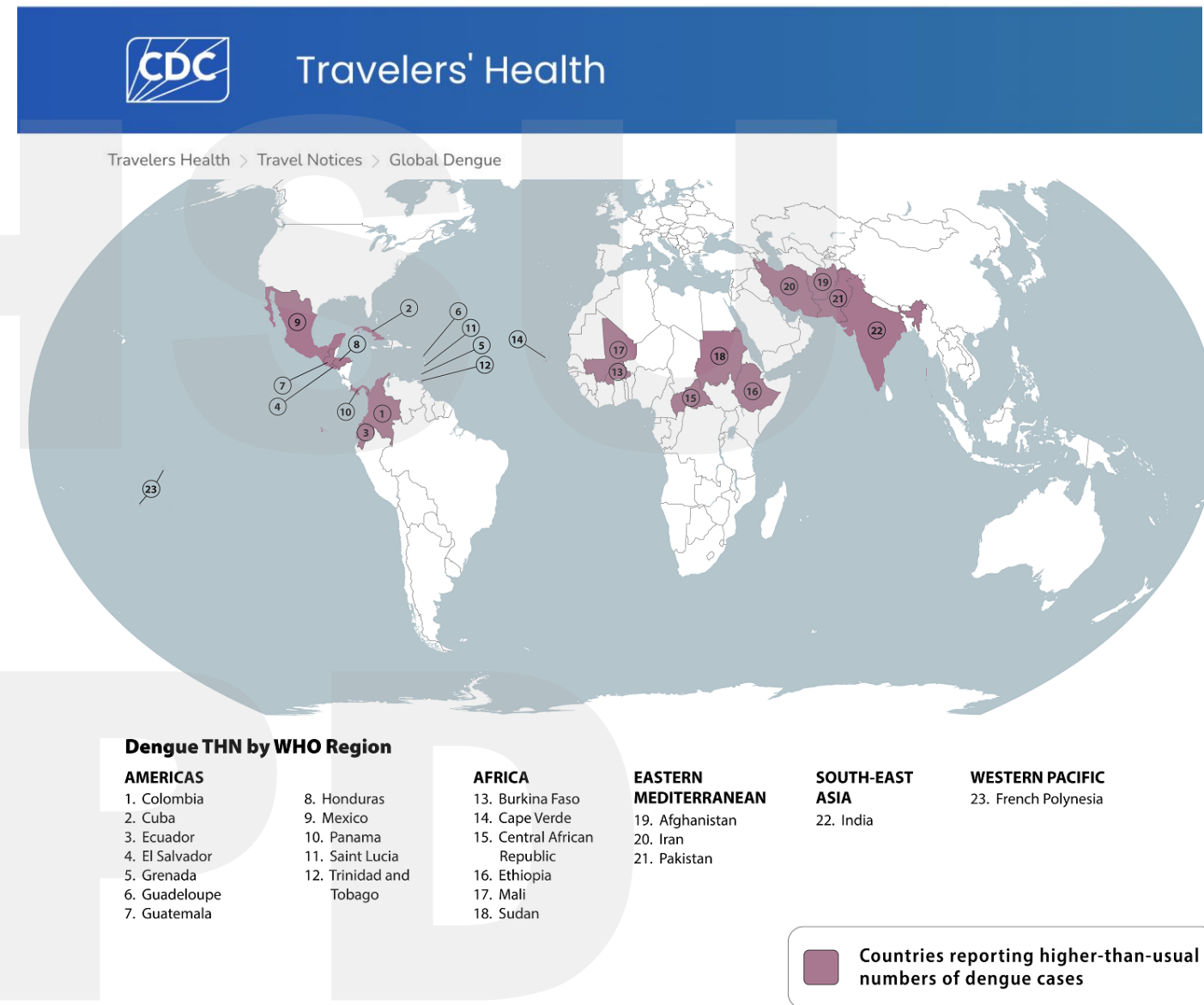
DENGUE ON THE RISE

Changes in temperature and rainfall patterns in the Americas might help to explain high incidences of dengue in recent years.



Dengue virus

- Dengue virus has been “emerging” and “re-emerging” since the 1970s
- 2024 had higher than usual cases worldwide



Names and boundary representation are not necessarily authoritative.



Dengue virus

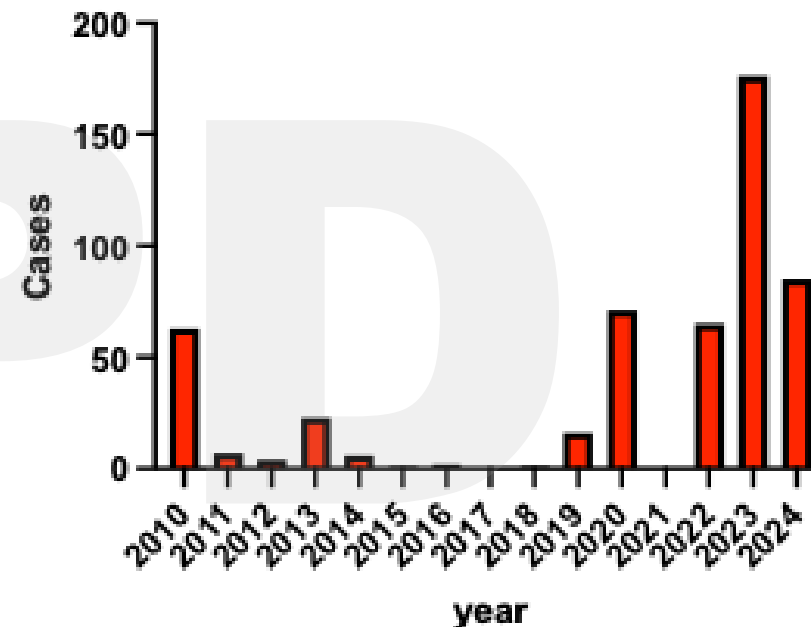
- Dengue virus has been “emerging” and “re-emerging” since the 1970s
- 2024 had higher than usual cases worldwide
- Now may be emerging in the US.
 - Florida

Florida Arbovirus Surveillance Week 52: December 22-28, 2024

Dengue Cases Acquired in Florida: No cases of locally acquired dengue were reported this week. In 2024, 85 cases of locally acquired dengue have been reported from ten counties.

County of Exposure	DENV-1	DENV-3	Unknown	Total
Hillsborough	2	1		3
Manatee		1		1
Miami-Dade		20	2	22
Monroe	2		1	3
Orange		2		2
Palm Beach			1	1
Pasco		3		3
Total	4	27	4	35

Local dengue transmission, FL 2010-2024



Dengue virus

- Dengue virus has been “emerging” and “re-emerging” since the 1970s
- 2024 had higher than usual cases worldwide
- Now may be emerging in the US.
 - Florida
 - California
 - Texas

CDPH Monthly Update on Number of Dengue Infections in California January 1, 2025

The following table provides the number of infections with dengue virus in California residents from 2016 to 2025. Nearly all dengue cases reported in California have been associated with exposure through travel to an area affected by dengue outside of California.

- There have been 18 locally acquired infections reported in California in 2024. Locally acquired dengue cases are indicated by an asterisk (*) in the table below.

Dengue virus infections in California, 2016-2024 (as of January 1, 2025)

County	2016	2017	2018	2019	2020	2021	2022	2023	2024
Los Angeles Total	52	20	28	55	24	5	35	78, 2*	166, 14*
(City of Long Beach)	(0)	(1)	(2)	(2)	(2)	(0)	(1)	(7, 1*)	(5)
(City of Pasadena)	(3)	(0)	(1)	(2)	(0)	(0)	(0)	(1, 1*)	(6, 1*)
San Bernardino	7	3	0	6	3	0	0	5	20, 1*
San Diego	23	8	9	26	4	3	14	25	35, 3*

 NEWS RELEASE

November 25, 2024

The first locally acquired case of dengue virus in 2024 was reported in a Cameron County resident. It has been a highly active year for dengue virus globally. As of today, there have been 106 travel-associated dengue cases, including one death reported in Texas. This is the highest annual case count in Texas since 2002. Precautions should be taken to protect against mosquito bites in Texas and while traveling internationally to countries [where dengue is endemic](#).

Dengue virus

- Dengue virus has been “emerging” and “re-emerging” since the 1970s
- 2024 had higher than usual cases worldwide
- Now may be emerging in the US.
 - Florida
 - California
 - Texas
- 2024 *Aedes aegypti* in OR



PUBLIC HEALTH ADVISORY: AEDES AEGYPTI MOSQUITO

WE STILL HAVE A CHANCE TO GET RID OF IT, IF YOU HELP!

Aedes aegypti is an invasive mosquito species new to Jackson County and Oregon. *Aedes aegypti* was first detected in California in 2013 and is now considered endemic throughout much of the southern and central part of the state. On July 23, 2024, a single *Aedes aegypti* was found in Talent, marking the first time this species has been found in Oregon. Since the initial detection, JCVCD has detected 77 *Aedes aegypti* mosquitos from 18 trap locations throughout northwest Talent.

Unlike our native mosquitoes, *Aedes aegypti* prefer to feed on humans and they bite aggressively. They are primarily active during the day when people are more likely to be outdoors. They also require much less standing water for breeding, making it easier for them to spread in residential neighborhoods. *Aedes aegypti* have the potential to transmit several diseases such as dengue, yellow fever, chikungunya, and the Zika virus but the risk of these diseases to residents is currently very low.

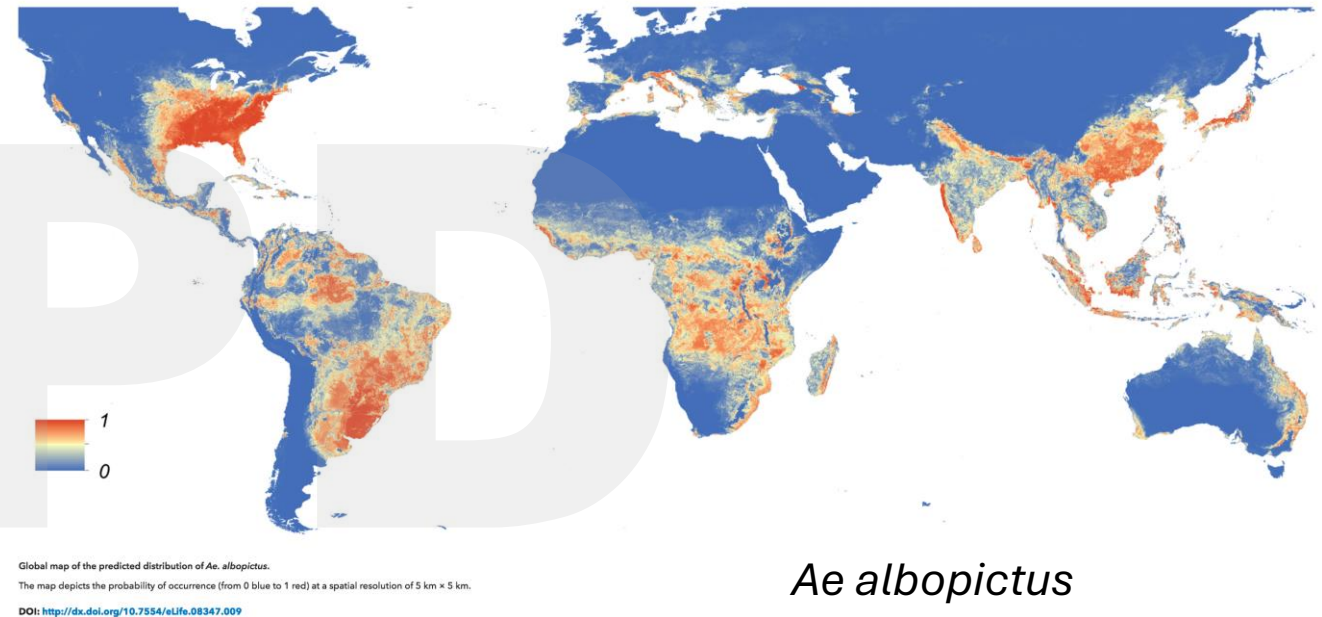
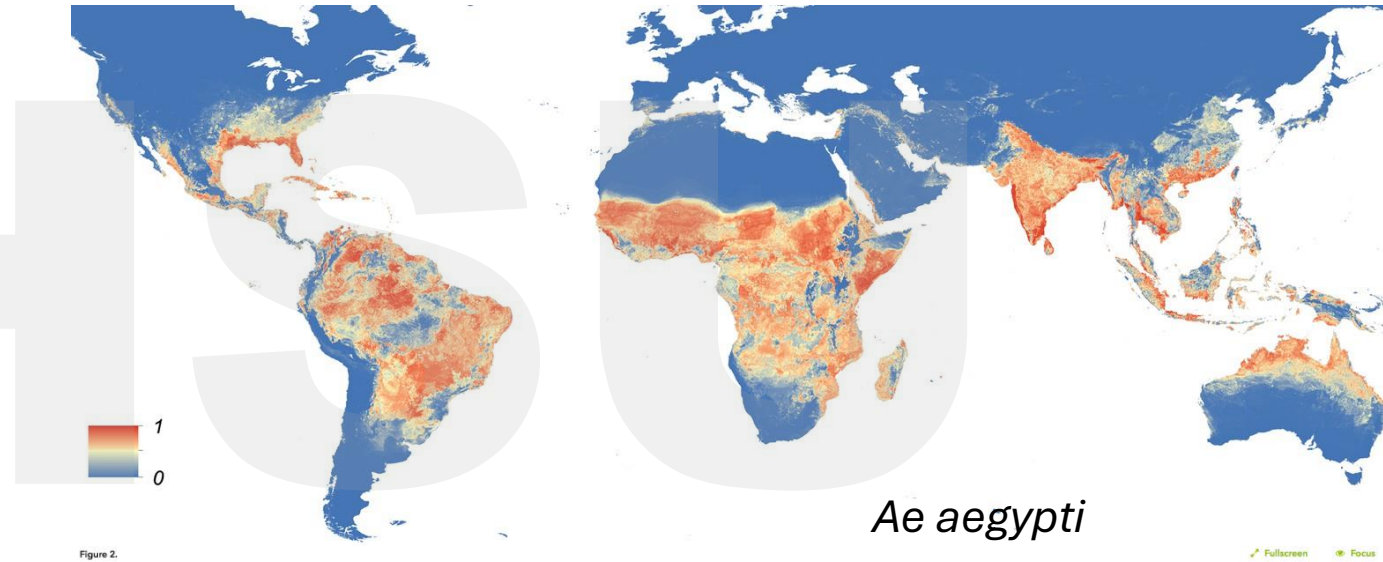


Dengue virus

- Clinical pearls
 - Supportive care with oral rehydration and APAP for fever
 - Avoid ASA, NSAIDS because of bleeding risk
 - IV fluids should be administered cautiously, high risk for 3rd spacing, esp pulmonary
 - Monitor HCT for rise (hemoconcentration/vascular leak) and platelets for fall (bleeding risk).

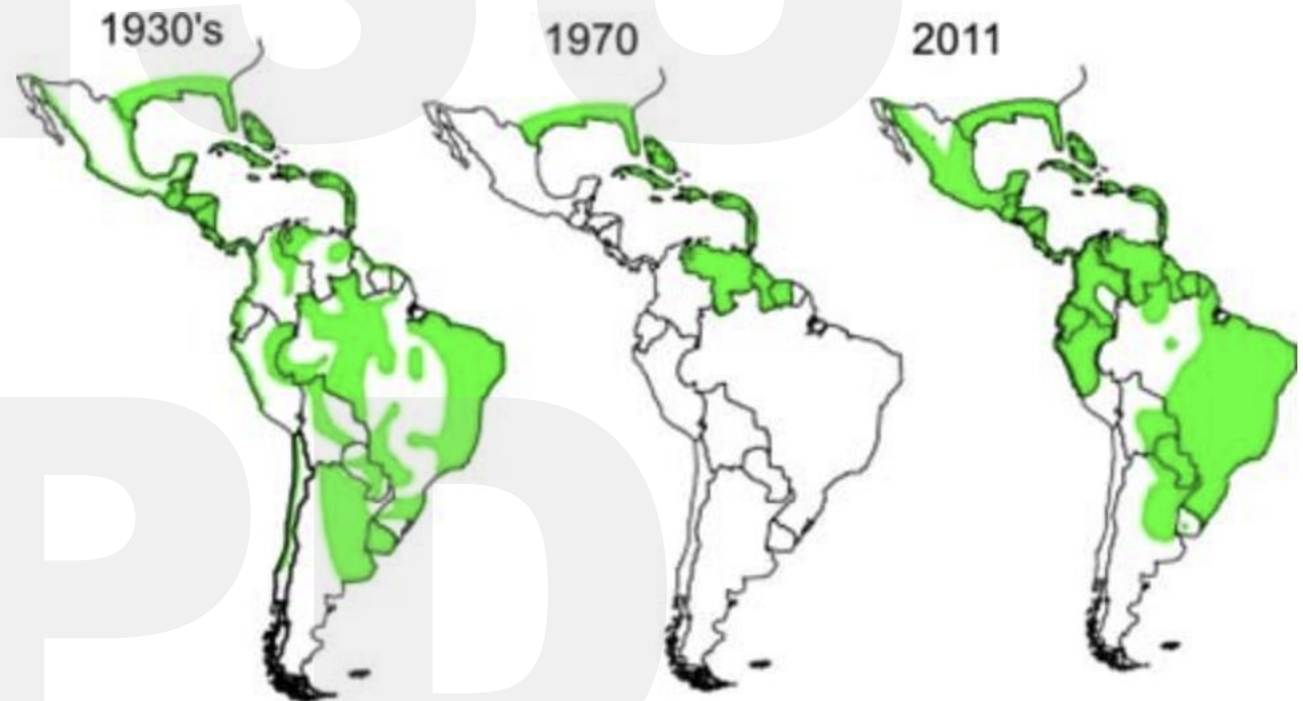
Dengue virus

- Climate pearls
 - Dengue has occurred as far North (Lat 39.9°) as Philadelphia (1780) in the US and Athens (Lat 38.0°, 1927-28) in Europe.
- *Aedes aegypti* and *albopictus* have expanded their range.
 - Adaptation to human-made breeding containers
 - International trade
 - Warming global temperatures
 - Abandoned eradication efforts



Dengue virus

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Dengue virus

- Climate pearls

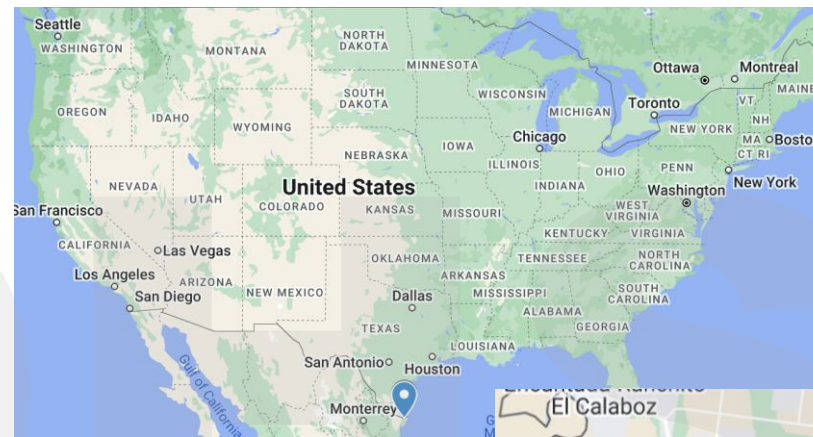
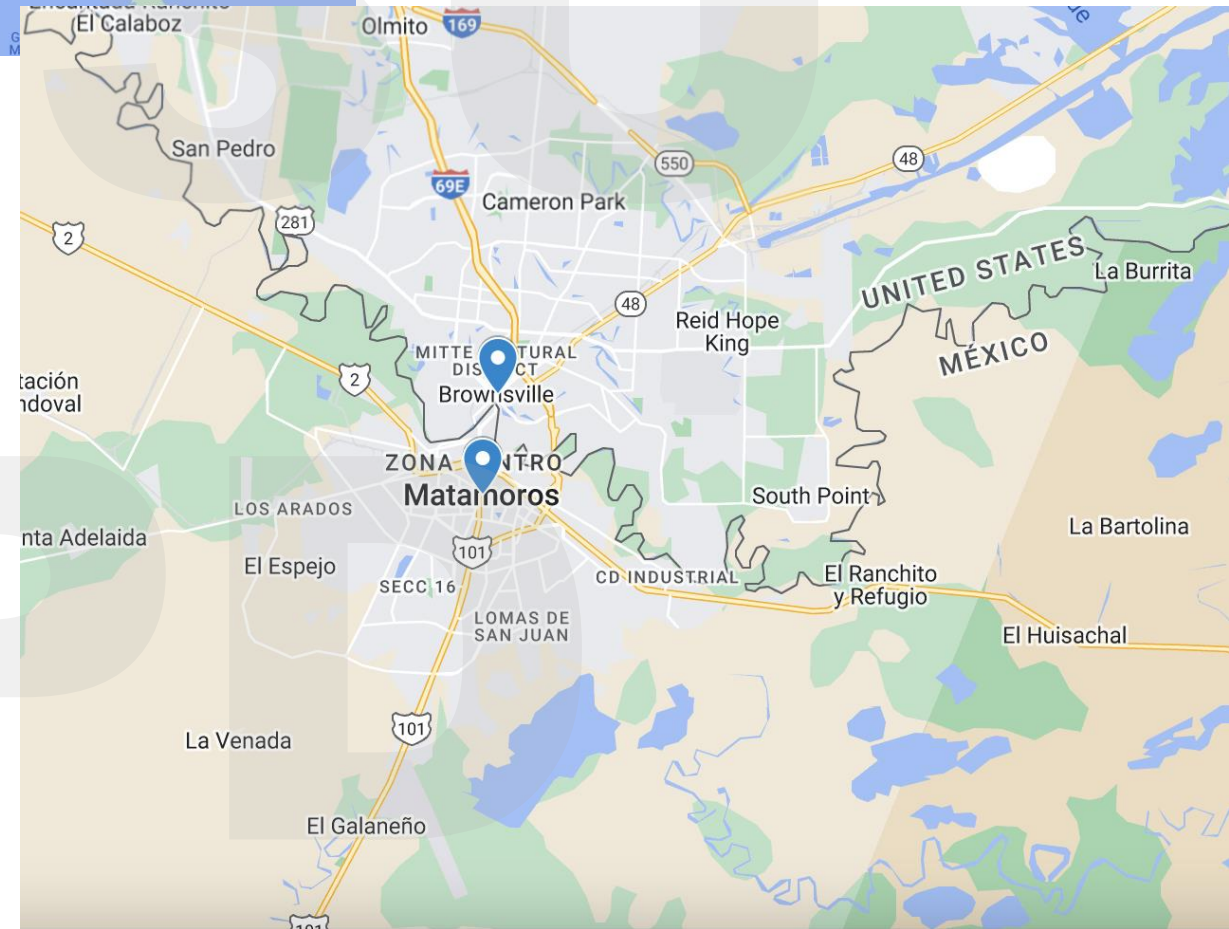


Table 1. Prevalence of IgG dengue antibodies by age and sex, Brownsville, Texas, and Matamoros, Mexico, 2004*

Characteristic	Brownsville, %	Matamoros, %
Age group, y		
15–24	8	79
25–34	45	75
35–44	43	72
45–54	45	80
55–64	35	79
65–74	43	95
≥75	38	90
Sex		
Male	35	72
Female	42	80

*IgG, immunoglobulin G.



Emerg Infect Dis. 2007 Oct;13(10):1477–1483. doi: [10.3201/eid1310.061586](https://doi.org/10.3201/eid1310.061586)

Dengue Fever Seroprevalence and Risk Factors, Texas–Mexico Border, 2004

Joan Marie Brunkard ^{*,¶}, Jose Luis Robles López [†], Josue Ramirez [‡], Enrique Cifuentes [§], Stephen J Rothenberg ^{¶,¶}, Elizabeth A Hunsperger [#],
Chester G Moore ^{**}, Regina M Brussole ^{††}, Norma A Villarreal ^{††}, Brent M Haddad [†]

Dengue virus

- Climate pearls
 - Built environment

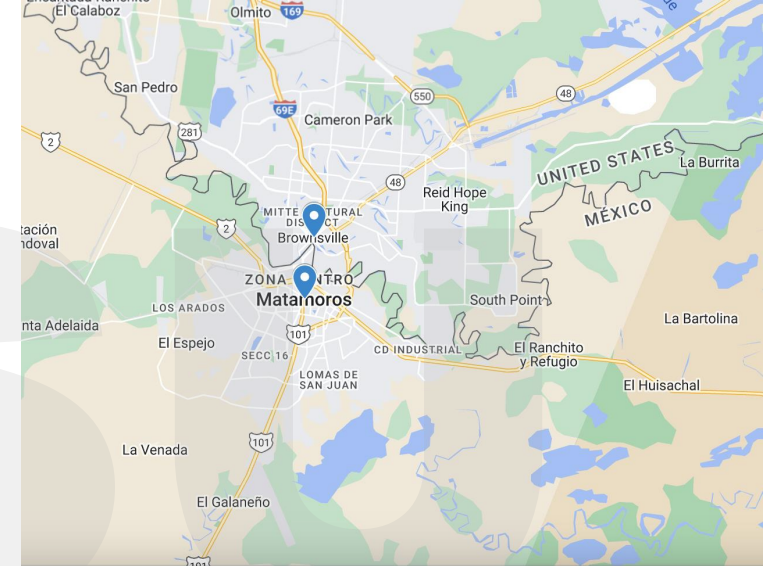


Table 5. Logistic regression results for serologic evidence of past dengue infection in Brownsville, Texas, and Matamoros, Mexico, 2004*

Variable	Adjusted odds ratio	p value	95% Confidence interval	Deff
Income ≤\$100	2.59	0.000	1.58–4.26	0.92
Missing income	0.90	0.679	0.54–1.50	0.83
Street drainage	0.57	0.009	0.37–0.87	1.07
Larval habitat	2.35	0.008	1.26–4.41	1.00
Air-conditioning	0.58	0.014	0.38–0.89	1.04
Intact screens	1.35	0.111	0.93–1.95	0.90
Store water	1.62	0.079	0.95–2.76	1.19
<i>Aedes aegypti</i>	0.84	0.476	0.53–1.35	1.05
Cross border, 3 mo	0.90	0.581	0.62–1.31	0.93
People/household	1.06	0.300	0.95–1.19	1.31

*Missing data in independent variables (n = 22) did not significantly change prevalence of recent or past dengue infection (p>0.10) in the remaining 578 observations used in subsequent models. Deff, design effect, the ratio of variance between the survey design and simple random sampling.

Emerg Infect Dis. 2007 Oct;13(10):1471–1483. doi: 10.3201/1310.061588

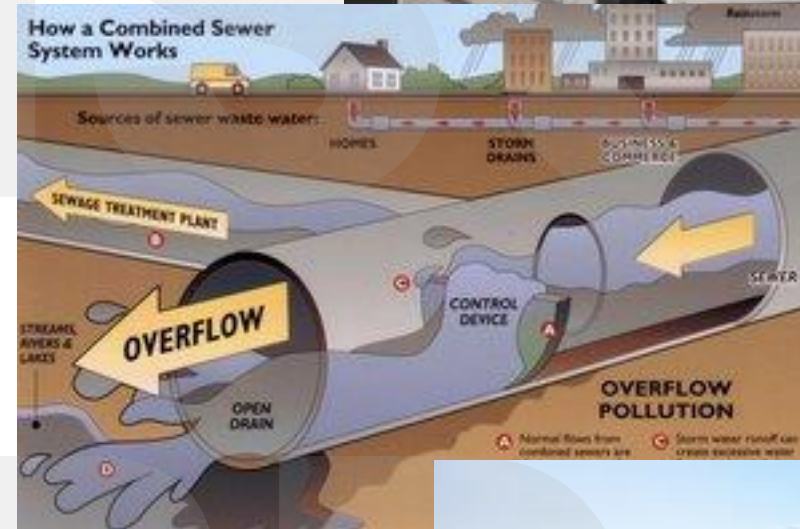
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Dengue virus

- Climate pearls
 - Built environment
 - Air conditioning*
 - Sealed windows and doors
 - Indoor/outdoor behavior
 - Economic wealth
 - Drainage
 - Breeding abatement
 - Infrastructure development
 - Economic wealth



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Summary

- Recognize virology, epidemiology, and origins of viral emergences in 2024
- Describe viral genomic recombination as a driver of virus emergence and re-emergence
- Summarize clinical pearls for each pathogen
- Identify key factors driving viral emergence in 2024
- Critique the environment's role in the emergence and spread of dengue virus

Thanks for your attention!

OHSU

CPD