Killer Viruses: The Why and The How

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@AmeshAA

JOHNS HOPKINS BLOOMBERG SCHOOL of PUBLIC HEALTH | Center for Health Security

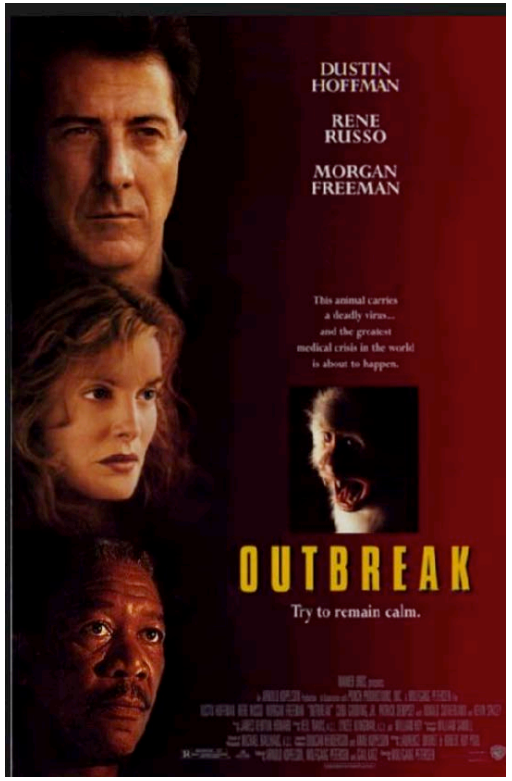
TRACKING ZEBRA

Disclosures

- Stockholder: Merck, Luminex, Evolent
- Bondholder: UPMC
- Speaker’s Bureau: Merck, Roche
- Consultant: Roche
- Funding: Open Philanthropy Project

Purpose

- New, unrecognized infectious diseases continue to emerge
- Major potential for disruption
  - Societal
  - Healthcare
- Chance favors the prepared mind
- Endlessly fascinating



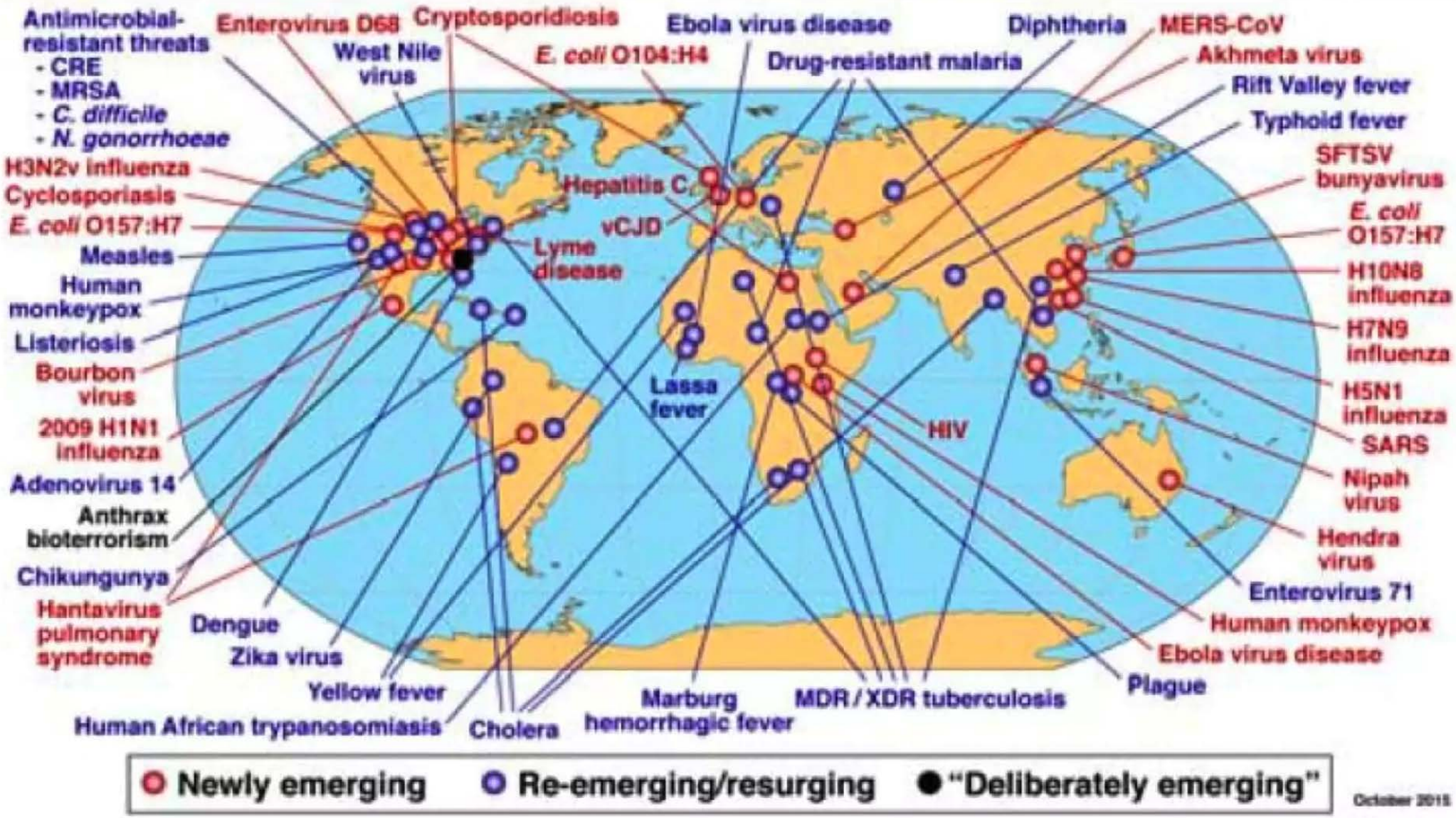
Outline

- A Snapshot of the Current Situation
- Causes
  - It’s a Small World
  - Human - human interactions
  - Human - animal interactions
  - Human – environmental interactions
  - Vectors
- Surveillance and the Tools of discovery

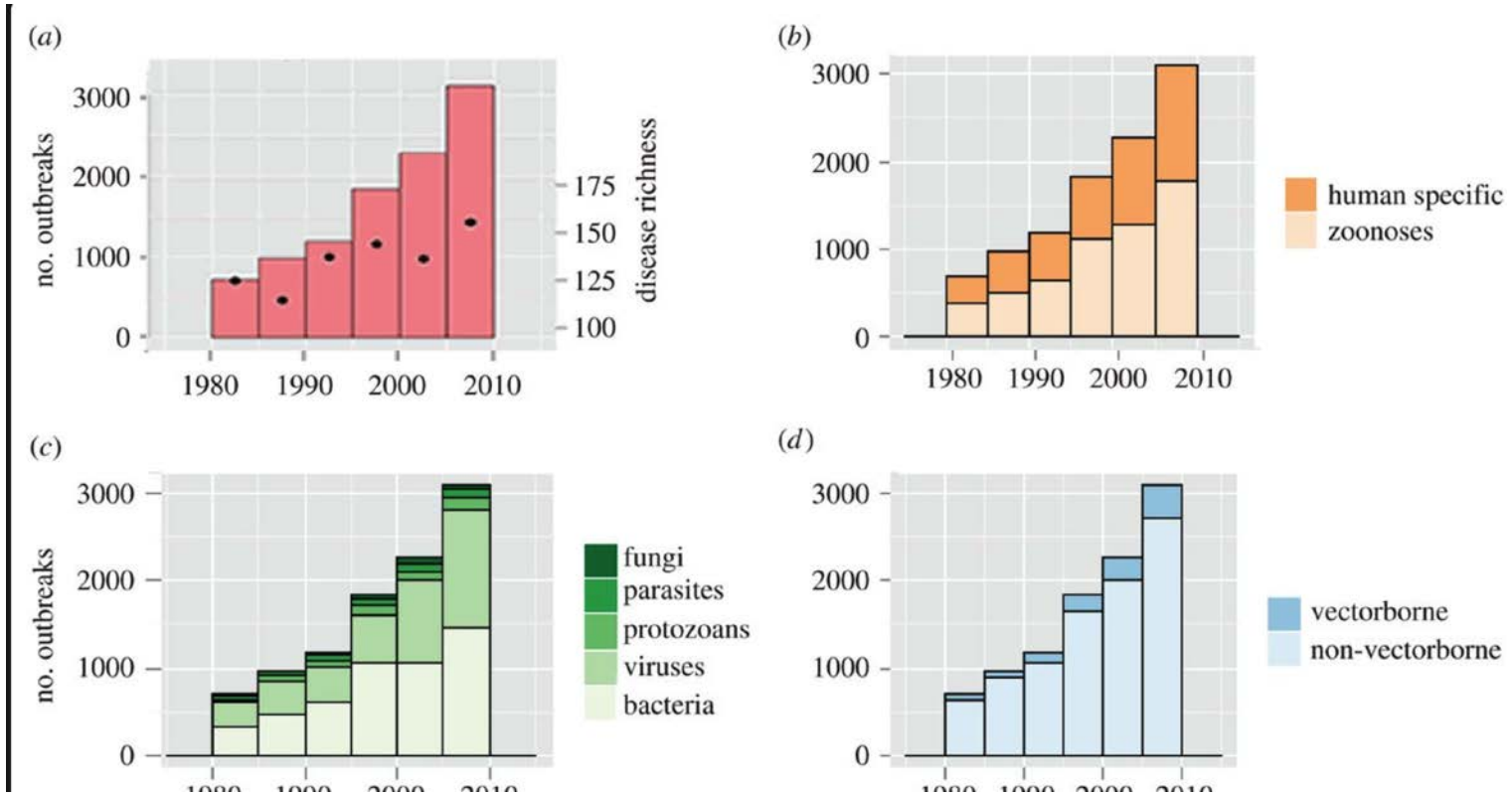
Snapshot

- MERS
- Yellow Fever
- Zika
- Ebola
- Powassan
- SFTS (Severe Fever with Thrombocytopenia Syndrome)
- West Nile
- SARS
- Measles
- Monkeypox
- Chikungunya
- Dengue
- Avian Influenza (H5, H7)
- Swine Influenza
- Hepatitis A

Global Examples of Emerging and Re-Emerging Infectious Diseases



The Trend

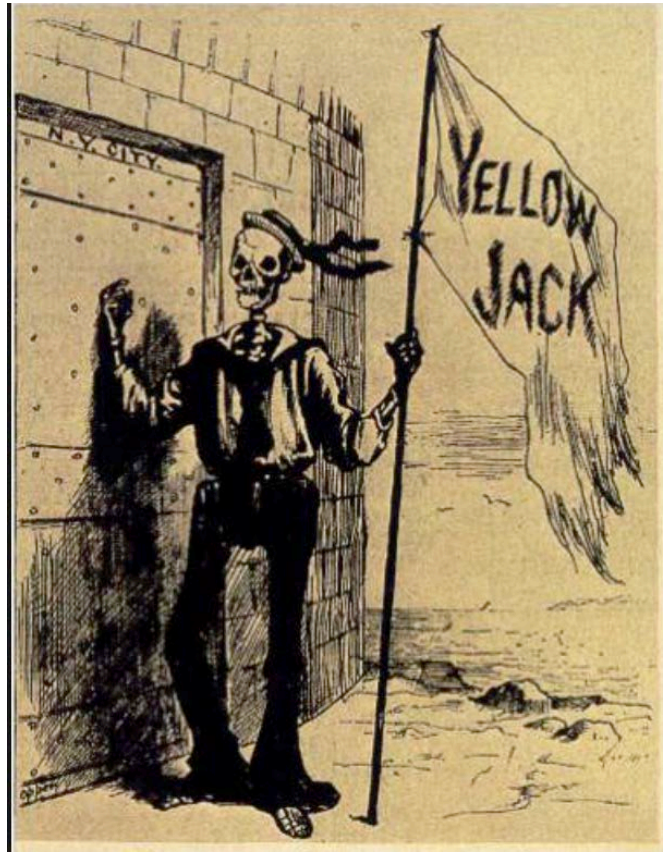

(a)
no. outbreaks
disease richness
3000
2000
1000
0
175
150
125
100
1980
1990
2000
2010
(b)
human specific
zoonoses
(c)
fungi
parasites
protozoans
viruses
bacteria
(d)
vectorborne
non-vectorborne

A little bit of mathematical reasoning

- Incubation period
- Period of contagiousness
- Travel Time

➔If travel time < incubation period and/or period contagiousness

➔Importation of disease


N. Y. CITY.
YELLOW
JACK

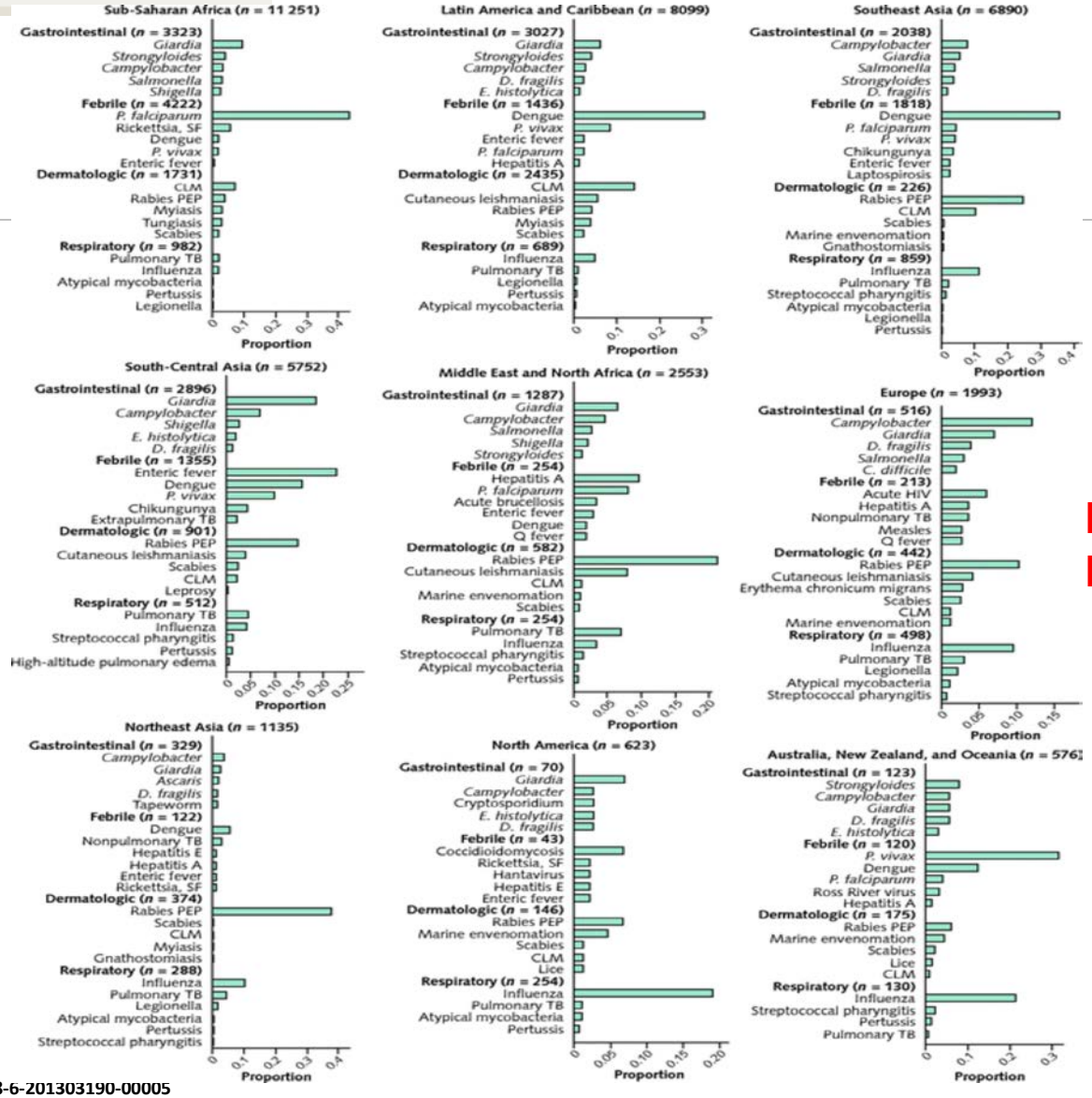
Global Flight Map


it's a
small world!

Origins of Globalization

Annals of Internal Medicine
Established in 1917 by the American College of Physicians

From: GeoSentinel Surveillance of Illness in Returned Travelers, 2007–2011



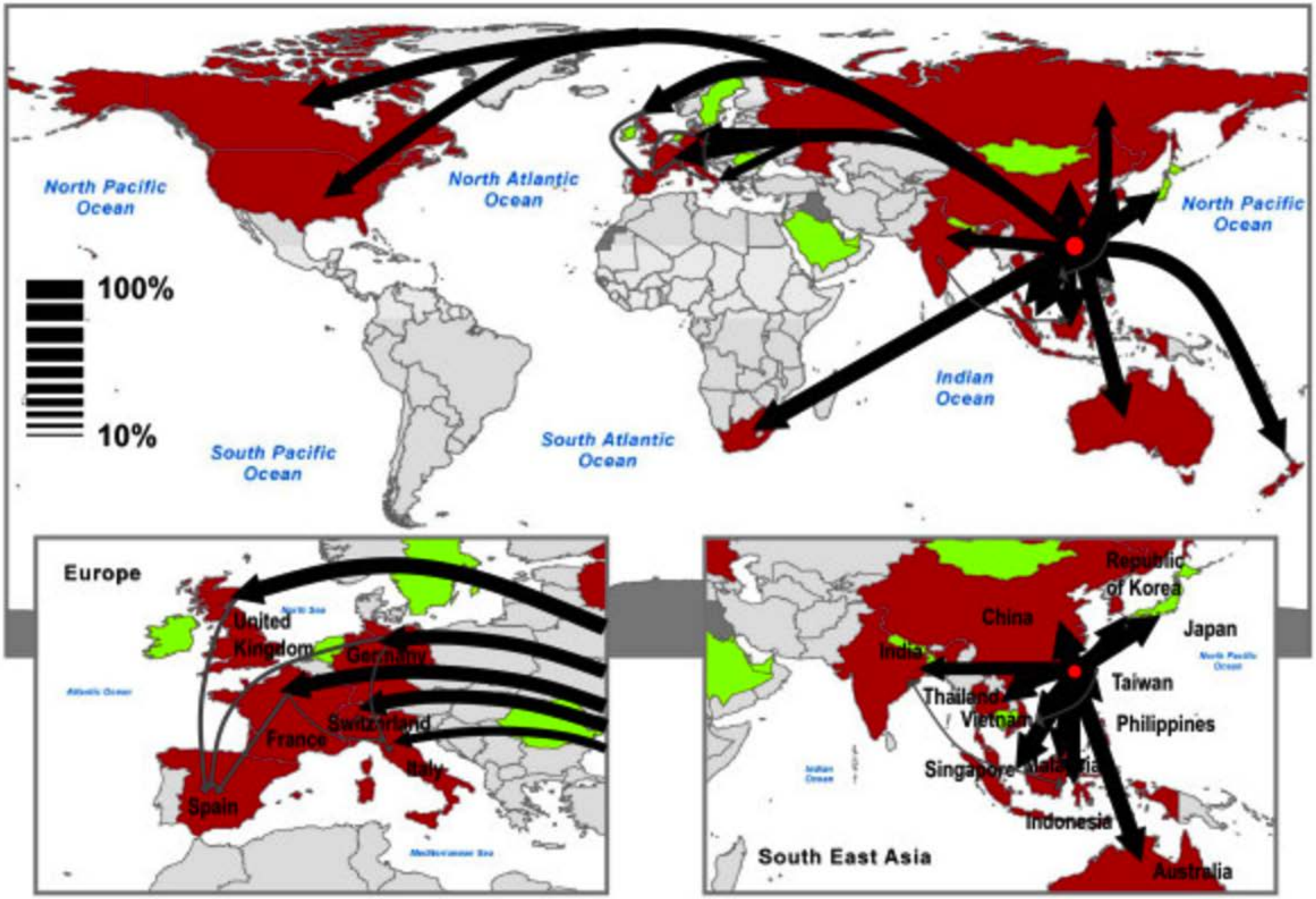
Malaria, Rabies, Campylobacter, Dengue, Influenza

Ann Intern Med. 2013;158(6):456-468. doi:10.7326/0003-4819-158-6-201303190-00005

Top identified specific causes for gastrointestinal, febrile, dermatologic, and respiratory illnesses by region among ill returned travelers.

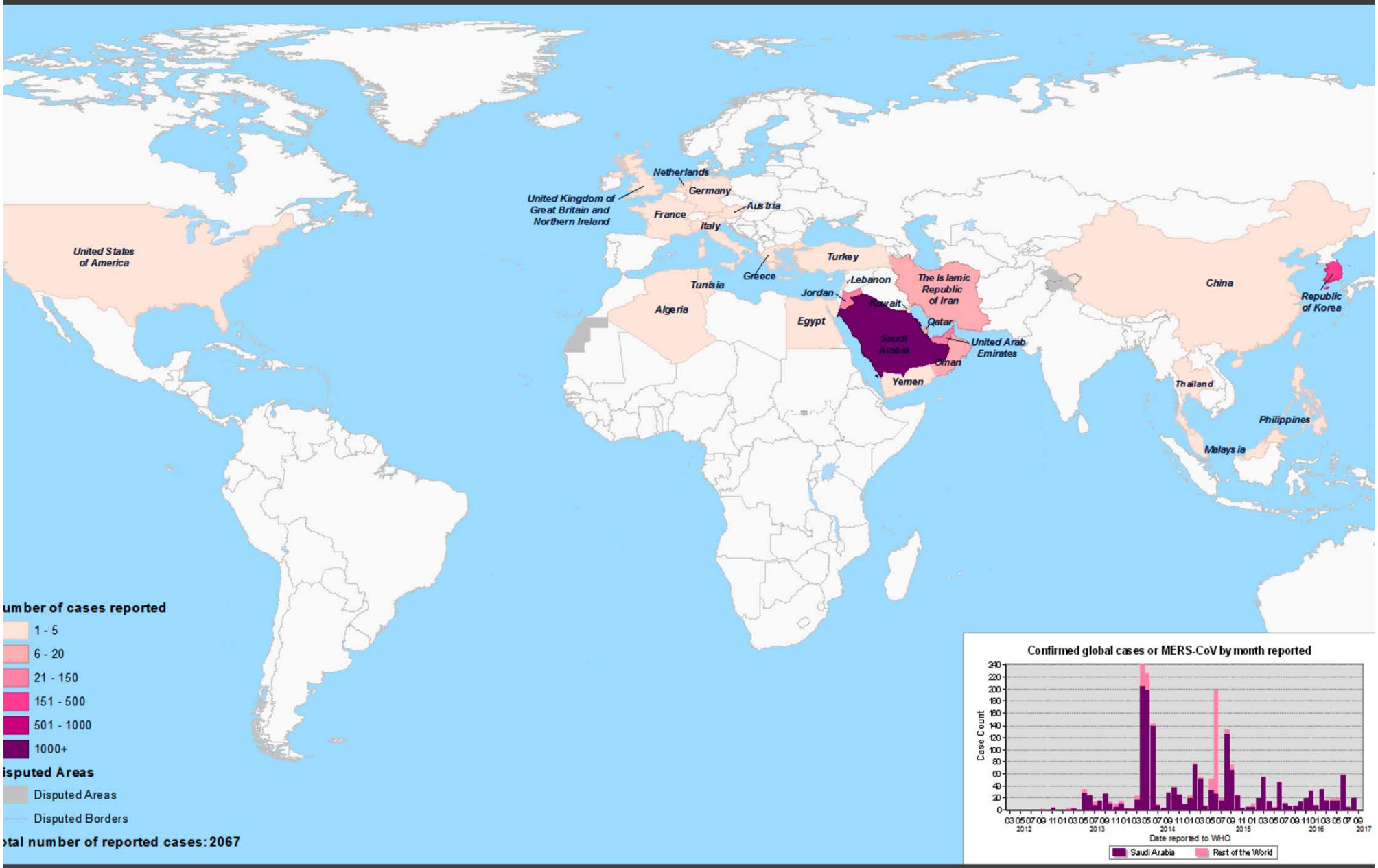
More than 5 diagnoses are shown if >1 cause had equal numbers of cases. These graphs represent proportions, and there is variability in the number of ill travelers represented from panel to panel (shown from largest to smallest traveler numbers). CLM = cutaneous larva migrans; D. fragilis = Dientamoeba fragilis; E. histolytica = Entamoeba histolytica; P. falciparum = Plasmodium falciparum; P. vivax = Plasmodium vivax; PEP = postexposure prophylaxis; SF = spotted fever; TB = tuberculosis.

SARS


North Pacific Ocean
North Atlantic Ocean
North Pacific Ocean
100%
10%
South Pacific Ocean
South Atlantic Ocean
Indian Ocean
Europe
United Kingdom
Germany
Switzerland
France
Italy
Spain
Republic of Korea
China
Japan
India
Taiwan
Thailand
Vietnam
Philippines
Singapore
Indonesia
South East Asia
Australia

Human Factors

CONFIRMED GLOBAL CASES OF MERS-COV 2012 - 2017



ap Scale (A3): 1:1,109,175,783
cm = 11,092 km
oordinate System: GCS WGS 1984
tum: WGS 1984
its: Degree

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

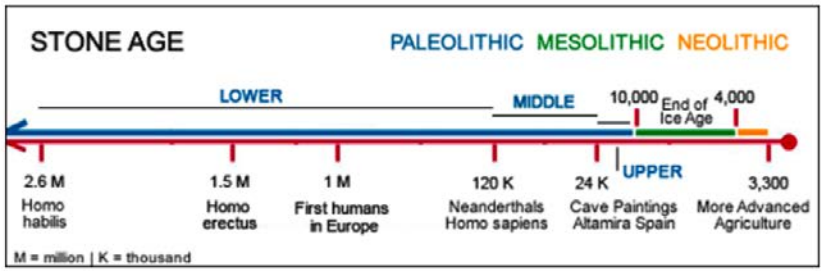
Data Source: World Health Organization

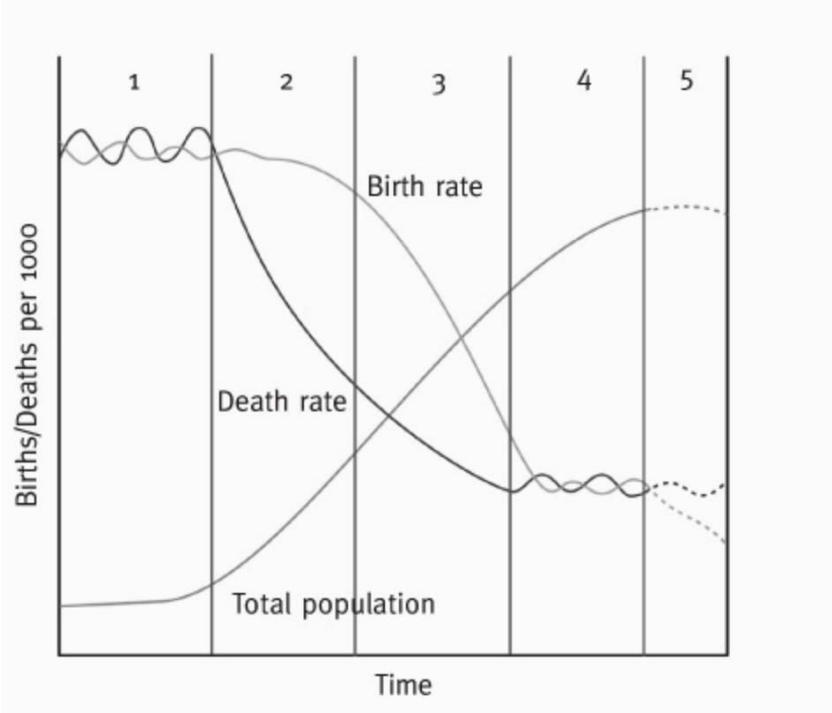
Map date:01/09/2017

World Health Organization

Epidemiological Transitions and Ages

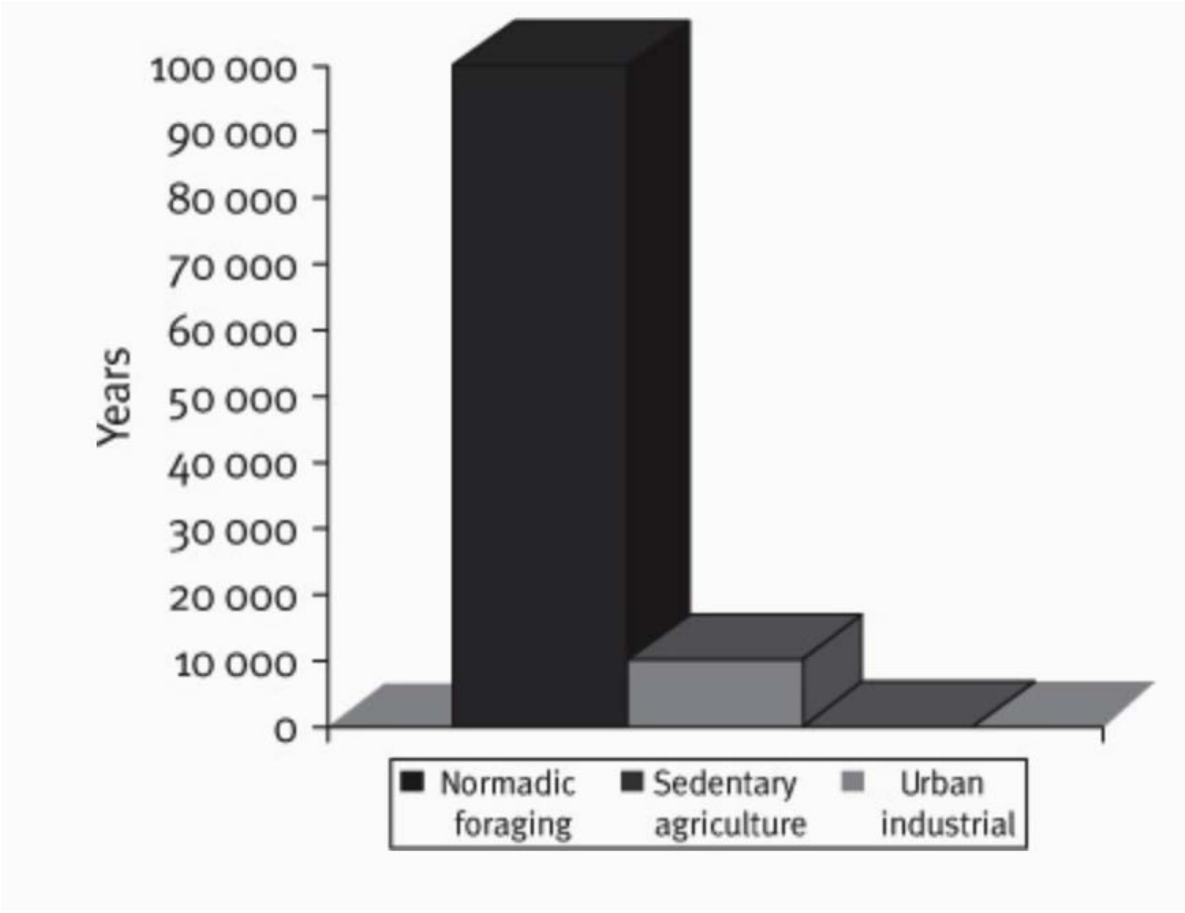
- 3 major transitions from Neolithic to modern area
  1. Nomadic → Agriculture 10,000 years ago (Age of Pestilence and Famine)
  2. Industrial Revolution (Age of Receding Epidemics)
  3. Globalization, Urbanization, Aging (Age of Degenerative and Manmade diseases)

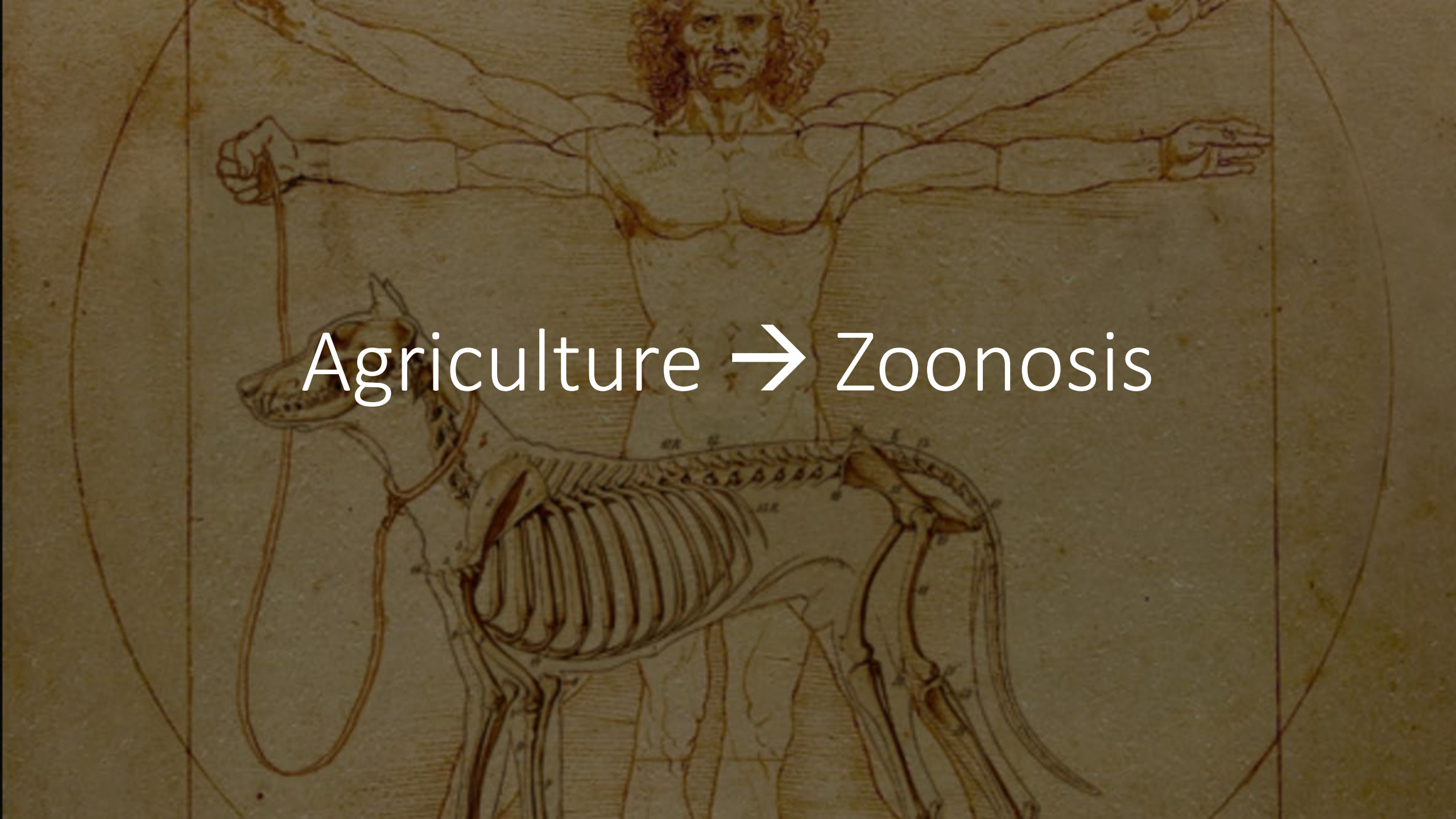




Nomadic → Stationary Transition

- Population density increases
- Human to human interaction increases
- Waste management
- Agriculture
- Lifestyle changes
- Evolution



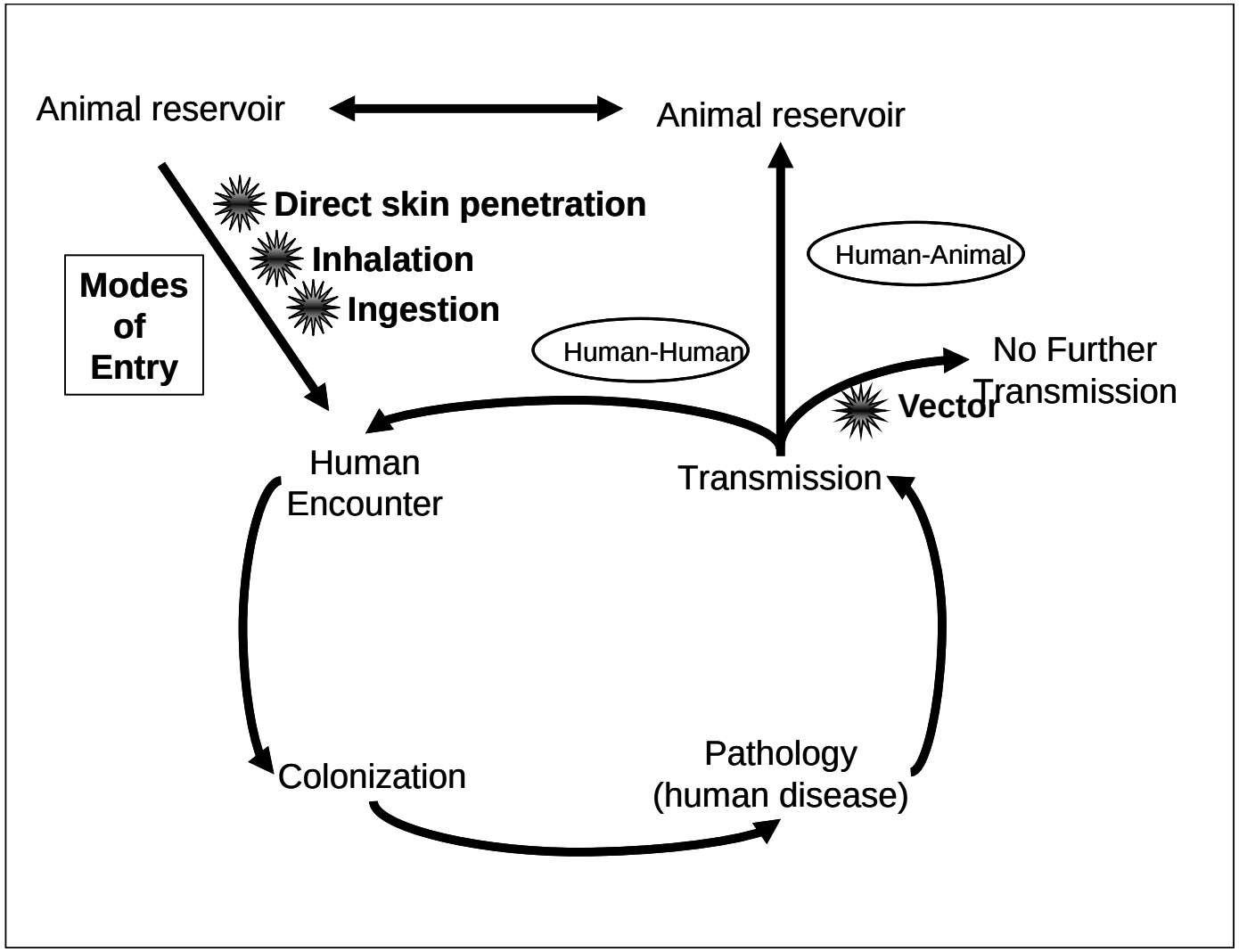


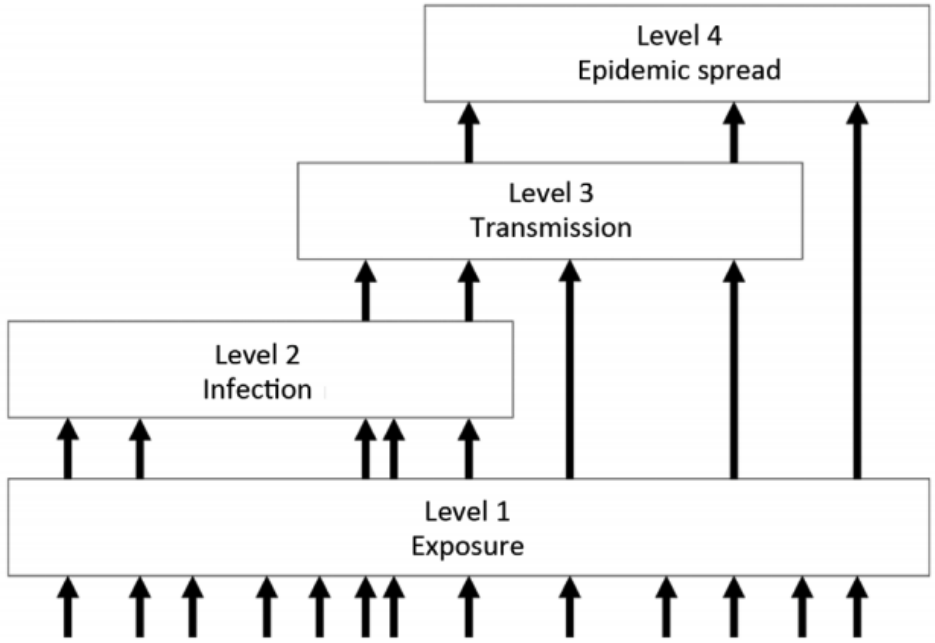
Agriculture → Zoonosis

Definitions

- **<u>Zoonotic</u>** = “zoo” meaning “animal” and “nosis” meaning “disease”
- **<u>Reservoir</u>** = animal where etiologic agent is maintained
- **<u>Vector</u>** = the medium (insect or other) transferring the etiologic agent between the animal reservoir and the human host.
- **Relatively infrequent cause of infection**
  - **But, most infections were zoonoses at one time**

Patterns of Zoonotic Infections





Factors Affecting Zoonotic Infections

- Improved diagnostics
- Recreational travel to rural areas
- International travel
- Population displacement due to warfare
- Homelessness
- Interactions with animals
- High population of reservoir host
- New reservoir or transmission cycle
- Weather patterns + events
- Translocation of reservoir host and ectoparasites
- Newly emerged or recognized organism

Los Angeles Times

Yosemite hantavirus outbreak has sickened 10, killed 3, CDC says

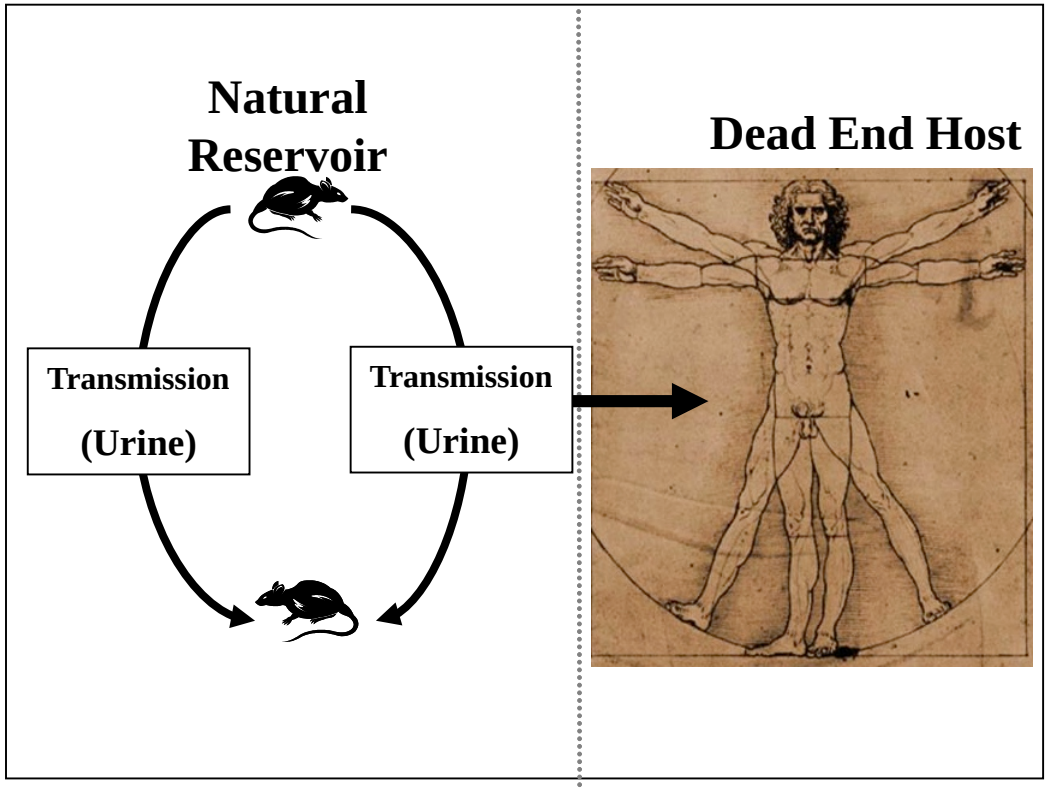
November 21, 2012 | By Eryn Brown | Los Angeles Times

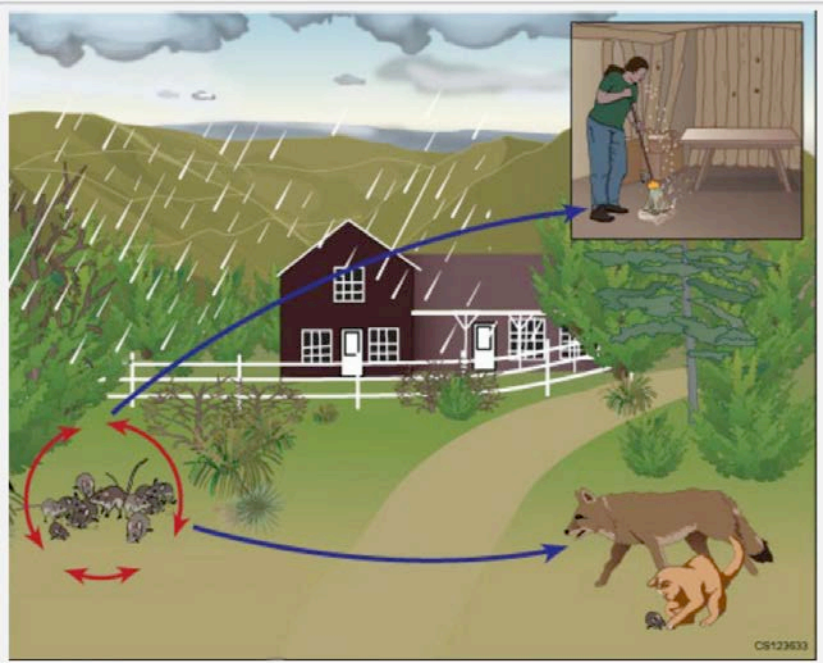
To date, 10 people have fallen ill — and three have died — in the hantavirus outbreak at Yosemite National Park's "signature" cabins in Curry Village, according to the U.S. Centers for Disease Control and Prevention.

The hantavirus outbreak in Yosemite this summer has sickened 10 and killed... (Michael Macor / San Francisco...)

Hantavirus only infects a handful of people in the U.S. each year, but when it strikes it is deadly about a third of the time, killing by shutting down the respiratory system. Humans can catch the virus by getting bitten by infected deer mice, which carry the disease, or by inhaling virus particles that are shed in mouse feces or urine. Hantavirus cannot pass from person to person.

Cycle of Transmission: Hantavirus





Ebola

Reservoirs of ZEBOV & MARV:
fruit bats species

Intermediary susceptible species:
virus amplification in great apes and duikers

Rousettus aeyptiacus: Egyptian Fruit Bat

Epomops franqueti:
Franquet's Epauletted Fruit Bat

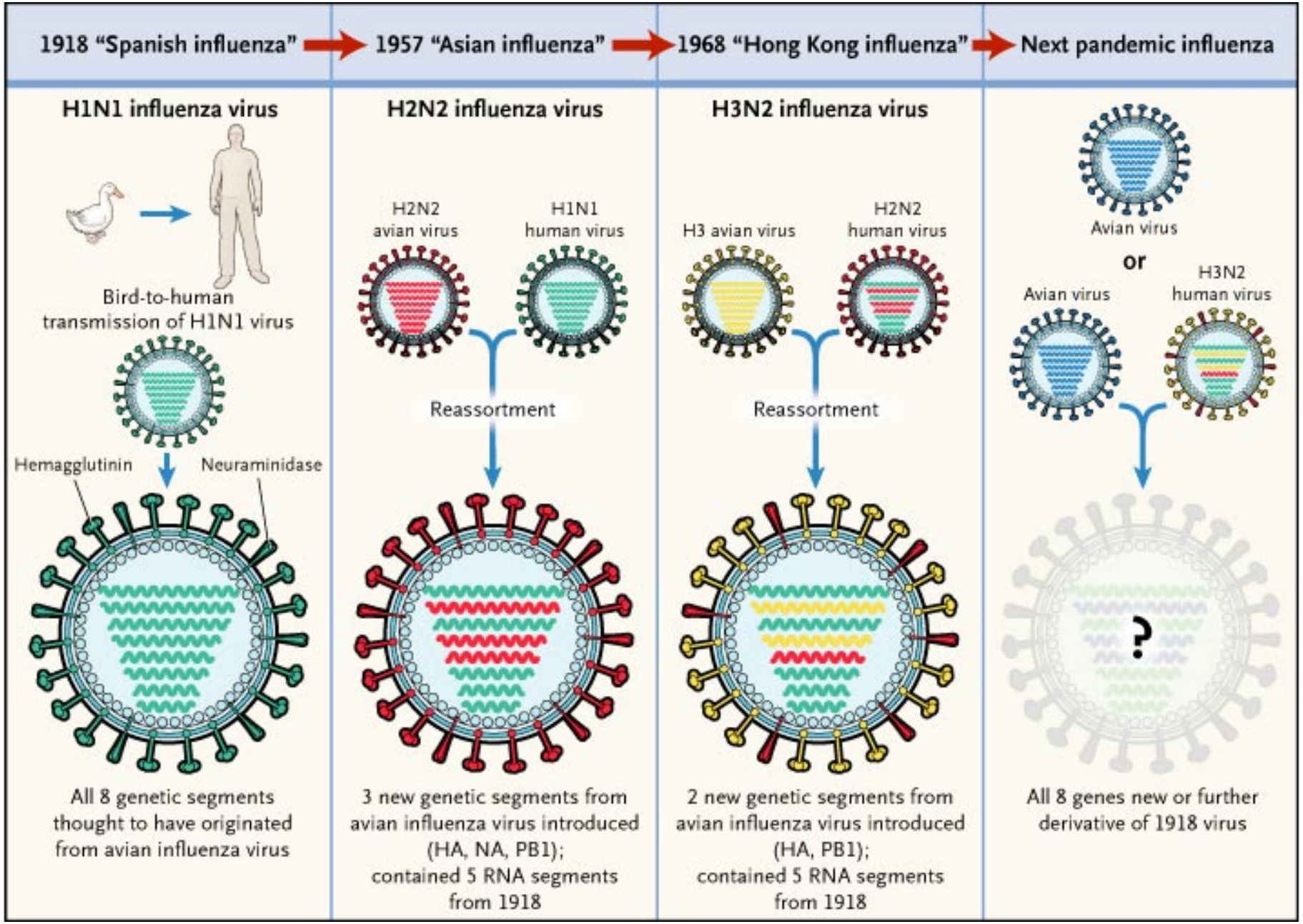
Myonycteris torquata:
Little Collared Fruit Bat

Hypsignathus monstrosus: Hammer-headed bat

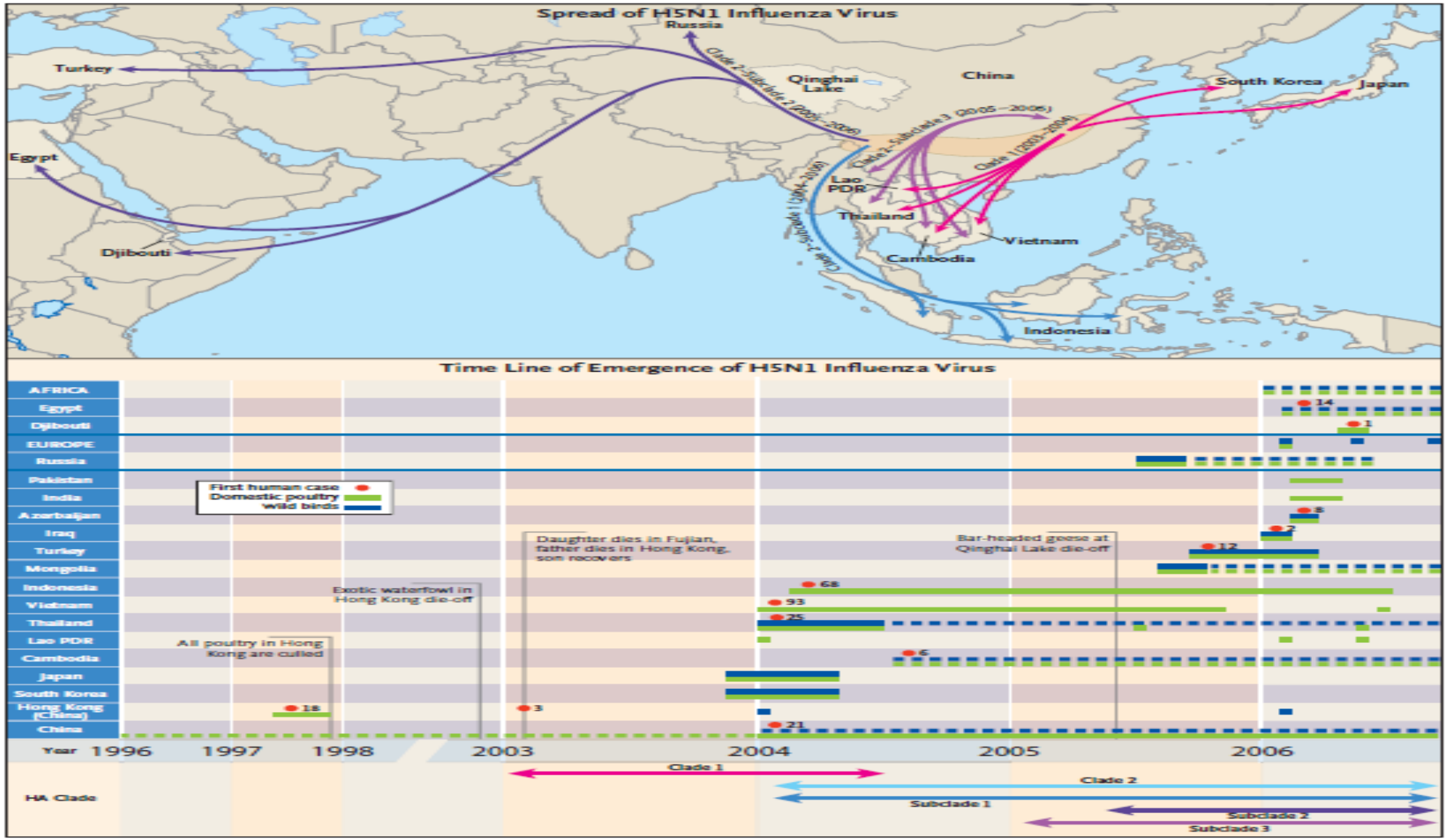
Why Bats?
--most populous mammalian species
--travel
--world wide

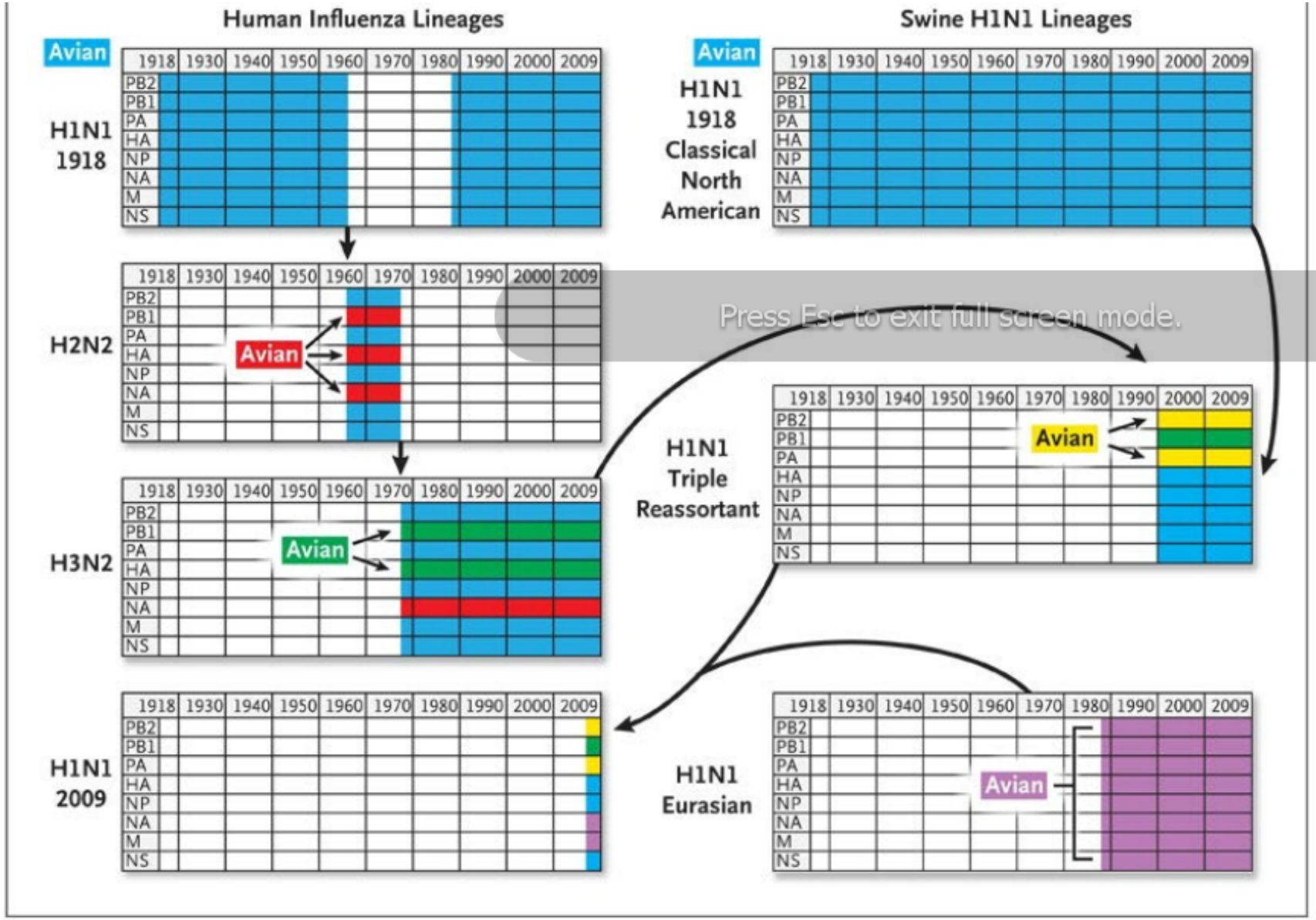
<u>Bat Zoonoses</u>
--rabies
--Nipah
--Hendra
--Marburg
--SARS
--MERS

Flu: H3N2v, H1N2v & Avian Influenza



Influenza
--RNA virus
--segmented genome
--multiple hosts
--reassortment
--respiratory transmission


Spread of H5N1 Influenza Virus
Russia
Turkey
Egypt
Djibouti
Qinghai Lake
China
South Korea
Japan
Clade 2-Subclade 2 (2005–2006)
Clade 2-Subclade 3 (2005–2006)
Clade 1 (2003–2004)
Clade 2-Subclade 1 (2004–2006)
Lao PDR
Thailand
Cambodia
Vietnam
Indonesia
Time Line of Emergence of H5N1 Influenza Virus
AFRICA
Egypt
Djibouti
EUROPE
Russia
Pakistan
India
Azerbaijan
Iraq
Turkey
Mongolia
Indonesia
Vietnam
Thailand
Lao PDR
Cambodia
Japan
South Korea
Hong Kong (China)
China
First human case
Domestic poultry
wild birds
Exotic waterfowl in Hong Kong die-off
All poultry in Hong Kong are culled
Daughter dies in Fujian, father dies in Hong Kong, son recovers
Bar-headed geese at Qinghai Lake die-off
14
1
8
7
12
68
93
25
6
18
3
21
Year 1996 1997 1998 2003 2004 2005 2006
HA Clade
Clade 1
Clade 2
Subclade 1
Subclade 2
Subclade 3



composition of a particular influenza virus lineage over time. In each chart, gene segments are shown along the left side, and dates from 1918 to 2009 are shown along the top. Color coding shows the avian origins and history of each gene segment in each influenza virus lineage. The influenza virus gene segment reassortments that gave rise to the H2N2 and H3N2 strains of human influenza A are shown on the left side of the diagram, along with human influenza A (H1N1) viruses or their descendants. Swine influenza A (H1N1) viruses are shown on the right side of the diagram.

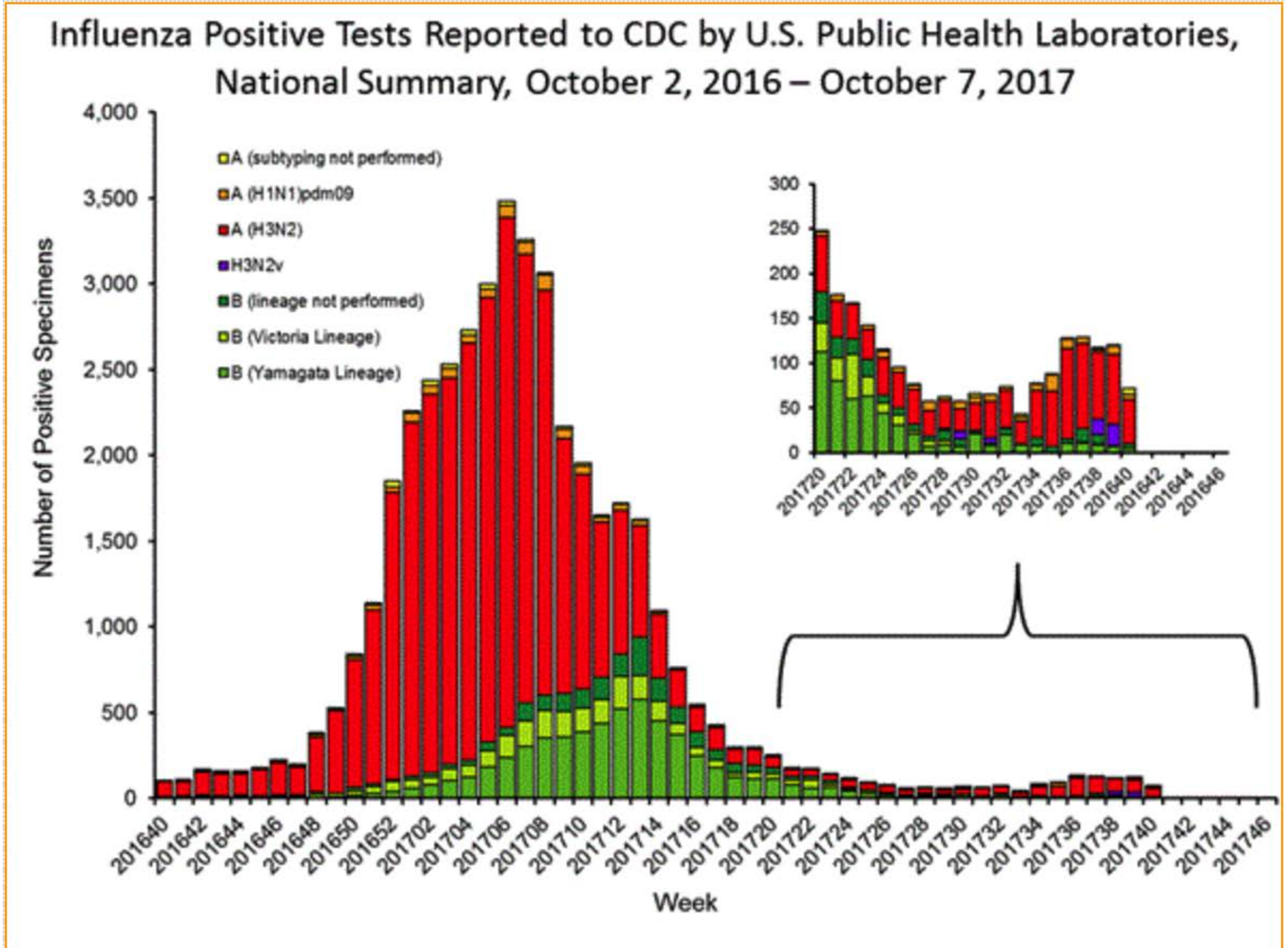
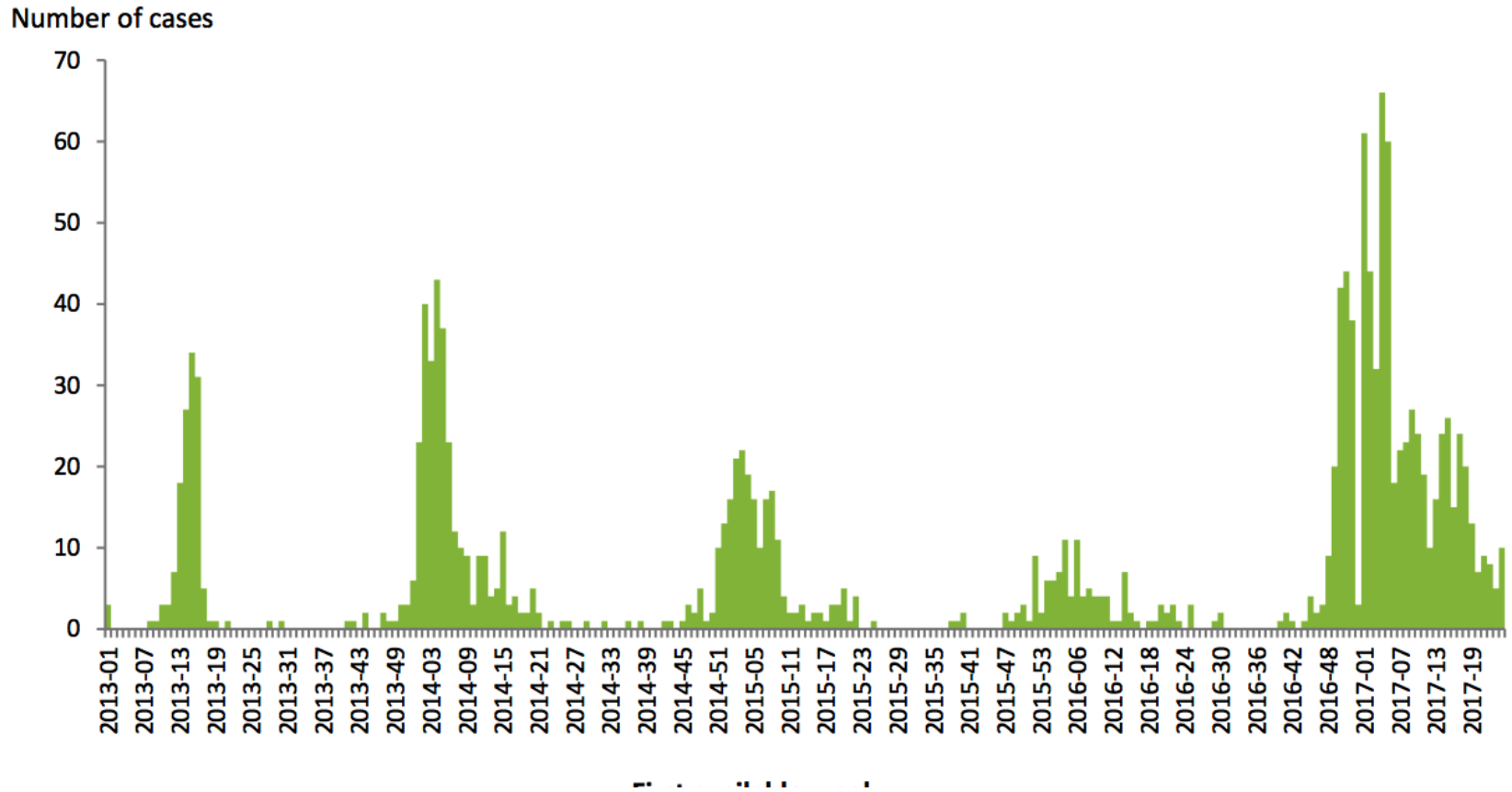
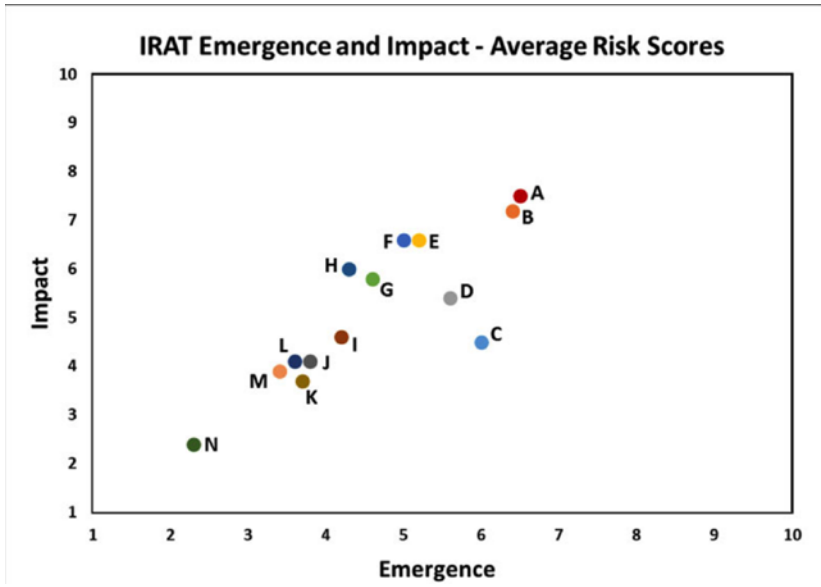

Influenza Positive Tests Reported to CDC by U.S. Public Health Laboratories, National Summary, October 2, 2016 – October 7, 2017
A (subtyping not performed)
A (H1N1)pdm09
A (H3N2)
H3N2v
B (lineage not performed)
B (Victoria Lineage)
B (Yamagata Lineage)
Number of Positive Specimens
Week

Figure 2. **Distribution of reported human influenza A(H7N9) cases in China by week, week 1/2013 to week 25/2017 (N=1 548)**



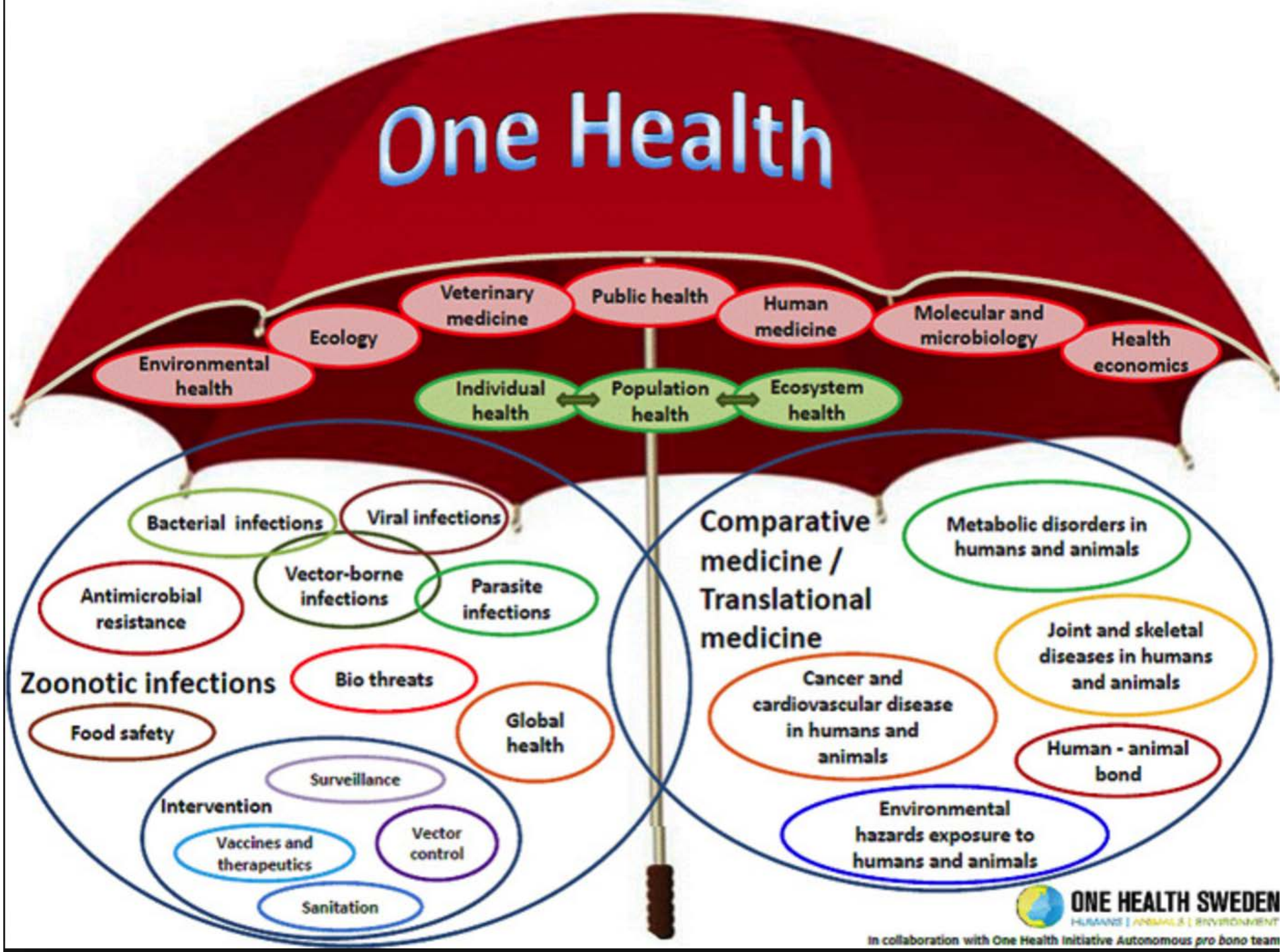


H7N9
--more cases in 3rd wave
--some changes showing human tropism
--antiviral resistance
--change in strain – vaccine mismatch
--high pathogencity variant in chickens

Box 1. Steps in pandemic emergence.

For an avian-adapted strain of influenza A to become a pandemic strain, several events are required:

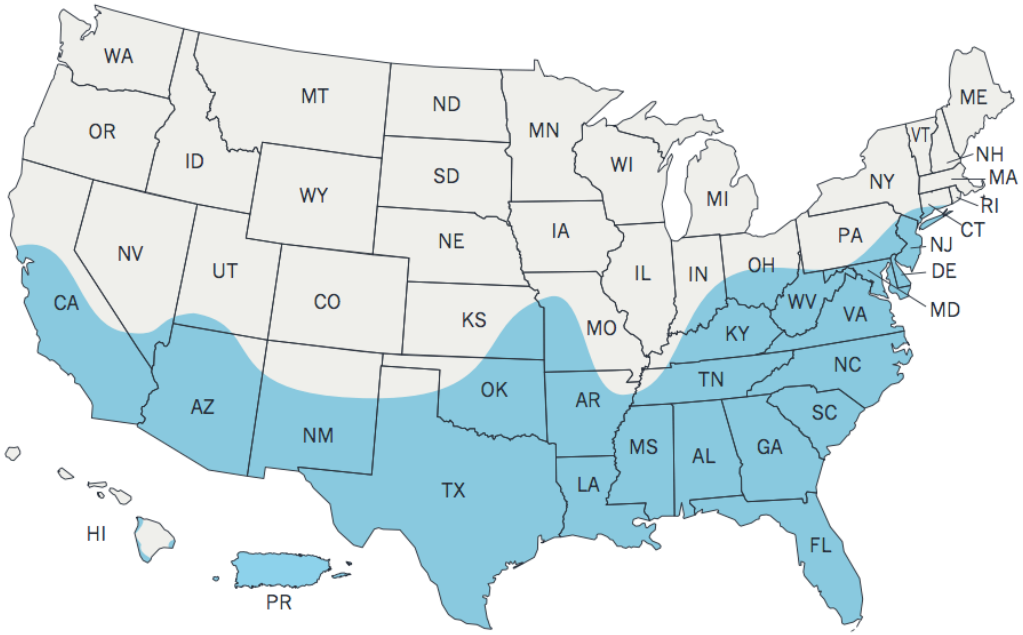
1. The avian-adapted strain must become sufficiently widespread in wild or domestic birds, swine or other reservoir species to expose at least one human to infection.
2. One or more humans must acquire infection from the reservoir species.
3. The infection must replicate sufficiently in a zoonotic case to produce infectious virus in respiratory or other secretions.
4. The infection must be transmitted to additional humans, avoiding an "early" termination of the transmission chain due to chance. Such early termination is a significant risk given the relatively low infectiousness of influenza and the moderate degree of overdispersion in the number of secondary cases infected by each case, both of which contribute to the probability that a transmission chain will terminate by chance (***Lloyd-Smith et al., 2005***; ***Lipsitch et al., 2003***). It must also avoid extinction due to deliberate control efforts put in place by public health authorities (***Ferguson et al., 2006***; ***Merler et al., 2013***).
5. Finally, the infection must spread beyond the local area to infect members of distant populations, a process accelerated by modern global travel (***Cooper et al., 2006***). This step and the one before are enhanced if the level of population susceptibility is high, as occurs when the surface proteins of the new strain are dissimilar to those on any currently or recently circulating human influenza A strains.


One Health
Veterinary medicine
Public health
Human medicine
Molecular and microbiology
Health economics
Ecology
Environmental health
Individual health
Population health
Ecosystem health
Bacterial infections
Viral infections
Vector-borne infections
Parasite infections
Antimicrobial resistance
Zoonotic infections
Bio threats
Food safety
Global health
Surveillance
Intervention
Vaccines and therapeutics
Vector control
Sanitation
Comparative medicine / Translational medicine
Metabolic disorders in humans and animals
Joint and skeletal diseases in humans and animals
Cancer and cardiovascular disease in humans and animals
Human - animal bond
Environmental hazards exposure to humans and animals
ONE HEALTH SWEDEN
In collaboration with One Health Initiative Autonomous pro bono team

Vector-borne Diseases Strike Back

Urbanization
Complacency

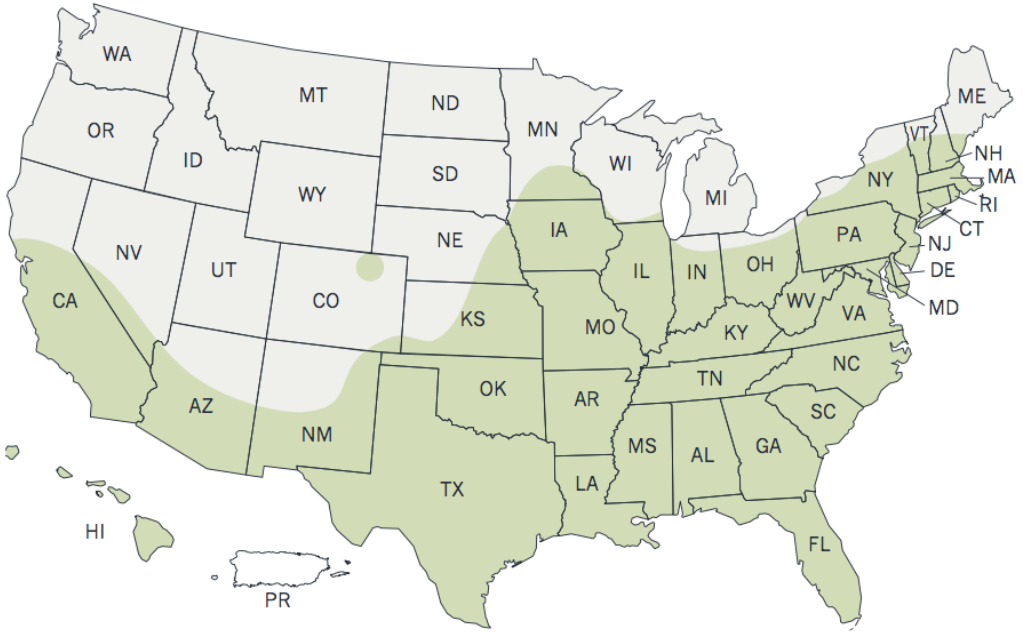
Where The



Approximate distributi
the United States*

of *Aedes albopictus* in

Aedes aegypti *Aedes albopictus*



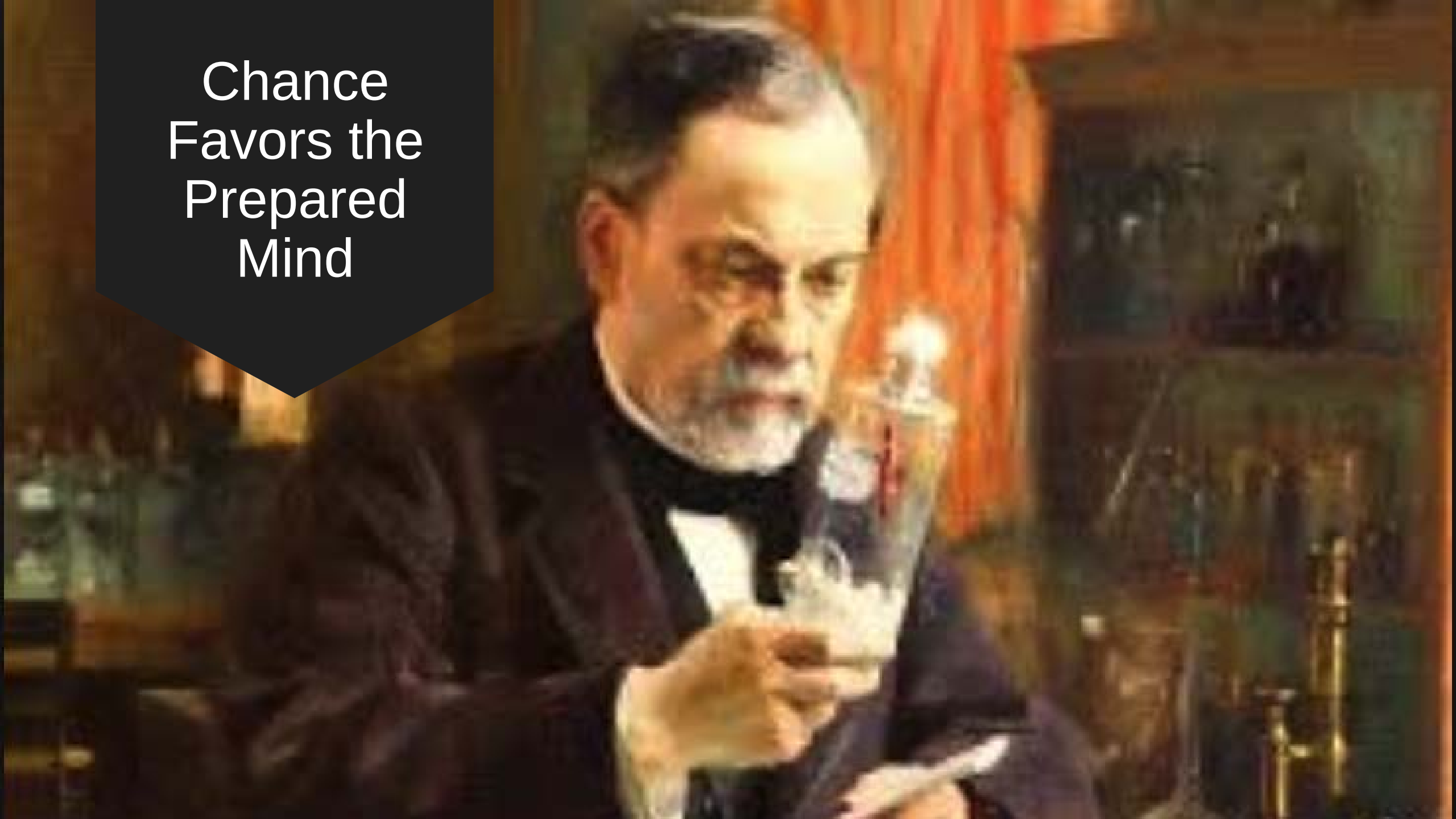
* Maps have been updated from a variety of sources. These maps represent CDC's

Historical US Yellow Fever Outbreaks

The Return of the Primitive: The Anti-vaccine Movement

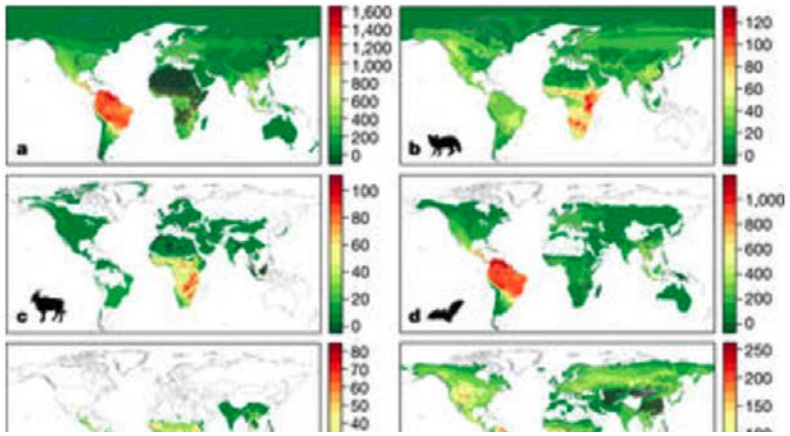
Table 1. Vaccination Status of Measles Cases and Crude Measles Incidence Rate (IR) by Age Group in the United States, 2001-2015

Age Group	No. of Measles Cases[a]	Vaccination Status, No. (%)[b]			Annual IR per Million Population (95% CI)
		Unvaccinated	Vaccinated	Unknown	
0-5 mo	31	31 (100.0)	0	0	1.03 (0.73-1.47)
6-11 mo	163	161 (98.8)	2 (1.2)	0	5.44 (4.67-6.34)
12-15 mo	106	95 (89.6)	7 (6.6)	4 (3.8)	5.38 (4.45-6.51)
16 mo-4 y	214	164 (76.6)	36 (16.8)	14 (6.5)	0.98 (0.86-1.12)
5-17 y	464	406 (87.5)	36 (7.8)	22 (4.7)	0.58 (0.53-0.63)
18-29 y	362	235 (64.9)	67 (18.5)	60 (16.6)	0.48 (0.43-0.53)
30-49 y	366	114 (31.1)	80 (21.9)	172 (47.0)	0.29 (0.26-0.32)
≥50 y	81	36 (44.4)	2 (2.5)	43 (53.1)	0.06 (0.05-0.07)
Overall[c]	**1789**	**1243 (69.5)**	**230 (12.9)**	**316 (17.7)**	**0.39 (0.37-0.41)**


Chance Favors the Prepared Mind

Tip of the Spear

- Bush meat hunters
- Abattoir workers
- Viral chatter
- Hot spots



Diagnostics

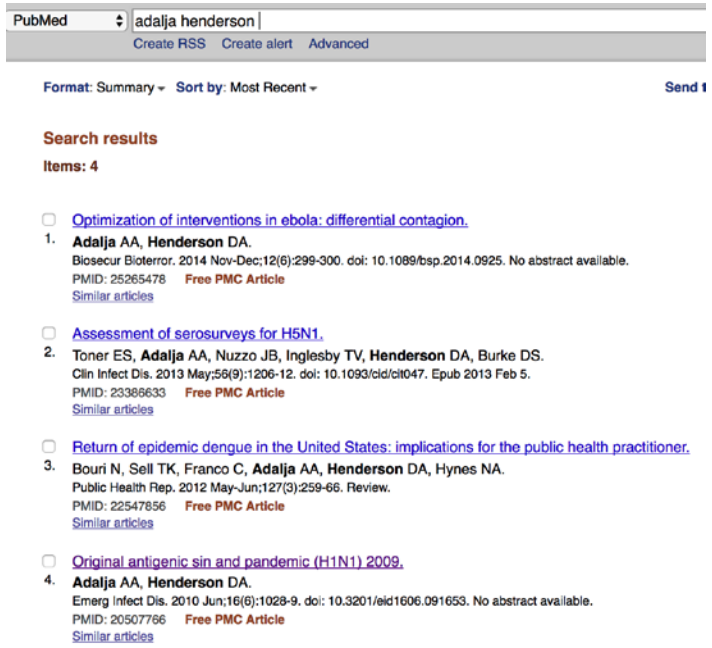
- Unknowns: Biological ”dark matter”
- Viral testing
- New technologies

central Africa, for instance Dr Bila Kapita, chief of internal medicine at Hôpital Mama Yemo in Kinshasa, reported that, at least since the mid-1970s, they started seeing cases that in retrospect were very likely to have been AIDS. This would be consistent with some degree of dissemination of the virus during the mid-1960s, given the average ten-year interval between infection and symptomatic disease. But could the disease have been present even earlier?[1,2]

In most district or regional hospitals of countries inhabited by *P.t. troglodytes*, the diagnostic facilities during the colonial era (and even now) were so minimal that it would have been difficult, even for astute and experienced clinicians, to recognise the emergence of a new disease characterised by intermittent fevers and profound wasting. Most such institutions did not have any kind of half-decent microbiology laboratory. No cultures were done, either for common bacterial pathogens or the agent of tuberculosis, and diagnoses were based on stains made directly on the specimens, or solely on the combination of symptoms and signs found during the clinical examination. Fifty years later, I found the same situation at the Nioki hospital in Zaire: nothing had changed. This approach was relatively effective for diagnosing parasitic diseases (malaria, sleeping sickness, filariasis, intestinal parasites) but very insensitive for most bacterial diseases. Little radiological investigation was available either; only in the best hospitals was it possible to get something as elementary as a chest x-ray. The first x-ray machine in Brazzaville was

Eradication of Smallpox (1980)

- Led by Dr. DA Henderson (1928-2016)
- First and only eradication of a human infectious disease
- Predicted by Jenner



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2. Assessment of serosurveys for H5N1.
   Toner ES, **Adalja** AA, Nuzzo JB, Inglesby TV, **Henderson** DA, Burke DS.
   Clin Infect Dis. 2013 May;56(9):1206-12. doi: 10.1093/cid/cit047. Epub 2013 Feb 5.
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3. Return of epidemic dengue in the United States: implications for the public health practitioner.
   Bouri N, Sell TK, Franco C, **Adalja** AA, **Henderson** DA, Hynes NA.
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4. Original antigenic sin and pandemic (H1N1) 2009.
   Adalja AA, **Henderson** DA.
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