Immunology II: Disease Ecology

Human Anatomy and Physiology

Outline

- Darwin: A Case Study
- Epidemiological Triangle
  - Agent
  - Environment
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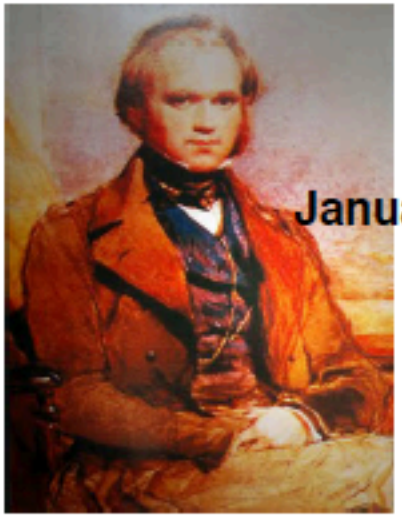
  - Hunter Gatherers vs. Modern Man
- Industrialization and the Eradication of Disease
- Zoonotic Diseases and Animal Domestication



January 29, 1839

Charles Darwin
1809-1882

Emma Wedgewood Darwin
1808-1896

1808 1818 1828 1838 1848 1858 1868 1878 1888 1898

William 1839-1914
December 27

Anne 1841-51

Mary 1842

Henrietta 1843-1927

George 1845-1912

Elizabeth 1847-1926

Francis 1848-1925

Leonard 1850-1943

Horace 1851-1928

Charles 1856-1858

Charles and William Darwin

William's drawing on a manuscript of *The Origin of Species*

Scarlet fever in 1849 at the age of 8 (along with Henrietta and Elizabeth).

After recovery, declining health and vigor, recurrent fevers, wasting.

Final illness in the spring of 1851 at Dr. James Manby Gully's hydrotherapy spa in Great Malvern.

Darwin suspected an inherited predisposition. The likely cause was tuberculosis.

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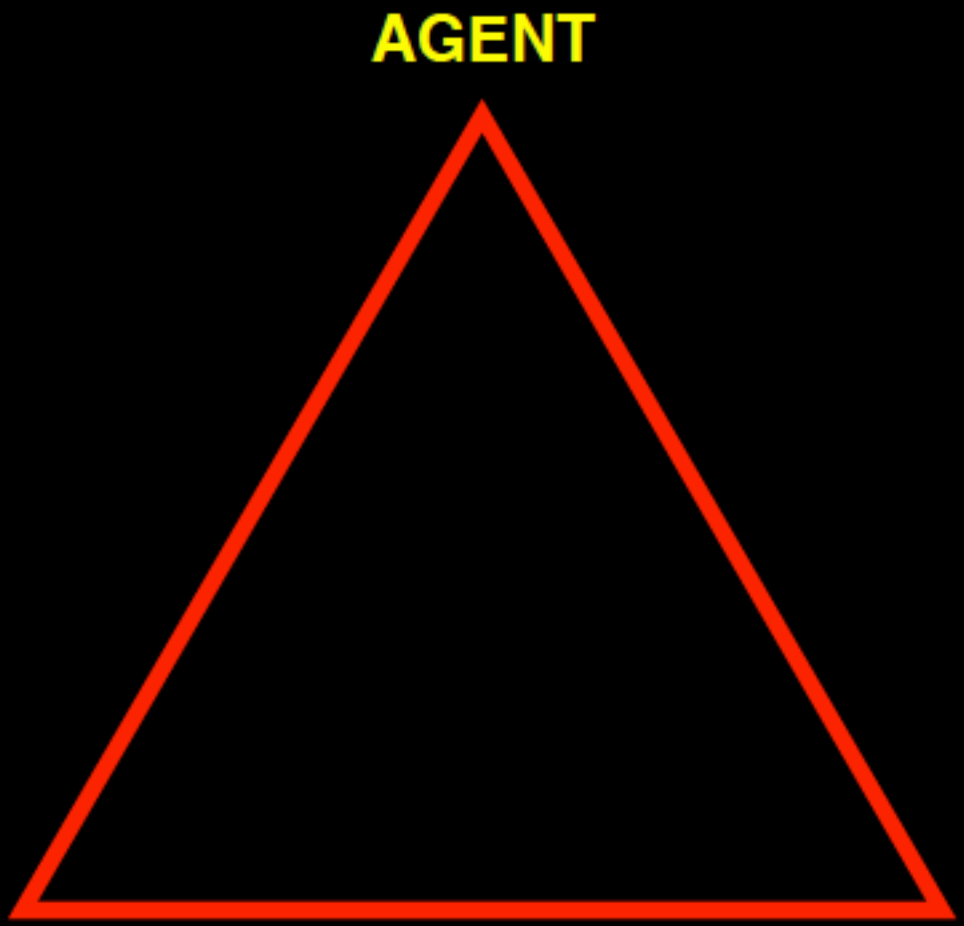
THE EPIDEMIOLOGICAL TRIANGLE



Agent Factors

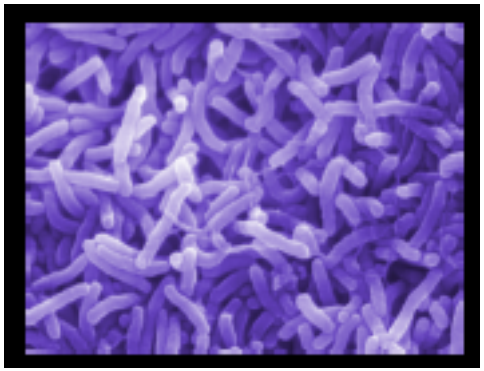
- Virulence
- Transmission (route and probability)
- Life Cycle
- Evasion

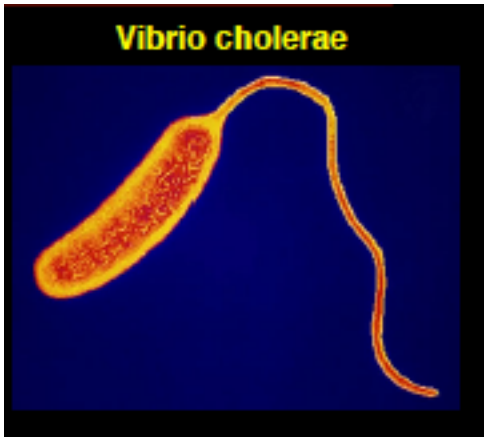
Evasion

- Outrun
- Lay low
- Outwit
- Disable

Evasion

- Outrun
- Lay low
- Outwit
- Disable





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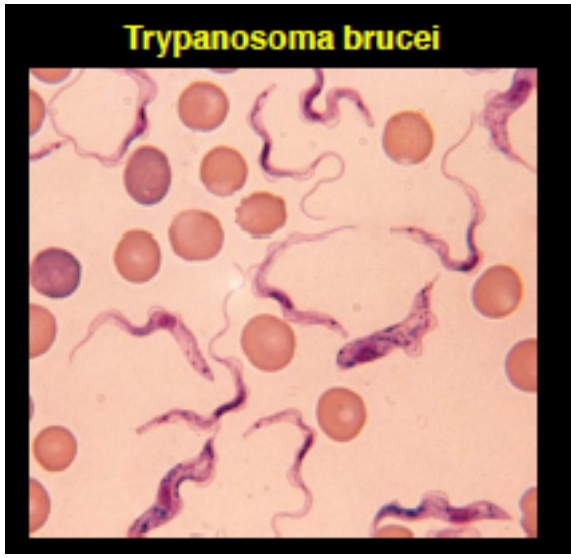

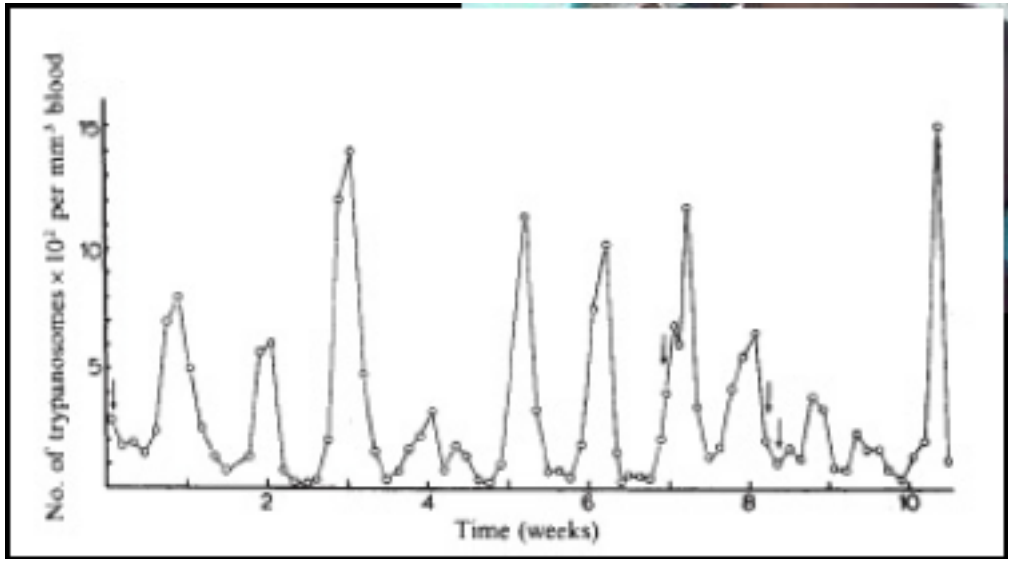

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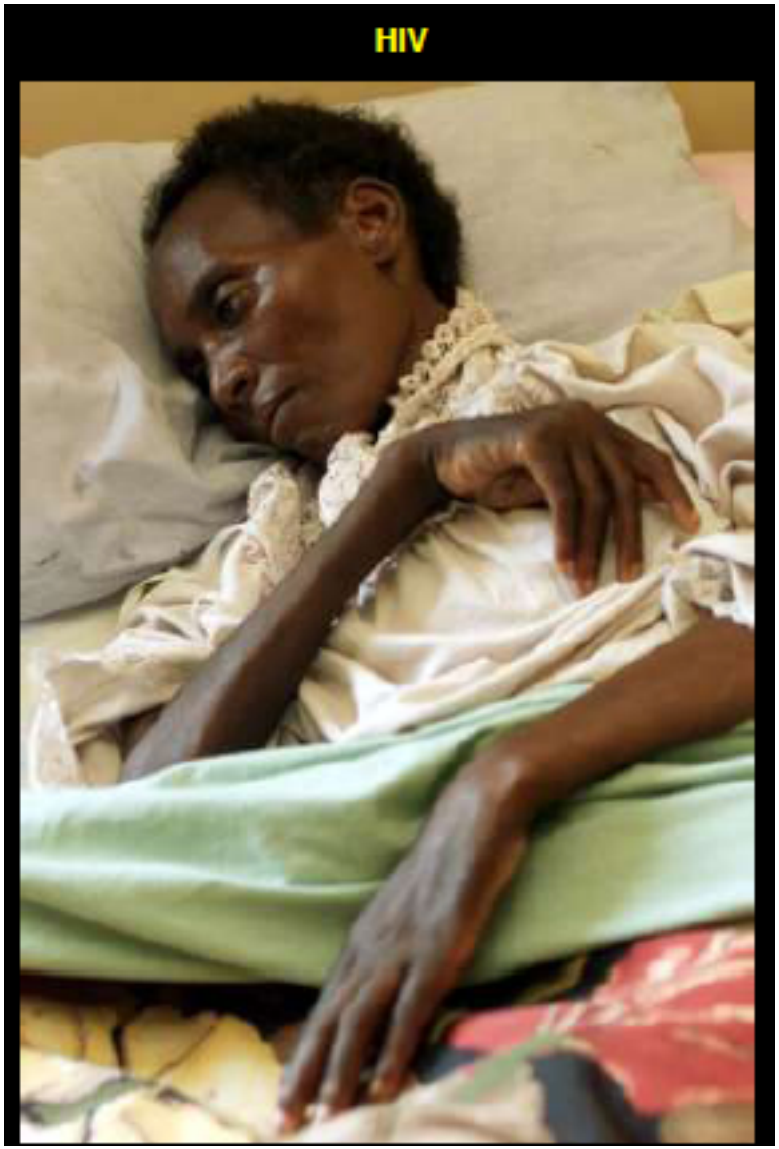

Host Factors

- Passive & Acquired Immunity
- Nutritional Status
- Age
- Reproductive Status
- Co-morbidity

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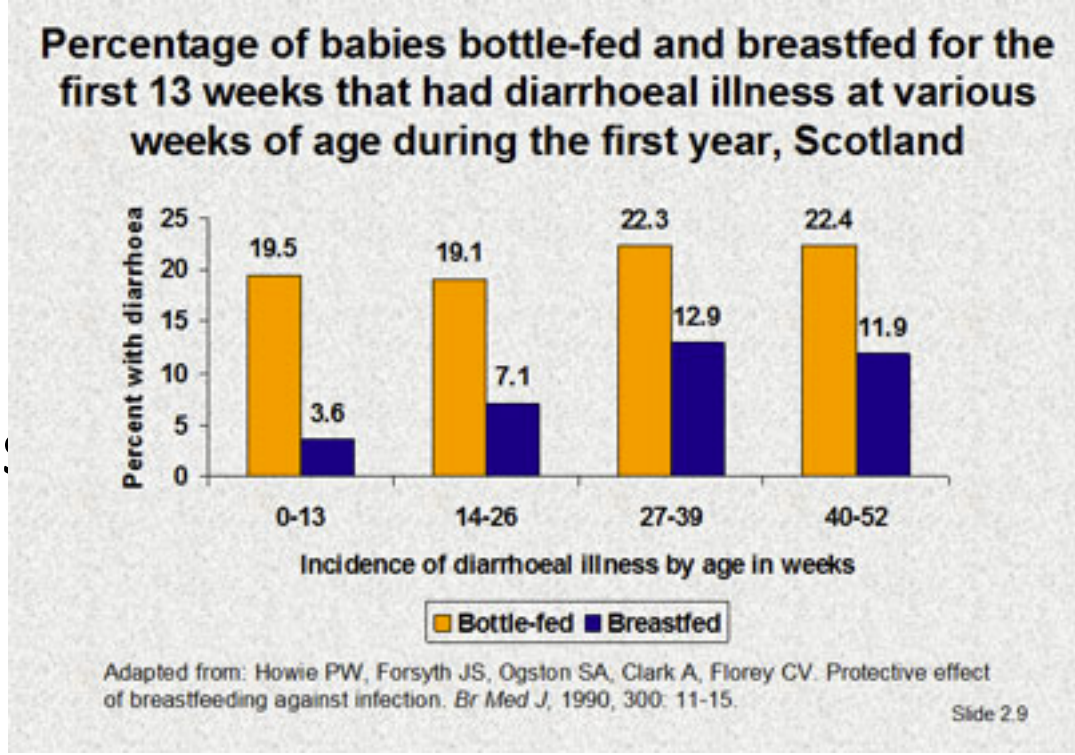

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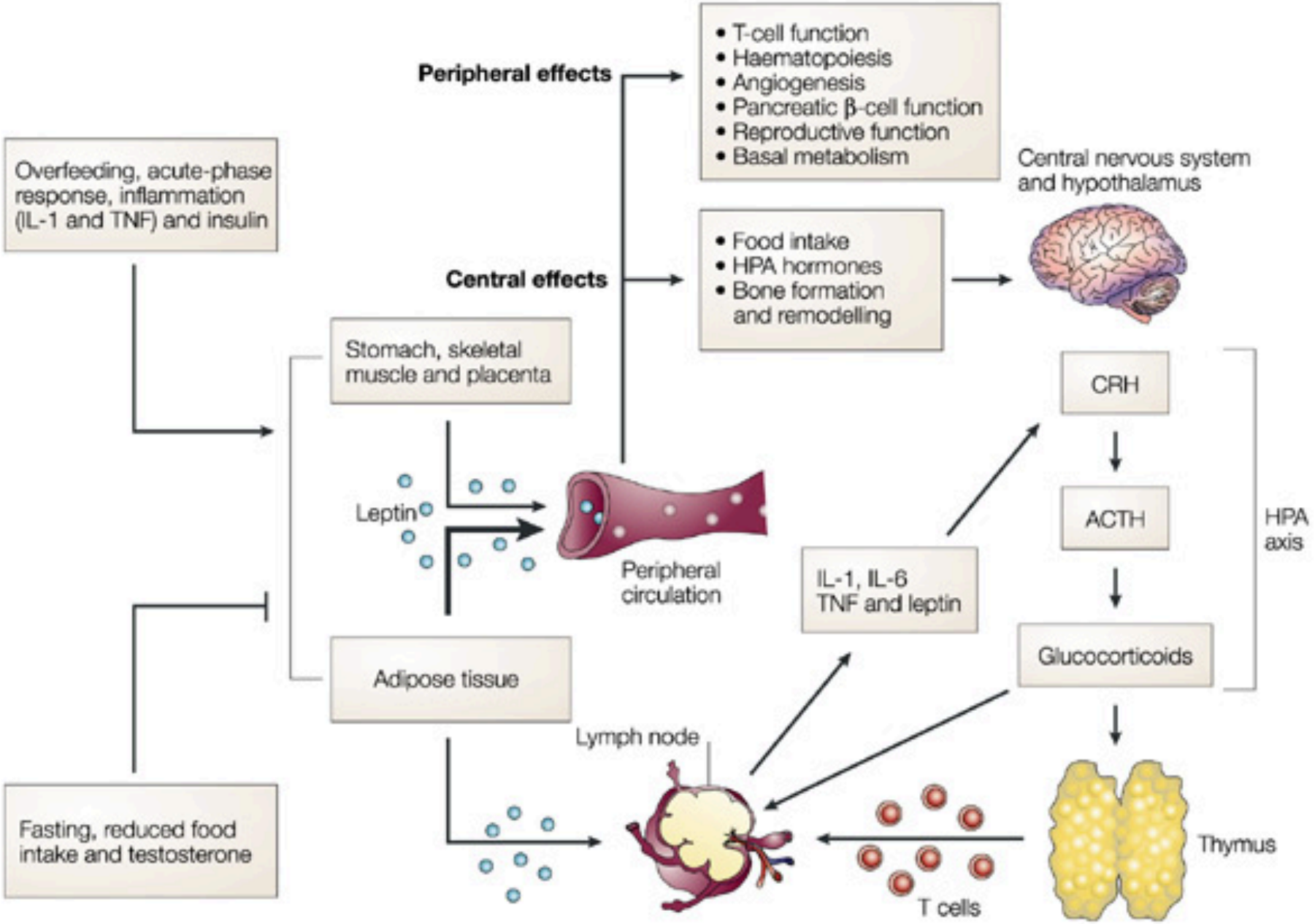
Peripheral effects
• T-cell function
• Haematopoiesis
• Angiogenesis
• Pancreatic β-cell function
• Reproductive function
• Basal metabolism
Overfeeding, acute-phase response, inflammation (IL-1 and TNF) and insulin
Central effects
• Food intake
• HPA hormones
• Bone formation and remodelling
Central nervous system and hypothalamus
Stomach, skeletal muscle and placenta
CRH
ACTH
HPA axis
Leptin
Peripheral circulation
IL-1, IL-6 TNF and leptin
Glucocorticoids
Adipose tissue
Lymph node
Fasting, reduced food intake and testosterone
T cells
Thymus

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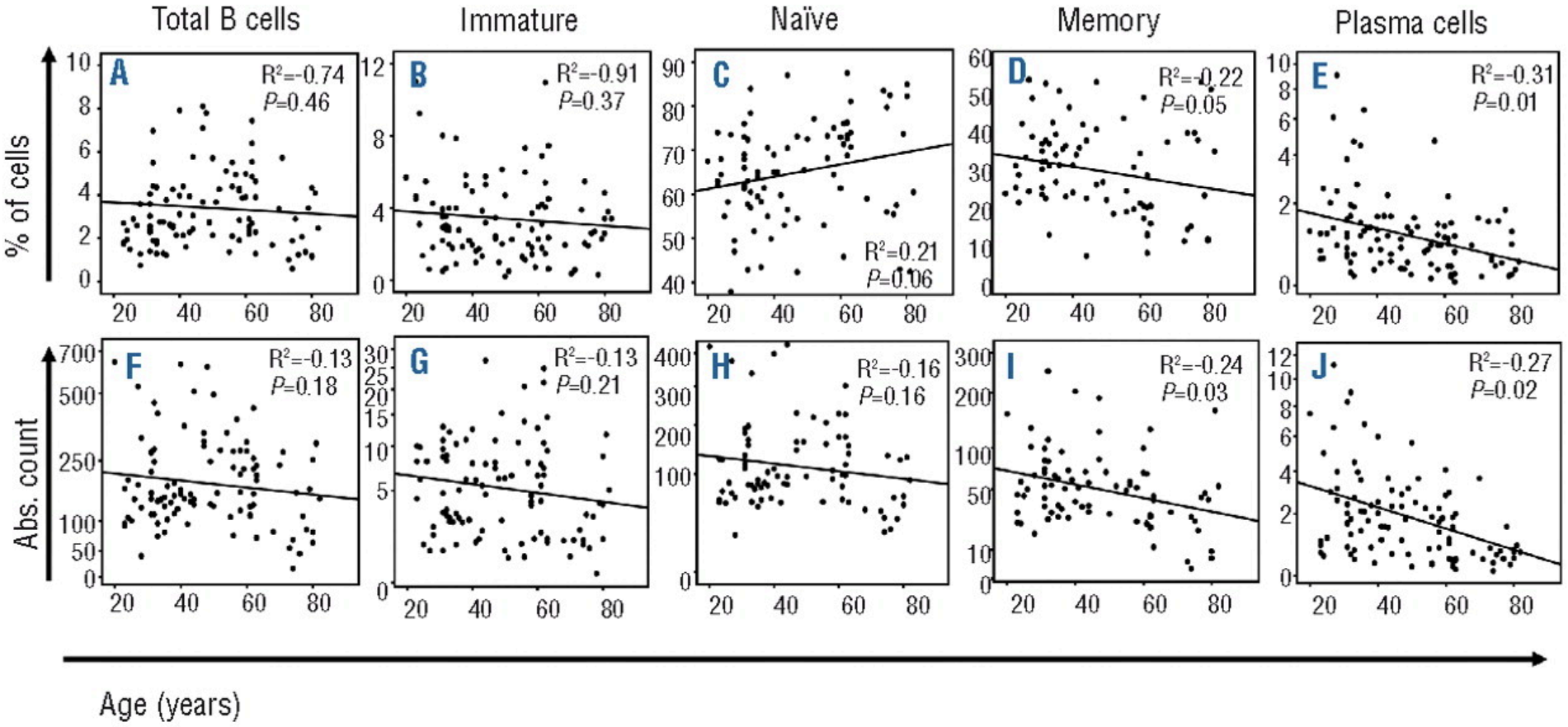

Anouk Caraux, Bernard Klein, Bruno Paiva, Caroline Bret, Alexander Schmitz, Gwenny M. Fuhler, Nico A. Bos, Hans E Johnsen, Alberto Orfao, Martin Perez-Andres,
Haematologica June 2010 95: 1016-1020; Doi:10.3324/haematol.2009.018689

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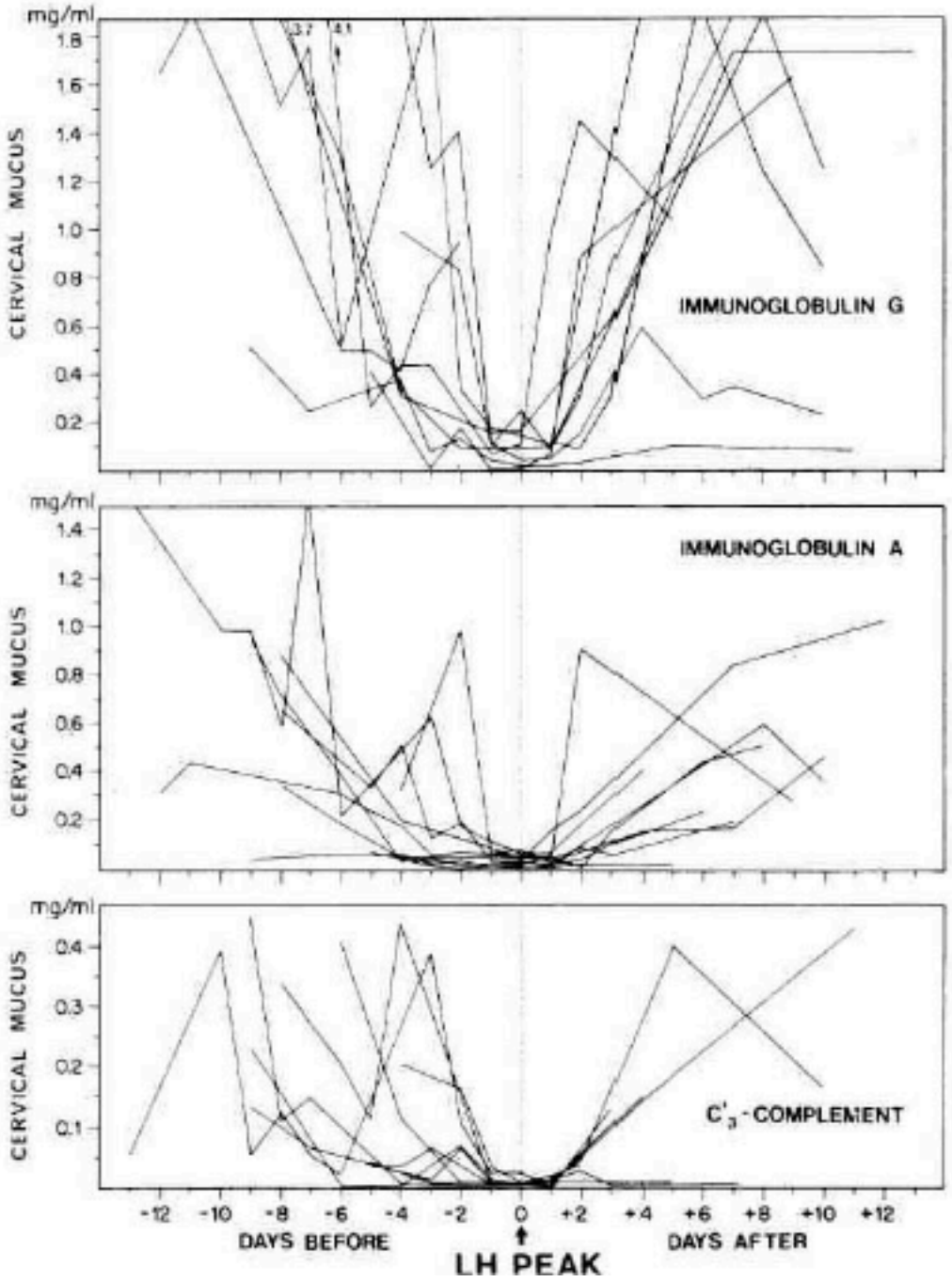
mg/ml
CERVICAL MUCUS
IMMUNOGLOBULIN G
IMMUNOGLOBULIN A
C'3-COMPLEMENT
DAYS BEFORE
LH PEAK
DAYS AFTER

Host Factors

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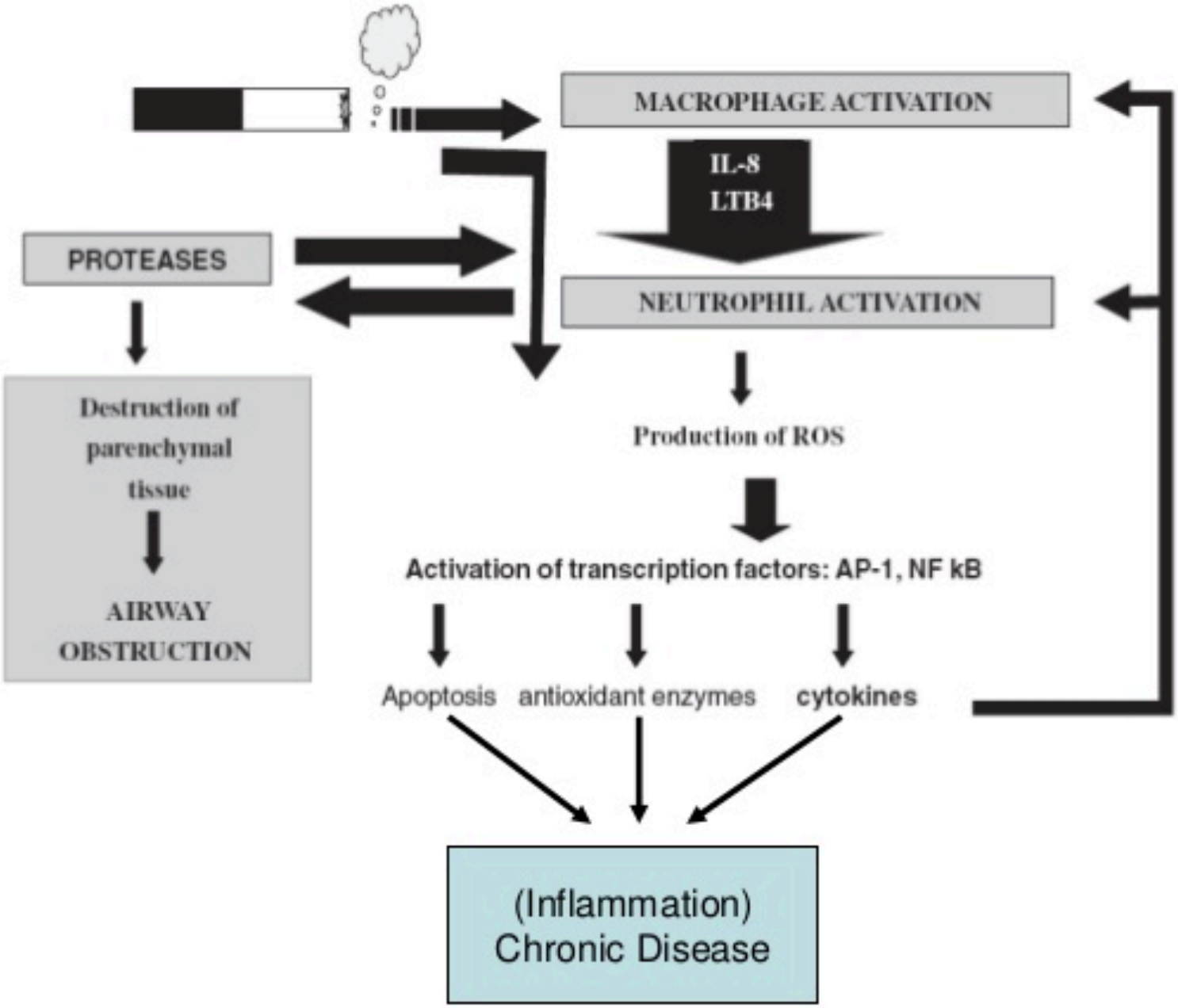
- Co-morbidity


MACROPHAGE ACTIVATION
IL-8
LTB4
PROTEASES
NEUTROPHIL ACTIVATION
Destruction of parenchymal tissue
AIRWAY OBSTRUCTION
Production of ROS
Activation of transcription factors: AP-1, NF kB
Apoptosis
antioxidant enzymes
cytokines
(Inflammation)
Chronic Disease

Common Comorbidities in COPD

Cardiovascular Disorders

- Pulmonary hypertension
- Right heart failure, Cor pulmonale
- Vascular disease
  - -Coronary artery disease
  - -Cerebrovascular disease
  - -Periferal vascular disease
- Systemic hypertension

Nutritional Disorders, Cachexia

Musculoskeletal Disorders

- Muscle dysfunction
- Osteoporosis

Cancer

Other

- Sleep disorders
- Sexual dysfunction
- Diabetes
- Depression, anxiety
- Anaemia
- Peptic ulcus
- Glocoma

Environmental Factors

- Encounter rates with agent
- Encounter rates with susceptibles
- Vectors
- Reservoirs
- Seasonality

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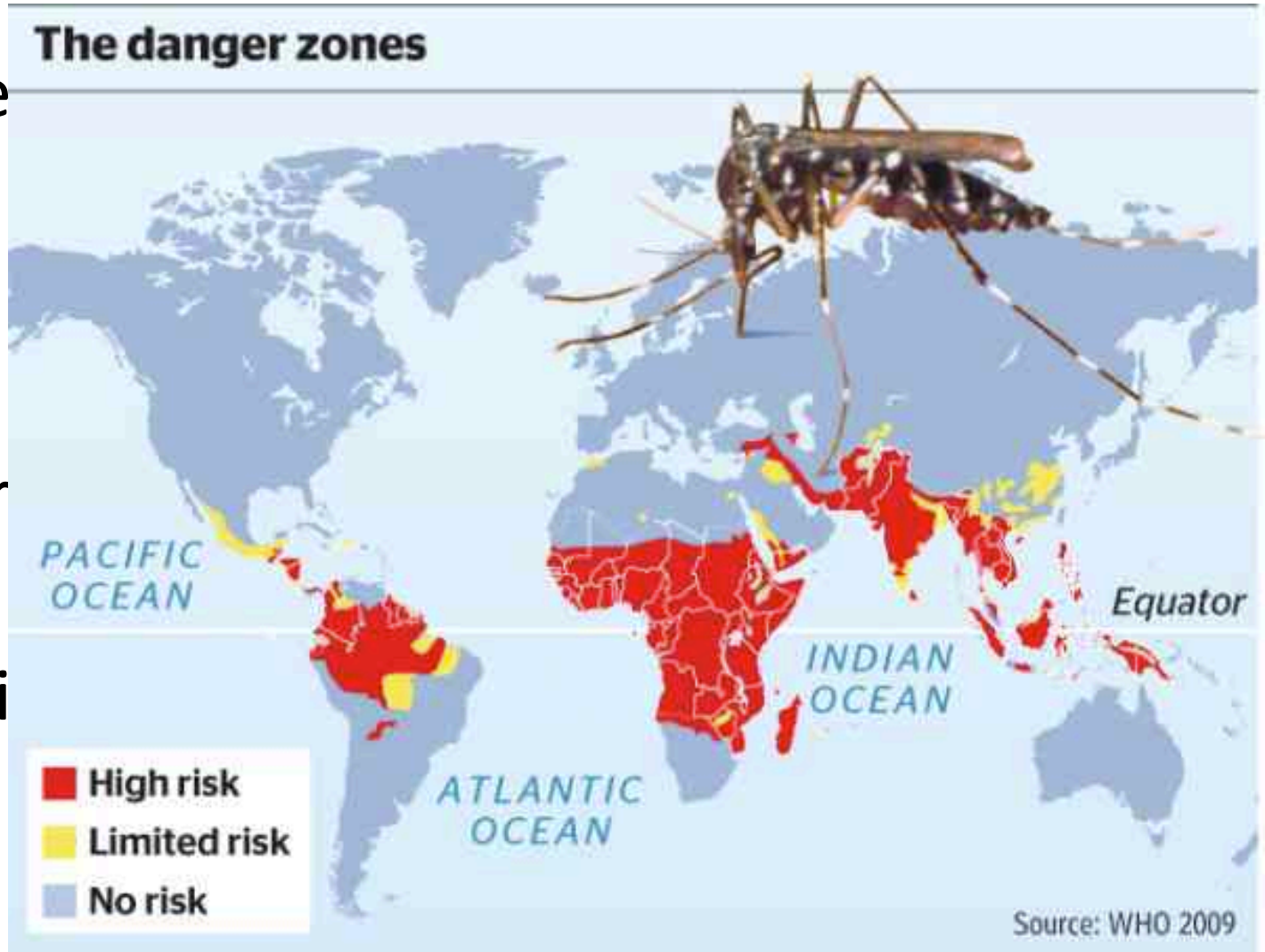

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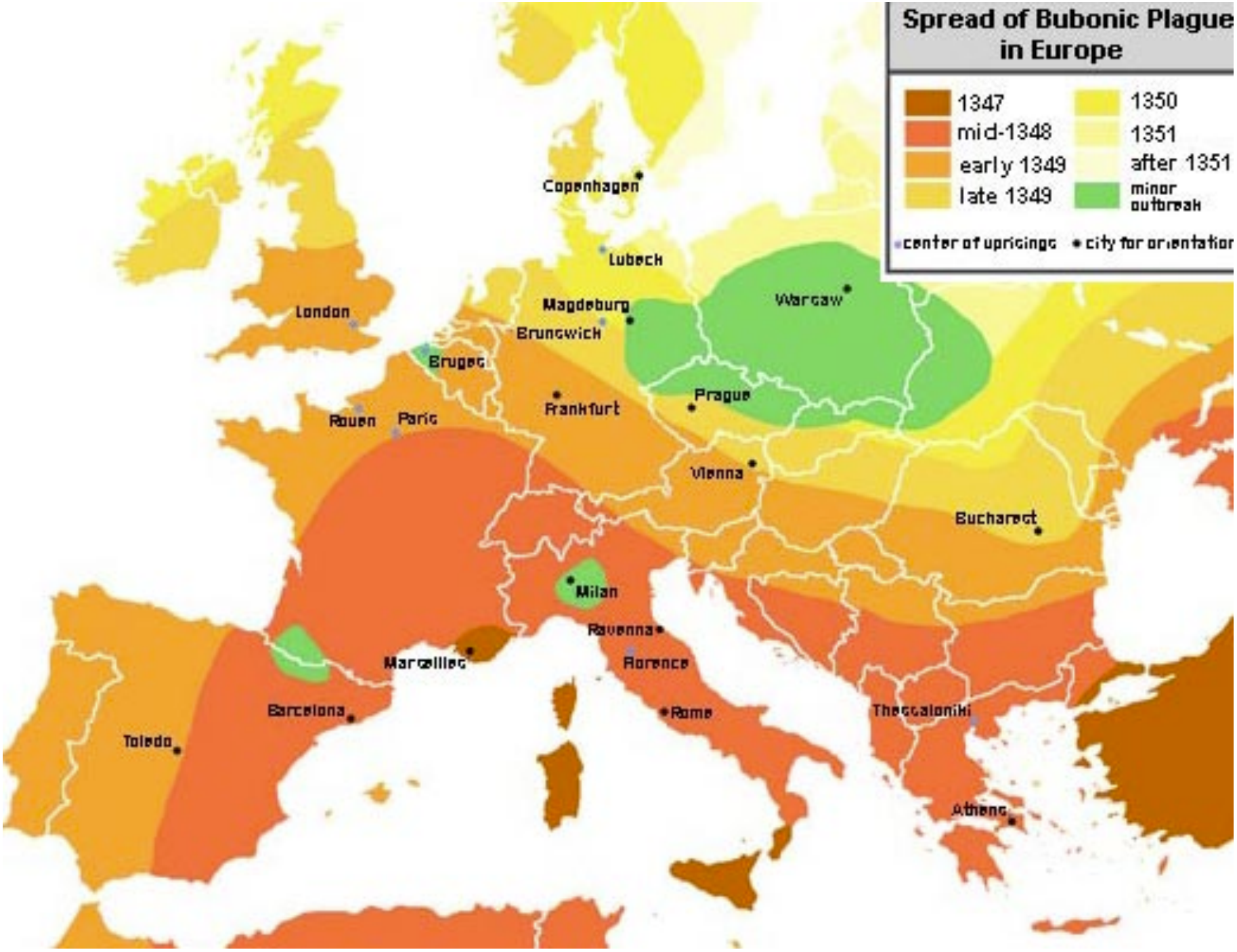
Spread of Bubonic Plague in Europe
1347
mid-1348
early 1349
late 1349
1350
1351
after 1351
minor outbreak
center of uprisings
city for orientation
Copenhagen
Lubeck
Warsaw
Magdeburg
Brunswick
London
Bruges
Prague
Frankfurt
Rouen
Paris
Vienna
Bucharest
Milan
Ravenna
Florence
Marseilles
Barcelona
Rome
Thessaloniki
Toledo
Athens

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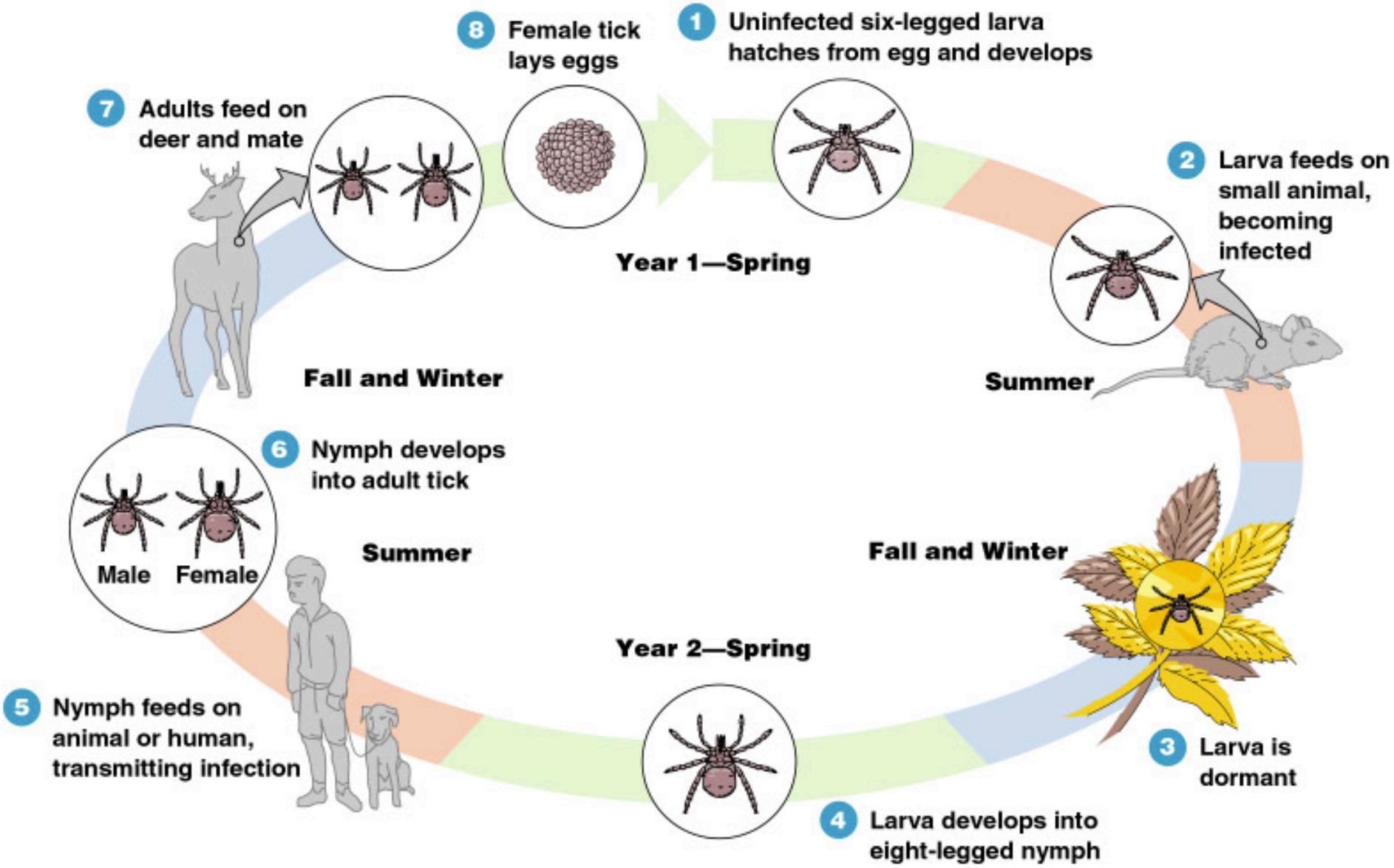
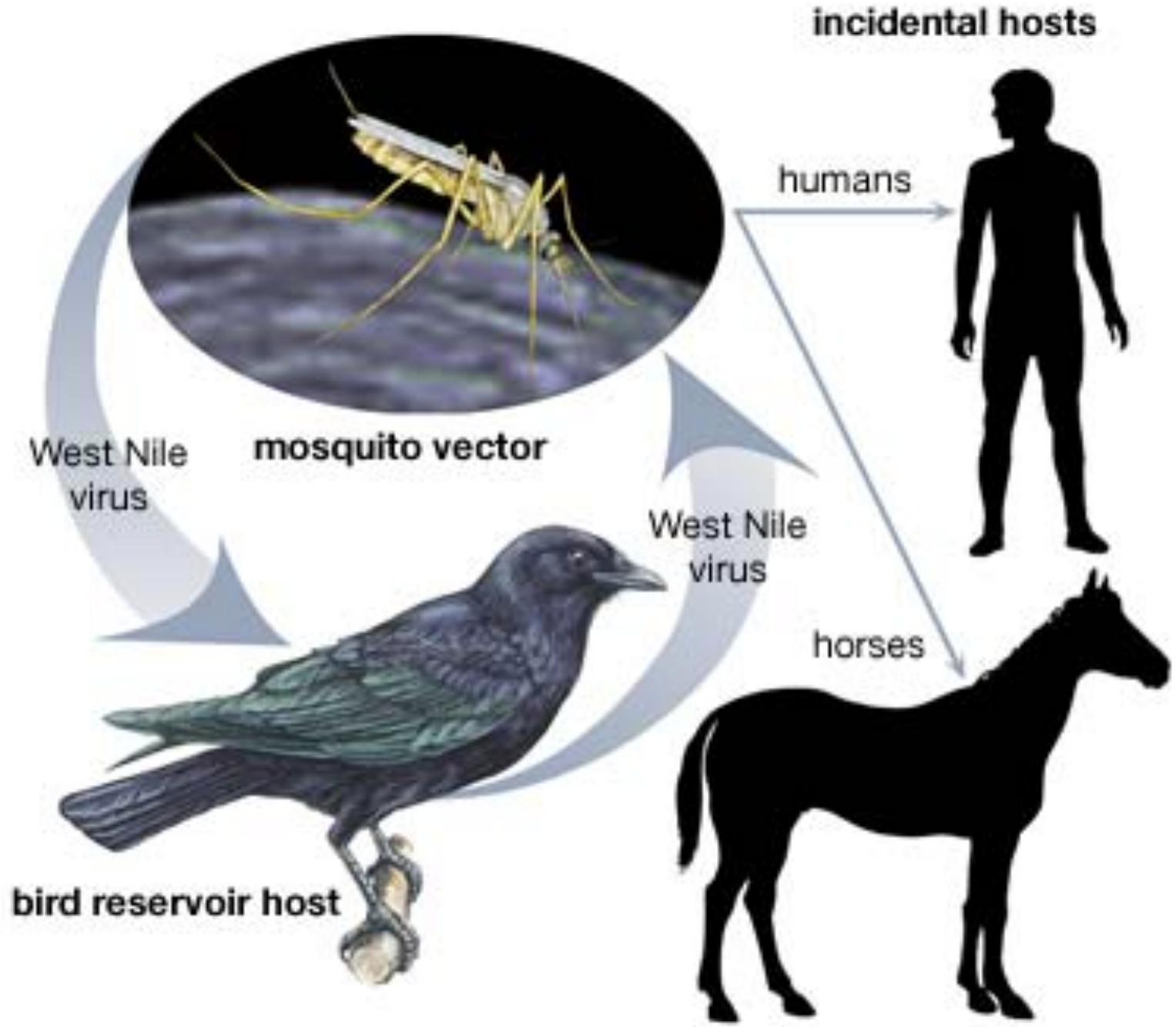


(a) The tick, *Ixodes scapularis*, has a two-year life cycle in which it requires three blood meals. The tick is infected by its first blood meal, and can pass on the infection to a human in its second.

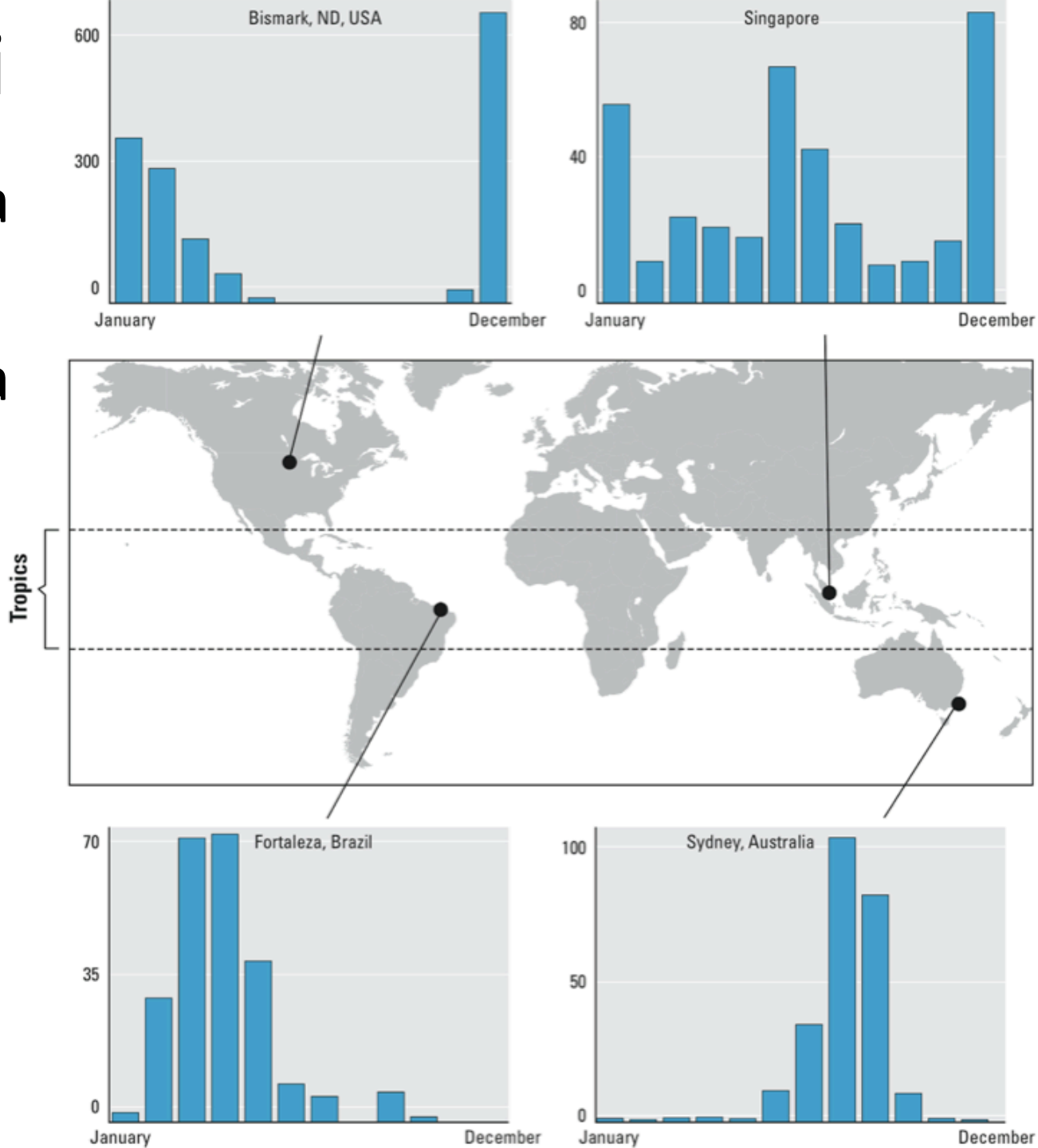
Environmental Factors

- Encounter rates with agent
- Encounter rates with susceptibles
- Vectors
- Reservoirs
- Seasonality



Envi

- Encounter ra
- Encounter ra
- Vectors
- Reservoirs
- Seasonality



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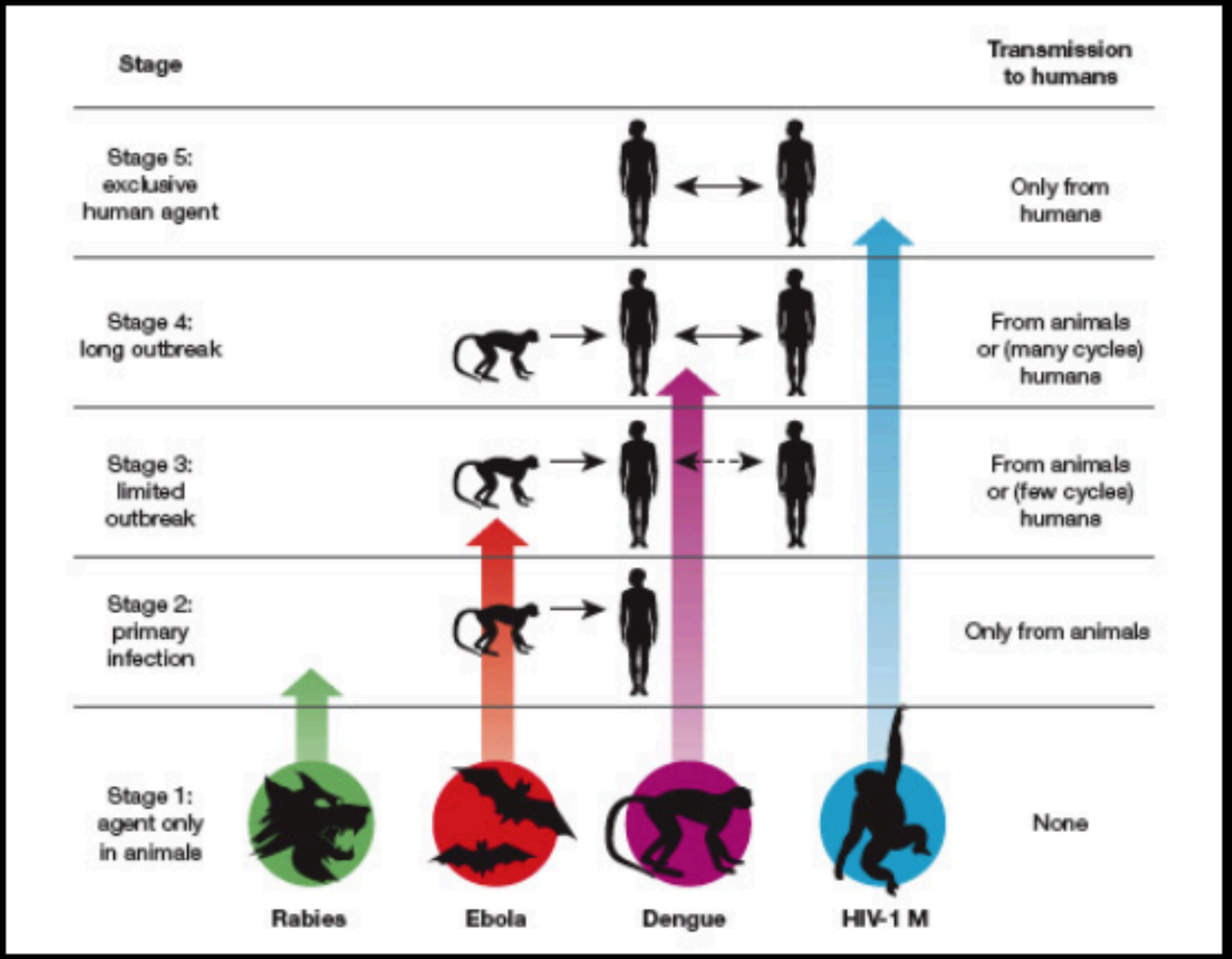
Hunting and Gathering

- Directly transmittable diseases rare

- Pathogens with long latencies, dormant life cycle stages, non-human reservoirs and transmission vectors were probably more common.

ANIMAL DOMESTICATION

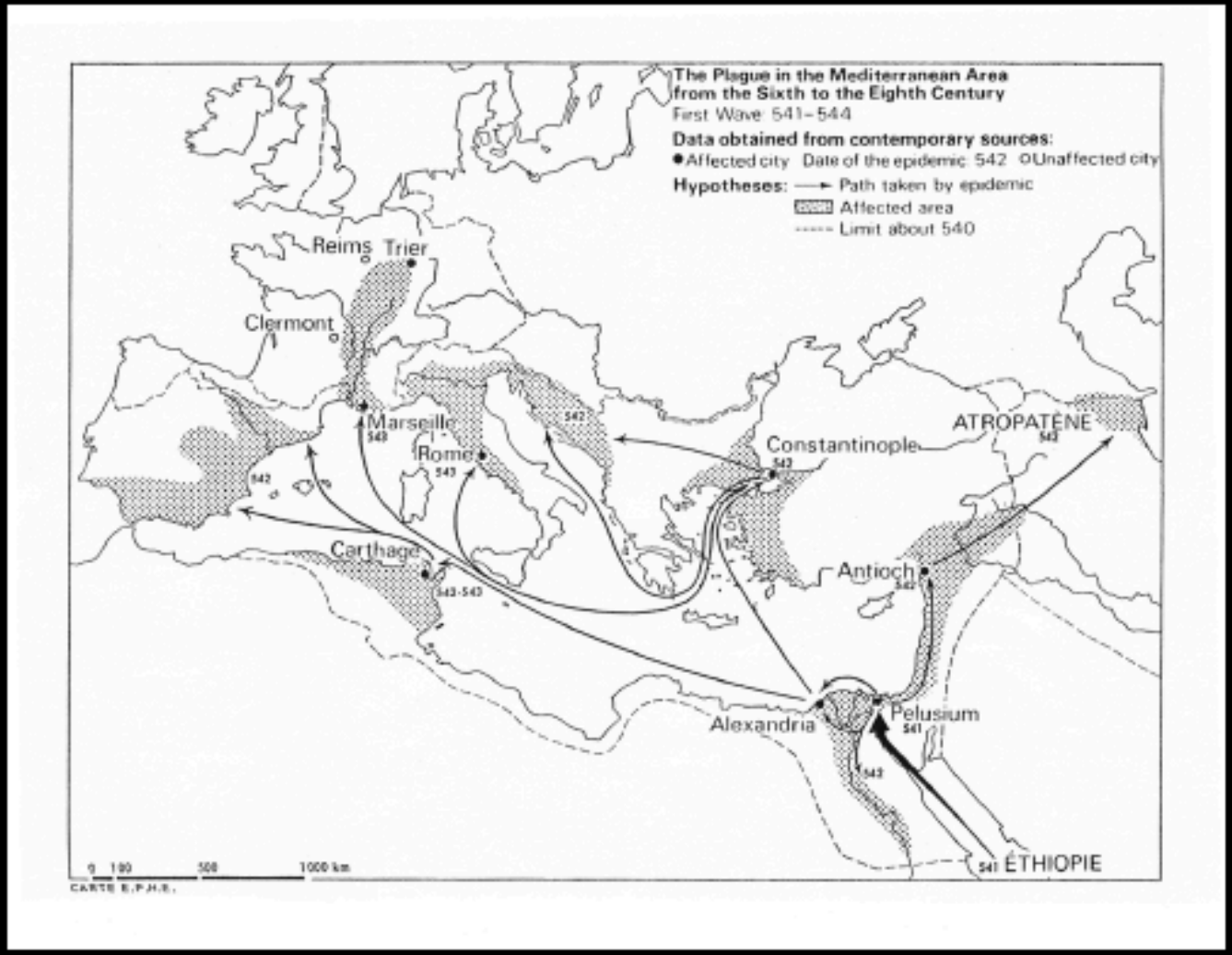
Most directly transmittable diseases in humans appear to have originated in domestic animals and have increased as our intimate contact with these species has increased.



Transfer of diseases from animals to humans (zoonotic diseases) continues to occur when humans and animals come into frequent, intimate contact.

Agriculture

Adoption of agriculture as a subsistence base led to larger populations, fixed residence, seasonality in workload and food abundance, and alteration of local ecology.



The emergence of long range sea and land based trade routes facilitated the spread of epidemic disease in the ancient and medieval worlds.

Conquest, invasion, and migration have also often introduced new diseases to previously unexposed populations.

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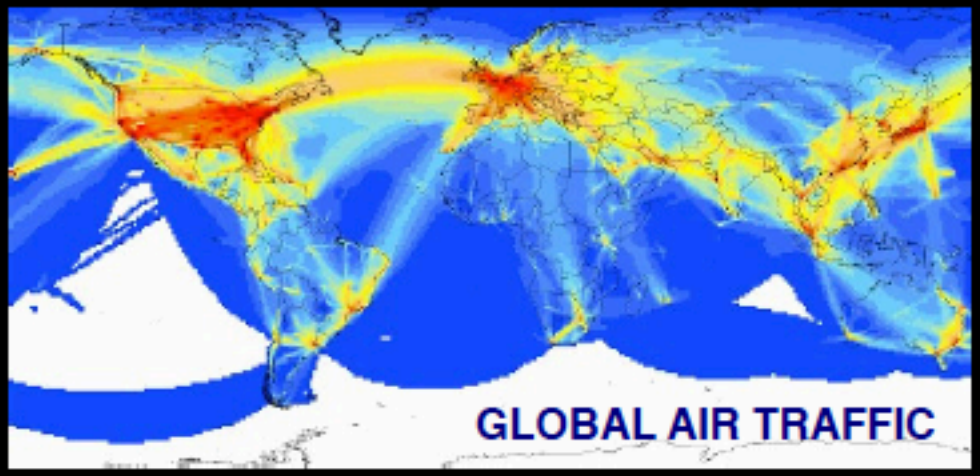
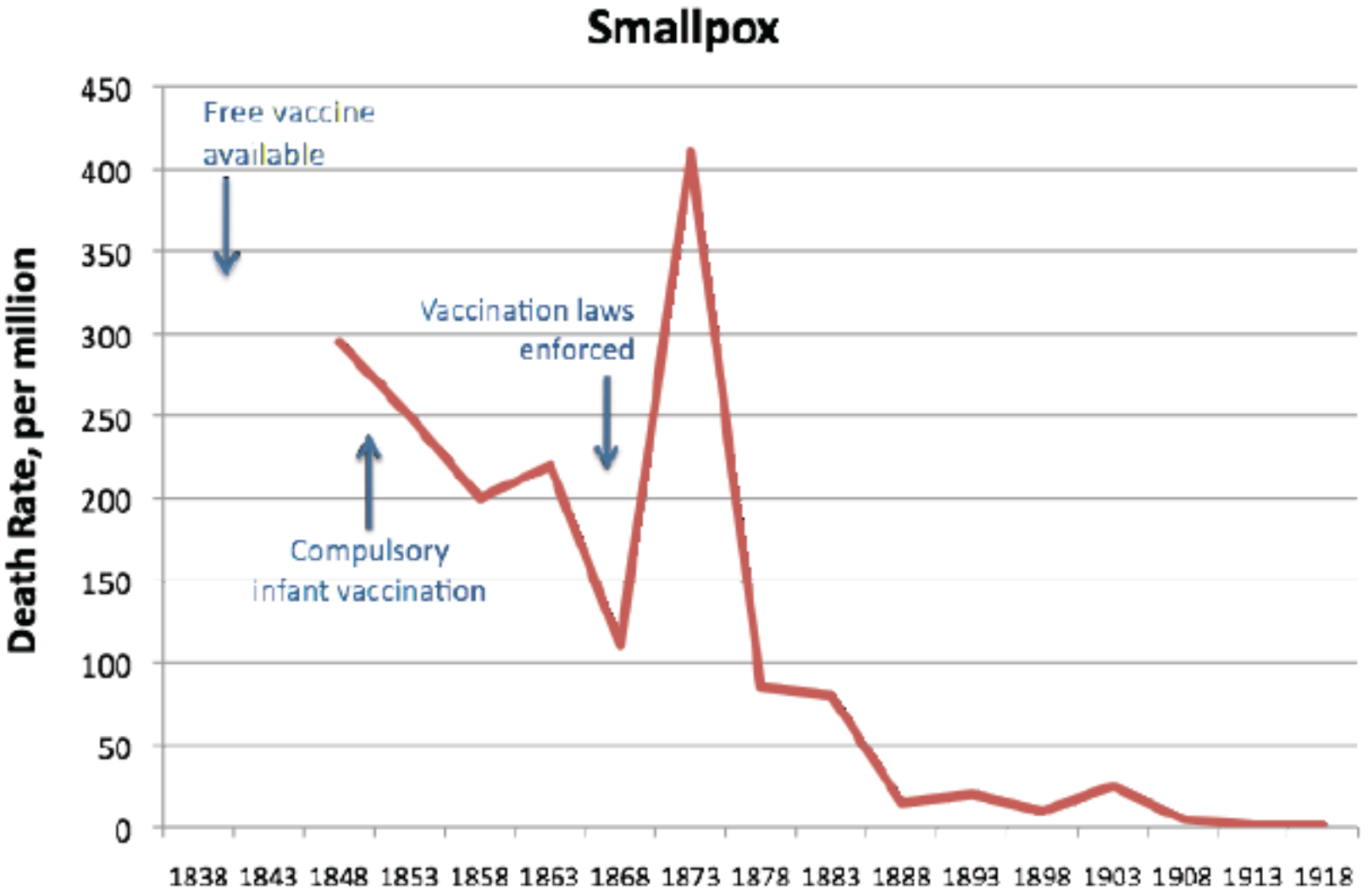
Industrialization

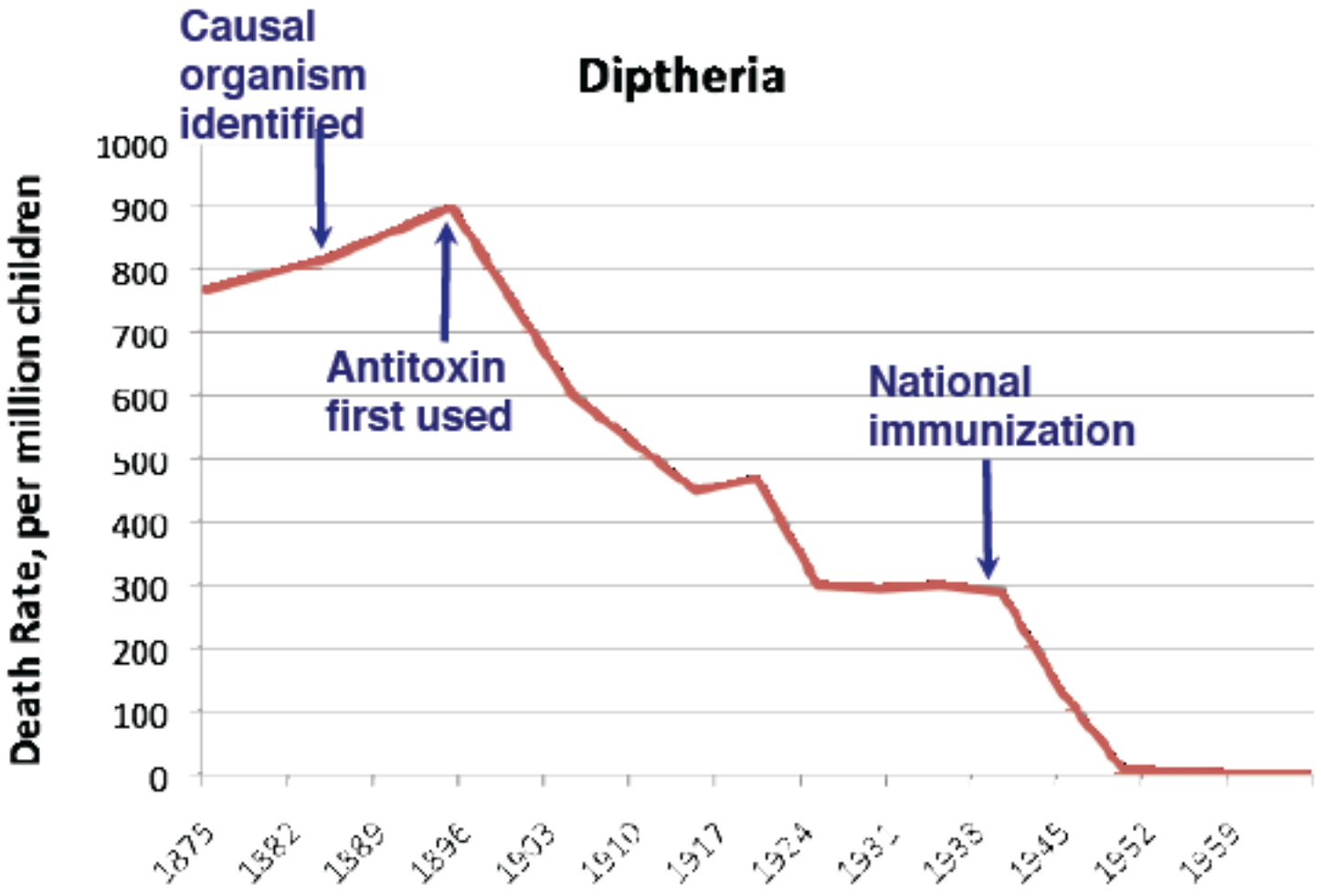


Modern urban-industrial societies have brought further changes in the degree of crowding, nutritional status, and the rate and extent of population mixing.



England and Wales

McKeown, T. 1976. ***The Rise of Modern Population***



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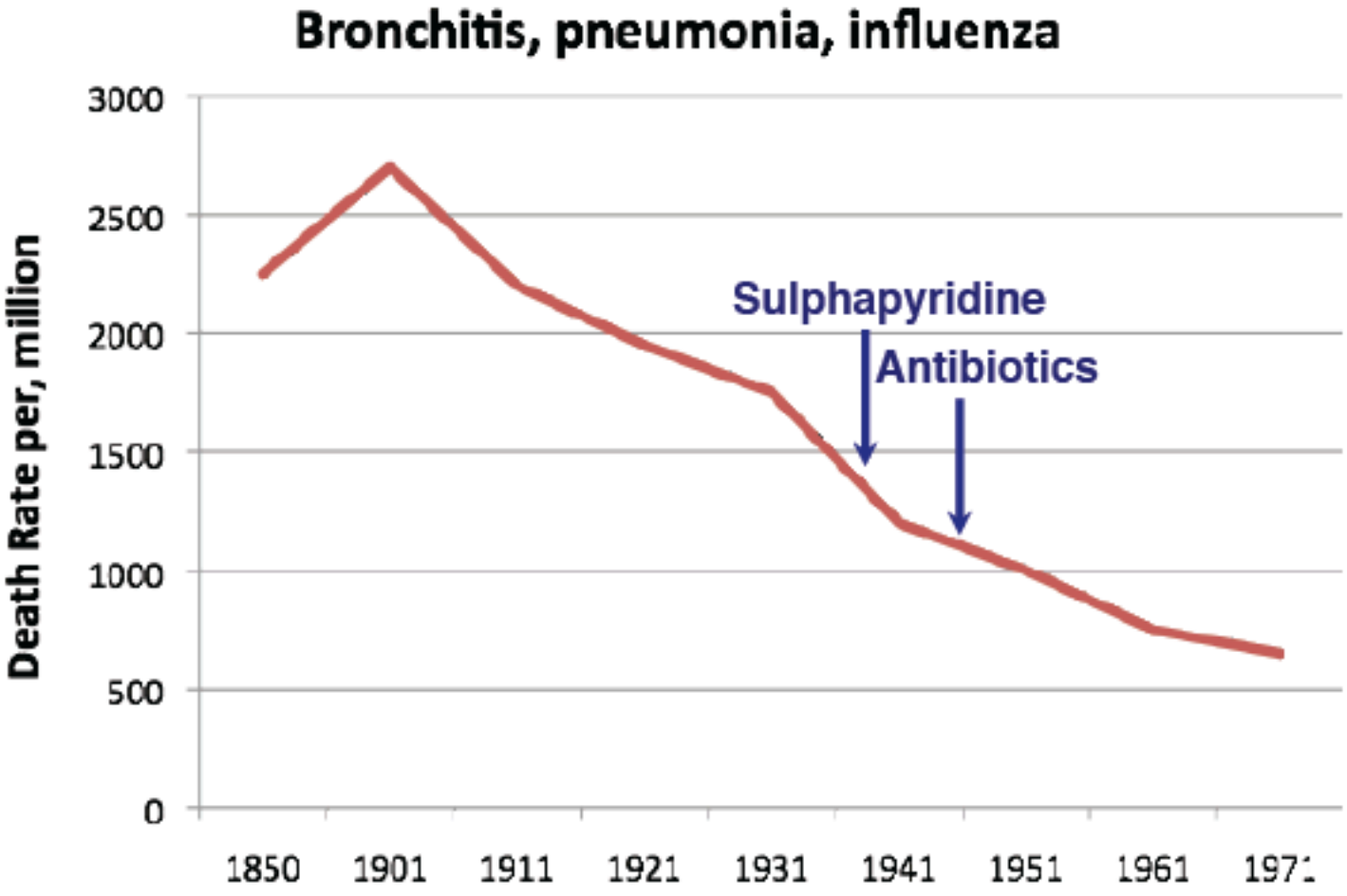

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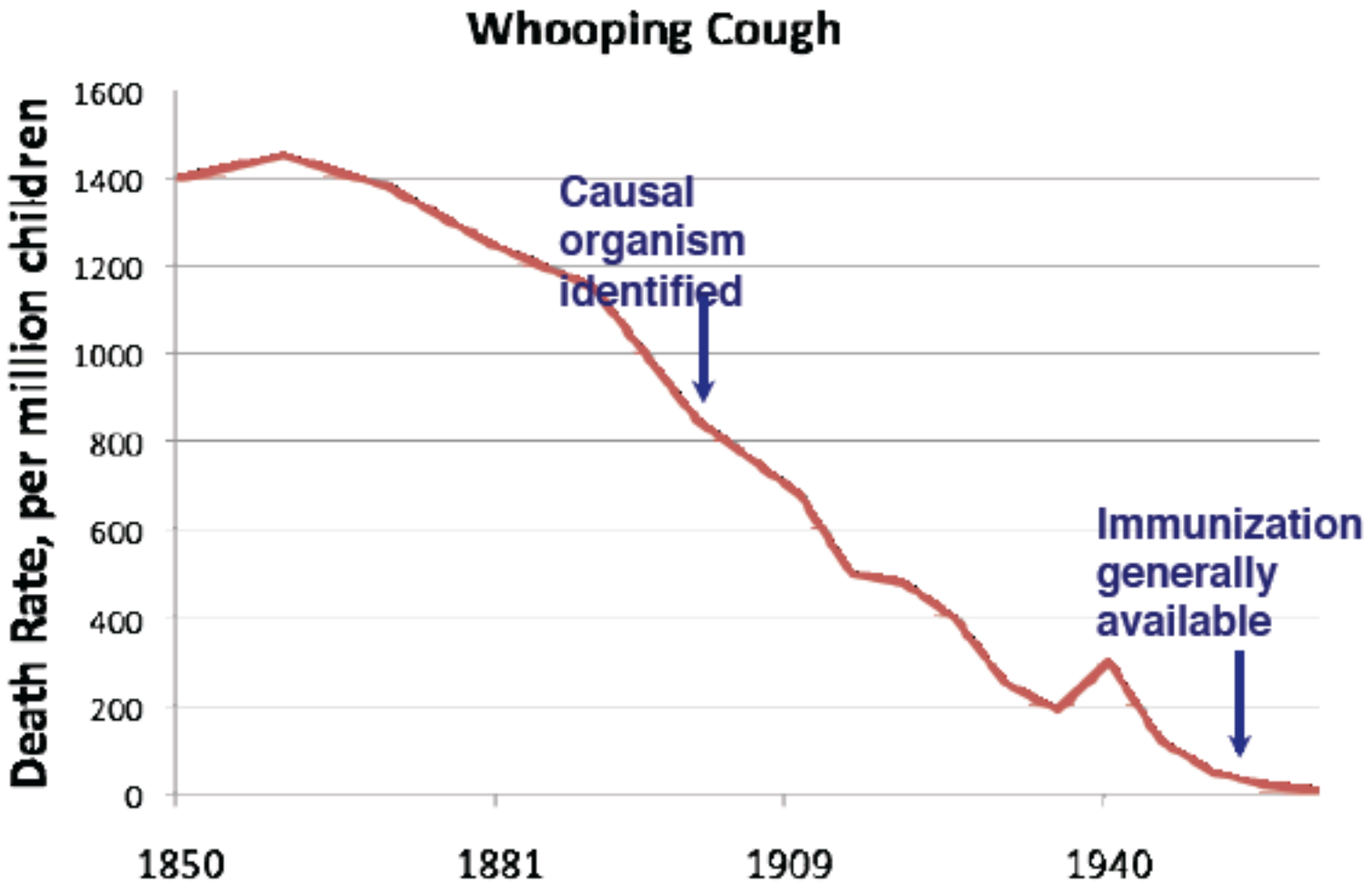

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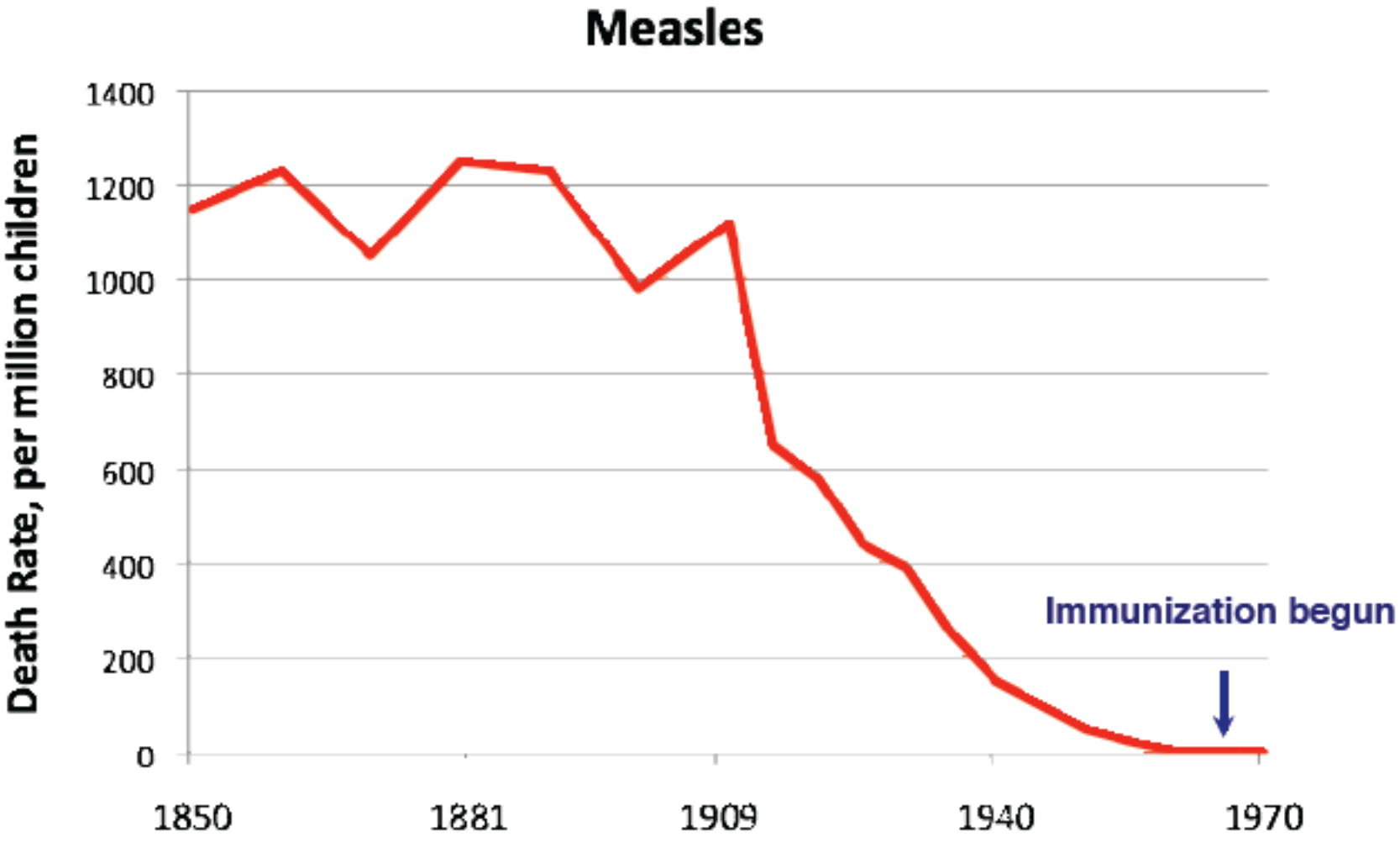


England and Wales

McKeown, T. 1976. ***The Rise of Modern Population***

ANNUAL MORTALITY RATE (PER MILLION)

4000
3000
2000
1000
0

1820
1860
1900
1940
1980

TUBERCULOSIS
SCARLET FEVER

†

Tubercle bacillus identified

Streptococcus bacillus identified

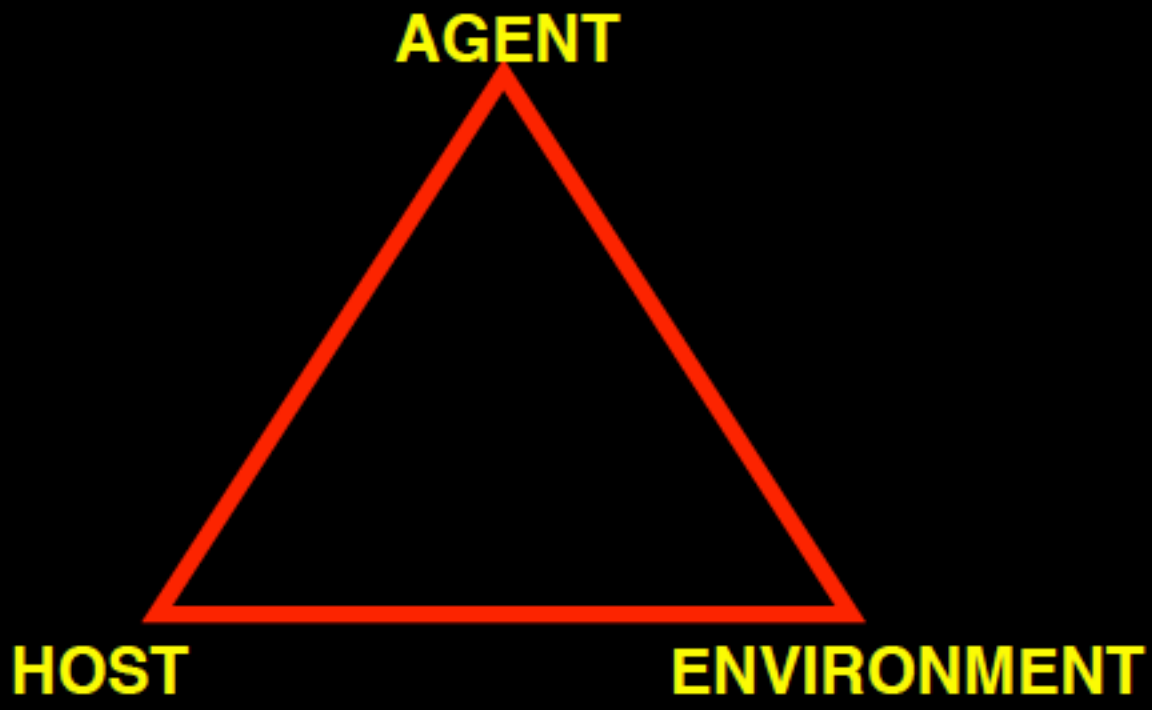
Chemotherapy

Vaccination

Sulpha drugs

Antibiotics

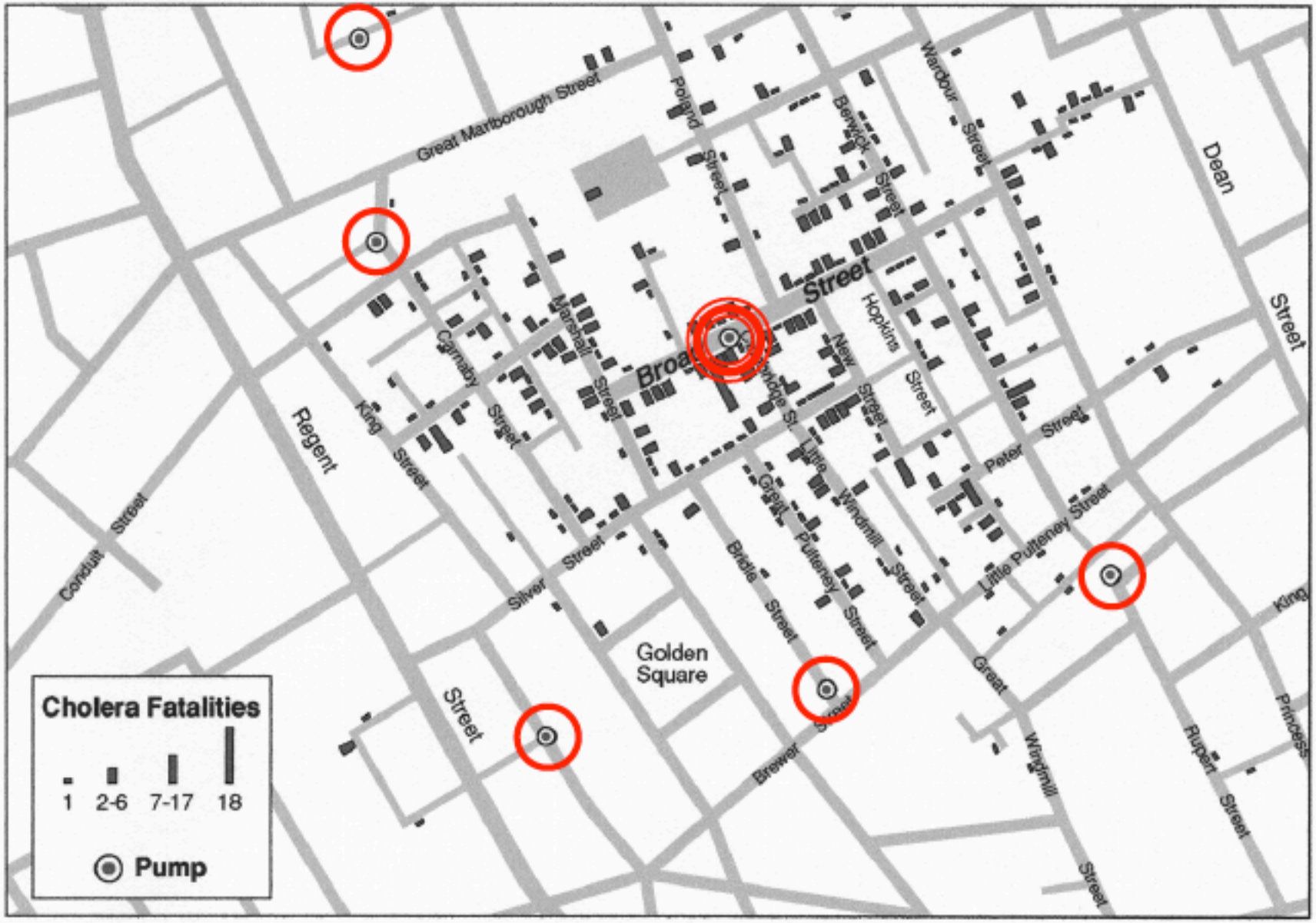
What caused the epidemiological transition?



$$R = (r_{encounter} * r_{transmission}) - r_{death} - r_{recovery}$$

Figure 1

Cluster Map of Fatal Cholera Cases in London, 1854



Source: Adapted from John Snow, *Snow on Cholera* (New York: Hafner, 1965).

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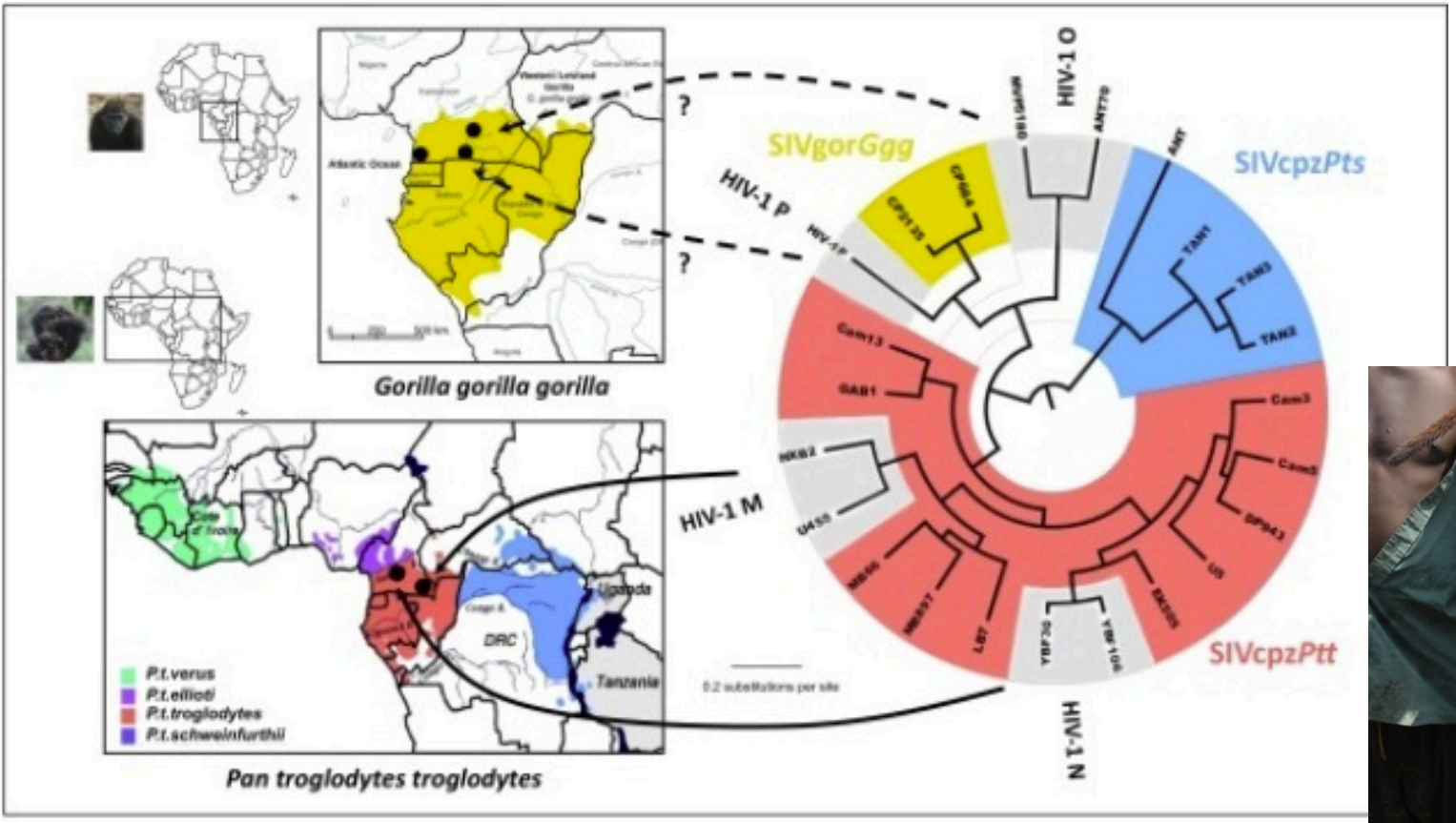
Zoonotic Diseases

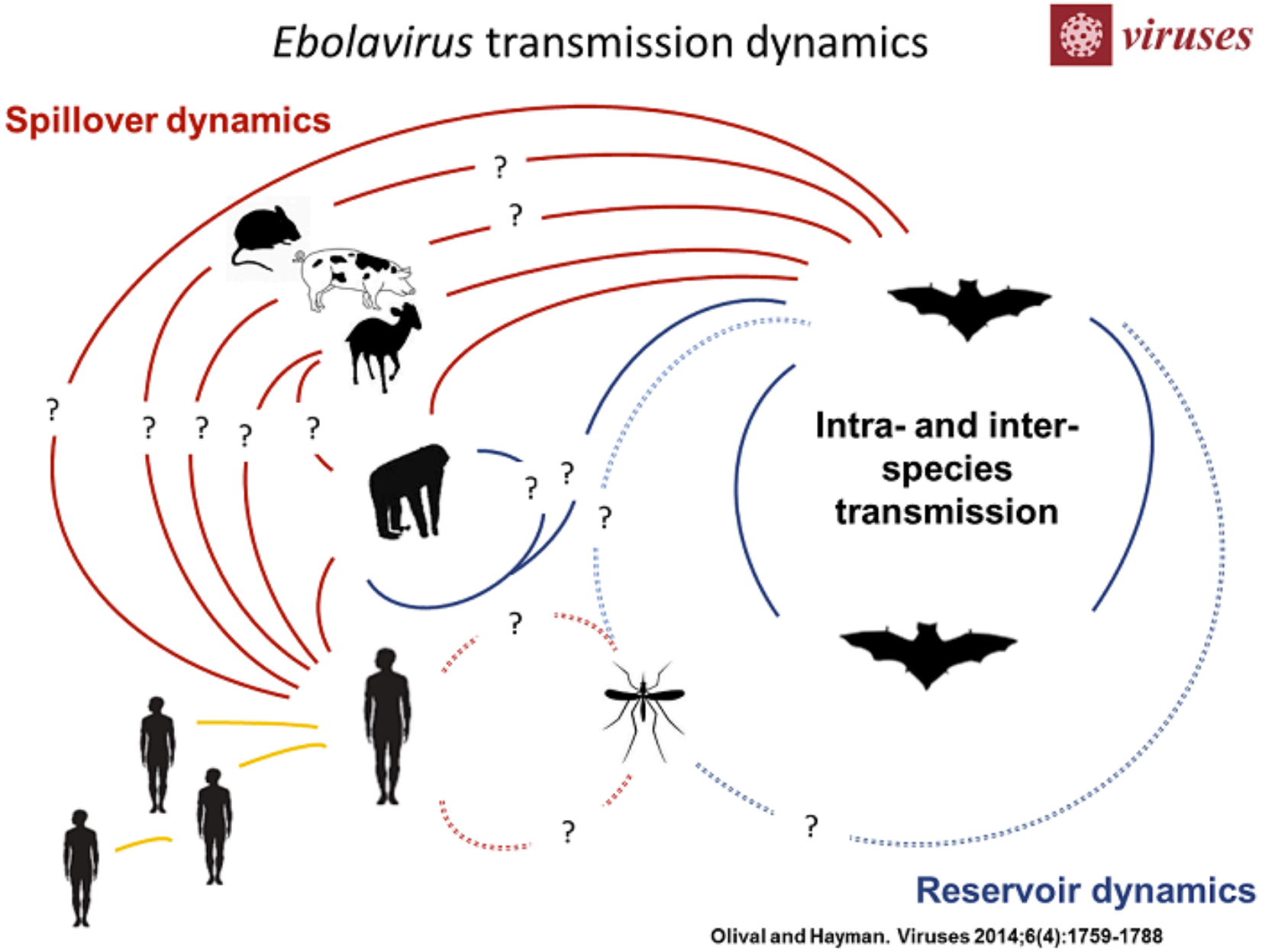
- Definition – a disease that can pass between animal and humans.

- Examples
  - HIV
  - Ebola
  - Avian Flu
  - SARS
  - Bubonic Plague

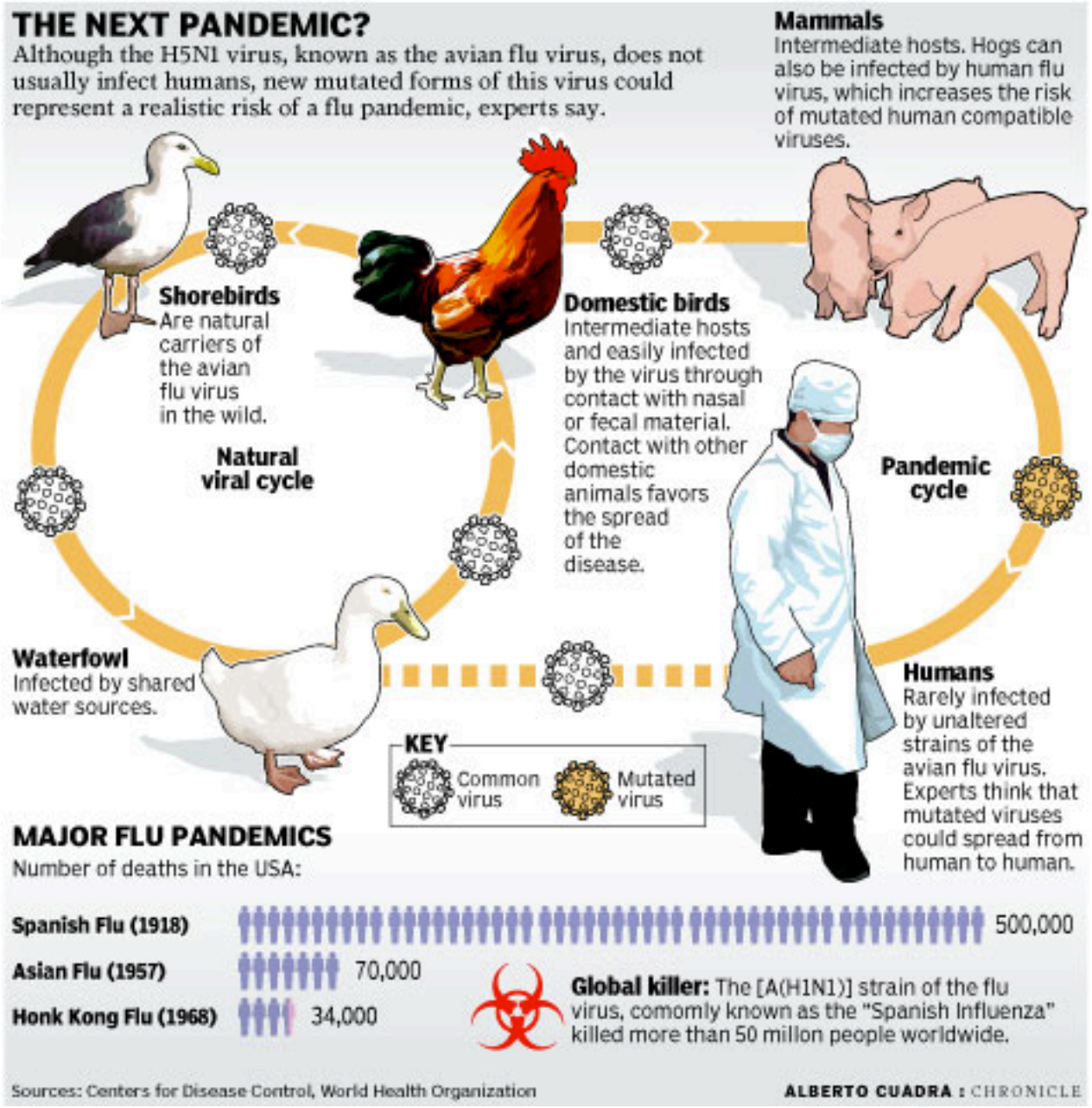
HIV

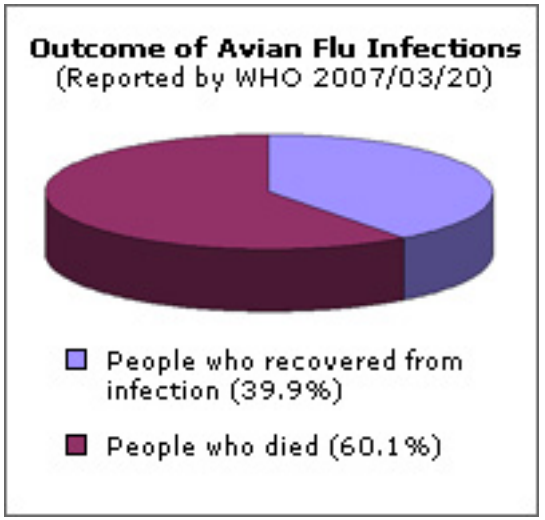

Gorilla gorilla gorilla
Pan troglodytes troglodytes
P.t.verus
P.t.ellioti
P.t.troglodytes
P.t.schweinfurthii
DRC
Tanzania
Uganda
HIV-1 O
HIV-1 P
HIV-1 M
HIV-1 N
SIVgorGgg
SIVcpzPts
SIVcpzPtt
0.2 substitutions per site

Ebolavirus


Ebolavirus transmission dynamics
viruses
Spillover dynamics
Intra- and inter-species transmission
Reservoir dynamics
Olival and Hayman. Viruses 2014;6(4):1759-1788

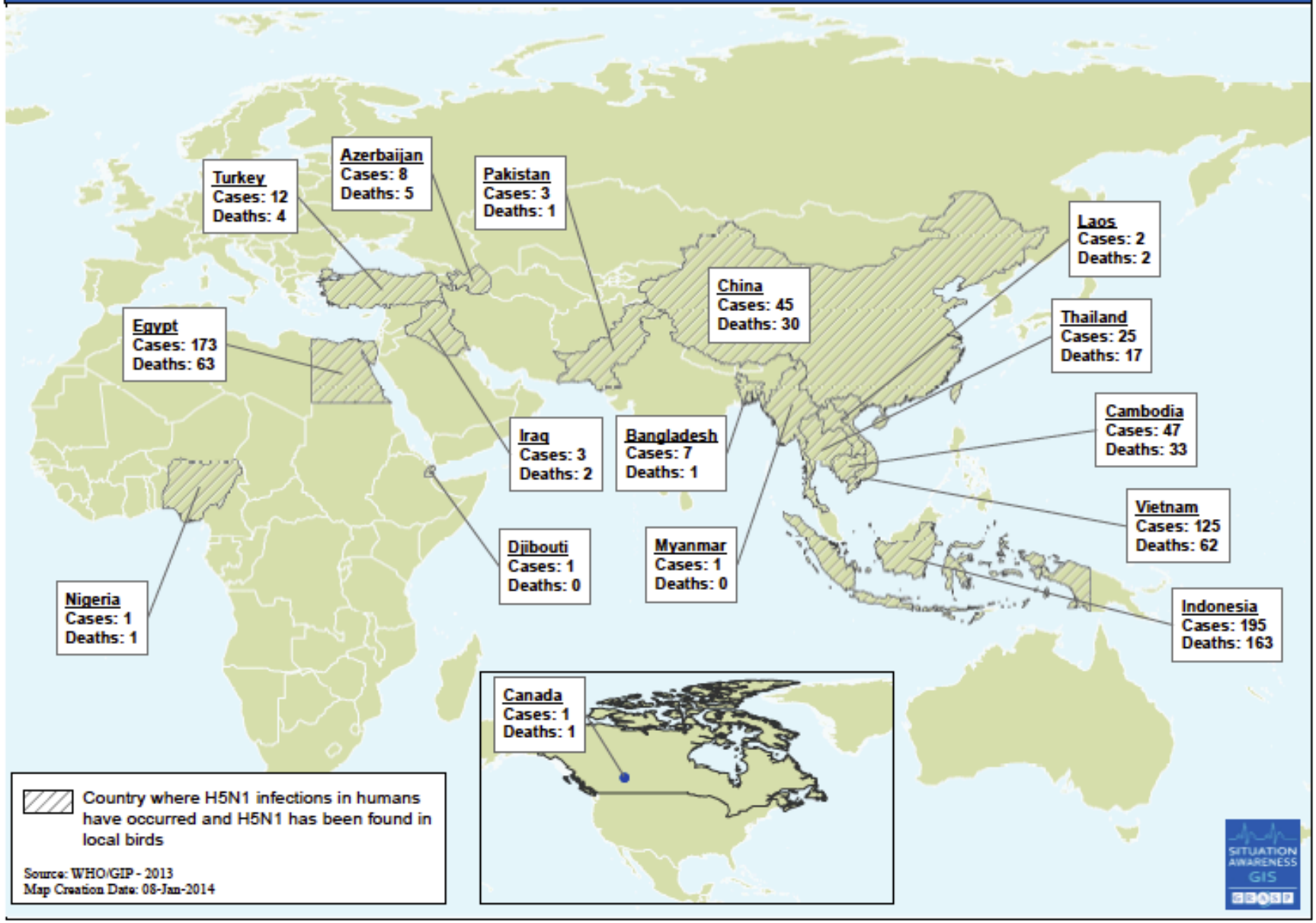
Avian Flu


THE NEXT PANDEMIC?
Although the H5N1 virus, known as the avian flu virus, does not usually infect humans, new mutated forms of this virus could represent a realistic risk of a flu pandemic, experts say.
Mammals
Intermediate hosts. Hogs can also be infected by human flu virus, which increases the risk of mutated human compatible viruses.
Shorebirds
Are natural carriers of the avian flu virus in the wild.
Natural viral cycle
Domestic birds
Intermediate hosts and easily infected by the virus through contact with nasal or fecal material. Contact with other domestic animals favors the spread of the disease.
Pandemic cycle
Waterfowl
Infected by shared water sources.
Humans
Rarely infected by unaltered strains of the avian flu virus. Experts think that mutated viruses could spread from human to human.
KEY
Common virus
Mutated virus
MAJOR FLU PANDEMICS
Number of deaths in the USA:
Spanish Flu (1918)
500,000
Asian Flu (1957)
70,000
Honk Kong Flu (1968)
34,000
Global killer: The [A(H1N1)] strain of the flu virus, comonly known as the "Spanish Influenza" killed more than 50 millon people worldwide.
Sources: Centers for Disease Control, World Health Organization
ALBERTO CUADRA : CHRONICLE


Outcome of Avian Flu Infections
(Reported by WHO 2007/03/20)
People who recovered from infection (39.9%)
People who died (60.1%)

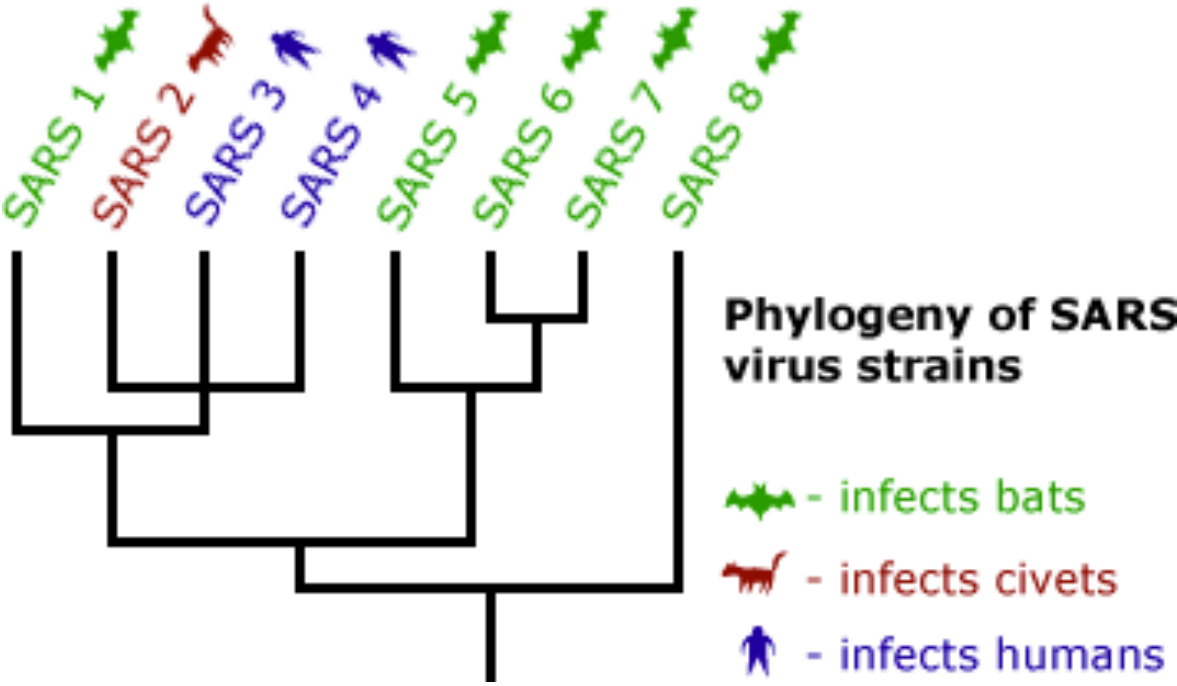
Highly Pathogenic Avian Influenza (H5N1) Human Cases and Deaths Since 2003

Status as of January 8, 2014
Latest available update

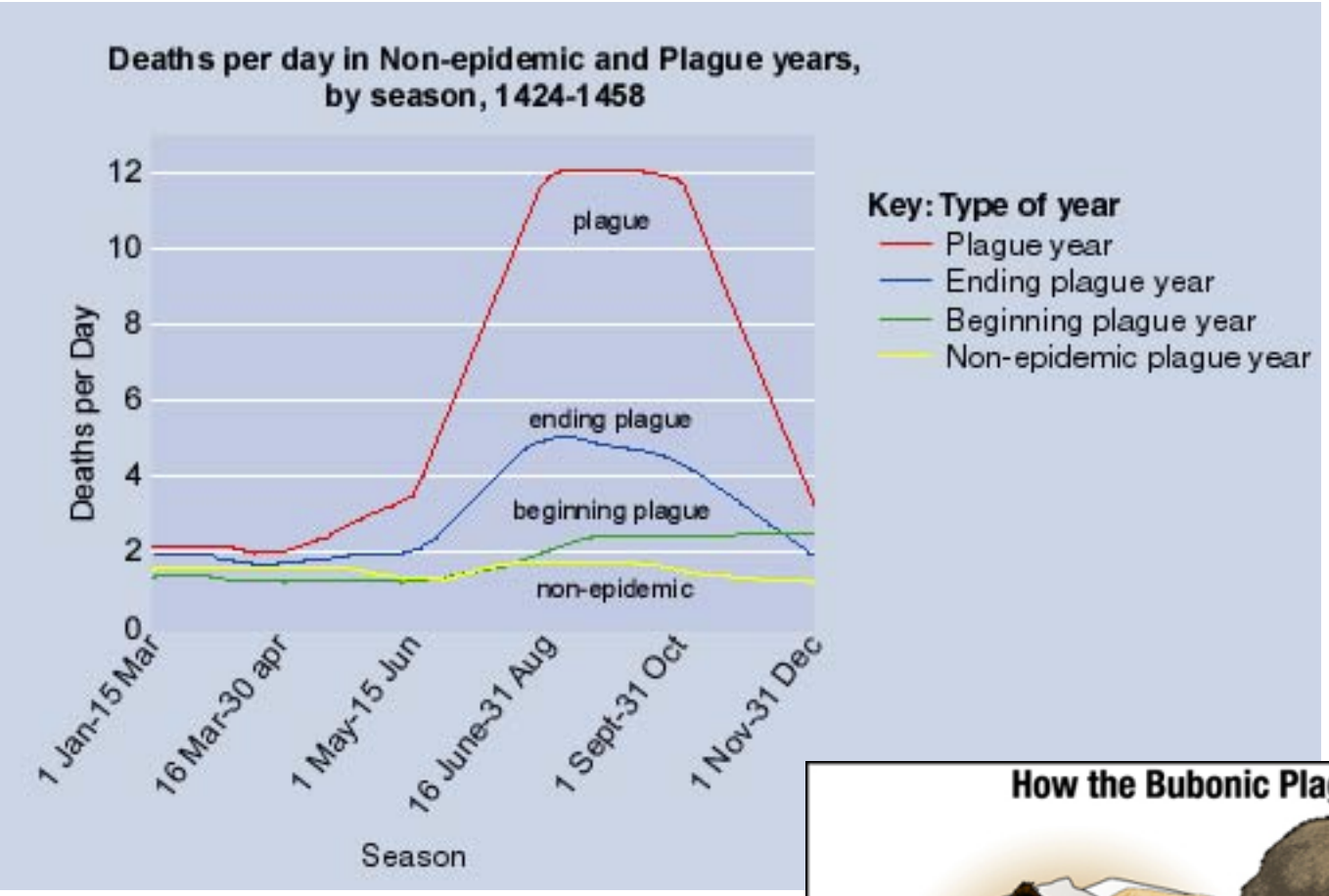


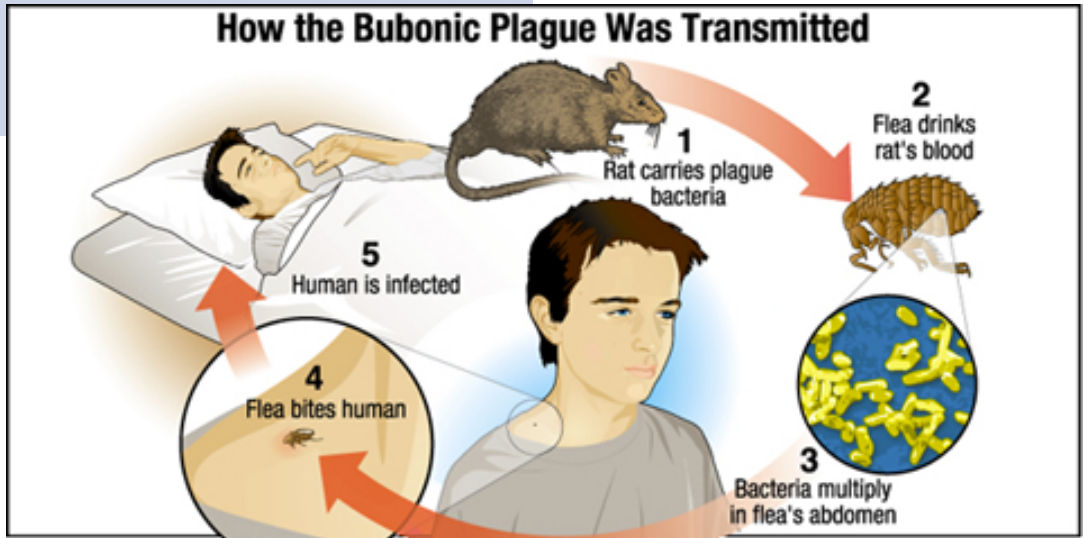
SARS – Severe Acute Respiratory Syndrome

????



Bubonic Plague





Thought Question

- What are some other zoonotic diseases and what are their hosts?

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Study Guide Questions

- Be able to describe in details the epidemiological triangle and the categories that contribute to host, agent and environmental factors using examples.
- How have disease changed as human populations have evolved?
- What contributed to the eradication of potentially life threatening diseases?
- What is a zoonotic infection? Be able to describe the zoonotic infections we discussed in class and their hosts.