EMERGING VIRAL INFECTIONS

Dr.H.T.Wickramasinghe

What is an Emerging infection?

Emerging infectious disease: An infectious disease that has newly appeared in a population or that has been known for some time but is rapidly increasing in incidence or geographic range.

Sir Peter Medawar (1915–1987) described a virus as "a piece of bad news wrapped in a protein coat"

1960 Nobel prize winner
for Physiology/ Medicine

US Surgeon General William H. Stewart remarked in 1967 “It’s time to close the book on infectious diseases and pay more attention to chronic ailments such as cancer and heart disease…the war against infectious diseases has been won.”

“The most likely forecast about the future of infectious disease is that it will be very dull. There may be some wholly unexpected emergence of a new and dangerous infectious disease, but nothing of the sort that has marked the past fifty years,”

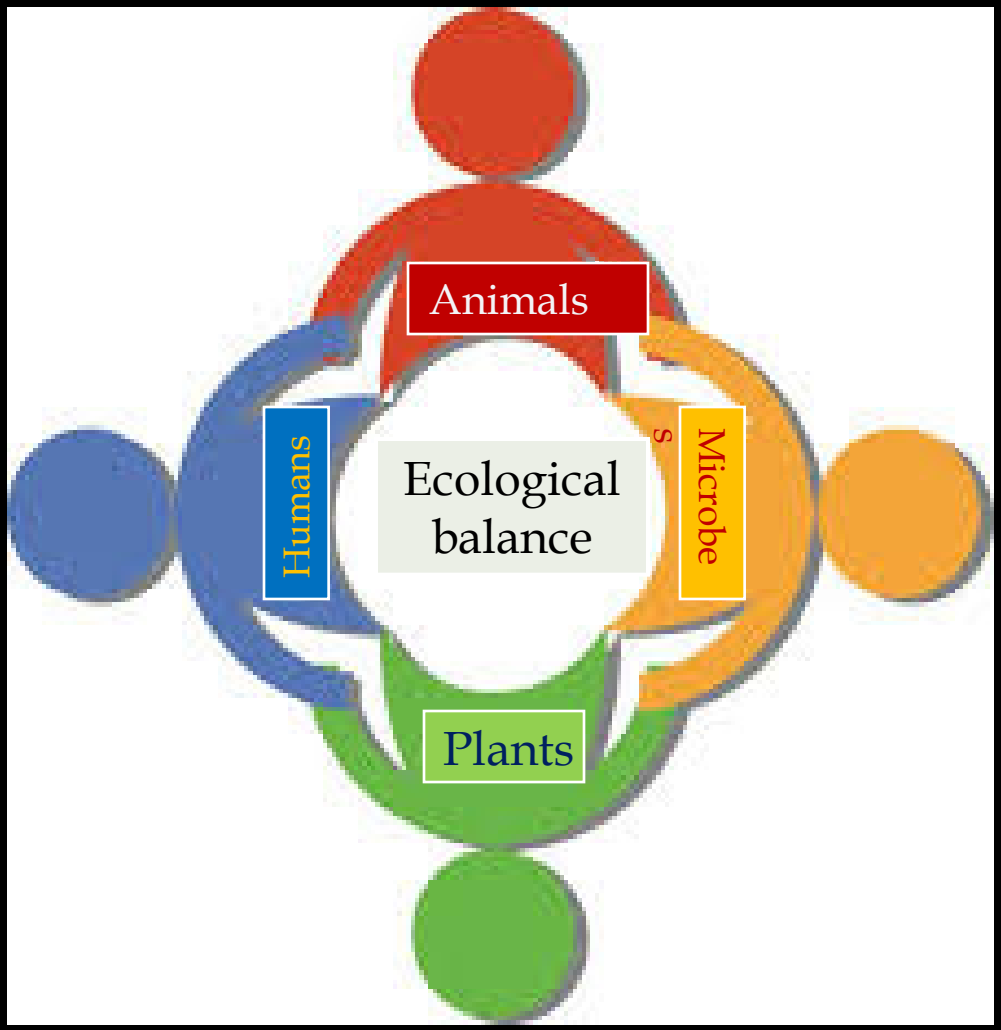
Australian virologist and Nobel Prize winner Macfarlane Burnet in 1970

Unfortunately history has proved them both wrong. Since those bold claims were made more than twenty novel diseases, including the worst pandemic humans have ever faced, AIDS, have emerged onto the world stage .

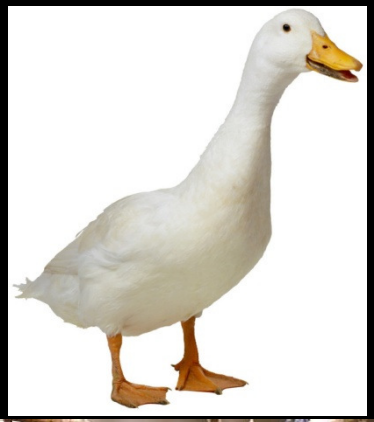
Globally, infectious diseases now account for over 25% of the fifty-seven million annual deaths worldwide.

But what are the origins of these new threats, and what provokes their appearance in the first place?

An axiomatic starting point for discussion of this topic is the simple recognition that microbes, plants, animals and humans are cohabitants of the planet.



Stable co-habitation and host-Virus partnership



All most all viruses causing human infections were originally living in harmony with their natural hosts , causing no harm to them.

- Small pox – rodent virus between 68,000 and 16,000 years ago[1]
- Measles- wild buffalos, antelopes etc 11000 Yrs ago[2]
- Influenza- aquatic birds around 10,000 Yrs ago[3]

"No virus is evolutionary successful in their continuance of existence, if they harm their host"

1.Esposito JJ, Sammons SA, Frace AM, *et al.* (August 2006). "Genome sequence diversity and clues to the evolution of variola (smallpox) virus". *Science* **313** (5788): 807–12.doi:10.1126/science.1125134. PMID 16873609.

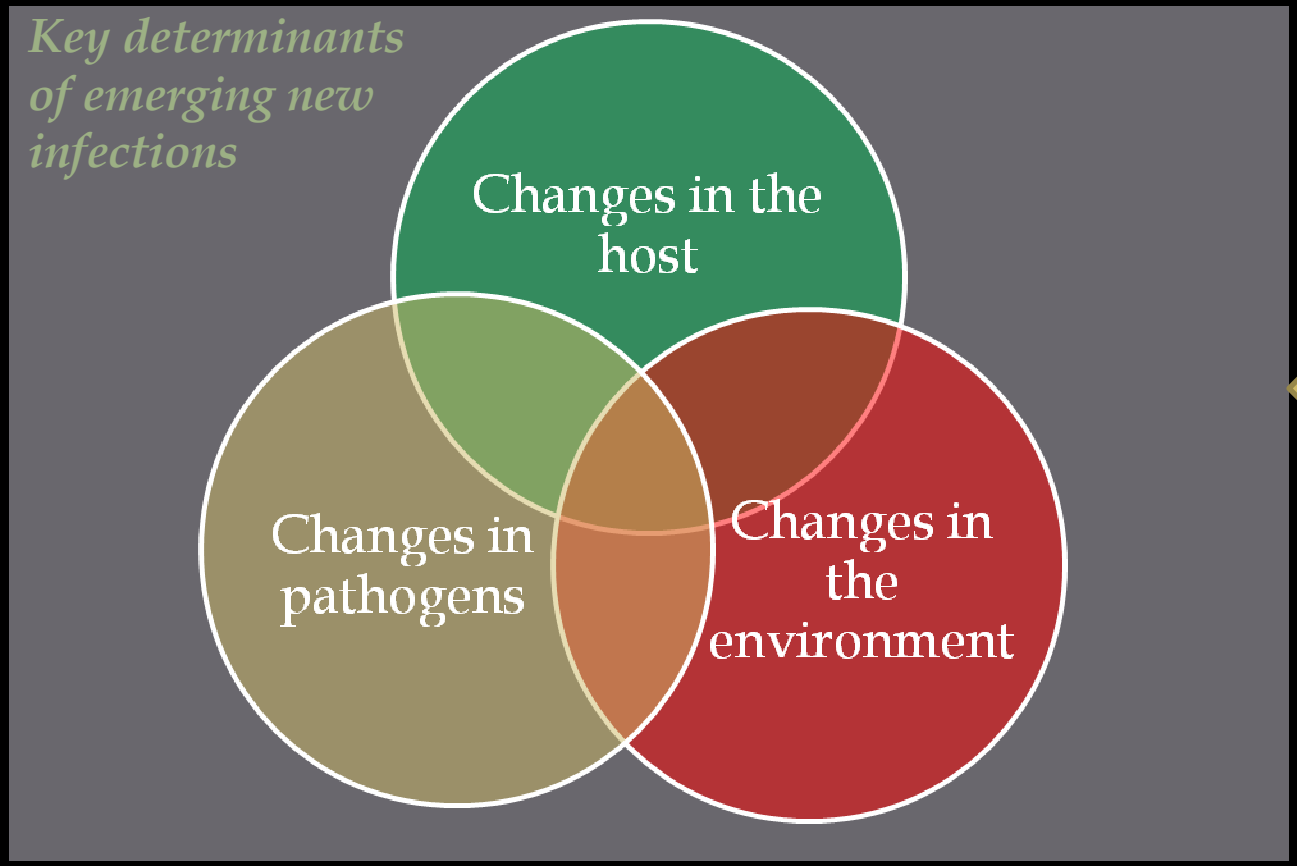
2. Furuse Y, Suzuki A, Oshitani H (2010).origin of measles virus: divergence from rinderpest virus between 11th and 12th centuries. *Virol. J.* **7**: 52. doi:10.1186/1743-422X-7-52. PMC 2838858. PMID 20202190.

3. Pearce-Duvet JMC 2006. Biol. Rev. 81: 369-382

Causes for instabilities within the context of stable cohabitation

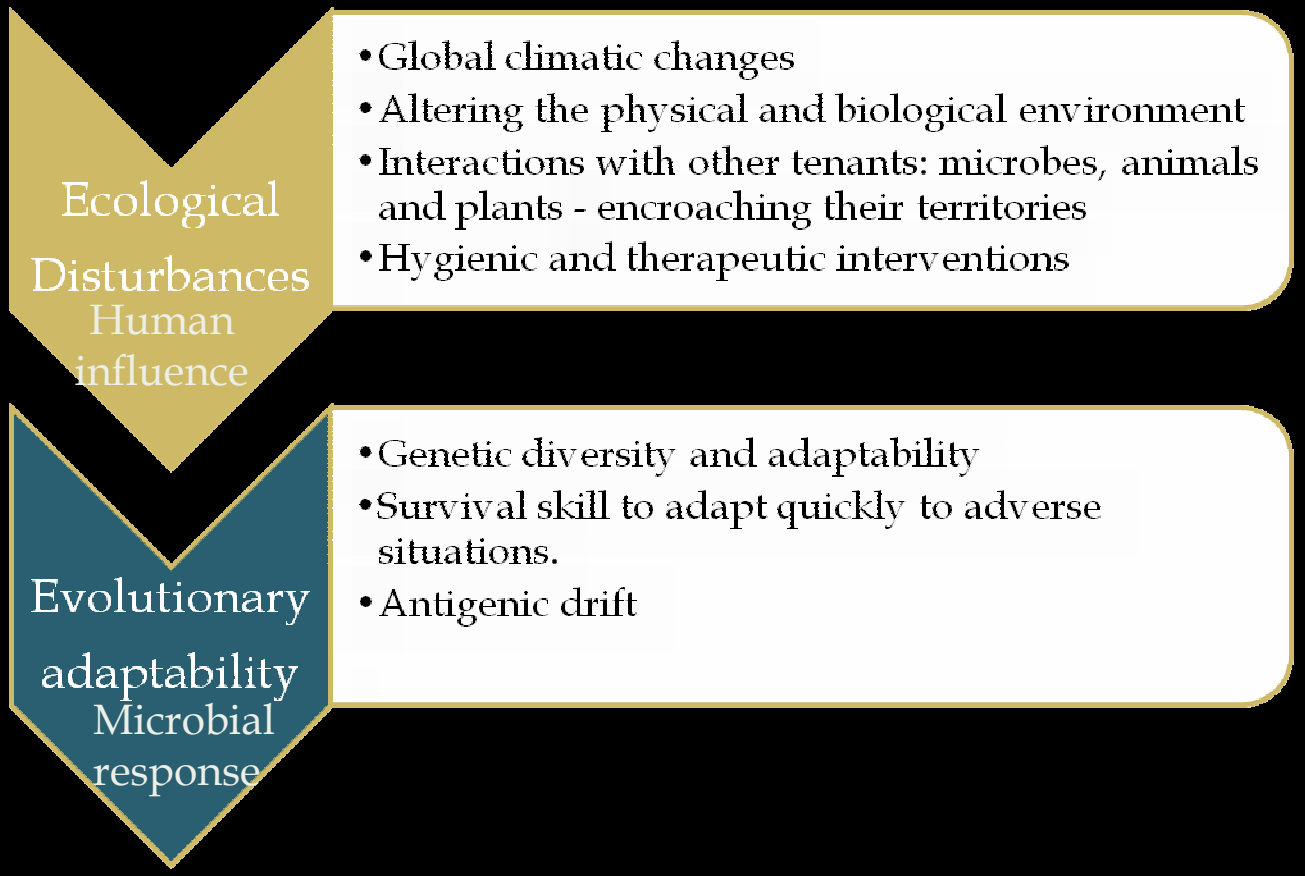
- Ecological and biological disturbances
- Evolutionary response

Ecological and biological disturbances caused by Humans and by nature

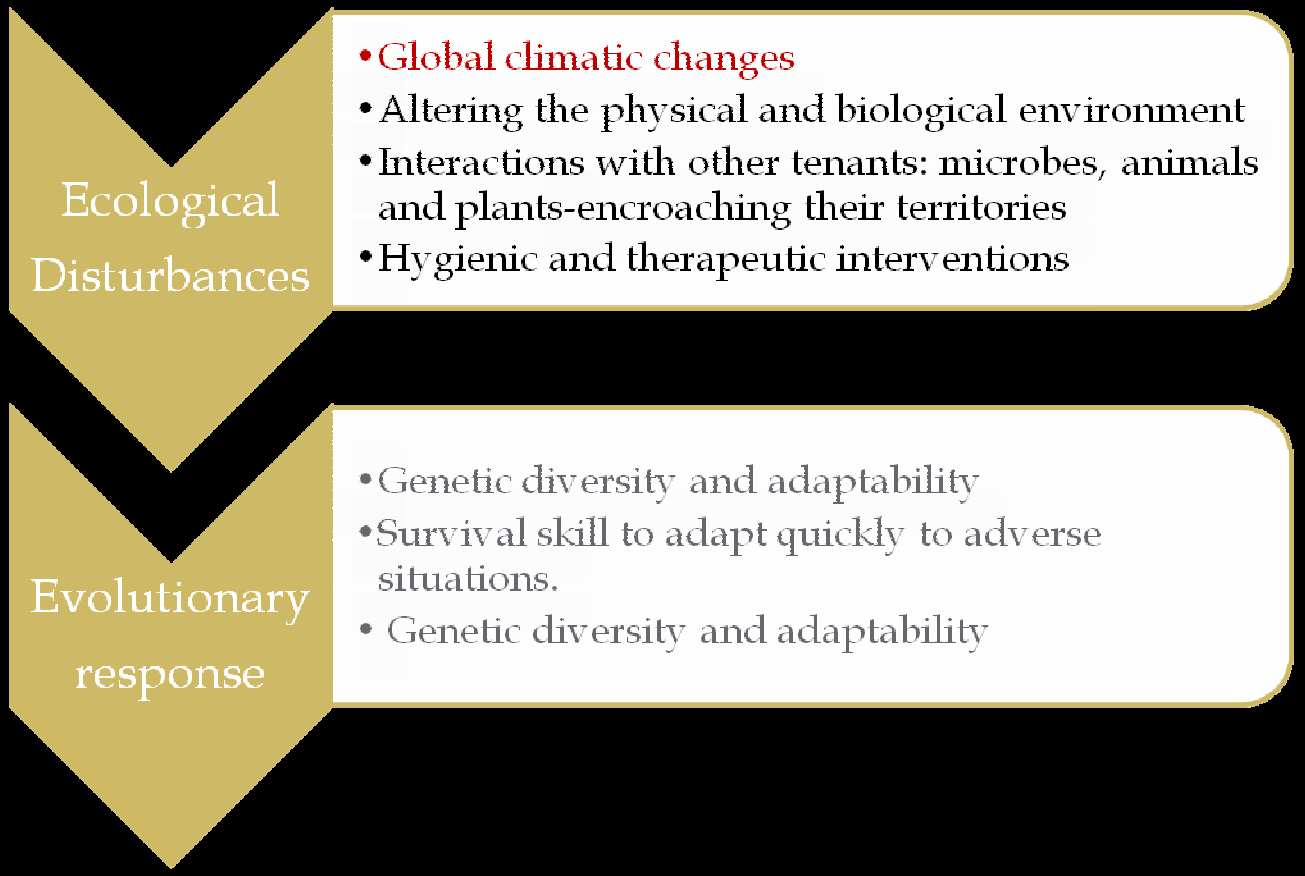


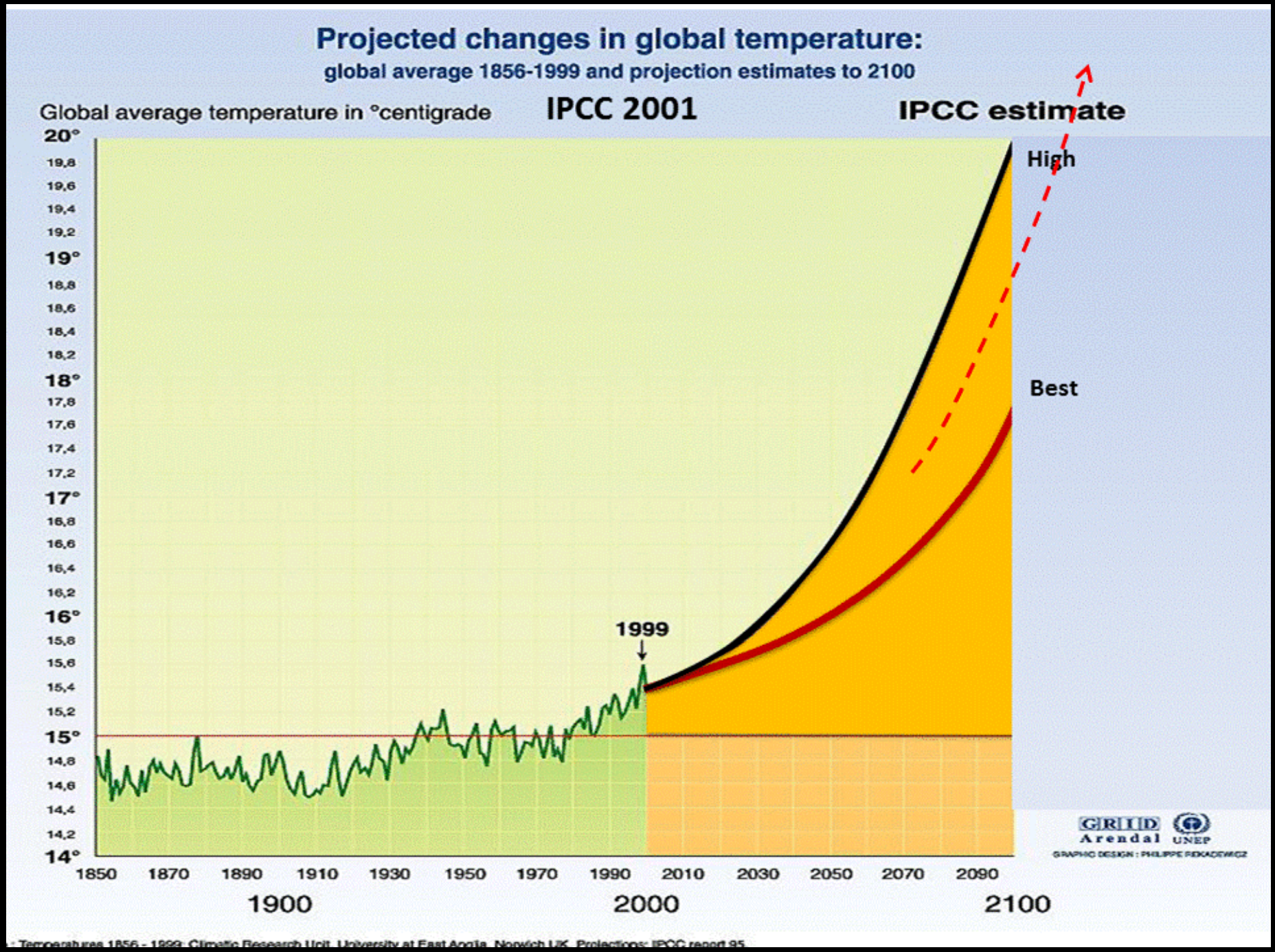
Evolutionary adaptations of the microbes

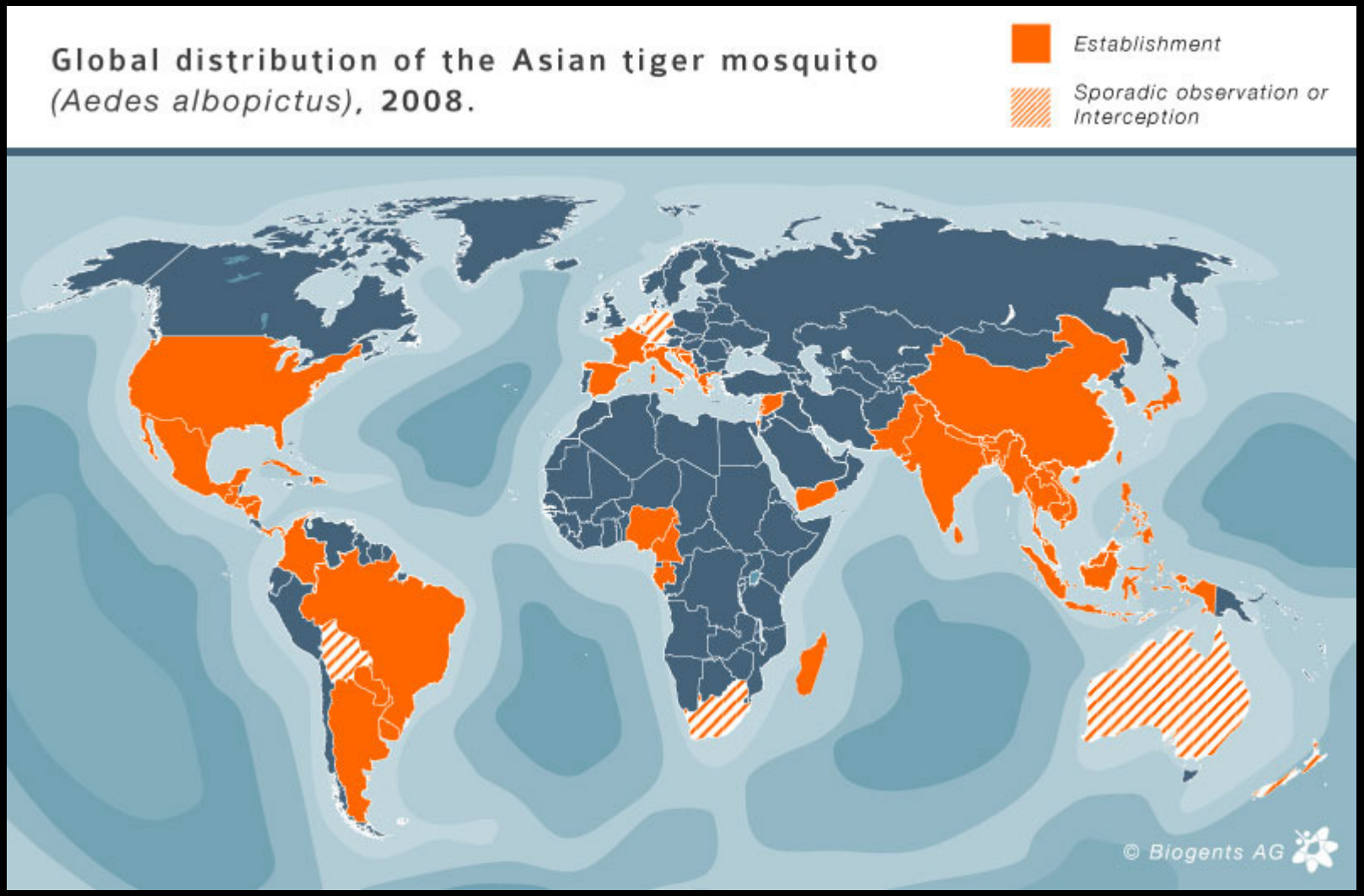
Causes for instabilities within the context of stable cohabitation

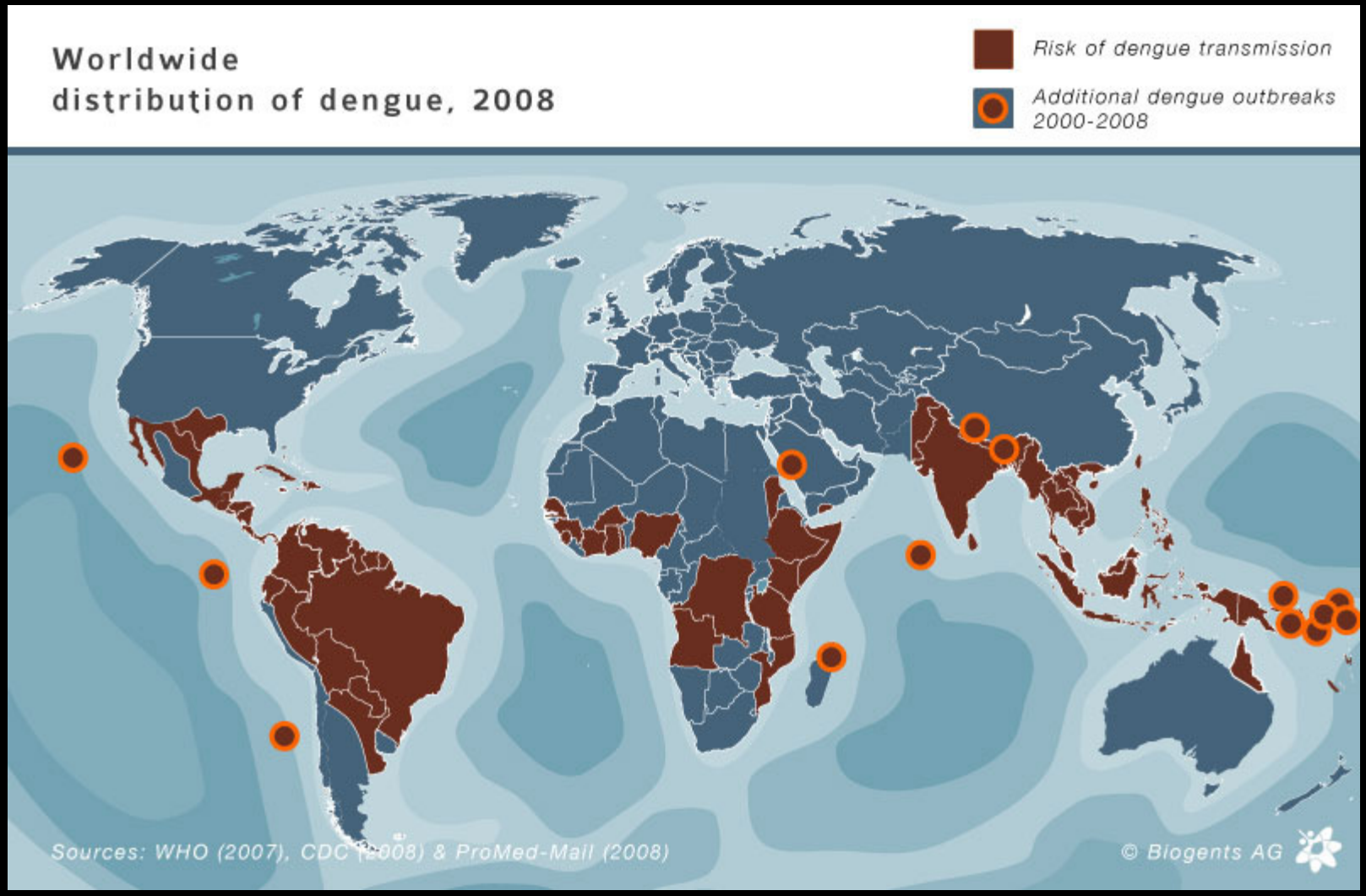


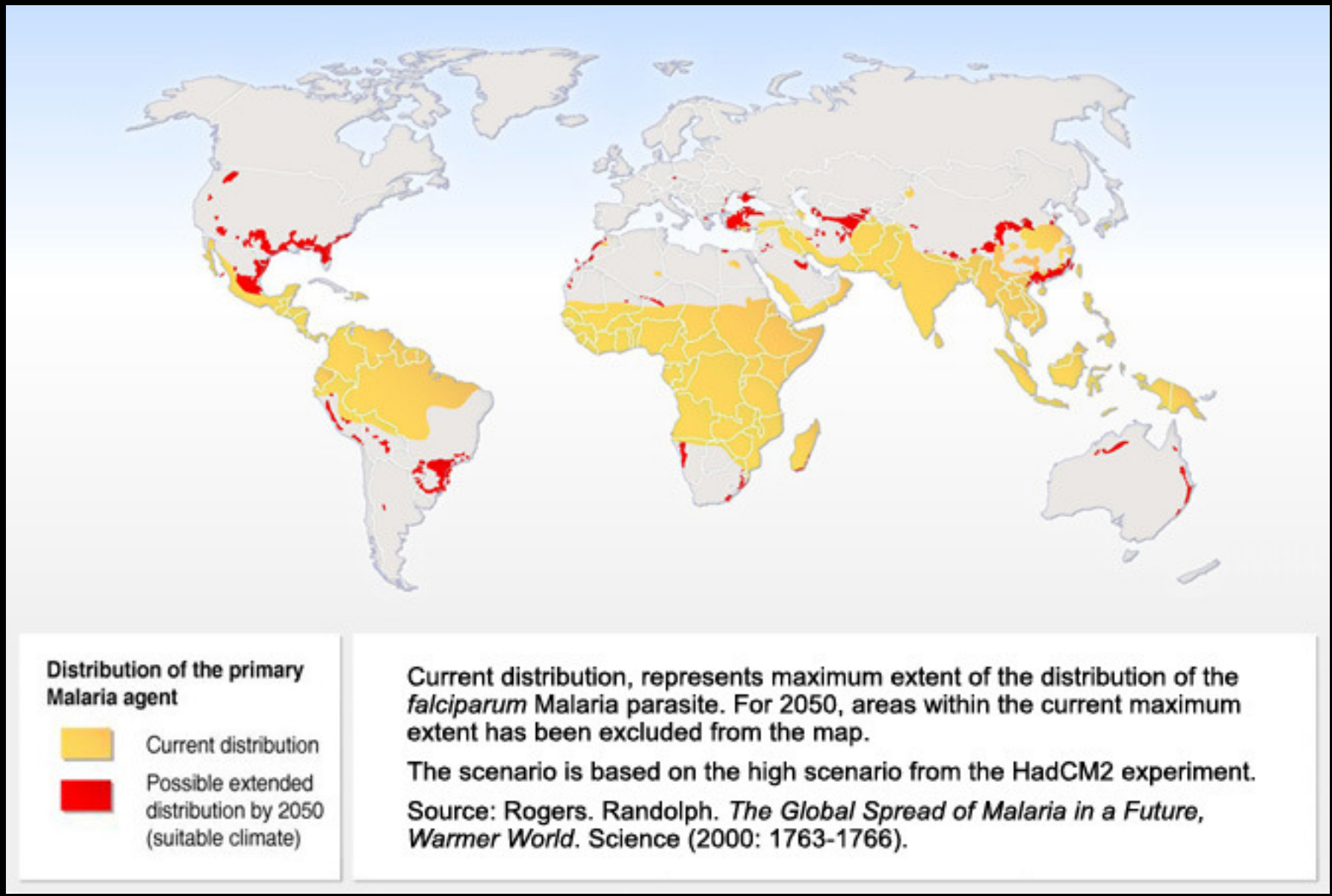
Causes for instabilities within the context of stable cohabitation

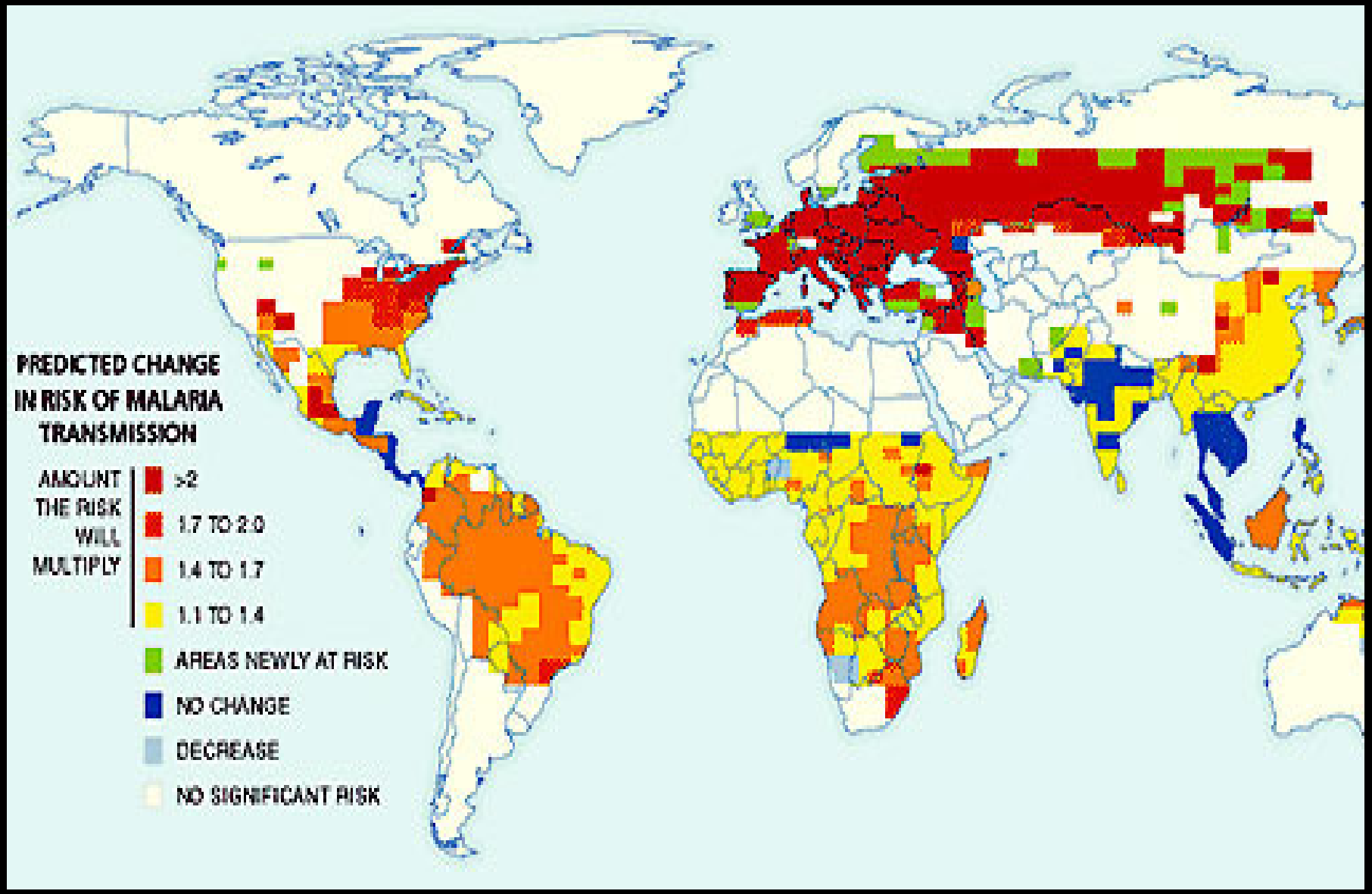



Projected changes in global temperature:
global average 1856-1999 and projection estimates to 2100
Global average temperature in °centigrade
IPCC 2001
IPCC estimate
High
Best
1999
20°
19,8
19,6
19,4
19,2
19°
18,8
18,6
18,4
18,2
18°
17,8
17,6
17,4
17,2
17°
16,8
16,6
16,4
16,2
16°
15,8
15,6
15,4
15,2
15°
14,8
14,6
14,4
14,2
14°
1850
1870
1890
1910
1930
1950
1970
1990
2010
2030
2050
2070
2090
1900
2000
2100
GRID Arendal
UNEP

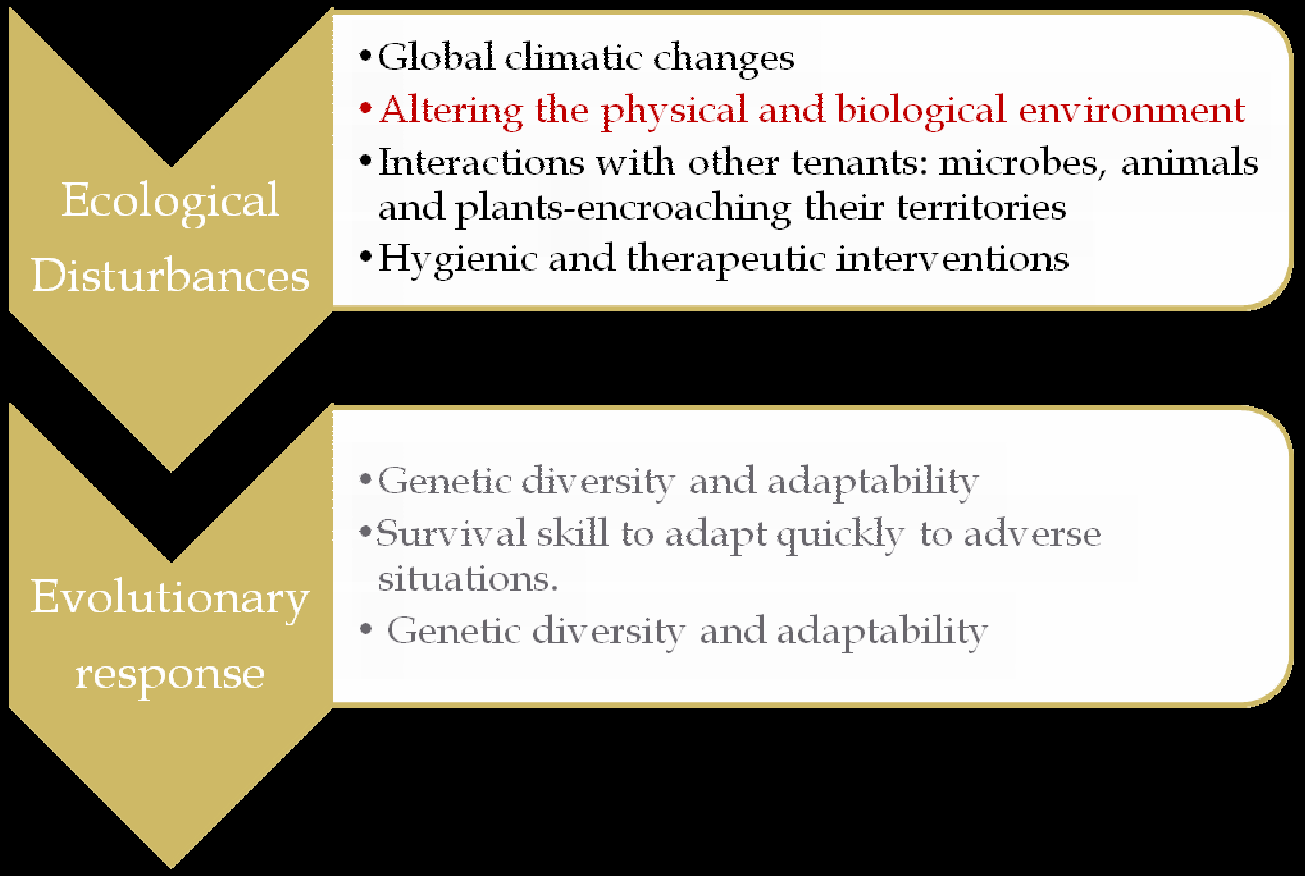

Global distribution of the Asian tiger mosquito
(Aedes albopictus), 2008.
Establishment
Sporadic observation or Interception
© Biogents AG


Worldwide
distribution of dengue, 2008
Risk of dengue transmission
Additional dengue outbreaks
2000-2008
Sources: WHO (2007), CDC (2008) & ProMed-Mail (2008)
© Biogents AG


Distribution of the primary Malaria agent
Current distribution
Possible extended distribution by 2050 (suitable climate)
Current distribution, represents maximum extent of the distribution of the *falciparum* Malaria parasite. For 2050, areas within the current maximum extent has been excluded from the map.
The scenario is based on the high scenario from the HadCM2 experiment.
Source: Rogers. Randolph. *The Global Spread of Malaria in a Future, Warmer World*. Science (2000: 1763-1766).


PREDICTED CHANGE IN RISK OF MALARIA TRANSMISSION
AMOUNT THE RISK WILL MULTIPLY
>2
1.7 TO 2.0
1.4 TO 1.7
1.1 TO 1.4
AREAS NEWLY AT RISK
NO CHANGE
DECREASE
NO SIGNIFICANT RISK

Causes for instabilities within the context of stable cohabitation



Hunting
to farming

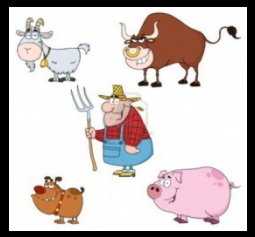
To Modern
man

Ruler of the world

Population explosion

colonization

Domestication
of animals



Mega
cities

deforestation

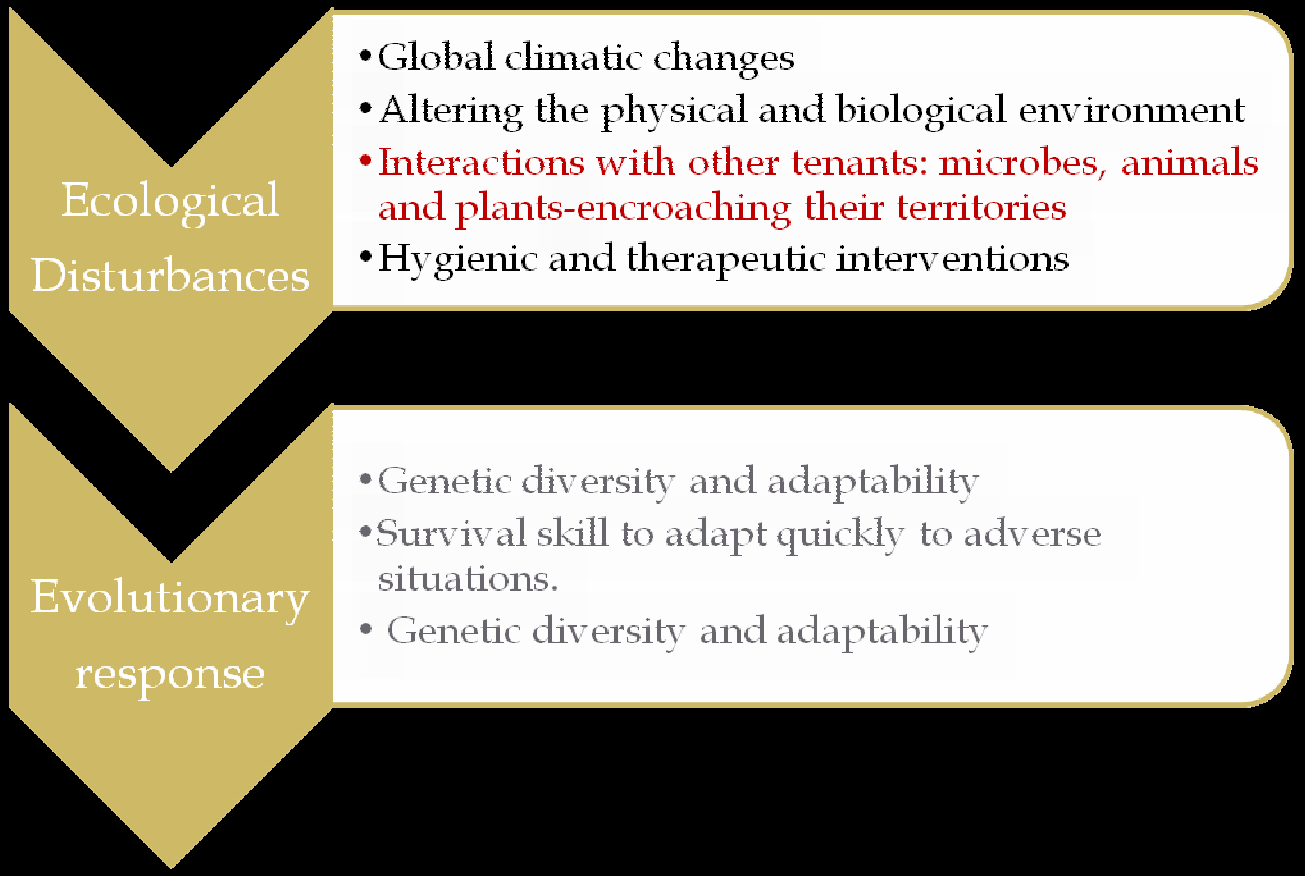
urbanization

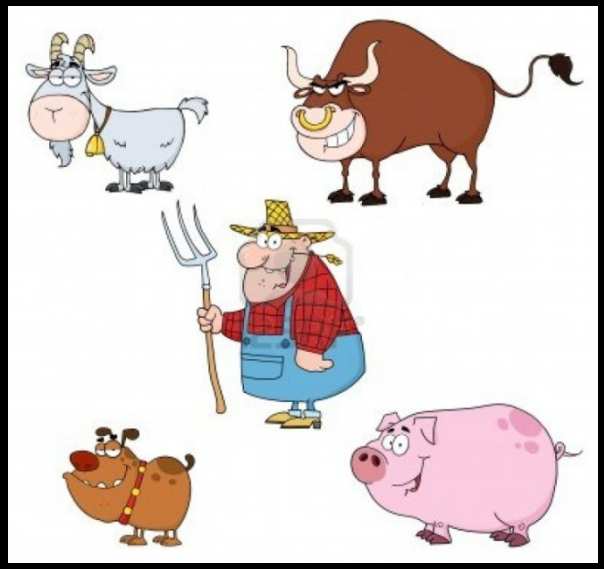
Pollution

Earth our home too…

Leave us a space to breath…

Causes for instabilities within the context of stable cohabitation

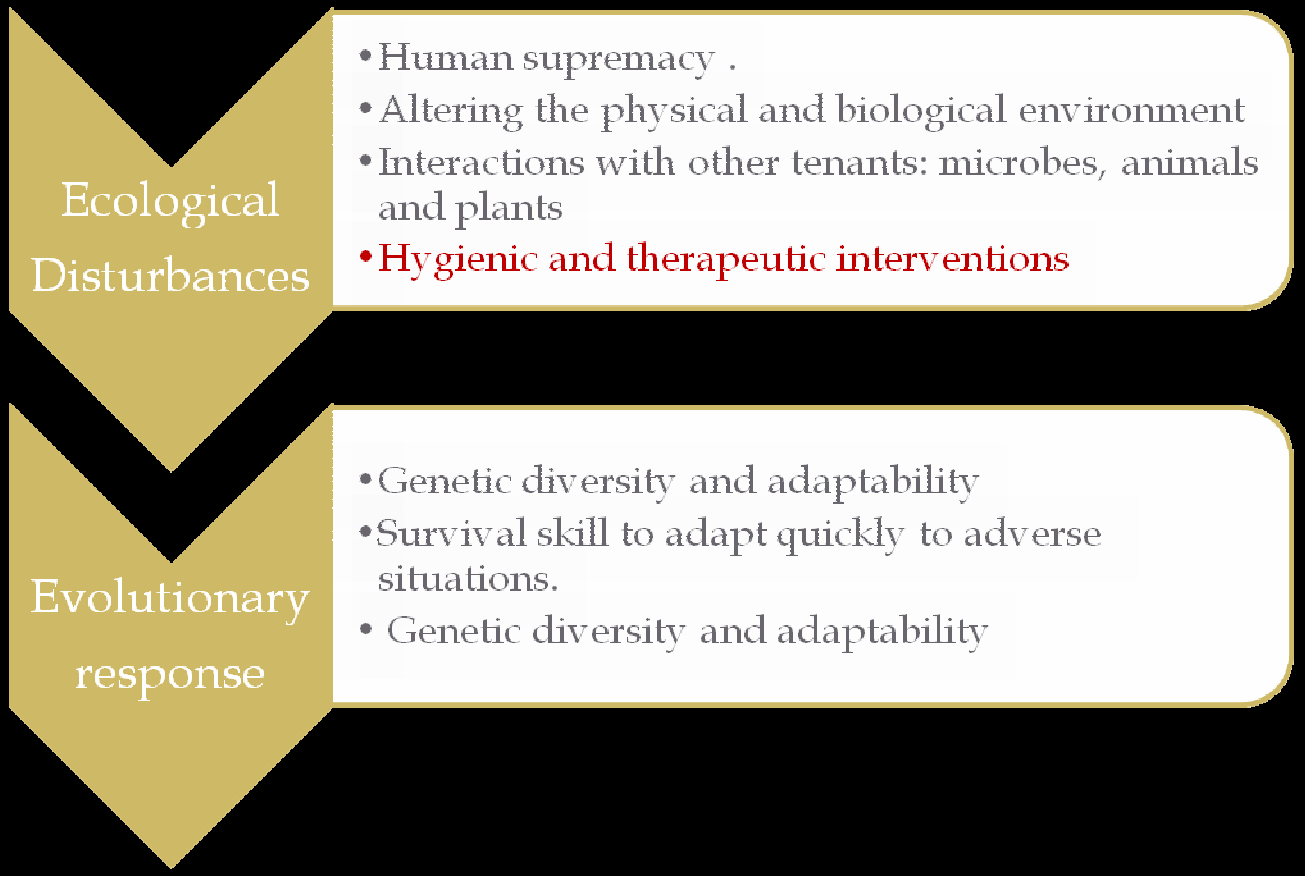




Deforestration and urbanization brings man and his domestic animals in close contact with wild animals

International wild animal trading

Causes for instabilities within the context of stable cohabitation



Hygienic and therapeutic interventions

Population explosion:

The average life expectancy has gone up from 35 years to 75.

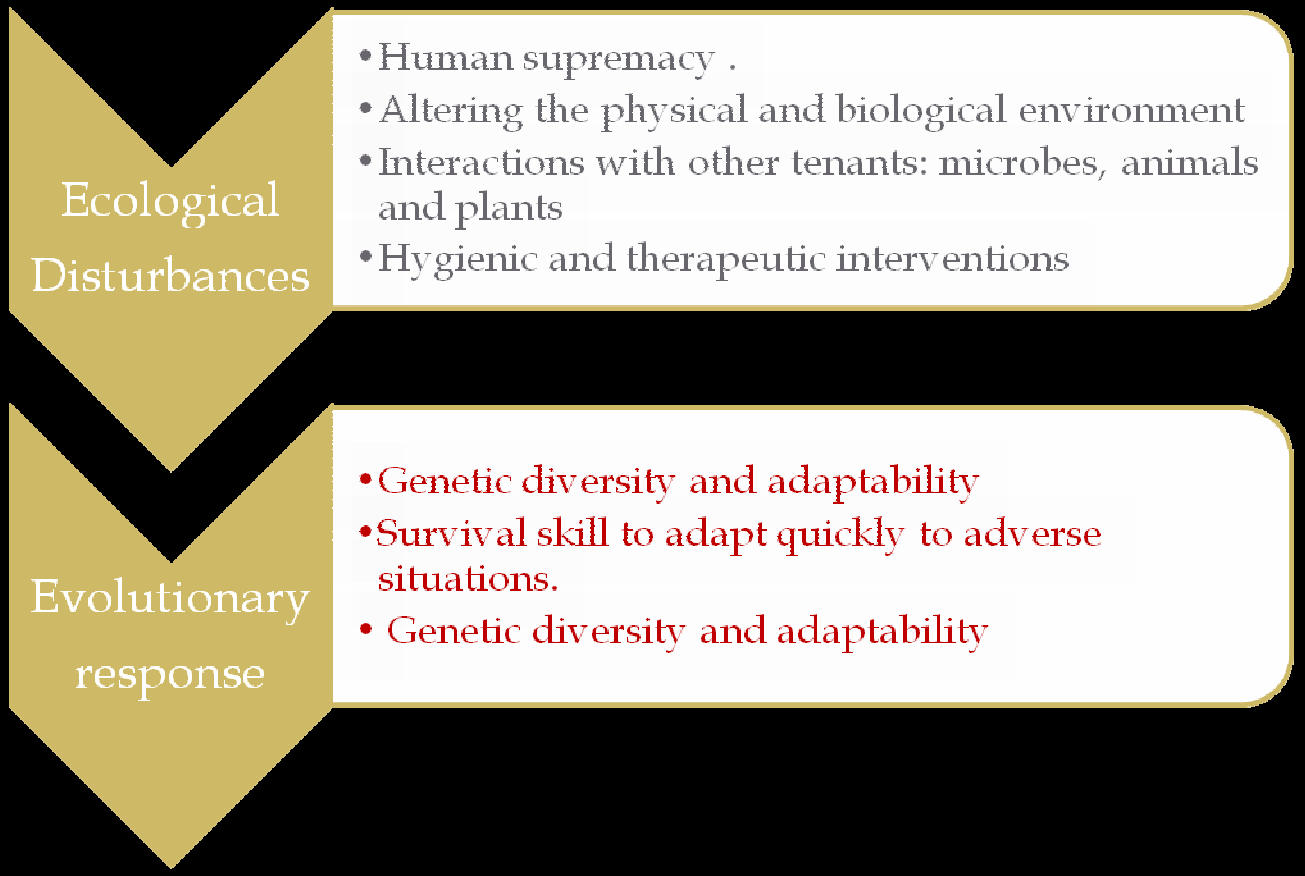
Doubling population in every 70 years. A global population explosion from about 1.6 billion in 1900 to its present level above 6 billion

Modern drugs and blood products

Needle sharing amongst drug users which can transmit HIV and HCV (hepatitis C

Organ transplantation and devices

Causes for instabilities within the context of stable cohabitation



Our Wits Versus Their Genes.

Human evolution is slow and plodding in contrast to rapid and dynamic genetic changes in microbes

We have inherited a robust immune system providing life long immunity to invaders, but successful immunological encounters do not become genetically inscribed and passed on to future generations of the host.

By contrast, the microbes quickly proliferate their successful genes, and transfer them to their offspring and they can use those enhancements to go on to new hosts, at least in the short run.

Why are microbes almost immortal?

Struggle for Life most severe between Individuals and Varieties of the same Species

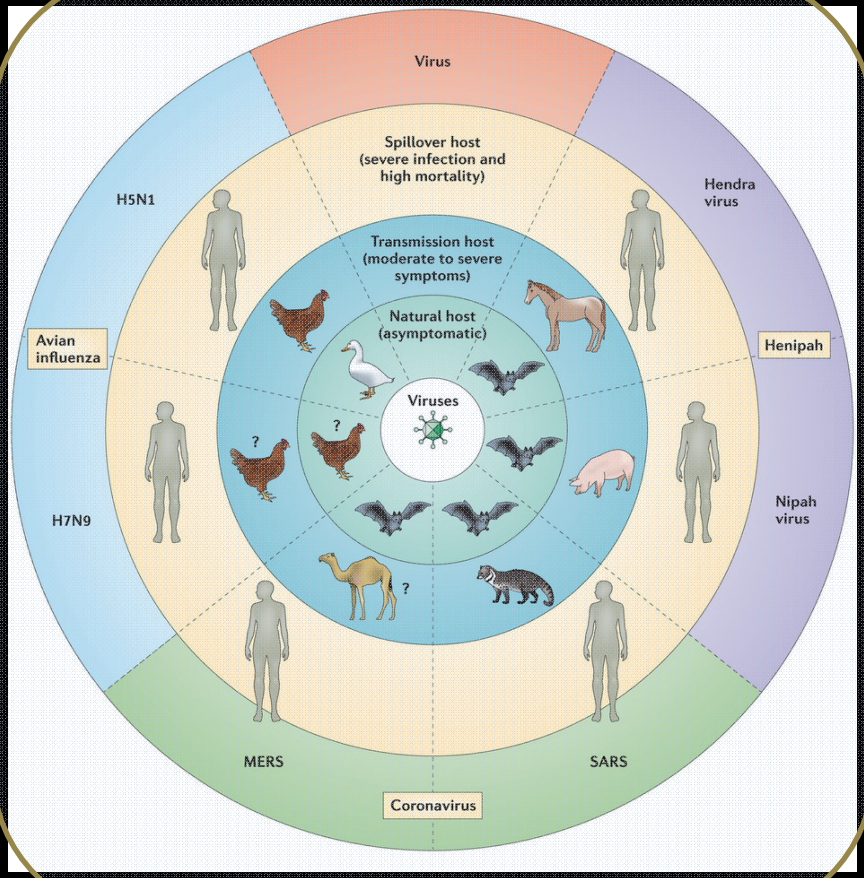
As the species of the same genus usually have, though by no means invariably, much similarity in habits and constitution, and always in structure, the struggle will generally be more severe between them, if they come into competition with each other, than between the species of distinct genera.

"From Darwin's On the Origin of Species.

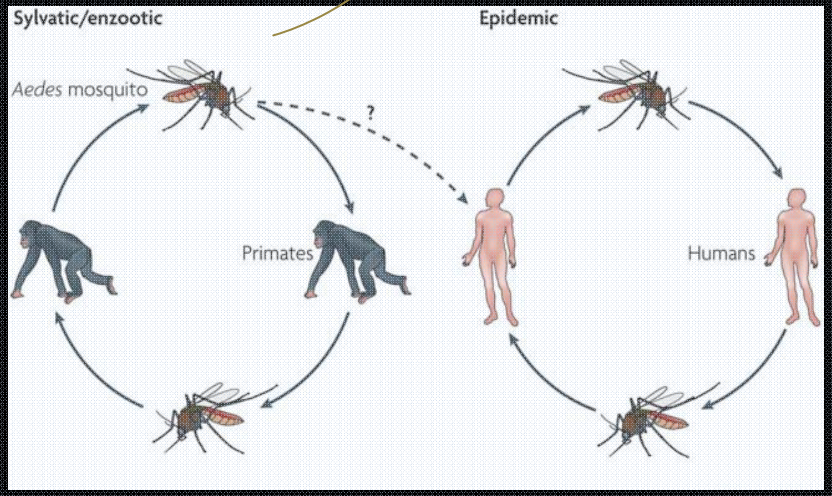
Why microbes are better than us in terms of survival?

Microbes	Animals and Humans
They try to share their survival kits with others	Compete with each other and keep their survival kits to themselves
Species survival	Individual survival
Overcome adverse periods by becoming dormant	overcome any shortage by fighting each other

Mode of transmission from wild animals to humans



Direct



Through Vectors

Bringing zoonoses to your doorstep…..

Why zoonoses so important?

Infectious Diseases where humans are the only host, complete eradication is possible. Eg. Small pox, Measles, Polio, whereas in emerging new zoonoses, as long as the natural host is living in the jungle, eradication is impossible.

It is predicted that the next global pandemic would be a Zoonotic disease probably from bats..

Major determinants of emerging diseases

Human activities

- Population explosion
- Human movement and international travel
- Urbanization
- Deforestation and land use
- Wild animal trading
- Poverty and social inequality
- War and Civil unrest
- Advance medical interventions, transplants and syringe use

Environmental factors

- Climate and weather changes E.g. El nino effect
- Changing ecosystems
- Man made environmental changes Eg. Pollution and ozone depletion

Changes in Viral behaviour

- Genetic recombinations and reassortments and changes in virulence
- Host shift and vector shift
- Adapting to new ecological nitches

What makes them spread across the globe?

Air travel

International animal trade

Human Mobility and global travel

At any given time there are more than half a million people airborne around the planet.

Select Committee on Science and Technology 2000. Fifth report to the UK Parliament

This level of population flux means that the geographical barriers faced by infectious diseases in the past have largely been removed. Journeys can be made so quickly that individuals can arrive at a destination well within the incubation period of an infectious disease thereby making outbreaks much more difficult to contain.

US Census Bureau, International Database (IDB)

NIPAH Virus

Hendra-related paramyxovirus called Nipah

The impact of human environmental modification and encroachment and its ability to facilitate the transmission of infectious agents to novel hosts: Nipah Virus

Sep 1998, a mystery illness appeared in Nothern Malaysia

In June 1999, 211 cases from Malaysia and 11 cases from Singapore with same symptoms were reported

?

C.N.S.Symptoms

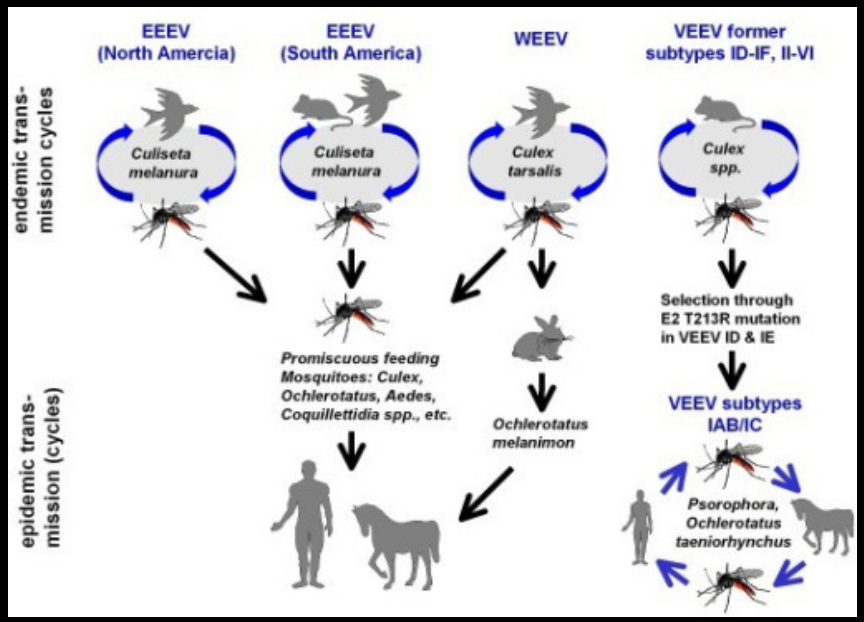
Respiratory symptoms

Japanese B Encephalitis

- Construction of large numbers of piggeries in virgin Malaysian rainforest.
- Orchards planted nearby attract fruit bats.
- Contamination of the pig-pens with bat excreta and partially-eaten pieces of fruit (potentially also containing bat saliva).
- Mild illness in pigs : longer duration of infectivity

Viruses are smarter than us…

- Equine encephalitis



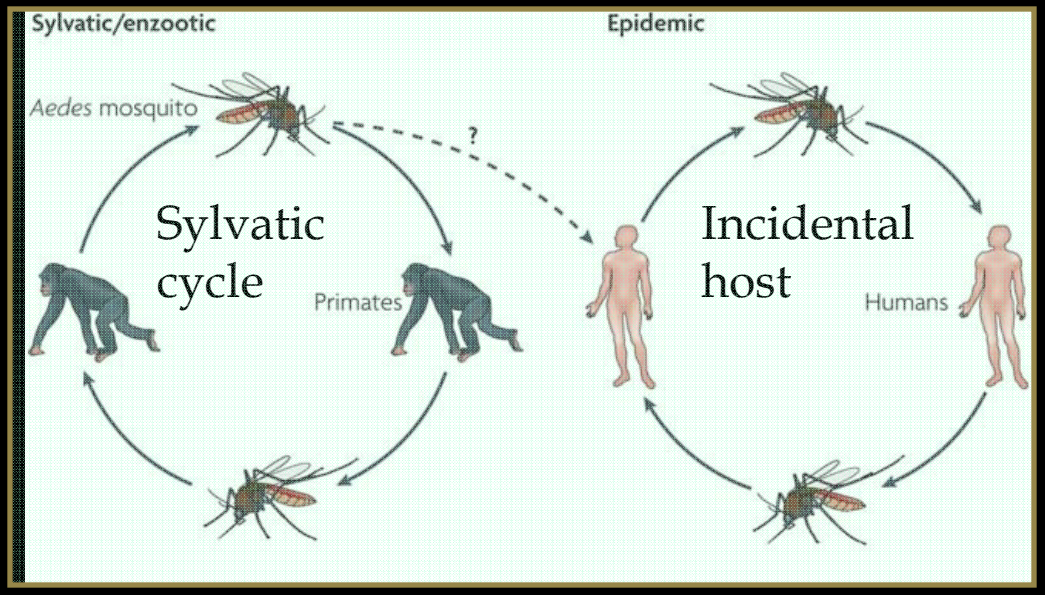
The natural hosts of VEE are small rodents, and the virus is transmitted by Culex taeniopus mosquitoes. Occasionally, highly viraemic strains of the virus emerge which enable it to be transmitted by other mosquito species, which can carry the virus between larger animals such as horses and humans. This is what triggers an outbreak

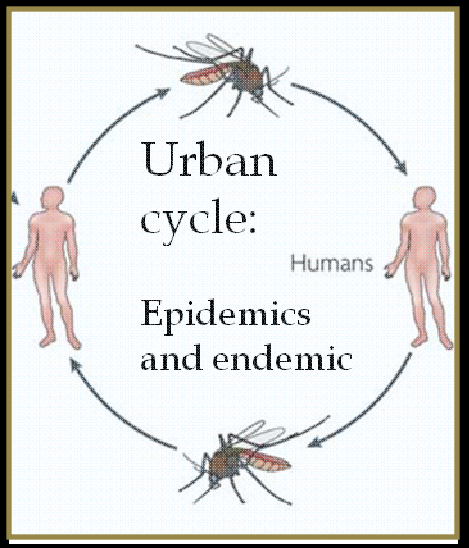
But the maxican outbreaks in 1993 and 1996 showed normal rodent strains which are not highly viraemic. A mutation in the viral E2 envelope glycoprotein which has allowed the agent to switch to a novel mosquito vector

How the population growth

Before emerging in humans dengue existed in a sylvatic cycle as an infection of non-human primates transmitted by Aedes stegomia mosquitoes. Humans were only incidental hosts infected when venturing through dengue-infected areas.

At the same time urbanisation attracted novel mosquito species including the anthropophilic vector Aedes aegypti





climate changes and emerging diseases.

Ebola virus is named after the Ebola River 1st epidemic occurred in 1976. second outbreak occurred in the Sudan at the same time.

Caused by two distinct species of the virus.

There have been about 25 outbreaks in central Africa since.

These have occurred on an annual or biannual basis since 1994. Some years, like 2012, have seen multiple outbreaks.

Ebola epidemics appear to peak at times of severe drought.

Before human out break, there is wild animal outbreaks noted by Dead carcass surveillance.

The best interpretation of this finding is that diverse groups of animals force to come together as they forage for dwindling water and food resources and this facilitates transmission.

Lahm SA, Kombila M, Swanepoel R, Barnes RF 2007 Trans R Soc Trop Med Hyg. 101(1):64-78

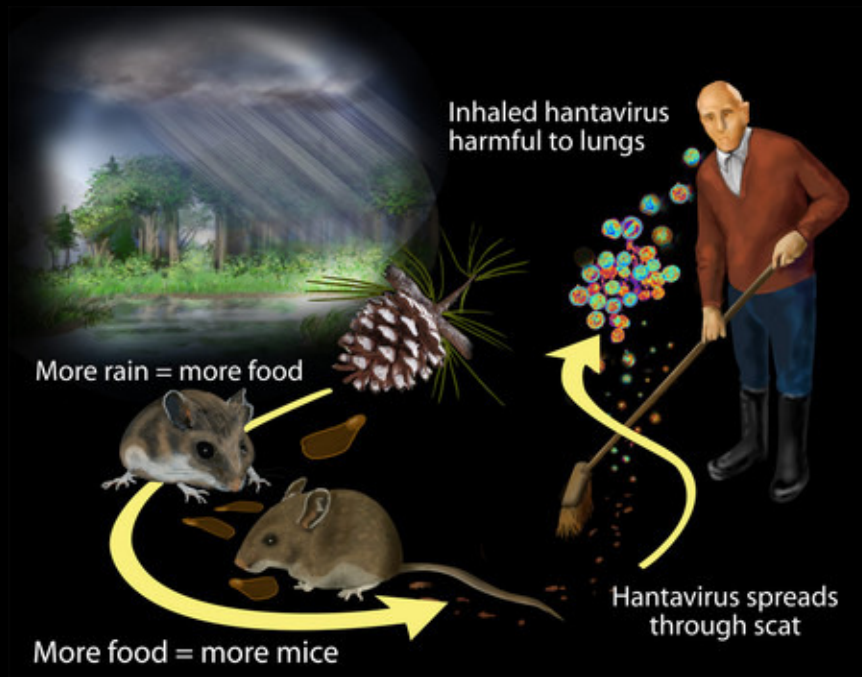
Could bats be the natural host of ebola virus?

Pierre Rouquet, Jean-Marc Froment, Magdalena Bermejo
Wild Animal Mortality Monitoring and Human Ebola Outbreaks, Gabon and Republic of Congo, 2001–2003
Emerging infectious disease journal:11: 2Feb 2005

Climate change?

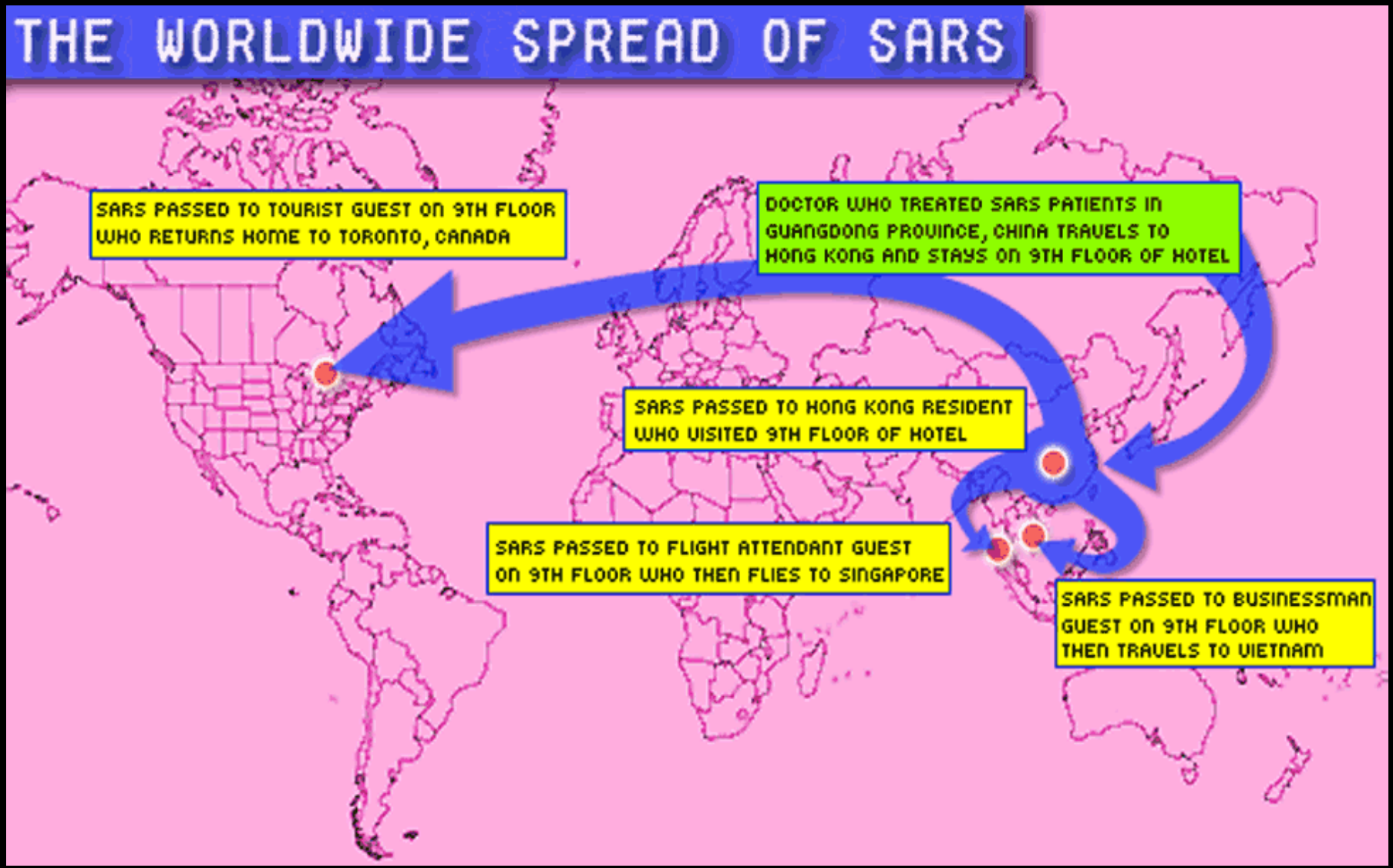
In 1993 first epidemic of hanta virus pulmonary syndrome occurred in the US.

The 1992 El Niño effect provoked heavy rainfall , led to proliferation of vegetation and an explosion in the rodent population, especially of deer mice, the natural hantavirus host.

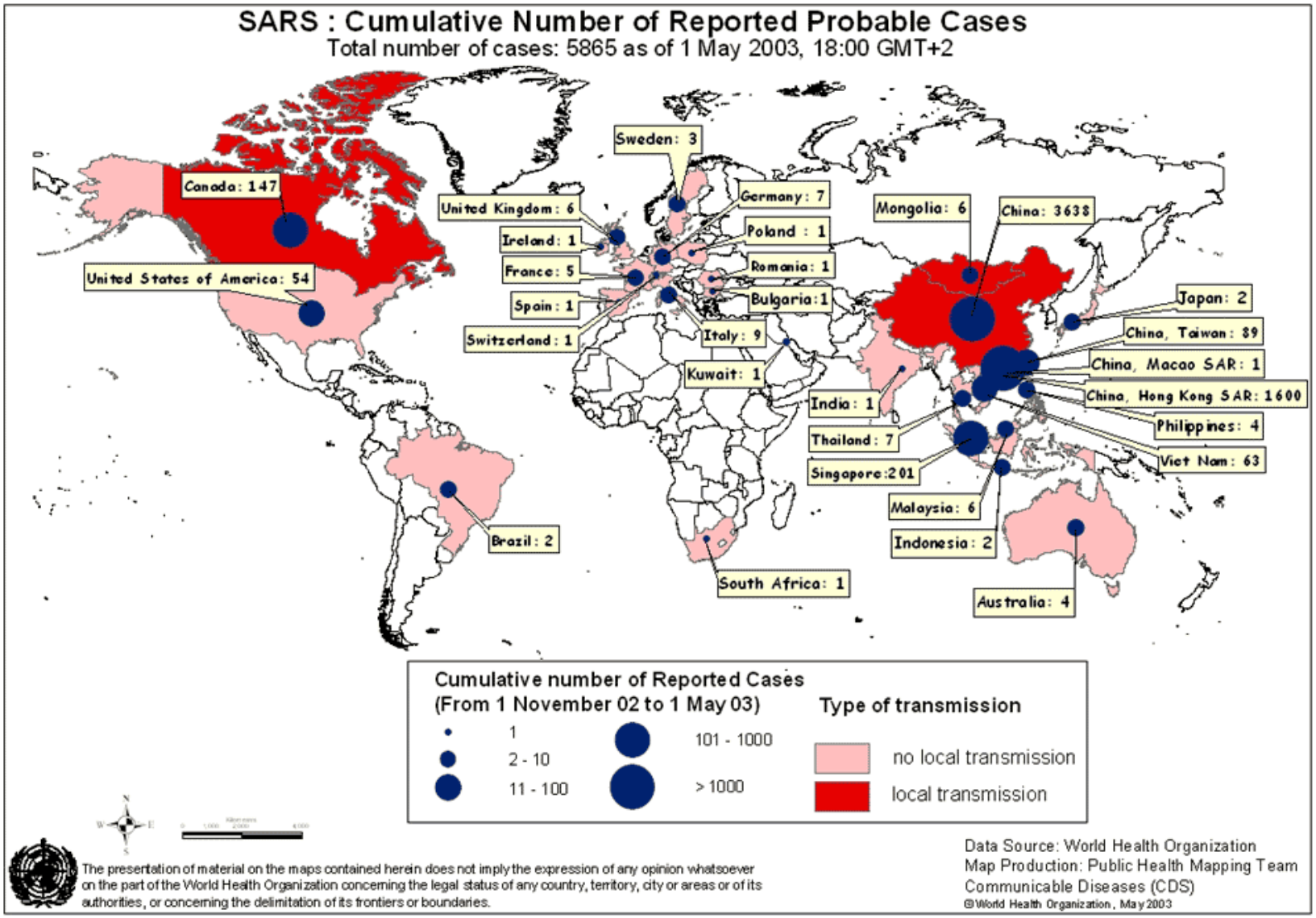


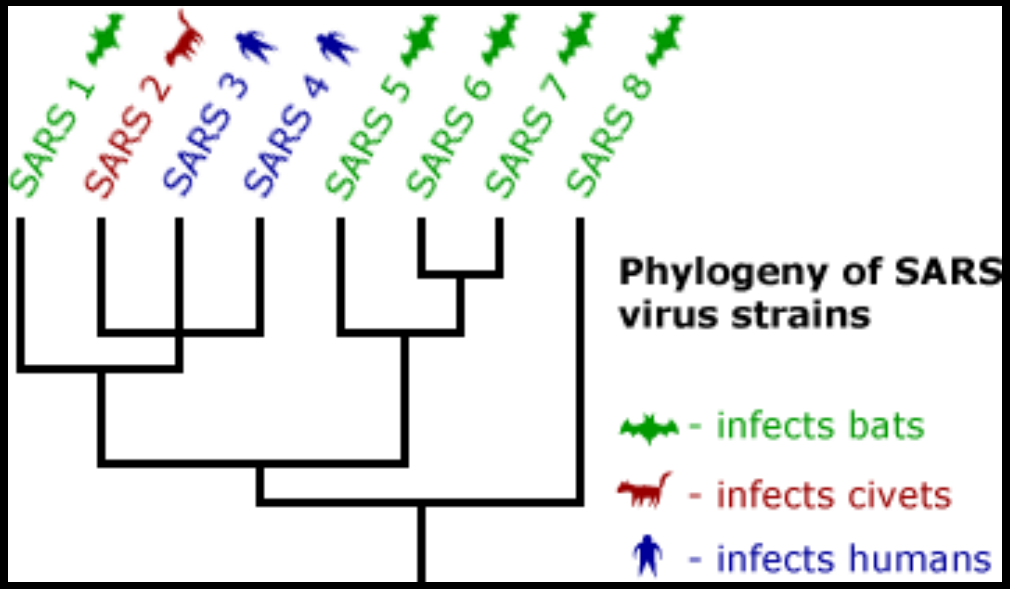
Second El Nino effect causing heavy rains again occur in 1998 followed by another severe epidemic in 1999.

Global travel and disease spread..



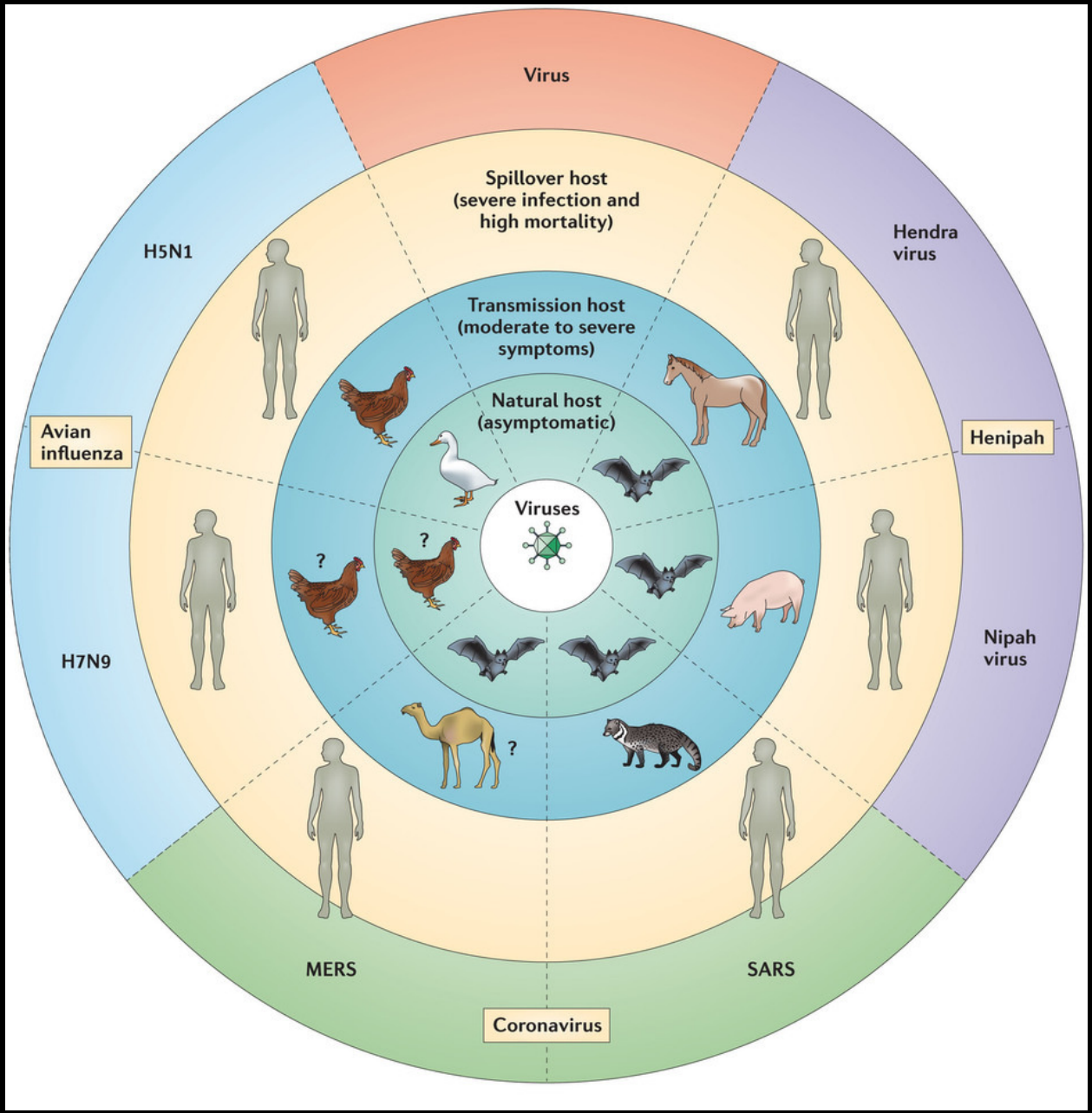
Globalization



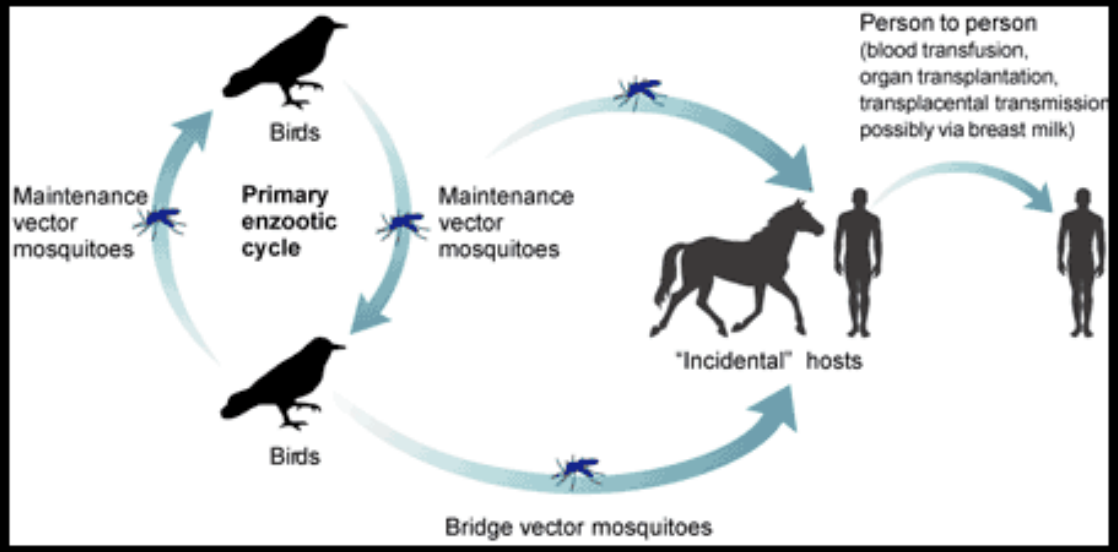

SARS 1
SARS 2
SARS 3
SARS 4
SARS 5
SARS 6
SARS 7
SARS 8
Phylogeny of SARS virus strains
- infects bats
- infects civets
- infects humans

Direct transmission from wild animals with or without intermediary host

Sylvatic symbiosis turns in to a serious infection in humans : penalty for encroaching others living space



West Nile Virus



Shipment of birds to Bronx Zoo

Early summer: warm weather ideal for mosquito breeding

Migration of infected birds to other areas of the country

Historical data:HIV and SIV

SIV and HIV :

- Cross species transmission events may be ongoing
- 33 species of Non-Human Primates (NHPs) harbor their own SIV species
- Hunting and butchering of NHPs for food common in central Africa
- SIVs isolated from bushmeat prepared for human consumption
- Ancestral strains of HIV-1 persist in wild chimps
- Precedent of laboratory worker acquired SIV infection
- 12 of 16 SIVs capable of infecting human

HIV-1and HIV-2 are direct descendants from SIVcpz (Chimpanzee) (Cameroon, Gabon, DRC, central Africa) and SIVsm (Sootey Mangabey) (Sierra Leone, Liberia).

SIV/HIV: retroviruses (RNA viral genome converted to DNA via enzyme reverse transcriptase)

- Origin of HIV 1: SIVcpz (Chimpanzee: *Pan troglodytes troglodytes)*
- Origin of HIV 2: SIVsm (Mangabee: *Cercocebus atys)*
- SIVcpz/SIVsm cause no discernable disease in their hosts
- SIVcpz and SIVsm have existed for millennia

- Same viruses cause lethal immunodeficiency in other primates, particularly Asian Macaques.
- Human contact with SIVs is likely longstanding (> 1000 years) through hunting of Non-Human Primates
- Despite longstanding human SIV exposure: epidemic HIV only emerges in last 60 years
- No HIV brought to the New World with >10 million African slaves
- Unclear mechanism of cross species transmission and origin of epidemic HIVs
- 11 individual cross species transmission events documented (HIV-1 subgroups M,N,O and HIV-2 subgroups A-G)

Dynamic gene mutations and successful survival..

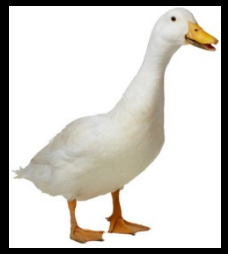
Influenza epidemics…

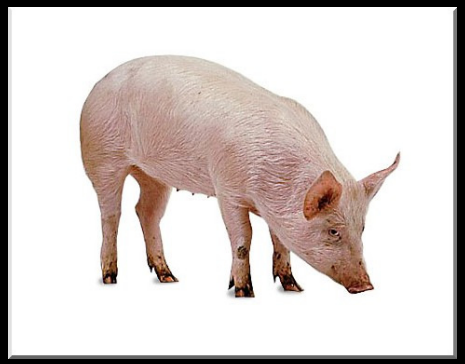
Influenza is an orthomyxovirus and originally an infection of aquatic birds.

It is believed to have made the transition to humans between nine thousand years ago, with increasing human urbanization, animal husbandry and animal domestication.

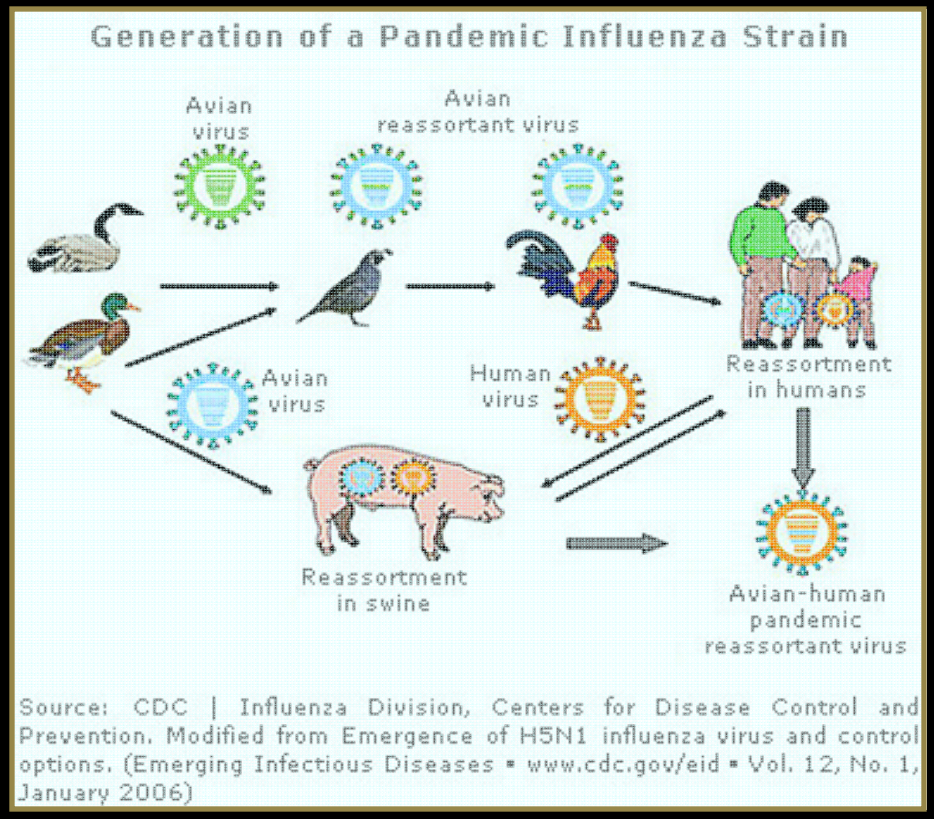
Historical jumps

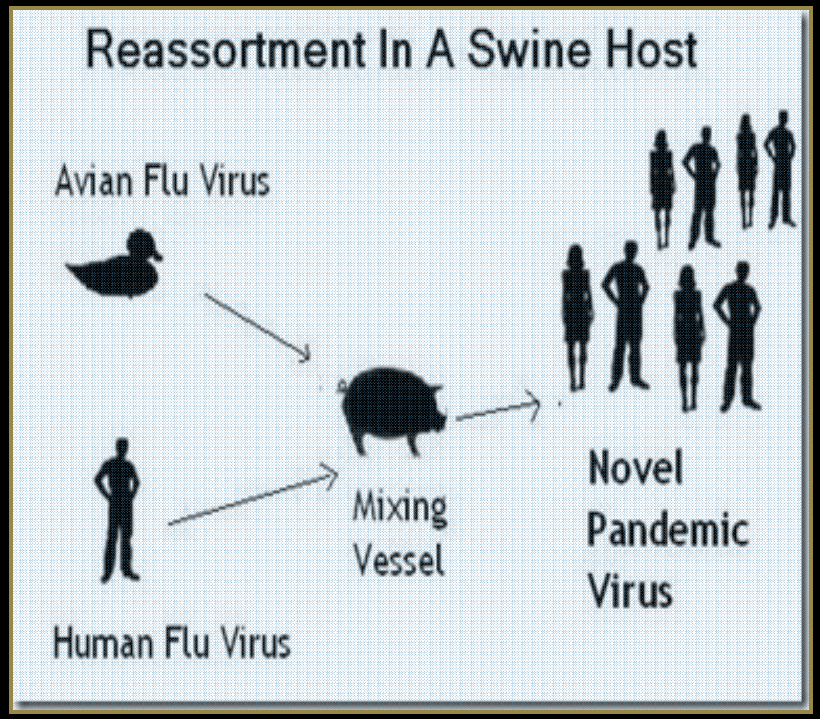
Influenza and Asian flu (1958) and H5N1 Hong Kong Avian flu (2008)





pandemic influenza H1N1 2009





Triple Reassortment of H3N2 Swine Influenza epidemic in US 2009

Should we worry about bats?

For some emerging pathogens the bat origin has been confirmed.

These include Hendra virus and Australian bat lyssavirus in Australia and Nipah virus in Malaysia and Bangladesh, where regular outbreaks reach mortality levels of 100%. Haemorrhagic fever viruses, including the feared and lethal Ebola and Marburg viruses, have also emerged from bats in Africa and Asia.

Presumable bat associated EIDs

Abbreviations:
RABV,=rabies virus;
EBLV-1,2=European bat lyssaviruses type 1 and 2;
WCBV=West Caucasian bat virus;
ARAV=Aravan virus;
KHUV=Khujand virus; IRKV=Irkut virus;
LBV=Lagos bat virus; SHIBV=Shimoni virus

Bat rabies—a global threat

66 virus types have been isolated from bats of 74 species.

Charles.H Calisher,James.E.Childs, Hume.e.Field, Kathlun.V. **Bats: Important Reservoir Hosts of Emerging Viruses** Clin Microbiol Rev. 2006 July; 19(3): 531–545.

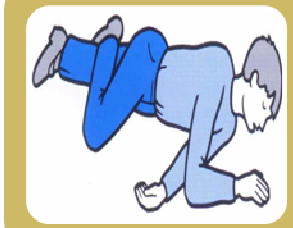
- Chiroptera are the oldest mammalian order .
- Only mammals capable of flight.
- Bats are the second largest order of mammals.
- Ecological flexibility, bats inhabit a wide variety of ecological niches.
- Many bat species roost together in very large and dense colonies.
- Roosting plasticity and broad food range, means that bats could transport viral material to many different animal species in various locations per unit time.
- Bats are capable of harboring large numbers of genetically diverse viruses within a geographic location and within a taxonomic group.
- Genes for interferon alpha family in both *Pteropus* and *Myotis* bats has revealed that both have up to 24IFNW genes, while humans have only one.

He G, He B, Racey PA, Cui J. Positive selection of the bat interferon alpha gene family. Biochem Genet. 2010;48:840–46

Clinical features

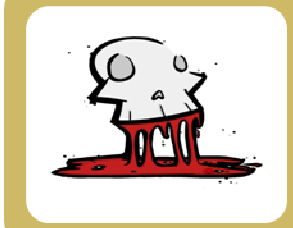
Respiratory symptoms

- SARS, MERS, Avian Influenza, etc.



Encephalitides

- JE, West Nile fever, VEE, Nipah



Hemorrhagic fevers

- Dengue, Ebola, Marburg,

Viral Hemorrhagic fevers

- Enveloped RNA viruses of diverse families
- May be arthropod borne with multiple, different animal reservoirs
- Symptoms and disease severity vary widely
- Precedent of international travel transporting viruses into non-endemic countries
- Precedent for nosocomial outbreaks healthcare workers and laboratory personnel

Viral Hemorrhagic fevers

Distinct VHF Families

- **Flaviviridae**
  - Dengue fever

- Filoviridae
- Ebola
- Marburg

- Arenaviridae
- Lassa Hemorrhagic Fever
- South American Hemorrhagic Fevers

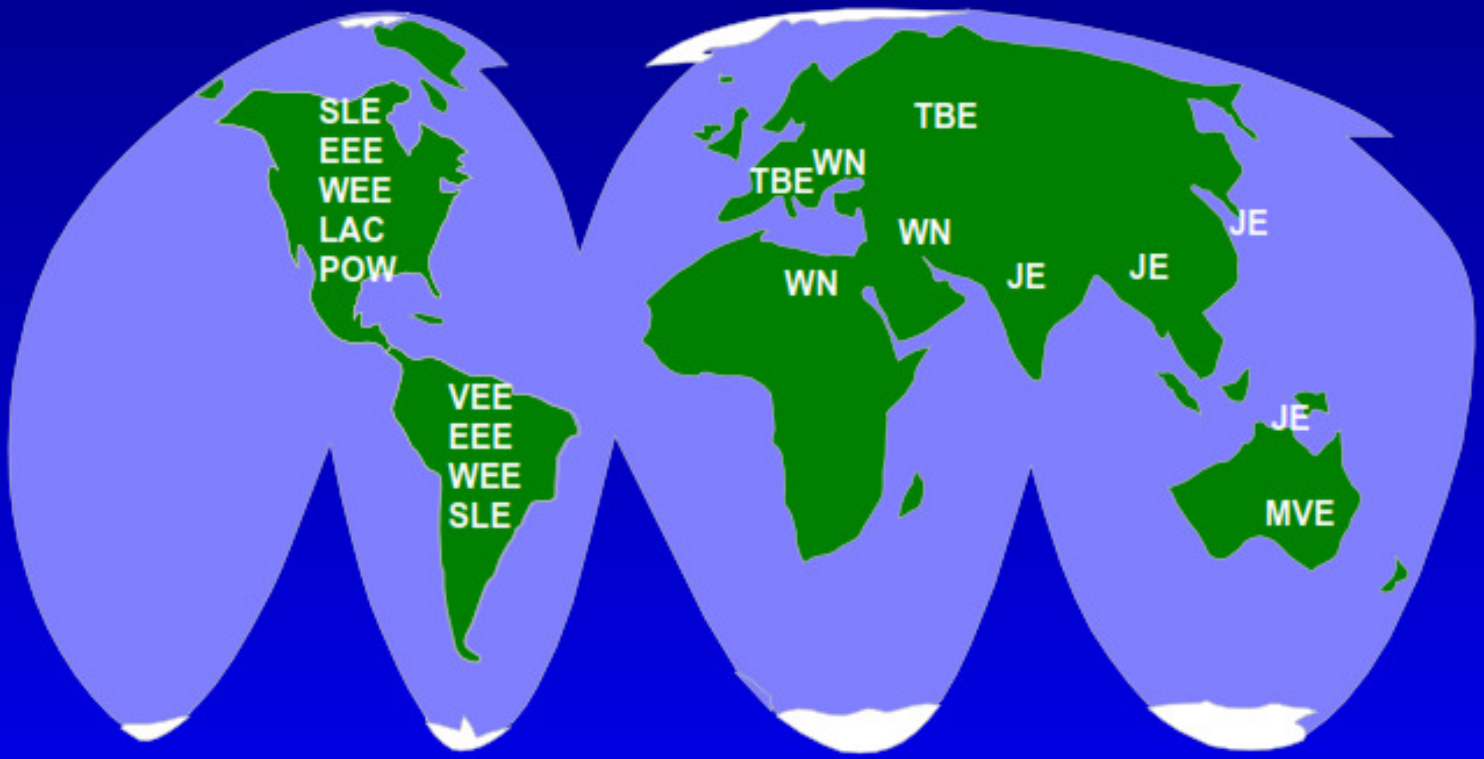
- Bunyaviridae
- Rift Valley Fever
- Crimean Congo Fever

Acute respiratory symptoms

- **Orthomyxoviridae**
  - Avian FLU, Swine Flu

- **CoronaViridae**
  - SARS, MERS

Worldwide Distribution of Major Arboviral Encephalitides



EEE: Eastern equine encephalitis
JE: Japanese encephalitis
LAC: LaCrosse encephalitis
MVE: Murray Valley encephalitis
POW: Powassan encephalitis
SLE: St. Louis encephalitis
TBE: Tick-borne encephalitis
WEE: Western equine encephalitis
WN: West Nile encephalitis
VEE: Venezuelan equine encephalitis

CDC

When to suspect

Occurrence of a cluster of cases with flu like symptoms in a limited geographical area at a certain time frame

In addition to flu like symptoms , at least some of the patients would show severe respiratory symptoms, or hemorrhagic events or features of encephalitides

Sickness among the domestic animals, particularly, pigs, horses, cattle, poultry may become evident at the time of human infection.

Global emerging-disease control plans

Strengthen international surveillance networks to detect, control, and reduce emerging diseases.

Improve the international public health infrastructure (e.g., laboratories, research facilities, technology, and communications links).

Develop better international standards, guidelines, and recommendations.
Improve international capabilities to respond to disease outbreaks with adequate medical and scientific resources and expertise.

Focus attention and resources on training and supporting medical and scientific expertise.

Encourage national governments to improve their public health care systems, devote resources to eliminating or controlling causes of emerging diseases and coordinate their public health activities with WHO and the international community.

Have we done enough?

The latest threat emerged on 19 October, when the WHO reported a cluster of cases of acute flaccid paralysis — a classic polio symptom — in Deir-ez-Zor, a conflict-ridden province in eastern Syria.

Two of the 22 cases were confirmed as polio
On 29 October, the WHO confirmed a total of 10.

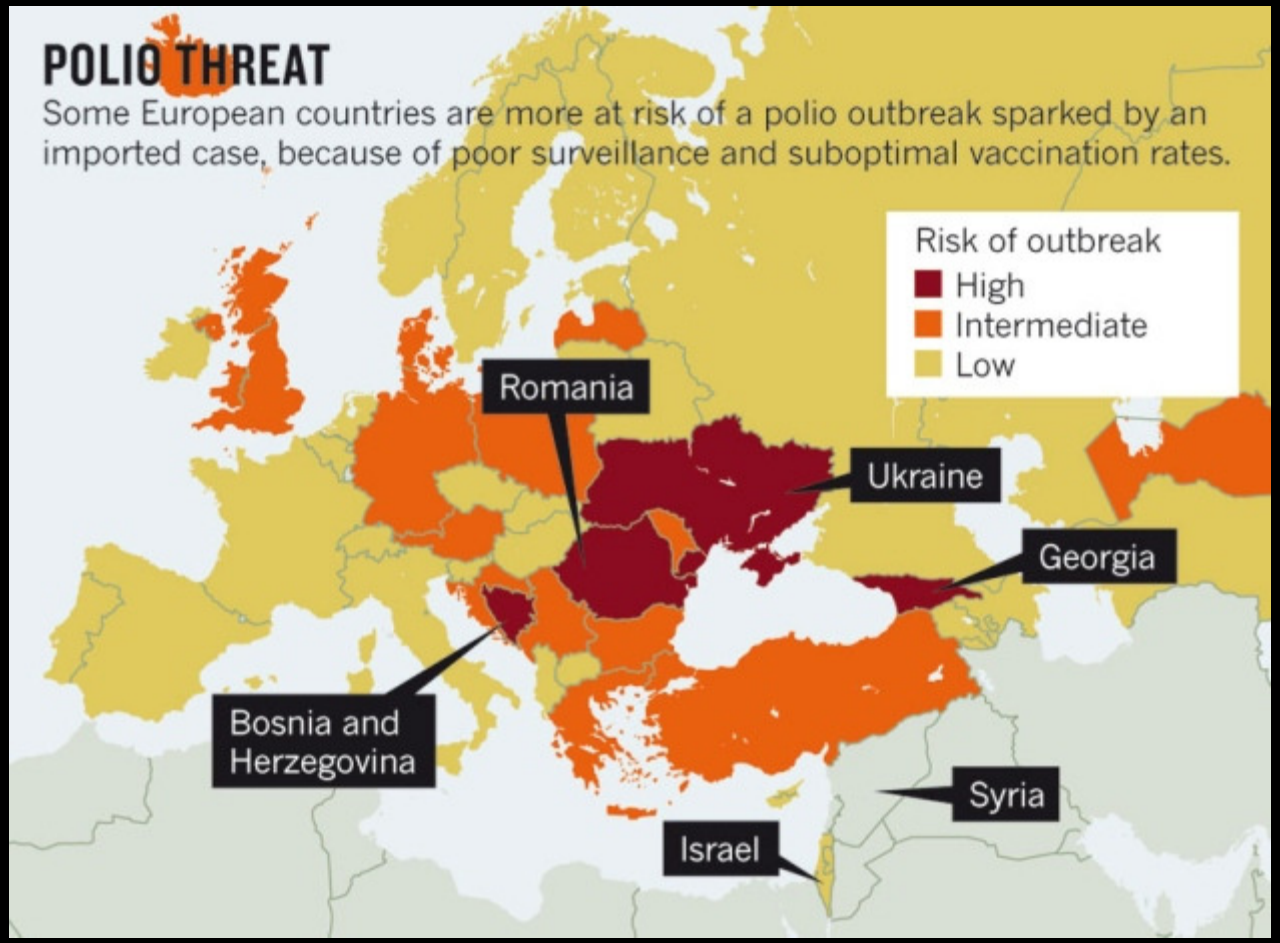
Situation in Israel..

Twenty-five years after it was dispatched, wild poliovirus is back and circulating widely in Israel but, surprisingly, there have been no human cases.

Israel relies on the inactivated polio vaccine, or IPV, to protect against this crippling disease.

Paradoxically, Israel's very high vaccination rate is what has allowed the virus to circulate silently for months.

Threat to Europe



Take home message…

Population explosion, modernization, urbanization all leads to encroachment of sylvatic territories exposing us to new diseases.

Global climatic and man made environmental changes force vectors to change hosts and infected birds to migrate to other areas .

Global travel and international wild animal trade facilitate global transmission.

Genetic diversity, ability to jump from species to species, together with natural host symbiosis allow the long term survival of viruses

Emerging diseases is a continuous process and there is no way we could prevent it.

The only option is to anticipate, detect, act, control and call for help (Global support)


Thank
you
©H. T. Wickramasinghe


©H. T. Wickramasinghe