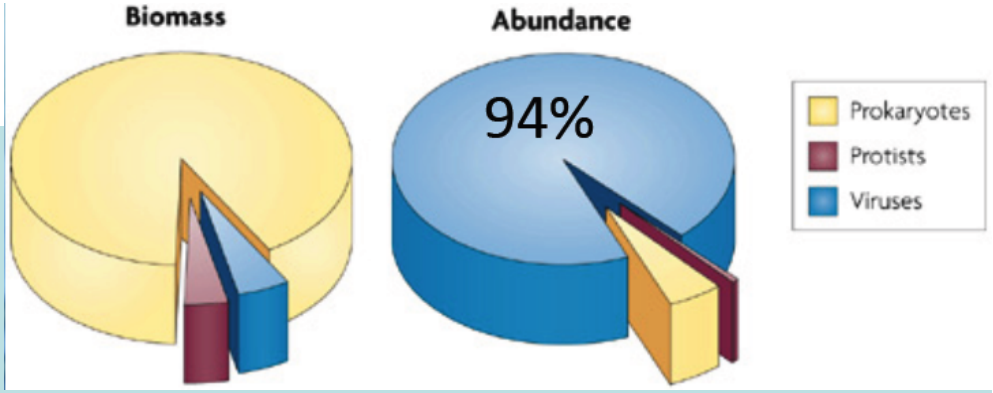
VIROLOGY

The science of Virology

The Viruses: the Invisible Enemy

Why do we need to study such a collections of monsters?

Why we have to study viruses?



✓Viruses Are Everywhere

✓Viruses Infect All Living Things

✓ Viruses are the Most Abundant Microorganisms on Earth.

✓ There are 10-50 million phages on average per ml of seawater.

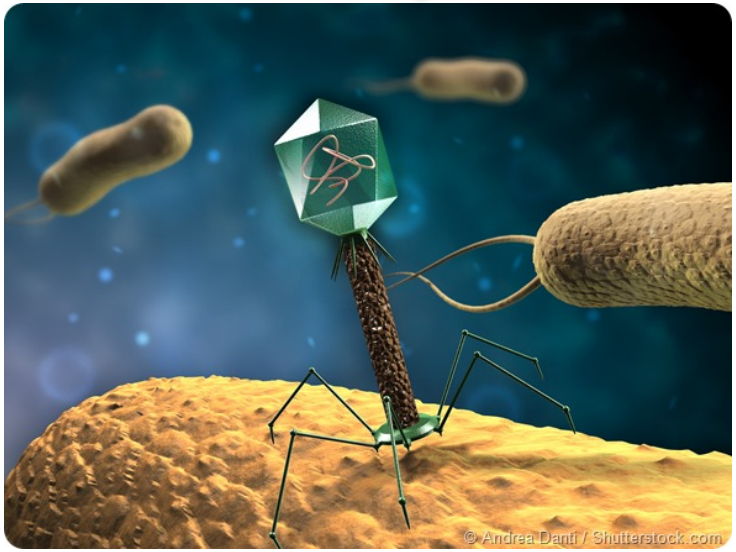
✓ More than 10^{31} bacteriophage particles in the world's oceans!

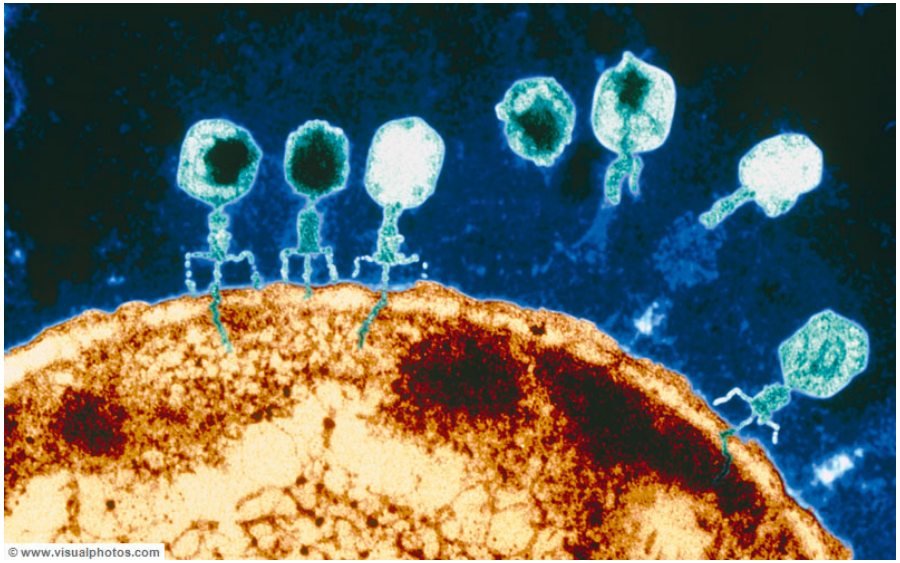
✓ A bacteriophage particle weighs about a femtogram (10^{-15} grams).

✓ 10^{31} X 10^{-15}= the biomass on the planet of ***bacterial viruses*** alone exceeds the biomass of elephants by more than 1000-fold!

✓ The length of a head to tail line of 10^{31} phages is 100 million light years!

Why We do Care about Viruses?



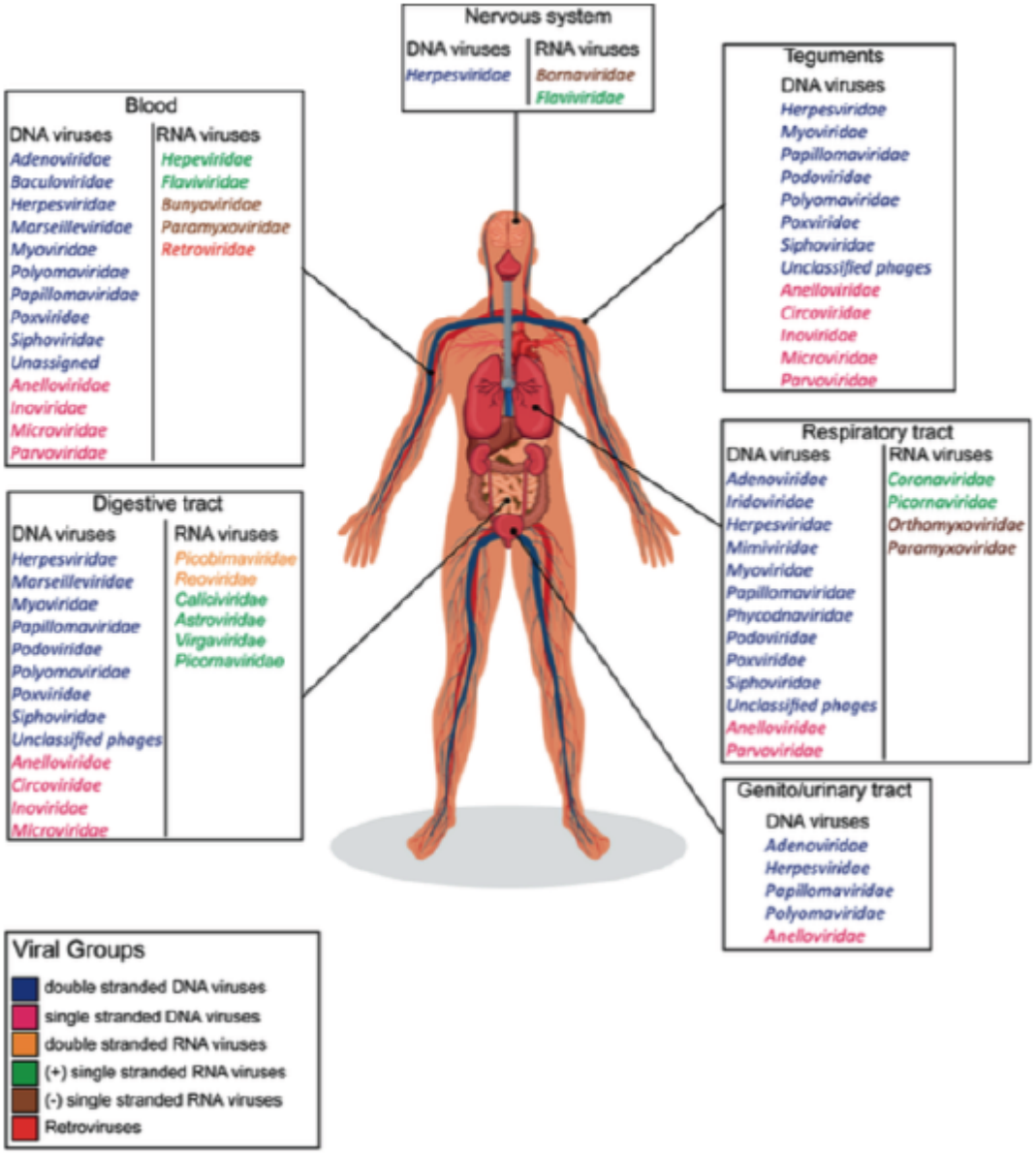


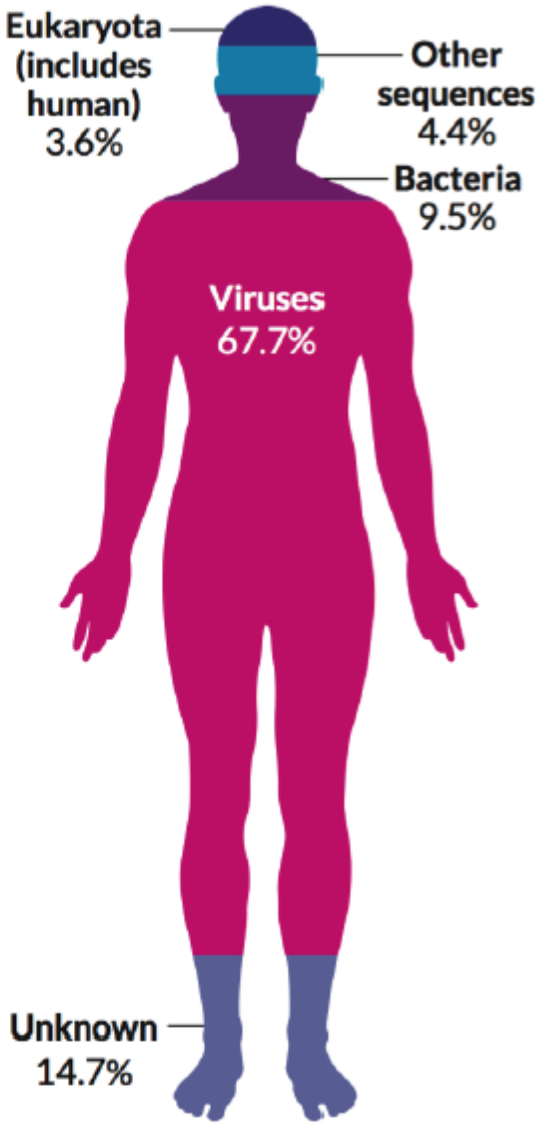
- ✓Viruses Outnumber Cellular Life by at least 10 fold.
- ✓Viruses show the greatest biodiversity on Earth.
- ✓Viruses Drive Global Cycles of Matter.
- ✓Beneficial Effects on Earth.
- ✓Viruses are source of New Pathogens

Why we have to study viruses?

- ✓ Viruses Cause Human Diseases
- ✓ However, amazingly the vast majority of viruses that infect humans have no or little impact on our health
- ✓ Viruses Can Cross Species Boundaries
- ✓ We Eat and Breathe Billions of Viruses Regularly
- ✓ Virus “R” Us (HERV proviruses make up nearly 8% of the human genome)
- ✓ Viruses Are Uniquely Valuable Tools to Study Biology
- ✓ Viruses Can Be Used To Manipulate Biology

The Human Virome





Nowadays, viruses have really an impact on mankind?

The facts: viral diseases exert a shocking toll on the developing world.

✓Over 2.5 million people die each year from AIDS, mostly in sub-Saharan Africa.

✓More than 3 billion people are at risk of infection with dengue fever.

✓Rotavirus, a cause of common diarrhoea, kills an estimated 450,000 children each year.

✓Three percent of the world's population, around 180 million people, are chronically infected with hepatitis C.

✓In West Africa alone, there are some 500,000 cases of Lassa fever every year.

✓Furthermore, many RNA viruses, such as the new H7N9 subtype of influenza and enteroviruses are emerging in developed countries.

Despite these facts, few drugs and vaccines are available for the treatment of these viral diseases.

Nowadays, viruses have really an impact on mankind?

- *We are all aware of the importance of virus diseases in our lives. The impact of viruses can be assessed in many ways.*
- *The economic effects of virus disease play an important role in the medical, animal and plant spheres.*
- *Consideration of the economic impact can often inform decisions about investment in exploring treatments for virus infections.*

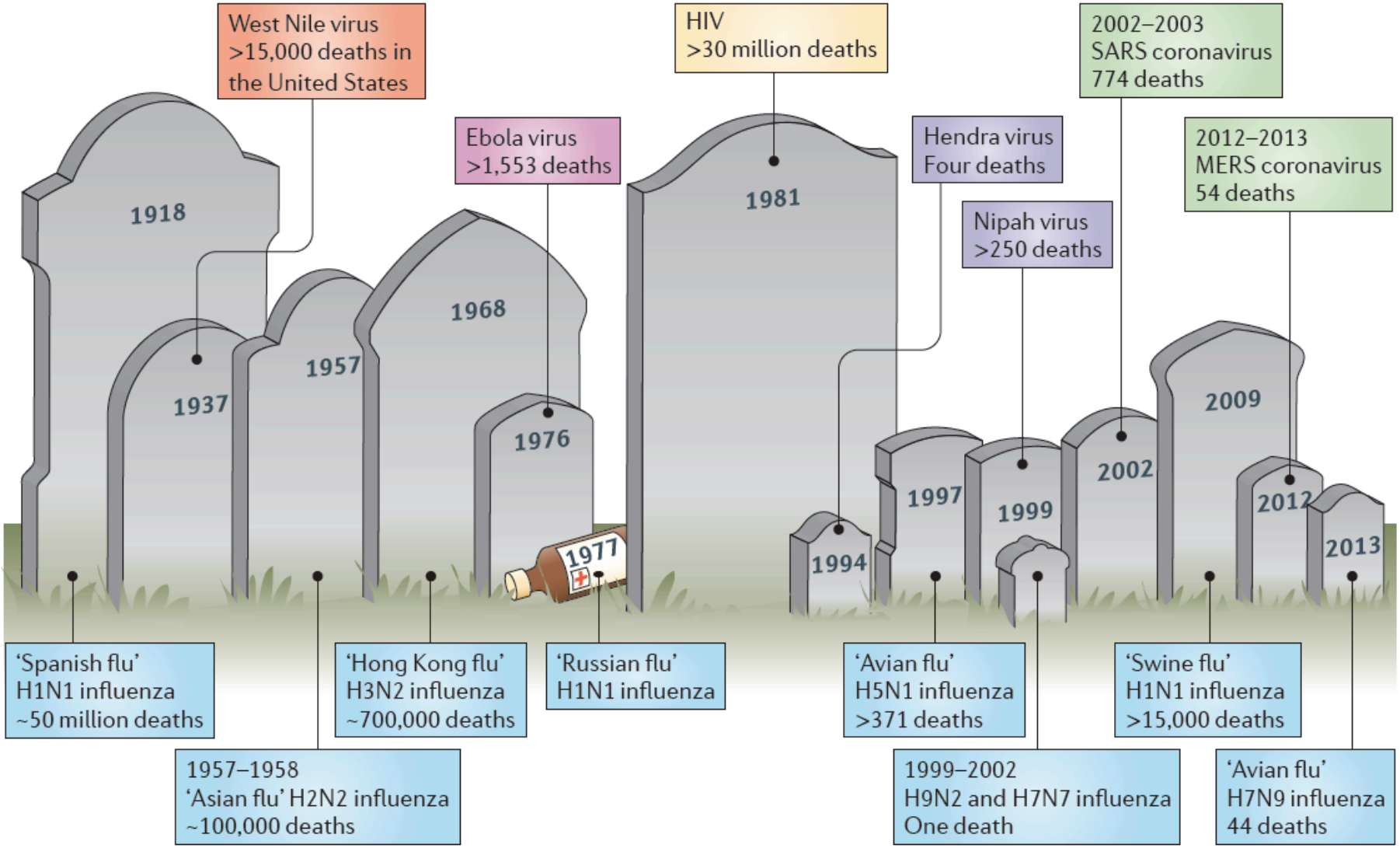
The economic cost of human infections includes both direct, medical, and indirect, social and employment, costs to the national economies of the world.

Examples of the impact: Exotic and emerging viral infections

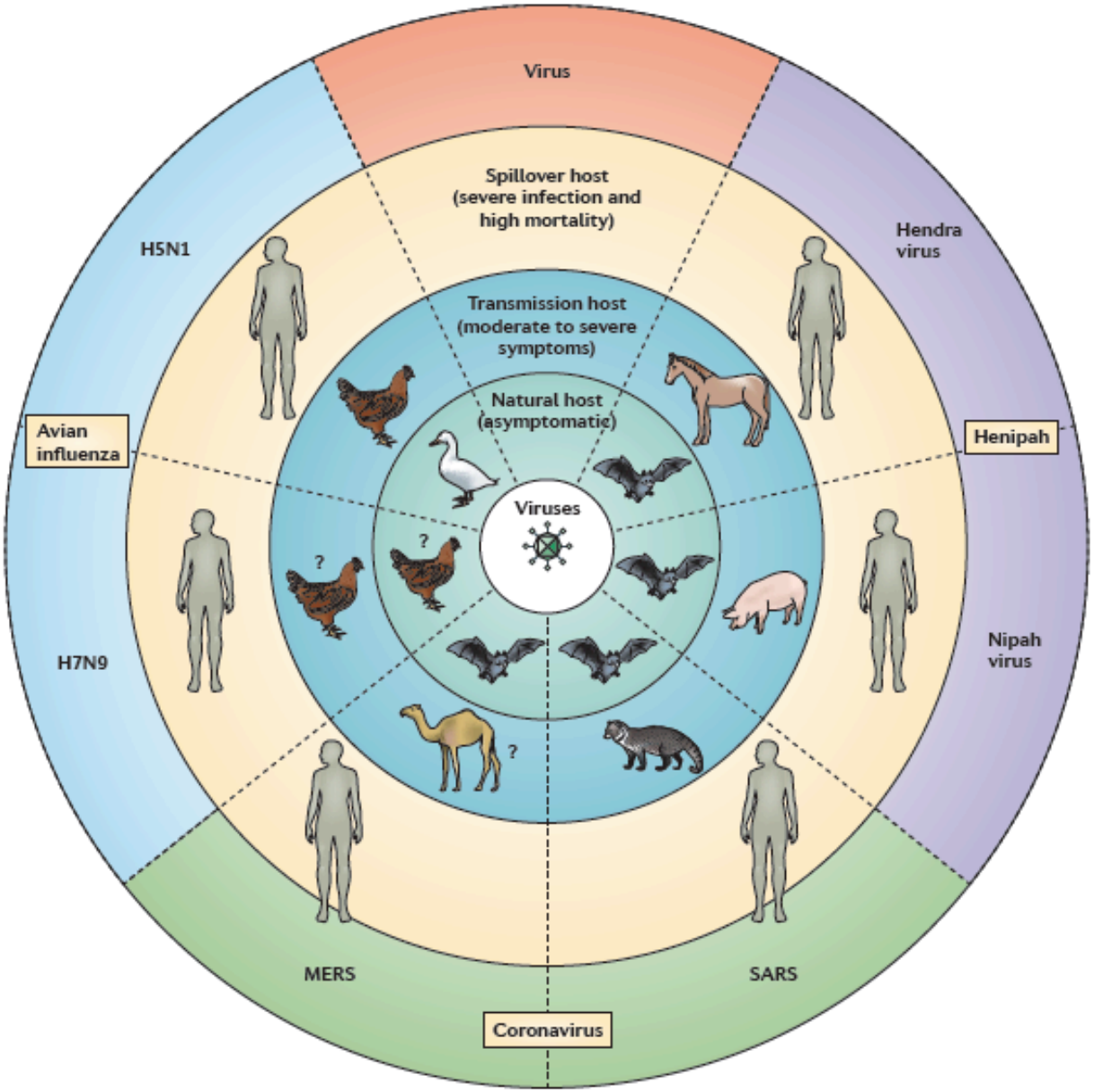
- *However, the most dramatic impacts are often seen when a previously unknown viral disease is encountered.*
- *This can arise either as an introduction of a virus from another species, or the appearance of an entirely new disease in a previously unaffected geographical area.*

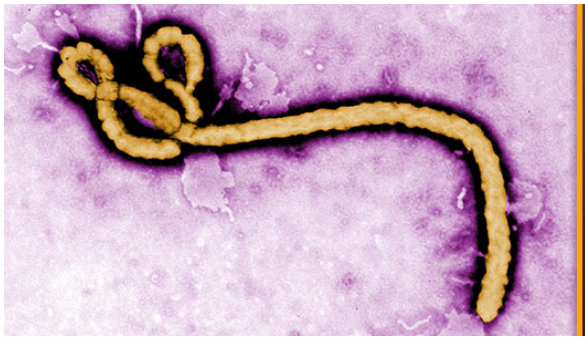
- Emerging viruses arise when humans explore new territories and become exposed to infection.
- Emerging viruses are transmitted to humans from other species in which they typically do not cause serious disease. Transmission often involves an intermediate host.

Emergence of viral zoonoses over the past century



The severity of emerging viral diseases is influenced by the host-pathogen interaction





Ebola Update

CDC and Texas Health Department Confirm First Ebola Case Diagnosed in the U.S.

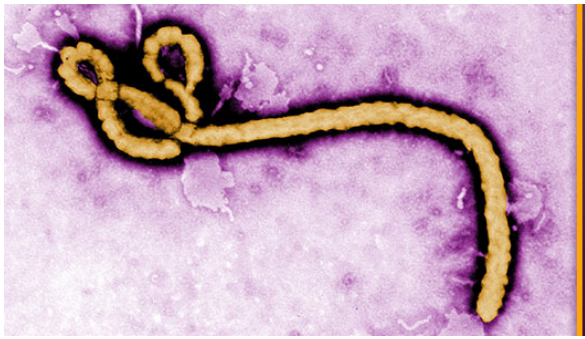
WEST AFRICA Ebola Outbreak

✓The 2014 Ebola epidemic in West Africa is the first in history.

✓The first case was reported in Guinea in March 2014, and the disease spread in the neighboring countries of Liberia and Sierra Leone.

✓ Over the span of a year, the Ebola epidemic has caused more than ten times as many cases of Ebola than the combined total of all those reported in previous Ebola outbreaks.

✓As the outbreak became more widespread, travel-associated cases appeared in Nigeria, Mali, Senegal, and even countries outside Africa, including the United States and European countries.



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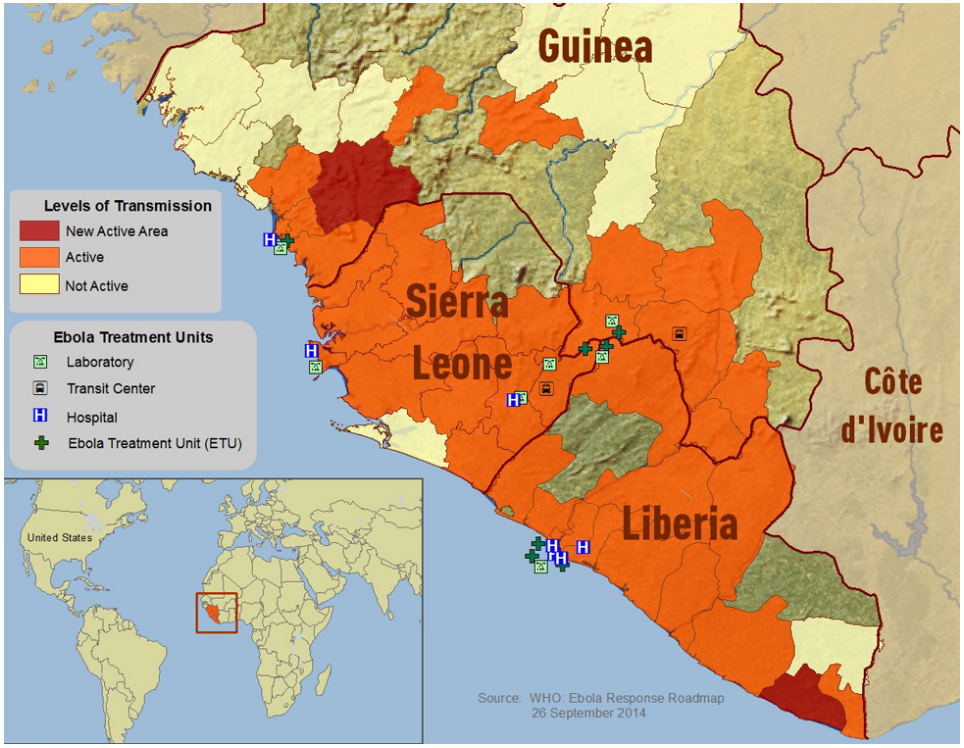


As of September 30, 2014

Case Counts*

*Case counts updated in conjunction with the World Health Organization updates and are based on information reported by the Ministries of Health.

As of September 30, 2014
(Updated October 3, 2014)

Countries with outbreaks

Totals for Guinea, Liberia & Sierra Leone

- Total Case Count: **7470**
- Total Deaths: **3431**
- Laboratory Confirmed Cases: **4087**

Countries with localized transmission

Nigeria

- Total Case Count: **20**
- Total Case Deaths: **8**
- Laboratory Confirmed Cases: **19**

Countries with travel-associated cases

Totals for Senegal and U.S.

- Total Cases: **2**
- Total Deaths: **0**
- Laboratory Confirmed Cases: **2**

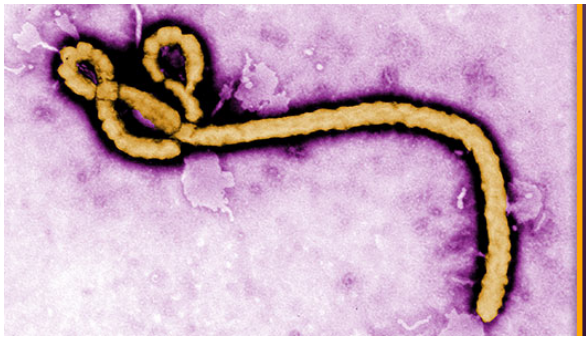
Senegal

- Total Case Count: **1**
- Total Case Deaths: **0**
- Laboratory Confirmed Cases: **1**

United States*

*In a traveler from Liberia

- Total Case Count: **1**
- Total Case Deaths: **0**
- Laboratory Confirmed Cases: **1**



Ebola Update

CDC and Texas Health Department Confirm First Ebola Case Diagnosed in the U.S.

WEST AFRICA Ebola Outbreak

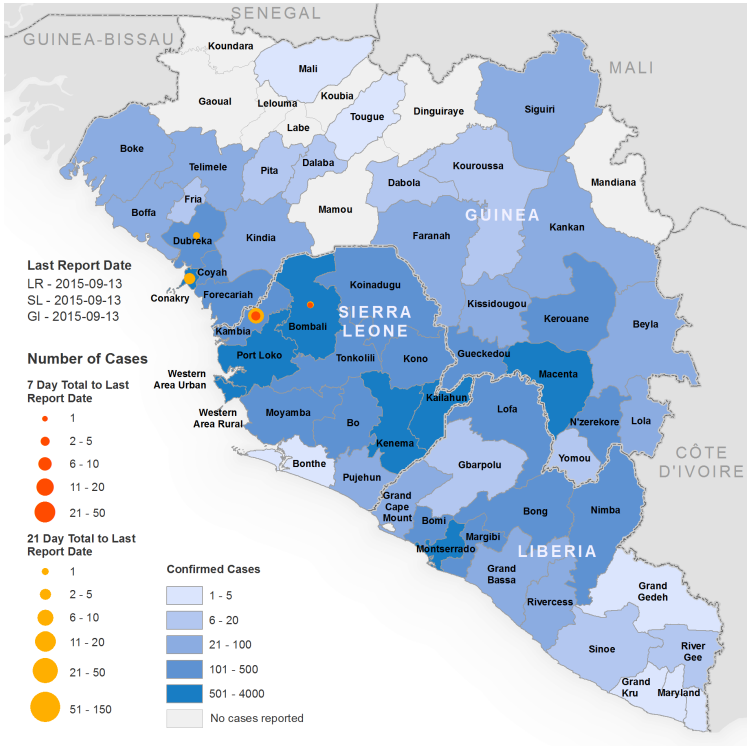
As of September 29, 2015

Ebola by the Numbers*

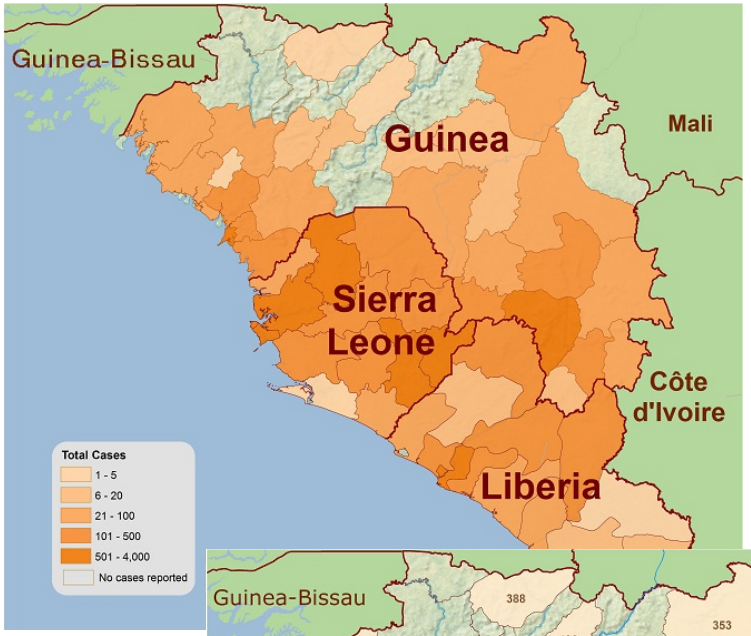
- **27,000+** Total number of cases
- **11,000+** Total number of deaths
- **24,665** Health workers trained by CDC in West Africa
- **2,471** CDC deployments
- **4** Patients diagnosed with Ebola in the U.S.
- **11** Patients with Ebola treated in the U.S.
- **600+** U.S. healthcare workers trained in Anniston
- **150,000** U.S. healthcare workers trained by webinars and calls

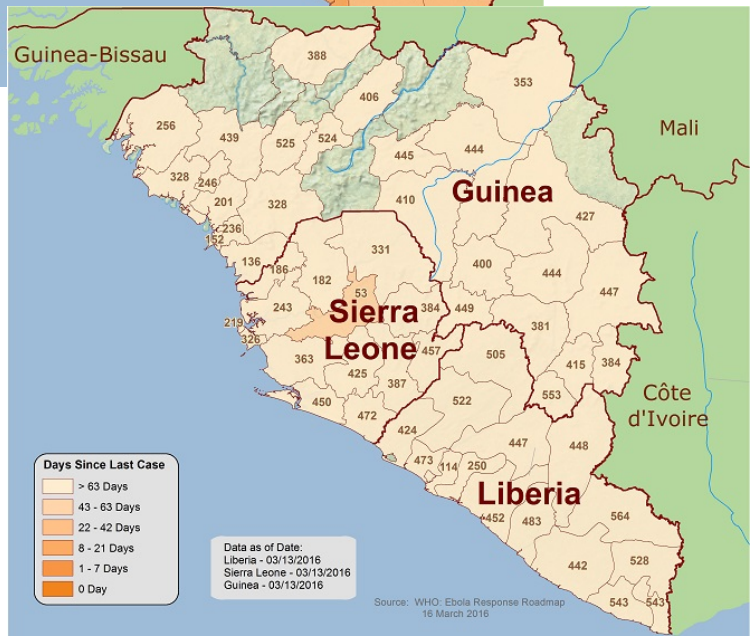
59,665,191 Number of views for CDC's Ebola website

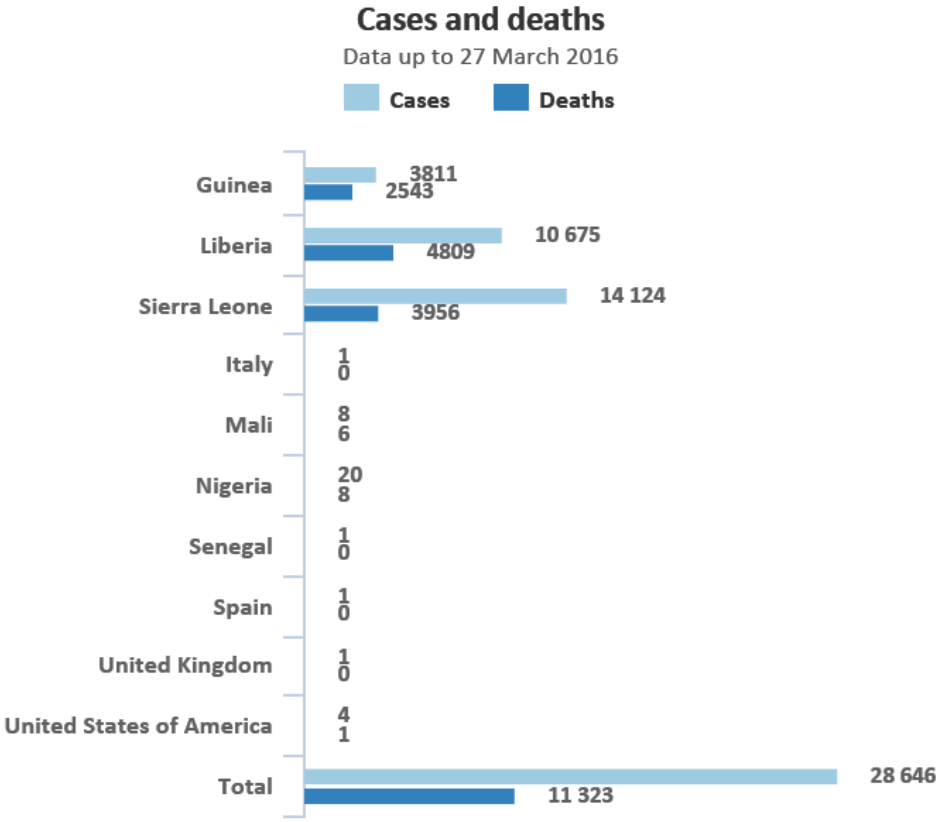
* As of June 12, 2015



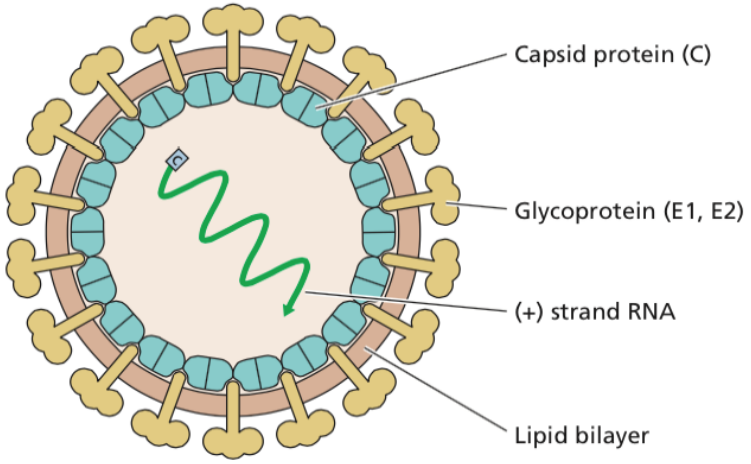
2014 Ebola Outbreak in West Africa
Situation Report March 30th, 2916







The Chigungunya outbreak in Lazio, 2017



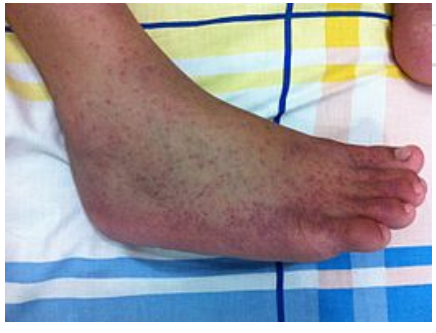
R.it Roma

Municipi: I II III IV V ALTRI | AREA METROPOLITANA | REGIONE

Chikungunya, gli esperti Ue "alto rischio epidemia, ecco le precauzioni"

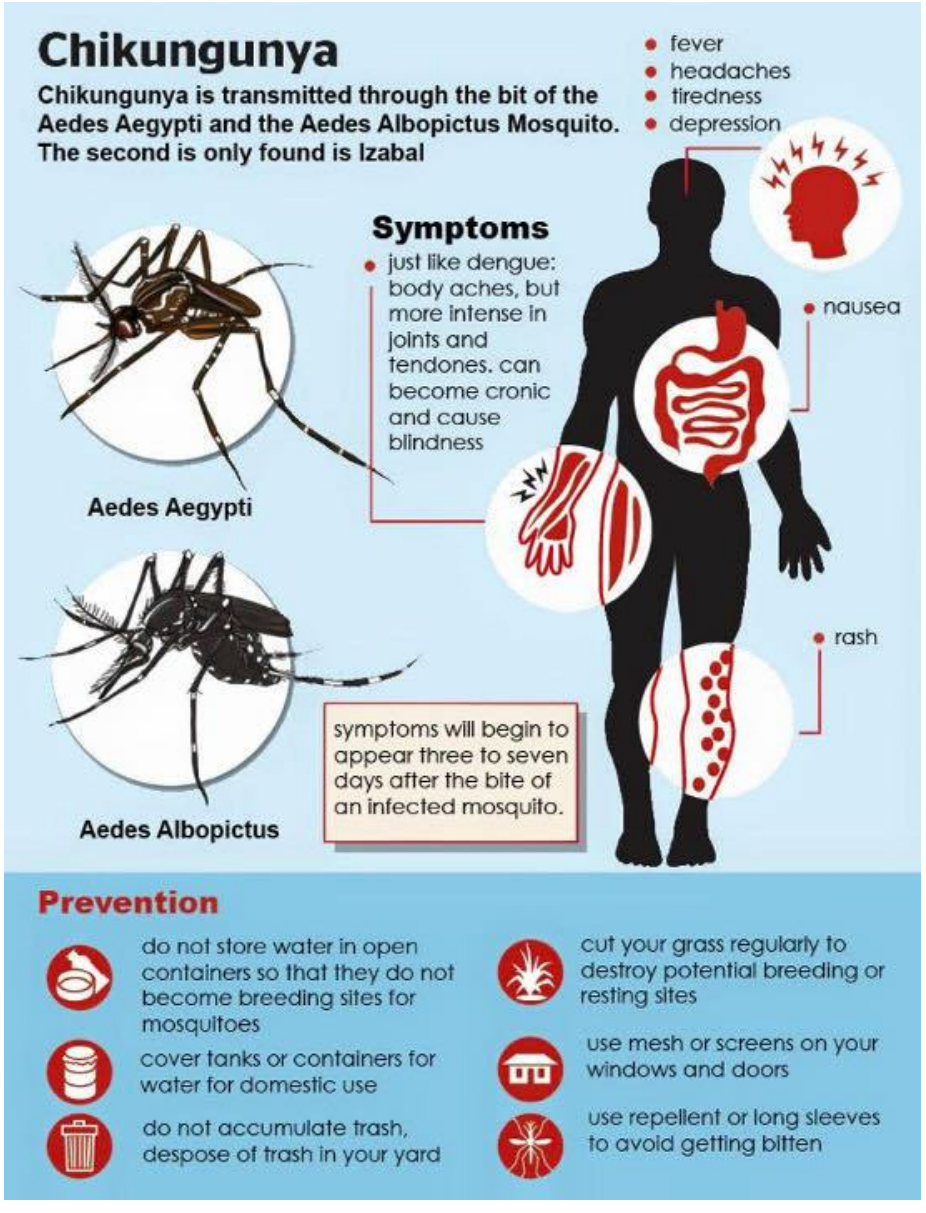
"Attenti prossime settimane". Appello della ministra Lorenzin: "Indispensabile disinfestare". Controlli sulle sacche di sangue

di CRISTINA PALAZZO

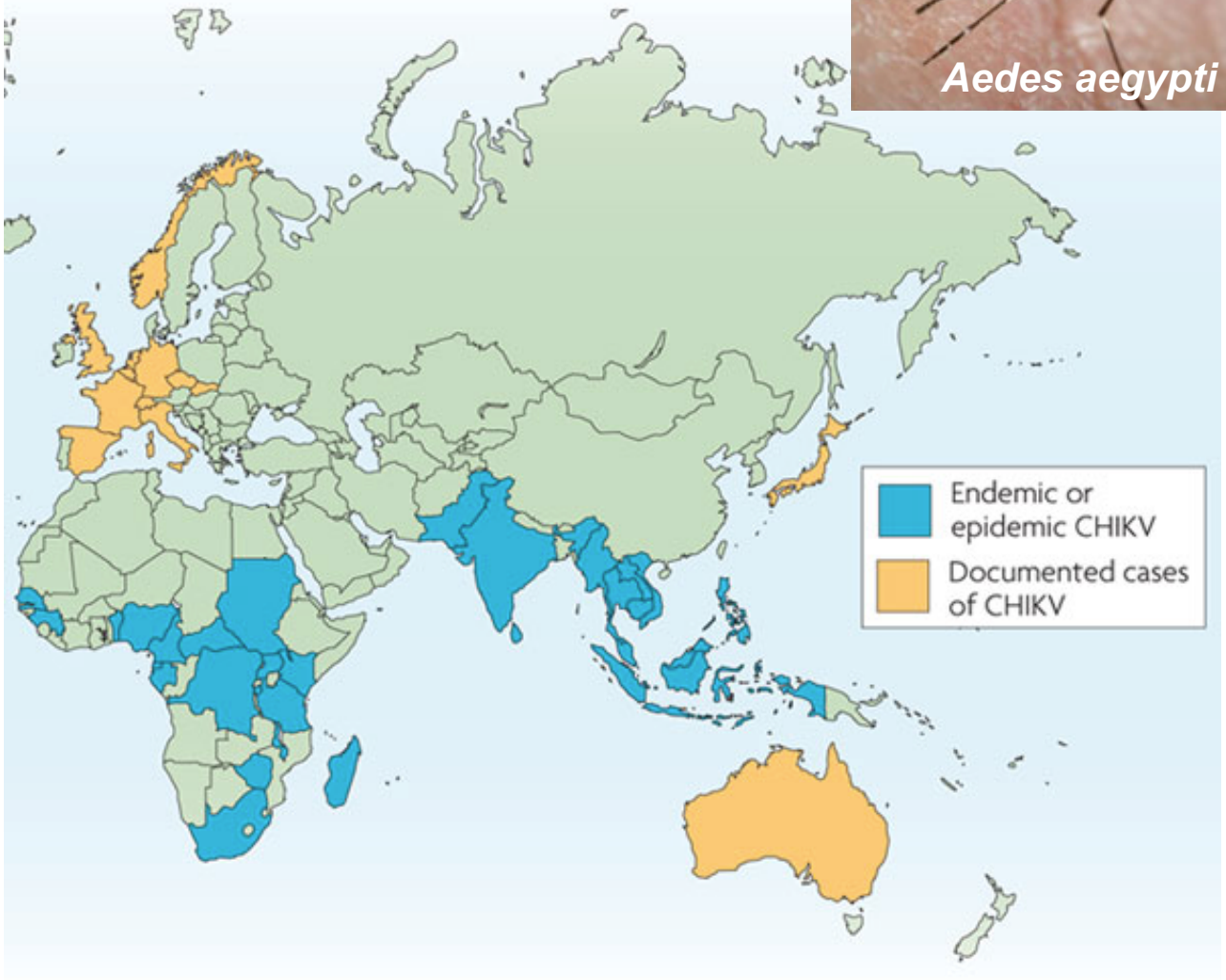


16 settembre 2017

Sono 47 i casi accertati di Chikungunya nel Lazio. Di questi uno in provincia di Latina, 6 di Roma e 40 sono residenti o hanno soggiornato ad Anzio.



The Chigungunya outbreak in Lazio, 2017



- Asia, Africa, never Europe or US
- 2004 – outbreaks spread from Kenya to India
- 2007 - outbreak in Italy, first in Europe
- Recent outbreaks associated with *A. albopictus*
- One amino acid change in viral gp E1

The Chigungunya outbreak in Lazio, 2017

BOX 1.7

DISCUSSION

An exotic virus on the move

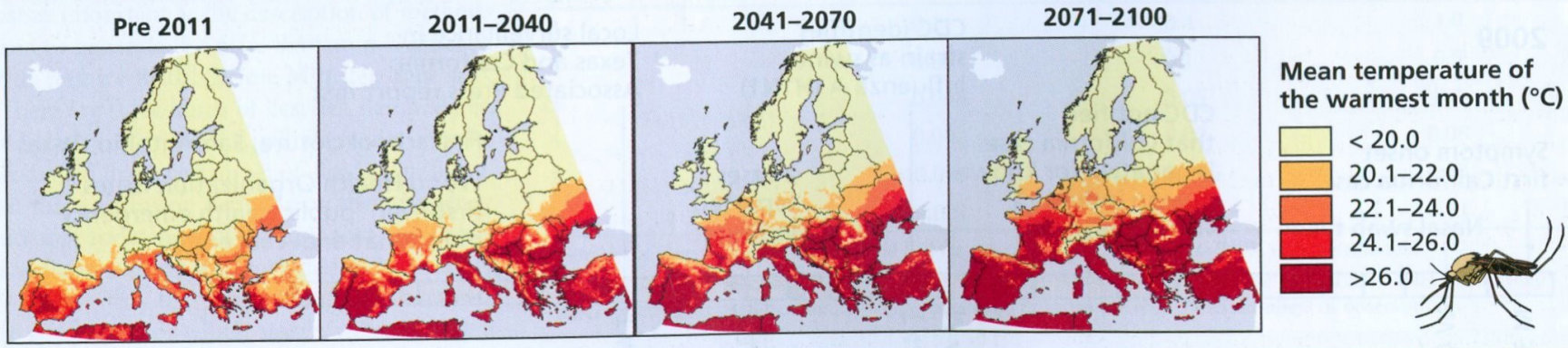
Chikungunya virus is a togavirus in the alphavirus genus. The virus is spread by mosquitoes (primarily the notorious *Aedes aegypti*). The viral disease has been known for more than 50 years in the tropics and savannahs of Asia and Africa but had never been a problem of the developed countries in Europe or the United States. The disease is uncomfortable (rashes and joint pains) but not fatal. In the last 5 years, however, something changed dramatically and brought this once exotic disease into the forefront of public concern.

In 2004, outbreaks of Chikungunya disease spread rapidly from Kenya to islands in the Indian Ocean and then to India, where it had not been reported in over 30 years. In some of the Indian Ocean islands, more than 40% of the population fell ill. In 2007, there was an outbreak in Italy, the first ever in Europe. What had happened to change the pattern of infection?

An alarming finding was that the Asian tiger mosquito (*Aedes albopictus*) became an efficient new vector for the virus. A point mutation in the viral genome appears to be the cause of the vector expansion and, perhaps, for the epidemic spread of the disease in areas where it had been unknown. *A. albopictus*, which has a greater geographical range than *A. aegypti*, is spreading across the globe from eastern Asia and is now found in mainland Europe and the United States. This mosquito is a maintenance (occasionally epidemic) vector of dengue viruses in parts of Asia and is a competent vector of several other viral diseases. Since its discovery in the United States, five arboviruses (Eastern equine encephalitis, Keystone, Tensaw, Cache Valley, and Potosi viruses) have been isolated from *A. albopictus*.

Enserink M. 2007. Chikungunya: no longer a Third World disease. *Science* **318:**1860–1861.

Projected distribution of *Aedes albopictus* in Europe, based on climate change models. Projections from two emission scenarios from the Intergovernmental Panel on Climate Change indicate that the habitat of *Aedes albopictus* will increase dramatically over the next century. From D. Fischer et al., *Int. J. Health Geogr.* **12:**51, 2013, with permission.



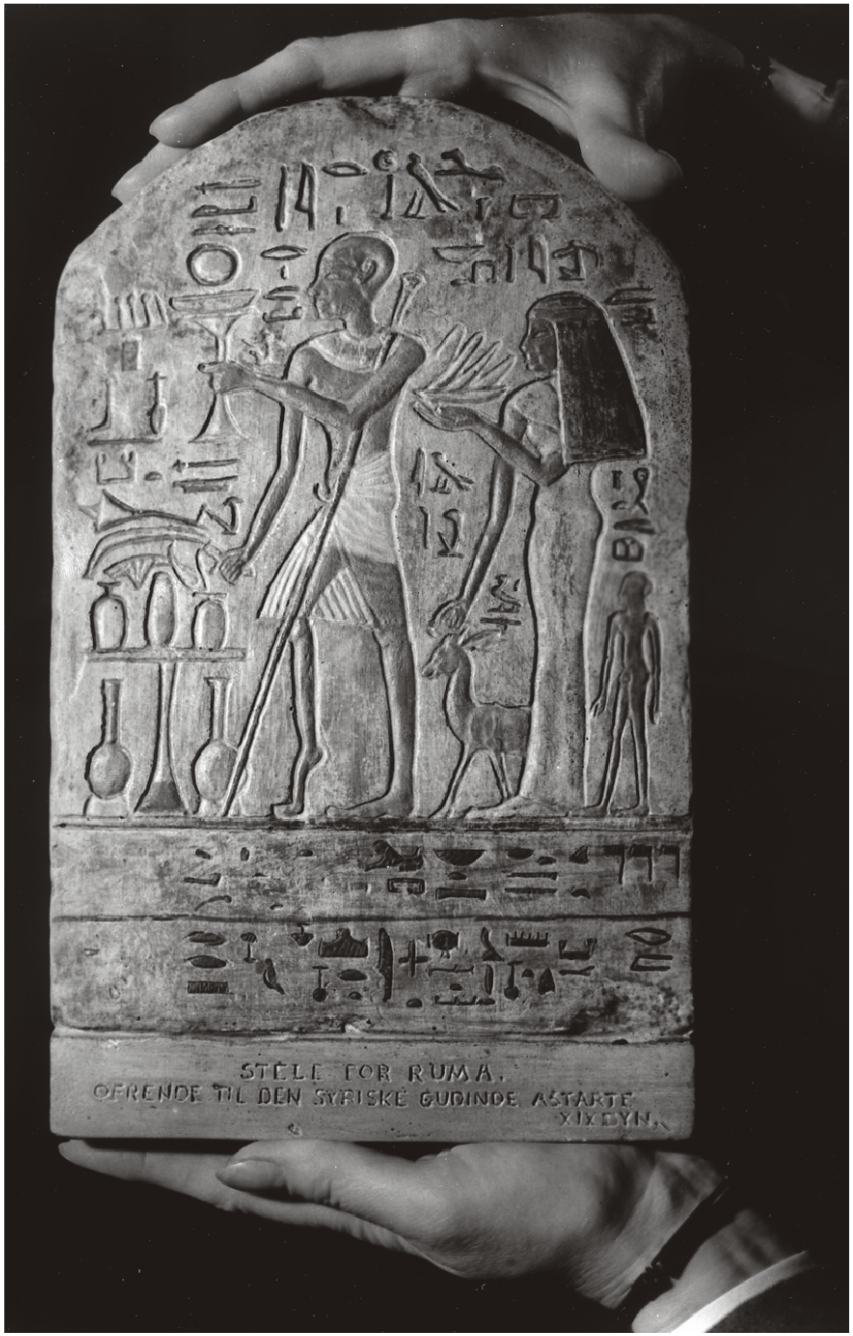
The science of Virology:

origin of Virology

Virus prehistory

Perhaps the first written record of a virus infection consists of a heiroglyph from Memphis, drawn in approximately **1400 BC**, which depicts a temple priest called **Ruma** showing typical clinical signs of paralytic poliomyelitis.

B



The Pharaoh **Siptah** (ruled Egypt from 1200-1193 BC) died suddenly at the age of about 20. His mummified body laid undisturbed in his tomb in the Valley of the Kings until 1905 when the tomb was excavated. The mummy shows that his left leg was withered and his foot was rigidly extended like a horse's hoof – classic paralytic *poliomyelitis*.

In addition, the Pharoh **Ramses V**, who died in **1196 BC**, is believed to have succumbed to *smallpox*.

Viral diseases were treated

•Smallpox was endemic in China and India by 11th century.

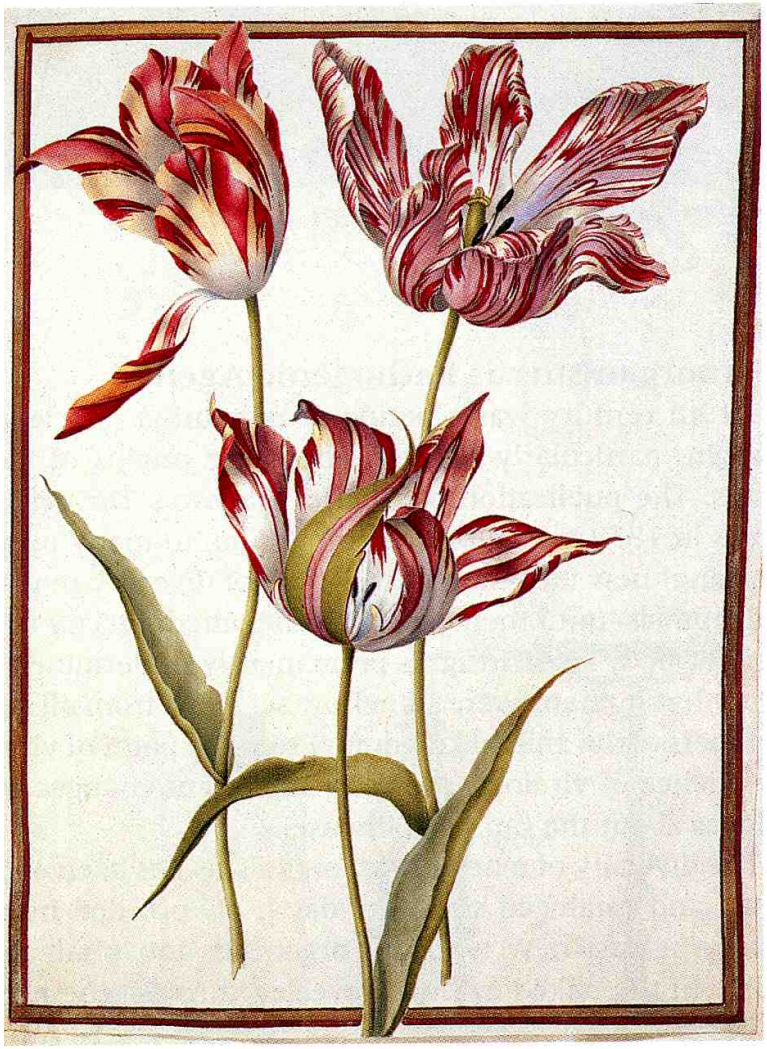
•Recognizing that survivors of smallpox outbreaks were protected from subsequent infection, the practice of **variolation** developed.

• Lady Montagu (1700s).

•Practice survived until last century.

•No knowledge of the causative agent.

Humans manipulate viruses



A painting by N. Robert (1624-1685). Striping patterns (color breaking) in tulips were described in 1576 in western europe and were caused by a viral infection (TMV, tulip mosaic virus)

Vaccines were developed

•On 14th May 1796, **Edward Jenner** used cowpox-infected material obtained from the hand of Sarah Nemes, a milkmaid from to vaccinate 8 year old James Phipps.

•On 1st July 1796, Jenner challenged the boy by deliberately inoculating him with material from a real case of smallpox!

He did not become infected!

The virus concept

•On 12th February 1892, **Dmitri Ivanovsky**, a Russian botanist, presented a paper to the St. Petersburg Academy of Science which showed that extracts from diseased tobacco plants could transmit disease to other plants after passage through ceramic filters fine enough to retain the smallest known bacteria (“filterable infectious agent”).

•Unfortunately, Iwanowski did not fully realize the significance of these results (not a distinctive infectious agents).

•In **1898**, **Martinus Beijerinick** confirmed and extended Iwanowski's results on tobacco mosaic virus.

•He was the first to develop the modern idea of the virus, as contagious element, which he referred to as ***contagium vivum fluidum*** ('soluble living germ').

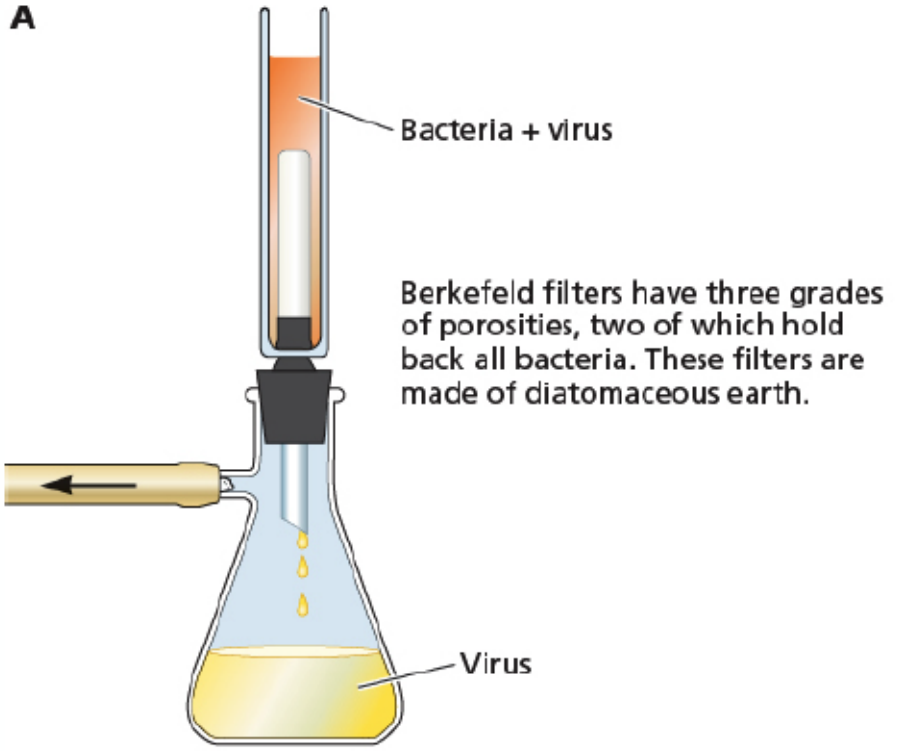
•This is generally recognised as the beginning of **Virology**.

•A new category of **ultrafiltrable**, **ultravisible** and **uncultivable** infectious agents were thus defined.

Virus discovery – filterable infectious agents

Lesions induced by Tobacco Mosaic Virus (TMV) on an infected tobacco leaf

An earliest filter (1891) probalbly used by Ivanosky, Loeffler and Frosch, to isolate the first plant and animal viruses



The virus concept

•Also in 1898, **Freidrich Loeffler** and Paul Frosch showed that a similar agent was responsible for foot-and-mouth disease in cattle (FMDV).

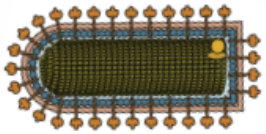
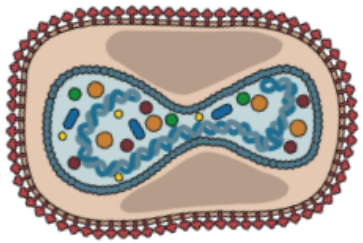
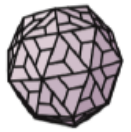
•Thus these new agents caused disease in animals as well as plants.

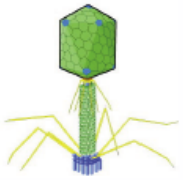
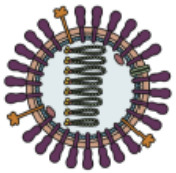
•In spite of these findings, there was resistanc
that these mysterious agents might have anythi
human diseases.

•**Frederick**
d'Herelle (in
viruses whic
called *bacteriophages*. In the 1930s &
subsequent decades, pioneering virologists such as Luria, Delbruck and many others utilized these viruses as model systems to investigate many aspects of virology, including virus structure, genetics, replication.

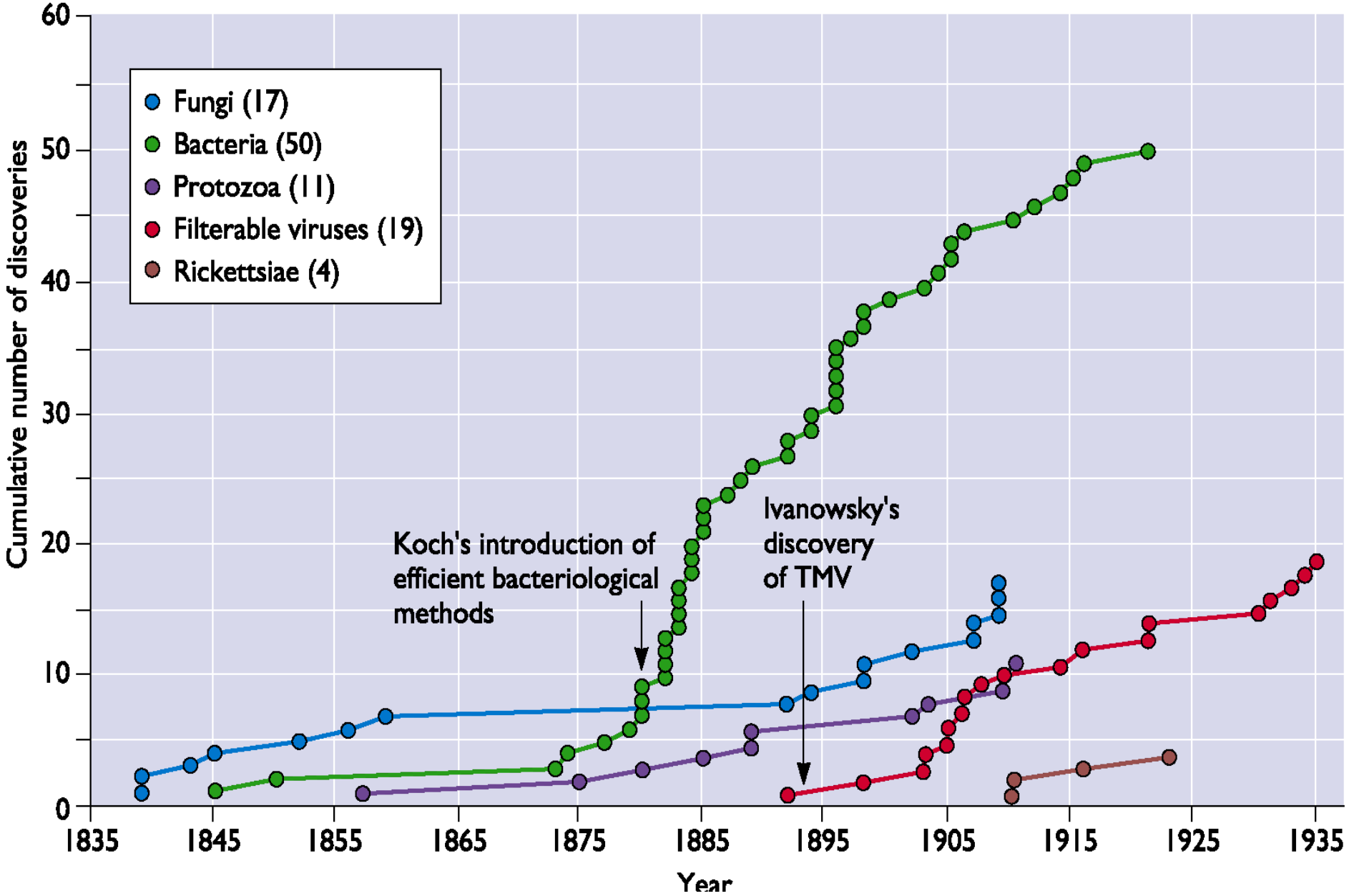
Virus Discovery

- 1901 - first human virus, yellow fever virus
- 1903 - rabies virus
- 1906 - variola virus
- 1908 - chicken leukemia virus, poliovirus
- 1911 - Rous sarcoma virus
- 1915 - bacteriophages
- 1933 - influenza virus

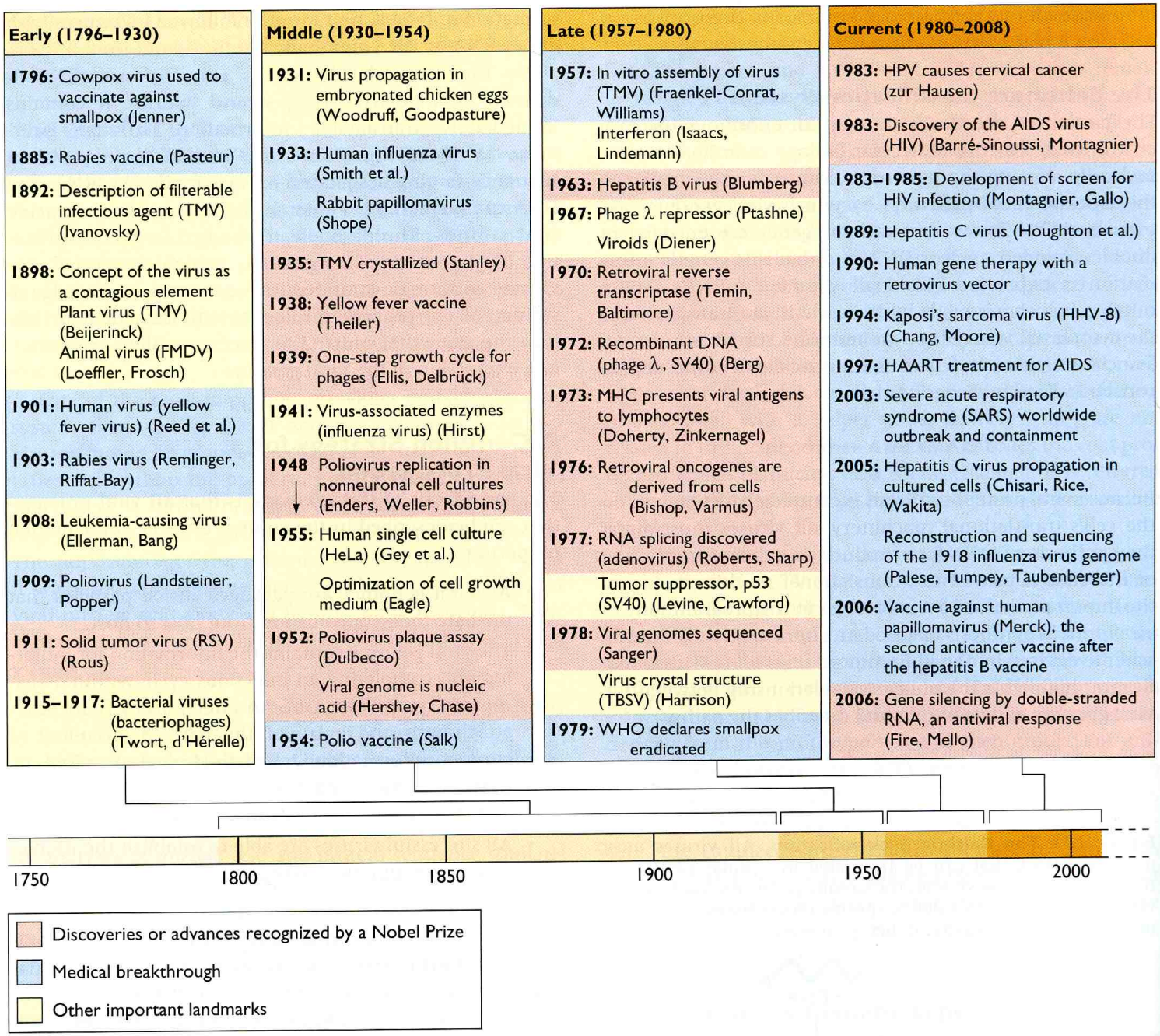





Discovery of new infectious agents in humans



Landmarks in the study of animal viruses (1796-2008)



Nobelprize.org

The Official Web Site of the Nobel Prize

1901 2010

2008

Sort and list Nobel Prizes and Nobel Laureat

Prize category: Medicine

The Nobel Prize in Physiology or Medicine 2008

Harald zur Hausen, Françoise Barré-Sinoussi, Luc Montagnier

The Nobel Prize in Physiology or Medicine 2008

Nobel Prize Award Ceremony

Harald zur Hausen

Françoise Barré-Sinoussi

Luc Montagnier

Photo: U. Montan

Harald zur Hausen

Photo: U. Montan

Françoise Barré-Sinoussi

Photo: U. Montan

Luc Montagnier

The Nobel Prize in Physiology or Medicine 2008 was divided, one half awarded to Harald zur Hausen *"for his discovery of human papilloma viruses causing cervical cancer"*,the other half jointly to Françoise Barré-Sinoussi and Luc Montagnier *"for their discovery of human immunodeficiency virus"*.

TUTTOSCIENZE

L'evento

GABRIELE BECCARIA

Un meeting tra paure e speranze

Cattive notizie dentro un involucro proteico». Ecco il ritratto dei virus, secondo il Nobel Peter Medawar.

Spesso citati a sproposito, motori di pandemie e metafore delle angosce collettive, dall'Aids fino ai disastri informatici, sono tanto popolari quanto sconosciuti. Proviamo a darci una spiegazione secca della loro natura e inciamperemo nelle contraddizioni di entità «monche» che hanno bisogno di un organismo ospite per replicarsi. Non è facile capire che cosa siano e anche agli scienziati fanno perdere il sonno: ne hanno classificati sì e no 5 mila, ma si pensa che esistano milioni di tipi diversi.

Dopo gli allarmi della Sars e dell'influenza A e mentre si moltiplicano le ricerche sui pericoli dei virus emergenti, la certezza è che ora sono arrivati al centro dell'attenzione e ci resteranno a lungo: la società globalizzata è l'habitat ideale per le loro metamorfosi e per la Grande Scienza dei team interdisciplinari si tratta di un'occasione unica di studio. E non solo. Dovrà dare risposte più efficaci per scongiurare possibili scenari catastrofici.

La verità è che di questi frammenti di materiale genetico siamo fragili ostaggi, per lo più inconsapevoli: ecco il tema della «Sesta Conferenza Mondiale sul Futuro della Scienza» che si apre il 19 settembre a Venezia. Un gruppo di scienziati, tra cui gli «ex nemici» Luc Montagnier e Robert Gallo, ha risposto all'invito di Umberto Veronesi e in questo meeting - intitolato «Virus: il nemico invisibile» - spiegherà perché temerli, come difenderci e come piegarli ai nostri scopi. Anche stavolta la scienza «sposta un po' più in là i confini dell'ignoranza» e ci provoca con un mix di paura e di speranza.

TUTTOSCIENZE
MERCOLEDÌ 15 SETTEMBRE 2010
NUMERO 1424

A CURA DI:
GABRIELE BECCARIA
REDAZIONE:
GIORDANO STABILE
tuttoscienze@lastampa.it
www.lastampa.it/tuttoscienze/

Virus: viaggio al centro di tutti i misteri

Così i nemici più temibili dell'uomo possono essere trasformati in amici

UMBERTO VERONESI

Nel 1969 il «Surgeon General» degli Stati Uniti annunciò che l'epoca delle malattie infettive era finita: i vaccini avevano risolto epidemie come il vaiolo (che aveva causato 120 milioni di morti nel secolo precedente) e la poliomielite, gli antibiotici avevano eliminato le malattie batteriche. Fu un sogno da cui ci risvegliammo bruscamente quando, 15 anni dopo, si scoprì l'esistenza di nuovo virus mortale, l'HIV. La sfida all'AIDS e il susseguirsi di allarmi-pandemie ha riportato i virus sulla scena scientifica e sociale e la Conferenza di Venezia, che si aprirà domenica prossima, mette in evidenza quanto il risveglio è stato potente.

Abbiamo indagato sull'origine di queste entità biologiche, sfuggenti ed indefinite, presenti a miliardi nel Pianeta; abbiamo imparato a difenderci dalla loro rinnovata minaccia con vaccini biotech, sicuri al 100%; addirittura abbiamo iniziato a sfruttare le loro caratteristiche straordinarie per curare alcune delle malattie più gravi. Ma il fermento non basta e, se vogliamo in futuro scacciare per sempre l'incombente paura dei virus, l'interesse scientifico e popolare deve essere rifocalizzato e sviluppato nelle nuove direzioni che la scienza stessa ha dischiuso con le conoscenze sul DNA.

Abbiamo scoperto, per esempio, che anche se l'origine dei virus rimane misteriosa, sono i grandi motori dell'evoluzione. Passando da un organismo vivente all'altro, sono uno stimolo continuo al cambiamento e i frammenti di materiale genetico che trasportano

Chi è Umberto Veronesi

RUOLO: ONCOLOGO, E' DIRETTORE SCIENTIFICO DELL'ISTITUTO EUROPEO DI ONCOLOGIA E IDEATORE DELLA FONDAZIONE CHE PORTA IL SUO NOME
IL SITO: HTTP://WWW.FONDAZIONEVERONESI.IT/INDEX.PHP

nel loro passaggio dentro e fuori le cellule possono lasciare tracce perenni. In particolare una famiglia di virus (i retrovirus) ha la capacità di integrare le sue informazioni genetiche con quelle dell'organismo «ospitante», creando un copia di DNA (chiamata provirus) che viene ereditata come parte del patrimonio genetico di tutti i discendenti dell'organismo in cui è avvenuta l'integrazione. Nel genoma umano ci sono circa 80 mila provirus (nessuno attivo, come avviene in altre specie animali), che ci possono dare informazioni preziose sulla nostra storia. Sono stati trovati provirus nella stessa posizione che hanno nel DNA dello scimpanzé. Il che conferma non solo la nostra indubbia discendenza dalla scimmia, ma anche che quel provirus ha almeno 5 milioni di anni.

E' affascinate pensare che cosa ancora potremmo scoprire sull'uomo, studiando le impronte genetiche «virali» nel suo DNA. Nel presente, la conoscenza dei geni e la possibilità di spostarli da un organismo all'altro ci ha dato nuove armi per difenderci dai virus: i vaccini moderni, ottenuti con il DNA ricombinante, utilizzano solo la proteina con potere immunizzante invece che tutta la molecola virale, con il suo potere infettivo. Viene così azzerato il rischio di sviluppare la malattia contro cui ci si vaccina. Anzi, oggi stiamo studiando forme di vaccinazione ancora più innovative: inserendo in piante o in frutti alcune molecole i cui geni sono stati modificati, sono stati creati cibi-vaccino che costano 50 volte di meno rispetto al farmaco e sono facili da somministrare. Se poi il cibo è trasformato in omogeneizzato, si risolvono molti problemi di conservazione, perché non è necessaria la catena del freddo.

Per ora la banana-vaccino è stata sperimentata per proteggere da un batterio, l'enterocolite, ma il principio è lo stesso per un virus. Negli Stati Uniti, quando nel 2001 ci fu il panico per l'attacco bioterroristico per posta, si è studiata invece l'insalata-antiantrace. Creata l'insalata-vaccino, si conservano i semi e in caso di epidemia si piantano e, invece che con farmaci, si protegge la popolazione con la lattuga. Dopo aver imparato ad usare i virus contro loro stessi, stiamo imparando ad usarli contro altre malattie: sono allo studio forme di terapia genica contro l'emofilia, la fibrosi cistica, il diabete, il cancro, il Parkinson's, l'Alzheimer che utilizzano come vettori dei virus «disattivati» che sono molecole ideali, perché nessuna come loro si riproduce velocemente e si integra nelle cellule. L'ultima frontiera sono vettori virali di terza generazione, che possono introdurre geni direttamente nel cervello, il fegato, i muscoli, le staminali emopoietiche e - scoperta recente - nella retina e in alcune cellule tumorali.

Non ho citato - è non è un caso - il bioterrorismo. E' innegabile che i progressi della scienza, in questo campo in particolare, possono essere utilizzati a beneficio dell'umanità, ma anche per la sua distruzione. E' dimostrato che Al Qaeda in Afghanistan studia armi batteriologiche. Questa consapevolezza non può fermare la scienza, ma rende indispensabile la diffusione e il radicamento del suo pensiero. Contro l'uso violento delle applicazioni scientifiche, quale è il bioterrorismo, l'unica arma è il radicamento e la diffusione della cultura scientifica. Occorre promuovere la scienza a tutti i livelli, renderla accessibile a tutti i Paesi e al maggior numero di persone, perché non diventi un privilegio e uno strumento di ricatto, sfruttando il suo potenziale civilizzatore e pacificatore. La Conferenza «The Future of Science» vuole essere un passo in questa direzione.

A Venezia

Dove
«Virus: il nemico invisibile»: è il titolo della Sesta Conferenza Mondiale sul Futuro della Scienza organizzata a Venezia dalle fondazioni «Umberto Veronesi», «Silvio Tronchetti Provera» e «Giorgio Cini».

Quando
Dal 19 al 21 settembre, alla «Fondazione Giorgio Cini» sull'Isola di San Giorgio Maggiore.

Informazioni
Sul sito http://www.thefutureofscience.org/.