

Nou coronavirus: qui t'avisa no et vol mal

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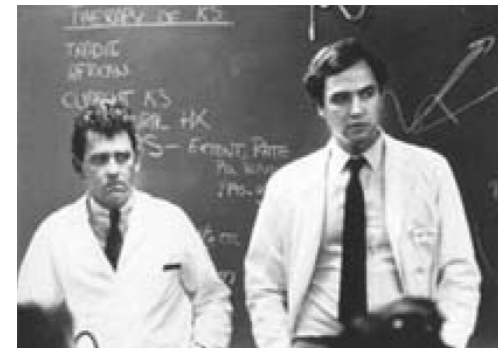
F.Xavier.Lopez@uv.es



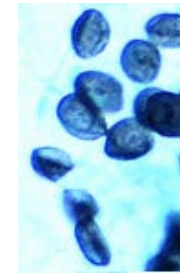
Començament dels 1980s: signes alarmants d'una nova epidèmia mundial

Juny 1981

- Identificació de la malaltia als EEUU
- Primeres observacions clíniques i epidemiològiques de pneumònia per *Pneumocystis carinii* i de sarcoma de Kaposi en homes homosexuals a EEUU (CDC, *MMWR Weekly*)



Drs. Conant i Volberg, CDC



Pneumònia per *Pneumocystis carinii* (jiroveci)



Sarcoma de Kaposi (HHV-8)

1982

- Descripció de l'acrònim AIDS "acquired immunodeficiency syndrome".
- Primers cassos de SIDA en pacients que han rebut transfusions de sang
- Primers cassos de SIDA en dones, infectades per transmissió heterosexual.

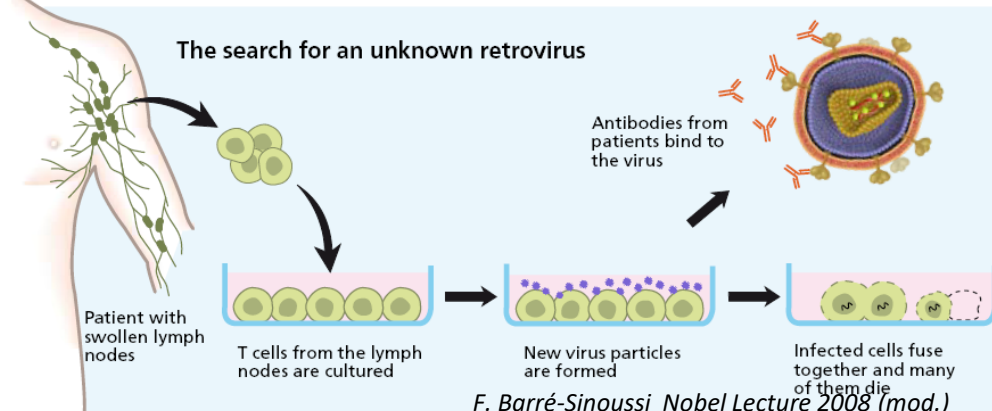
Desembre 1982

- Mobilització dels viròlegs de l'Institut Pasteur (i d'arreu)

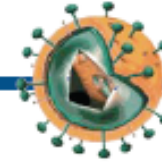
**Group of the Viral Oncology Unit
(L.Montagnier, F.Barré-Sinoussi,
J-C. Chermann)**

↓

**Biopsy of a lymph node from a gay men,
Lymphocytes put in culture (Protein A, IL2)**



Diversitat i origen del VIH



→ **HIV-1
group N**

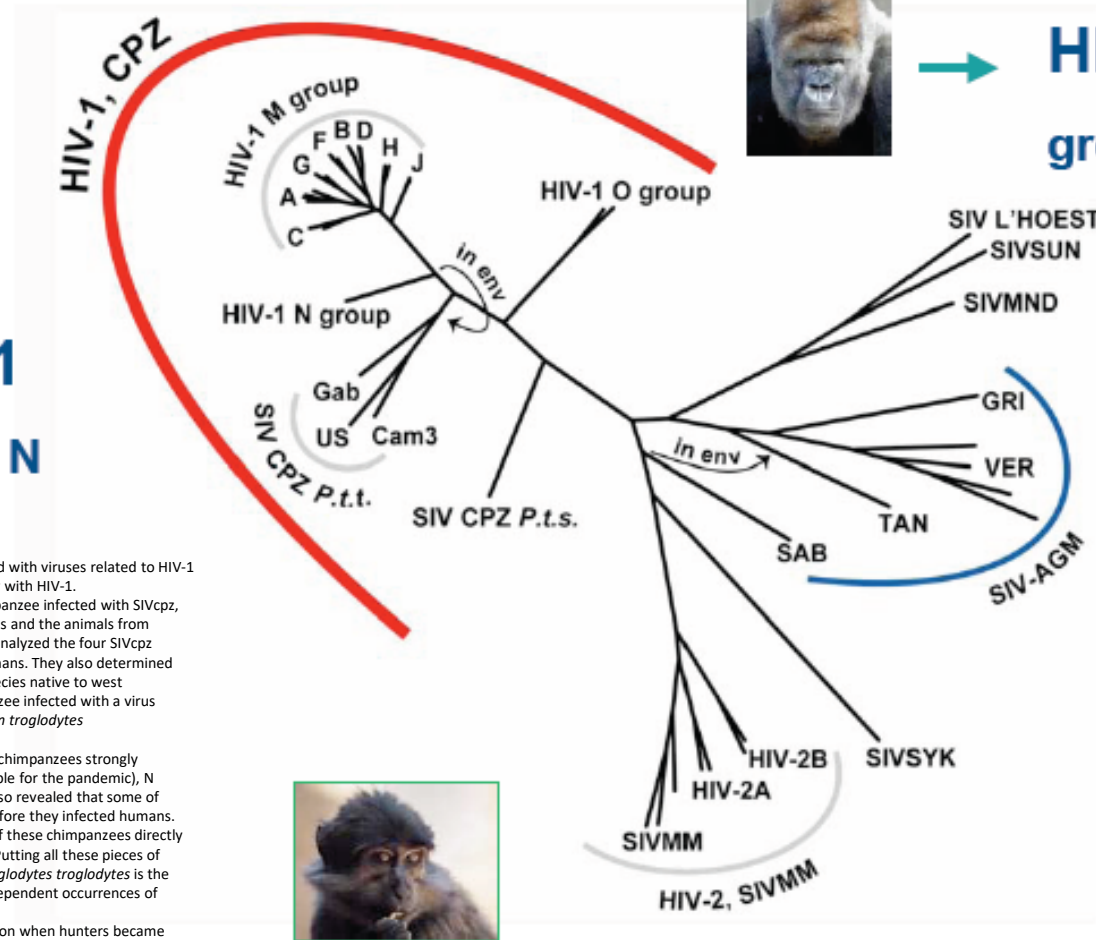
HIV descended from a primate species, only three chimpanzees infected with viruses related to HIV-1 had been documented, and one of these viruses correlated only weakly with HIV-1.

When Dr. Hahn and her collaborators recently identified a fourth chimpanzee infected with SIVcpz, they decided to use this opportunity to carefully examine all four viruses and the animals from which they were derived. With sophisticated genetic techniques, they analyzed the four SIVcpz isolates and compared them with various HIV-1 viruses taken from humans. They also determined the subspecies identity of the chimpanzees: three belonged to a subspecies native to west equatorial Africa, *Pan troglodytes troglodytes*. The fourth, the chimpanzee infected with a virus most unlike HIV-1, belonged to an east African subspecies known as *Pan troglodytes schweinfurthii*.

As it turns out, the three isolates from the *Pan troglodytes troglodytes* chimpanzees strongly resemble the different subgroups of HIV-1, namely groups M (responsible for the pandemic), N and O (both found only in west equatorial Africa). Their investigation also revealed that some of the viruses resulted from genetic recombination in the chimpanzees before they infected humans. Their other significant find, Dr. Fauci notes, is that the natural habitat of these chimpanzees directly coincides with the pattern of the HIV-1 epidemic in this area of Africa. Putting all these pieces of the puzzle together, Dr. Hahn and her colleagues conclude that *Pan troglodytes troglodytes* is the natural reservoir of HIV-1 and has been the source of at least three independent occurrences of cross-species virus transmission events from chimpanzees to humans.

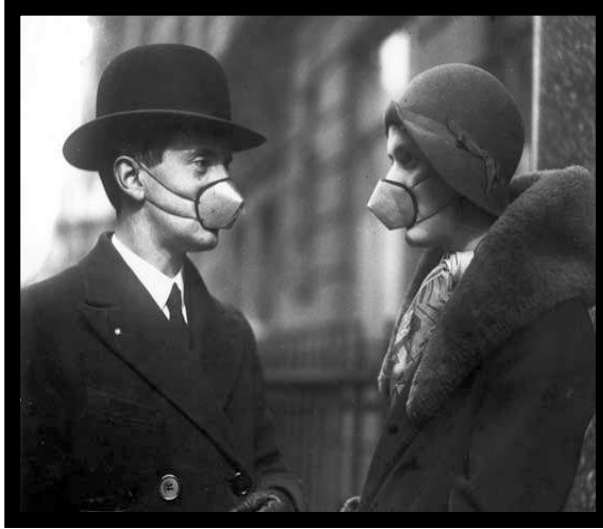
The authors believe that HIV-1 was introduced into the human population when hunters became exposed to infected blood. Furthermore, they speculate that humans might still be at risk for crossspecies transmission because the bushmeat trade – the hunting and killing of chimpanzees and other endangered animals for human consumption – is still common practice in west equatorial Africa.

F. Barré-Sinoussi Nobel Lecture 2008



→ **HIV-2**

1918-1919: Pandèmia de grip, 40-100 millions de morts



Pandèmies i introduccions de nous virus de la grip A

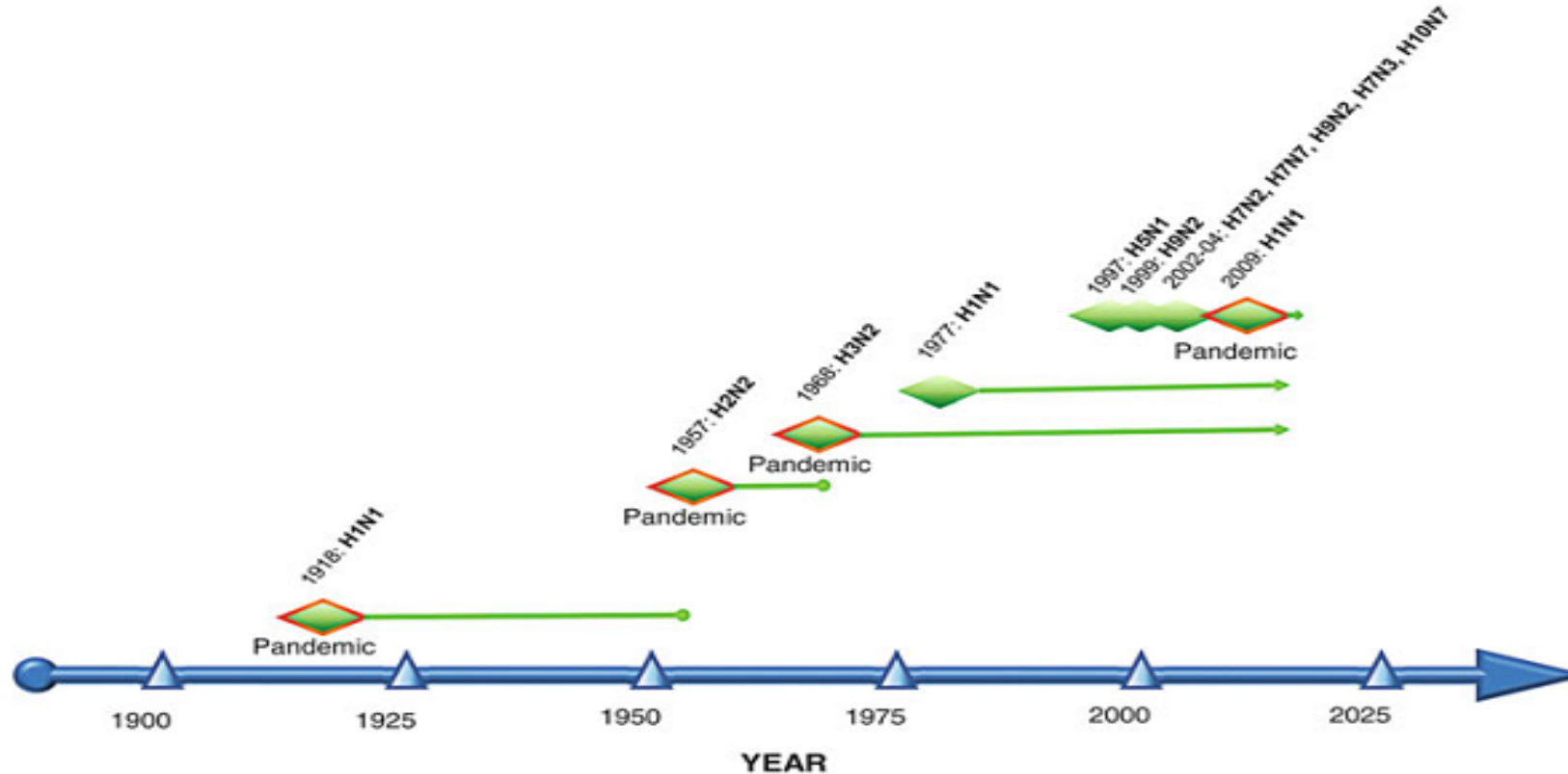
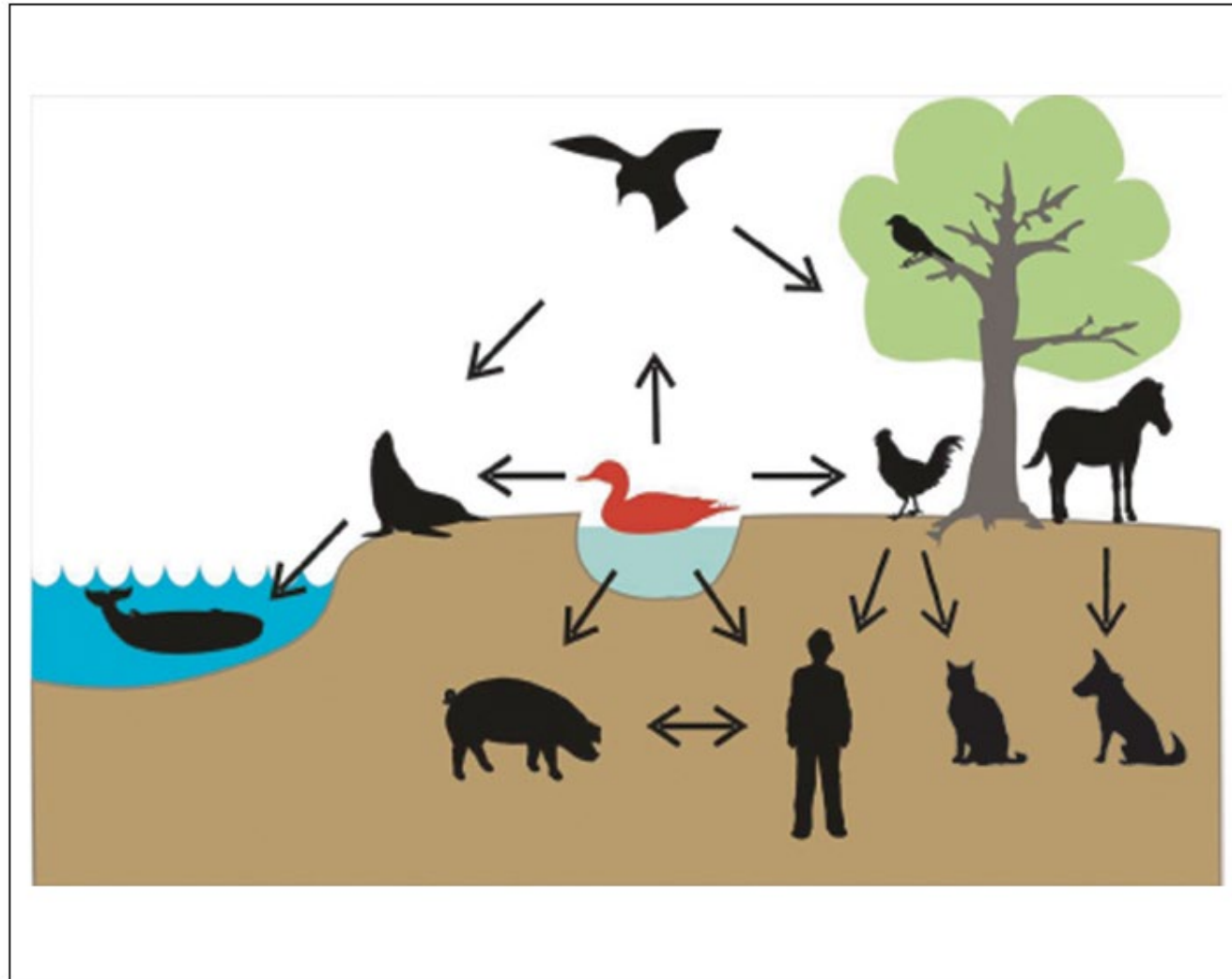


Fig. 4 Influenza A virus subtypes in humans. Three pandemics occurred during the twentieth century, including the “Spanish” influenza pandemic of 1918, the “Asian” pandemic in 1958, and the “Hong Kong” pandemic in 1968. H1N1 viruses re-emerged in 1977 and continue to circulate in the human population, along with the H3N2 subtype. In addition, H5N1 viruses have been reported to infect humans throughout Asia and Africa. Several other avian viruses have also recently caused sporadic infection in humans. A swine-origin influenza virus (pandemic influenza A H1N1 2009 virus) emerged during the spring of 2009 and spread globally, inciting the World Health Organization to declare a pandemic in June of 2009. Adapted from [68]

El reservori de la grip A són els ocells aquàtics



La pandèmia de grip A H1N1 2009 va ser provocada per *antigenic SHIFT* a causa d'un triple reordenament

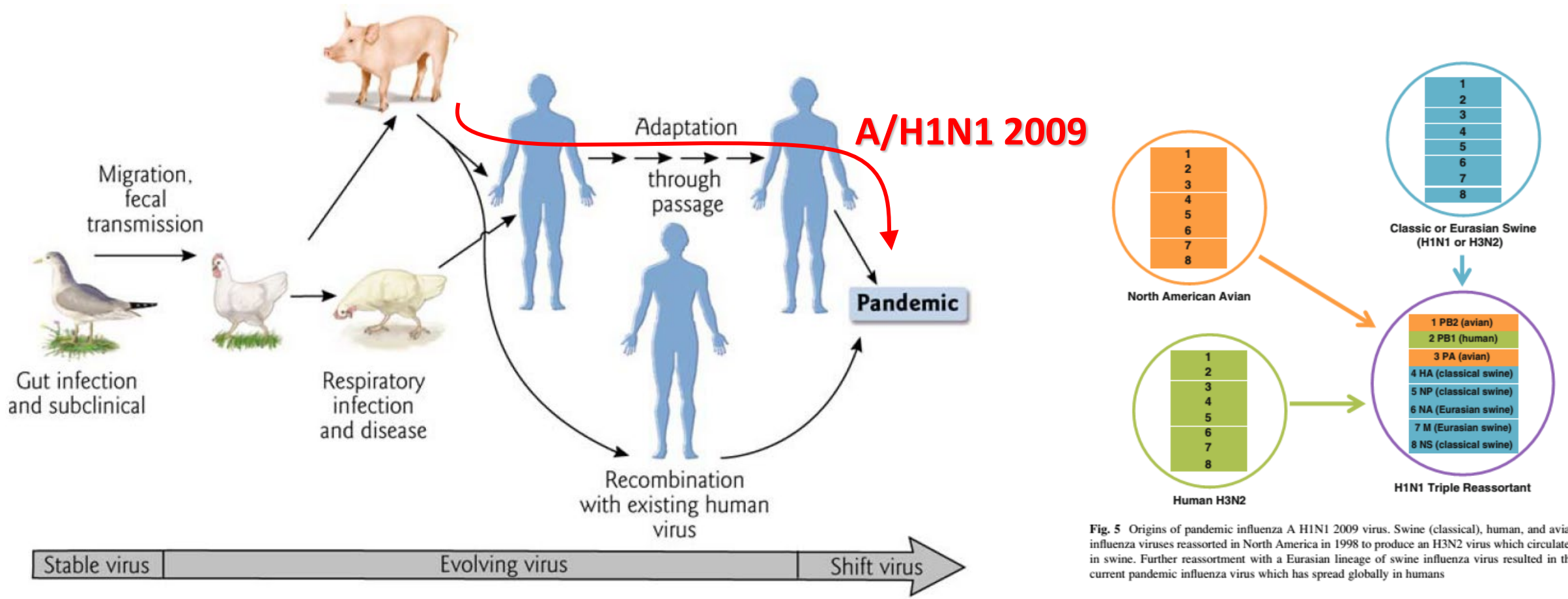
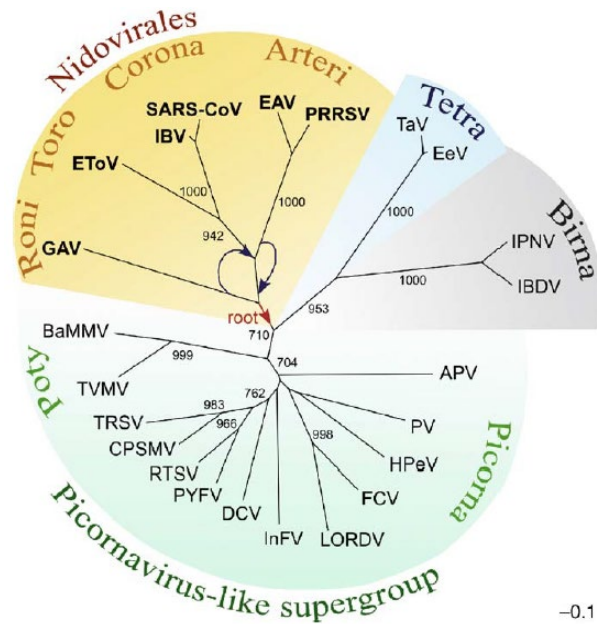
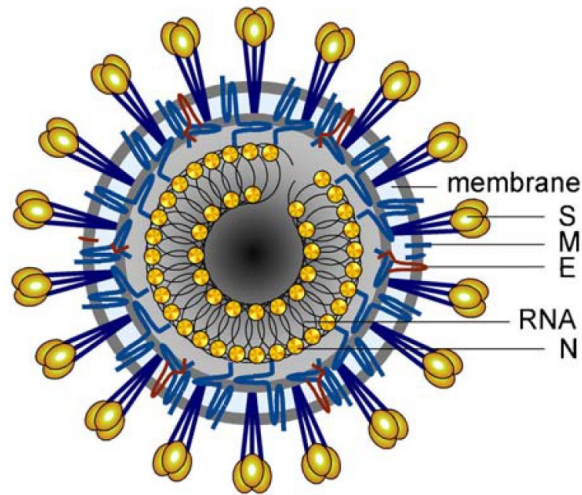


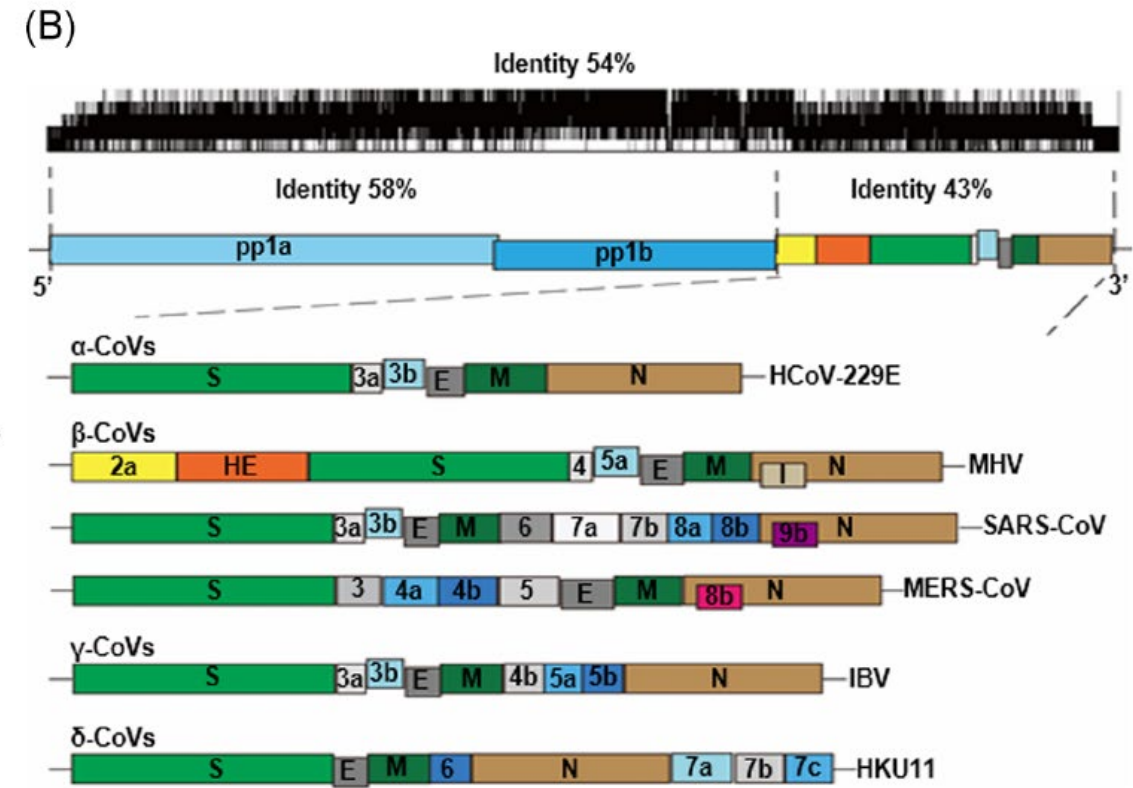
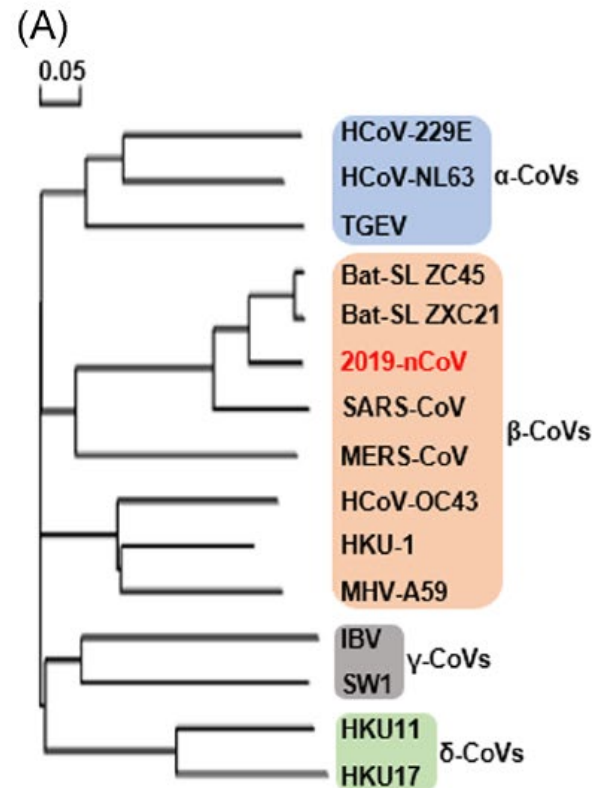
Fig. 5 Origins of pandemic influenza A H1N1 2009 virus. Swine (classical), human, and avian influenza viruses reassorted in North America in 1998 to produce an H3N2 virus which circulated in swine. Further reassortment with a Eurasian lineage of swine influenza virus resulted in the current pandemic influenza virus which has spread globally in humans

Coronavirus



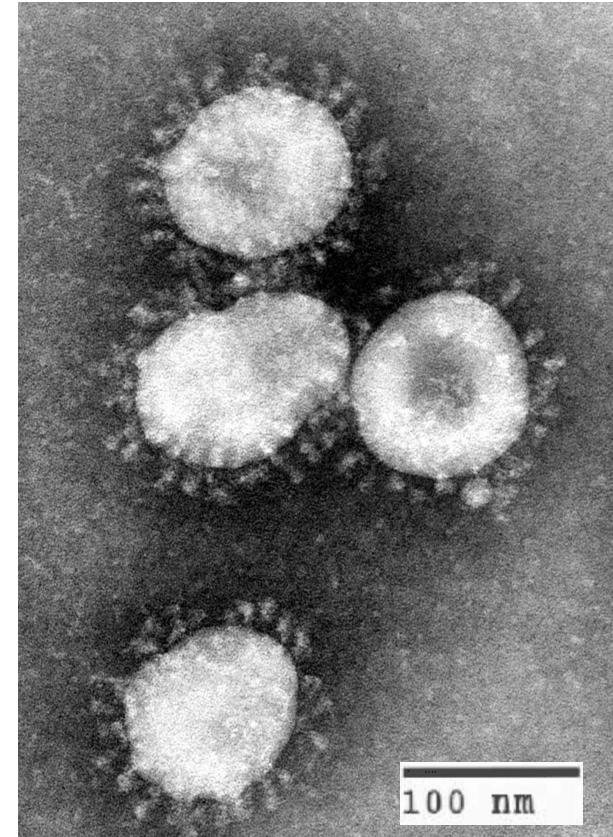
A.E. Gorbalenya et al. / Virus Research 117 (2006) 17–37

Coronaviridae



Primer avís: SARS – *Severe Acute Respiratory Syndrome*

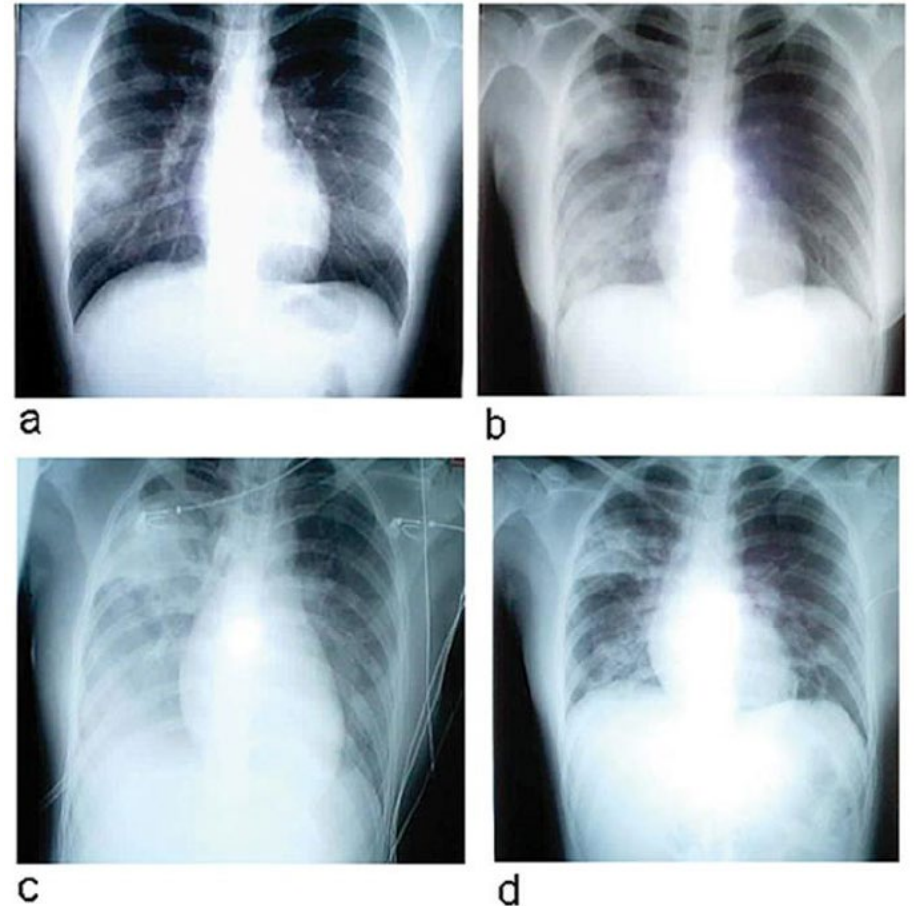
- **Produït per un beta-coronavirus, llinatge B**
- **Detectat en 2003**
- Transmissió persona a persona per contacte proper a través de gotetes.
- Important en recintes assistencials. (62–79% de casos).
- 22-39% transmissió entre familiars.
- Letalitat 10%



IBV (cdc.gov)

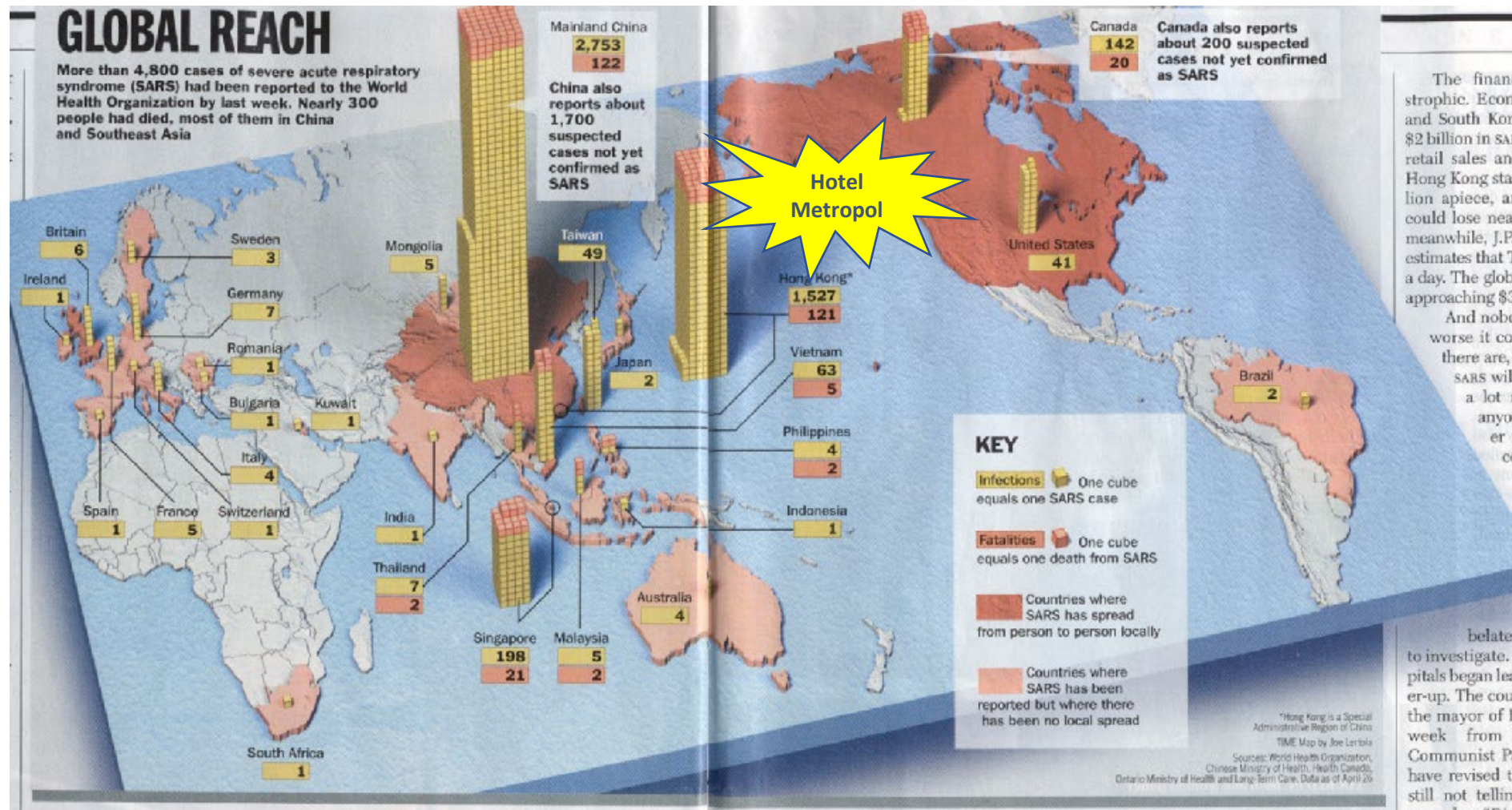
SARS – Severe Acute Respiratory Syndrome

- **Incubació SARS: 2-7 dies (max 14)**
- Febre alta ($>38^{\circ}\text{C}$)
- Cefalea
- Dolor generalitzat
- Síntomes respiratoris moderats
- Diarrea (10-20%)
- Tos seca (passats 2-7 dies)
- Pneumonia
- **Sense tractament específic ni vacuna**



Emerg Infect Dis. 2003 Jun;9(6):713-7.

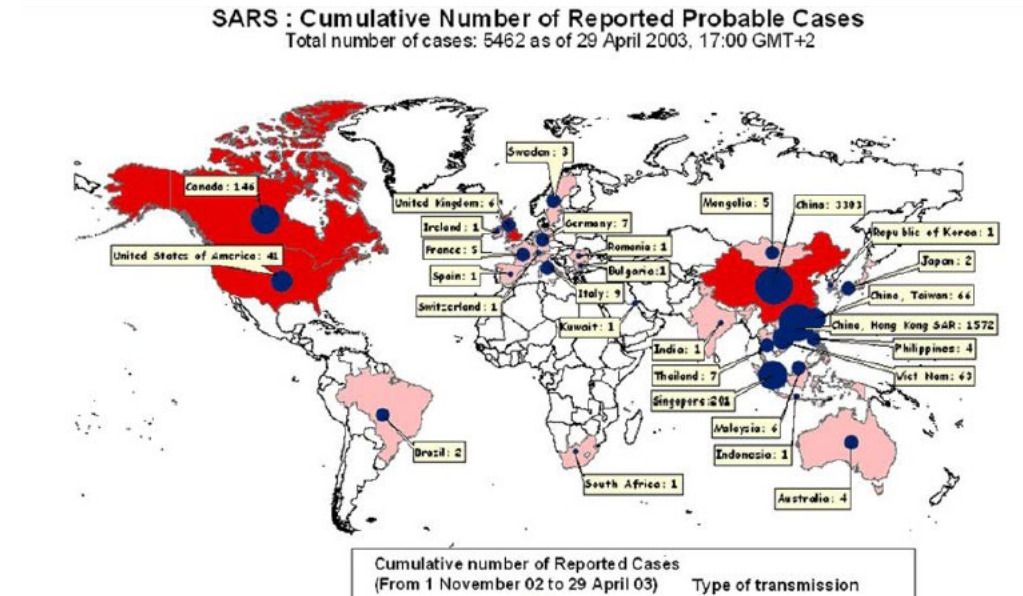
SARS – Severe Acute Respiratory Syndrome

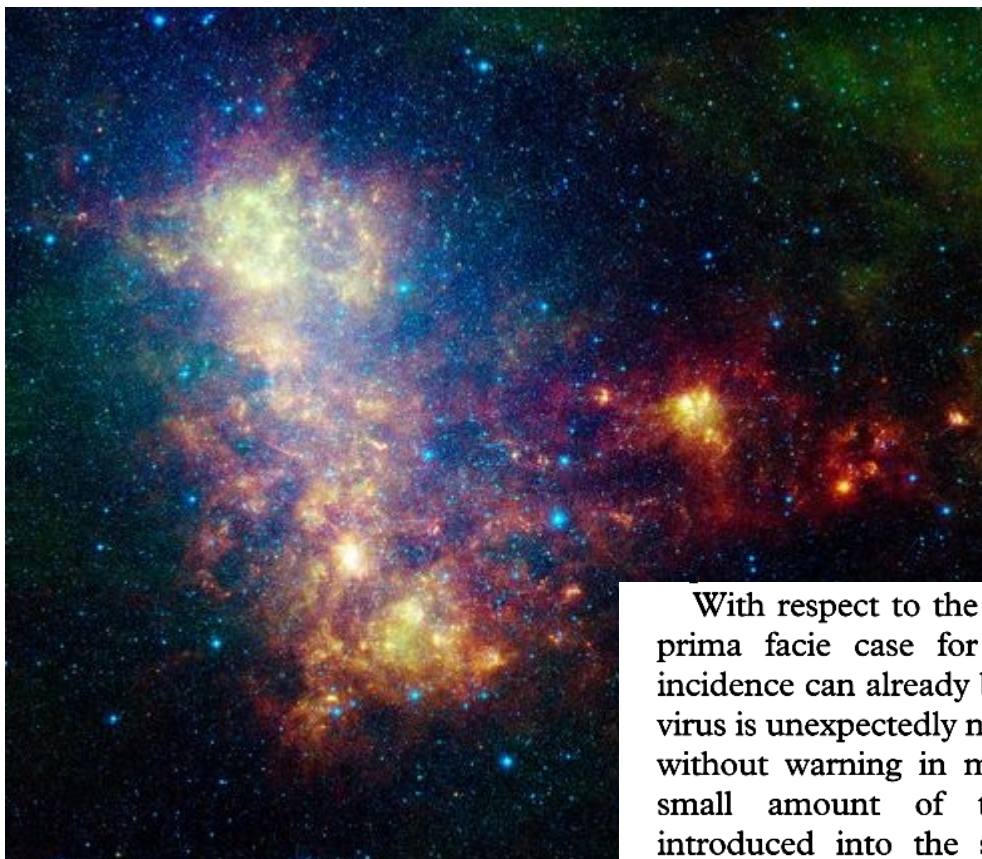


SARS – Severe Acute Respiratory Syndrome

Brot 2003

- Novembre 2002-Juliol 2003
- 8.098 persones, 29 països, 774 morts
- Des 2003 – Gen 2004 -> 5 casos zoonòtics.
- Infecció a laboratoris (2004).
- Publicació del Reglament Sanitari Internacional (2005).





Ens va arribar el SARS de l'espai exterior?

SARS—a clue to its origins?

Sir—We detected large quantities of viable microorganisms in samples of stratospheric air at an altitude of 41 km.^{1,2} We collected the samples in specially designed sterile cryosamplers carried aboard a balloon launched from the

With respect to the SARS outbreak, a prima facie case for a possible space incidence can already be made. First, the virus is unexpectedly novel, and appeared without warning in mainland China. A small amount of the culprit virus introduced into the stratosphere could make a first tentative fall out East of the great mountain range of the Himalayas, where the stratosphere is thinnest, followed by sporadic deposits in neighbouring areas. If the virus is only minimally infective, as it seems to be, the subsequent course of its global progress will depend on stratospheric transport and mixing, leading to a fall out

**Chandra Wickramasinghe, Milton Wainwright, Jayant Narlikar*

**Cardiff Centre for Astrobiology, Cardiff University, Cardiff CF10 3DY, UK (CW); Department of Molecular Biology and Biotechnology, Sheffield University, Sheffield, UK (MW); and Inter-University Centre for Astronomy and Astrophysics, Pune, India (JN)*



Probable cases of SARS by week of onset
Worldwide* (n=5,910), 1 November 2002 - 10 July 2003



* This graph does not include 2,527 probable cases of SARS (2,521 from Beijing, China), for whom no dates of onset are currently available.
Adapted from World Health Organization. Epidemic curves - Severe Acute Respiratory Disease (SARS)
<http://www.who.int/csr/sars/epicurves/epiindex/en/index1.html>

El SARS va ser a zoonosi



Horseshoe bat
Rhinolophus sp



Civet Cat
Paguma larvata

Segon avís: MERS – *Middle East Respiratory Syndrome*

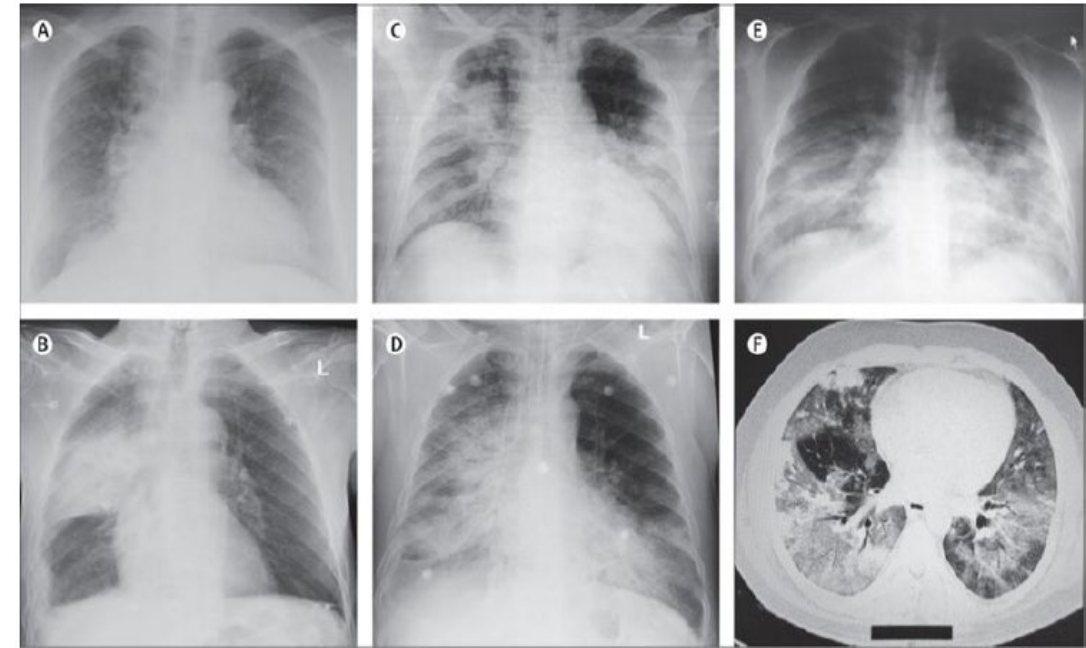
- **Produït per un beta-coronavirus, llinatge C**
- **Detectat al 2012, Arabia Saudita**
- **Transmissió sostinguda entre camèlids**
- Transmissió persona a persona per contacte proper a través de gotetes.
- Important en recintes hospitalaris (43.5–100% dels casos).
- 13–21% transmissió entre familiars



MERS – *Middle East Respiratory Syndrome*

Incubación MERS: 5-6 días (màx 14)

- Febre
- Tos
- Dificultat per respirar
- Diarrea y nausea/vòmits (no sempre)
- Complicacions: pneumonia y fallida renal
- Letalitat associada a presencia de comorbiditats
- Sense tractament específic, ni vacuna



Lancet Infect Dis. 2013 Sep;13(9):752-61.

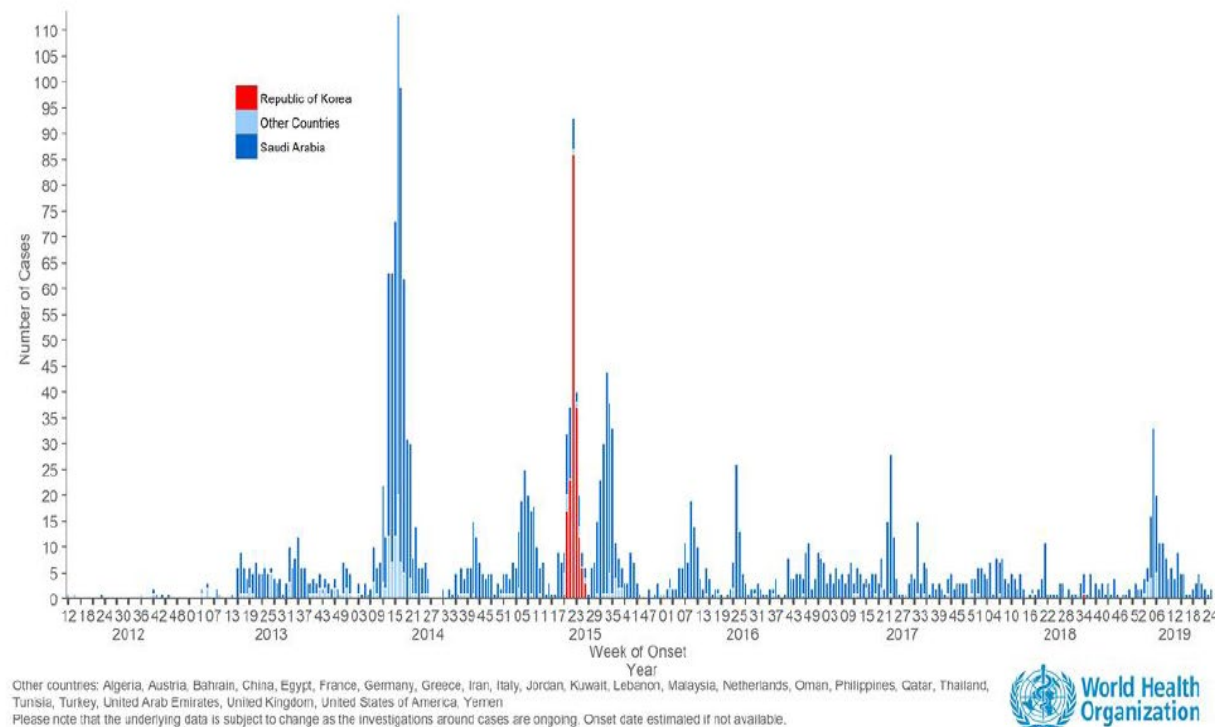
MERS – Middle East Respiratory Syndrome

Brot Corea del Sud Mai 2015-Abr 2016

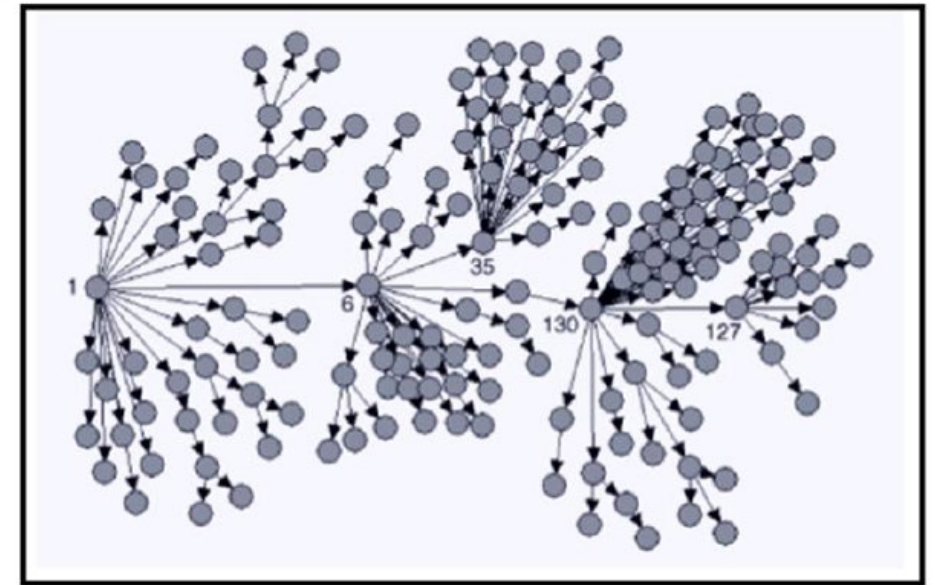
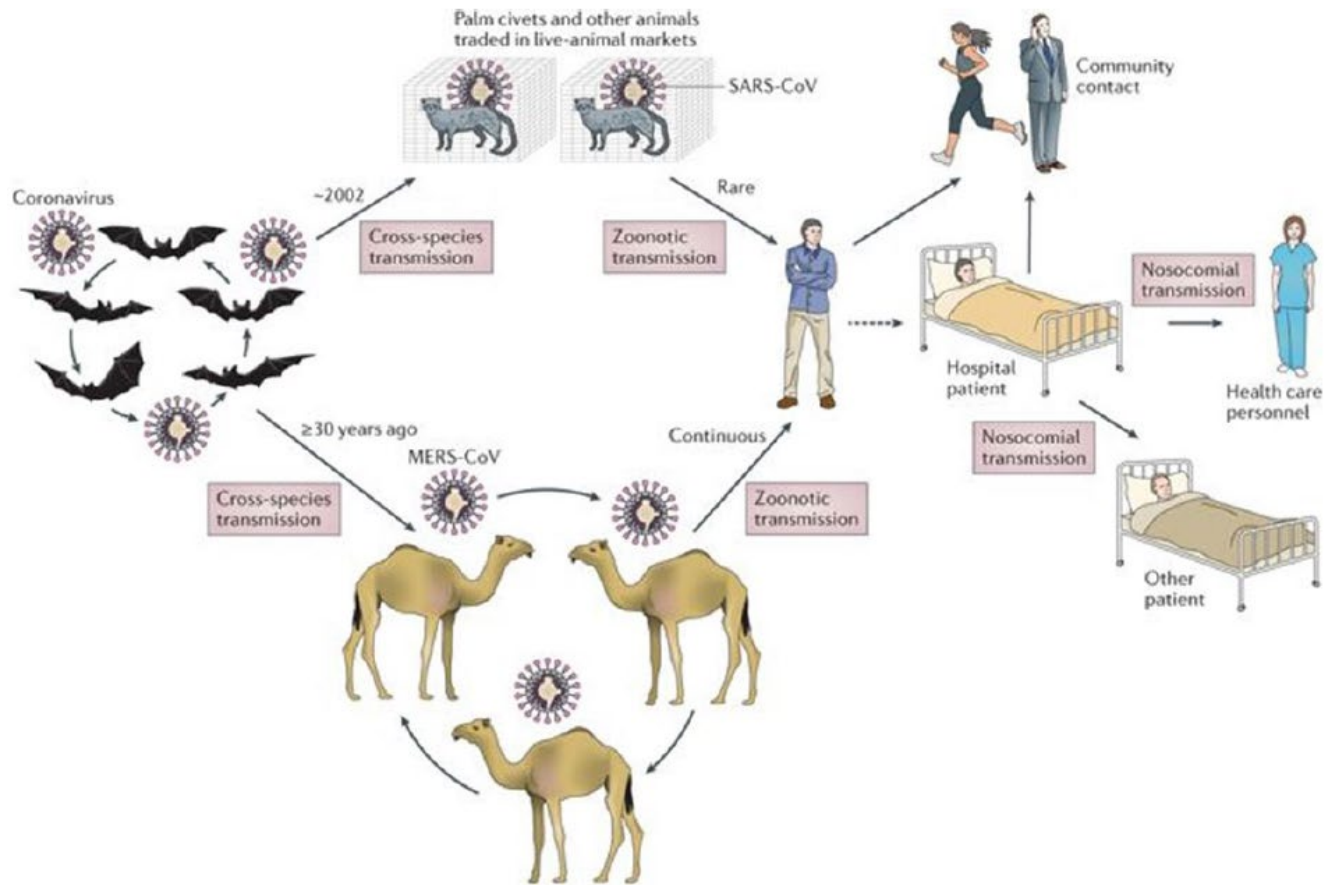
- 16 hospitales, 186 pacientes

2012 a Novembre 2019 (OMS)

- 2.494 casos confirmats, 858 morts (34,4% letalitat), 27 països
- Arabia Saudita: 2.102 casos, 780 morts (37,1% letalitat).



Transmissió SARS y MERS (superdiseminadors)



MMWR Morb Mortal Wkly Rep. 2003 May 9;52(18):405-11.

Nature Reviews | Microbiology

A la tercera...

Nou Coronavirus (SARS-CoV-2)

Brot a la Província de Wuhan, Xina

31 de desembre 2019

- 27 casos de síndrome respiratori, a Wuhan.
- Febre alta, dificultat per respirar y pneumonia.



Li Wenliang
李文亮



Nou Coronavirus (SARS-CoV-2)

- **1 de gen 2020:** Clausura del mercat de Wuhan.
- **7 de gen 2020:** S'identifica el nou coronavirus.
- **10 de gen 2020:** Genoma publicat
- **12 de gen 2020:** Els casos augmenten a **41**. S'informa de la **primera mort**, pacient amb comorbiditats
- **13 de gen 2020:** Primer assaig PCR (C. Dorsten, Berlin)
- **13 de gen:** **Tailandia** reporta el primer cas confirmat. Dona de 61 anys, resident de Wuhan.
- **15 de gen:** **Japó** informa cas amb antecedents de viatge a Wuhan y contacte amb malalt.
- **20 de gen:** **Corea** confirma cas de dona 35 anys resident a Wuhan.
- **21 de gen:** **EEUU** informa un cas a l'estat de Washington, el contagi va ser a Wuhan.



Nou Coronavirus (SARS-CoV-2)

Sintomatologia y quadre clínic

- Tos y dificultat per a respirar
- Febre alta sobre 38 °C
- Síndrome Respiratori Agut Greu
- **Historial de viatge recent a Xina**
- OMS declara alerta global pel nou Coronavirus (31 Gen)
- Recomana revisar respostes a la propagació de virus anteriors, adaptant-les proporcionalment al risc actual.
- OMS declara al virus pandèmic (11 Mar)
- Historial de viatge recent a Xina..... a Irán, a Italia, a Espanya, a Alemanya, a França, a EEUU, a Bèlgica, a Reino Unido....o a qualsevol lloc.....





Search by Country, Territory, or Area



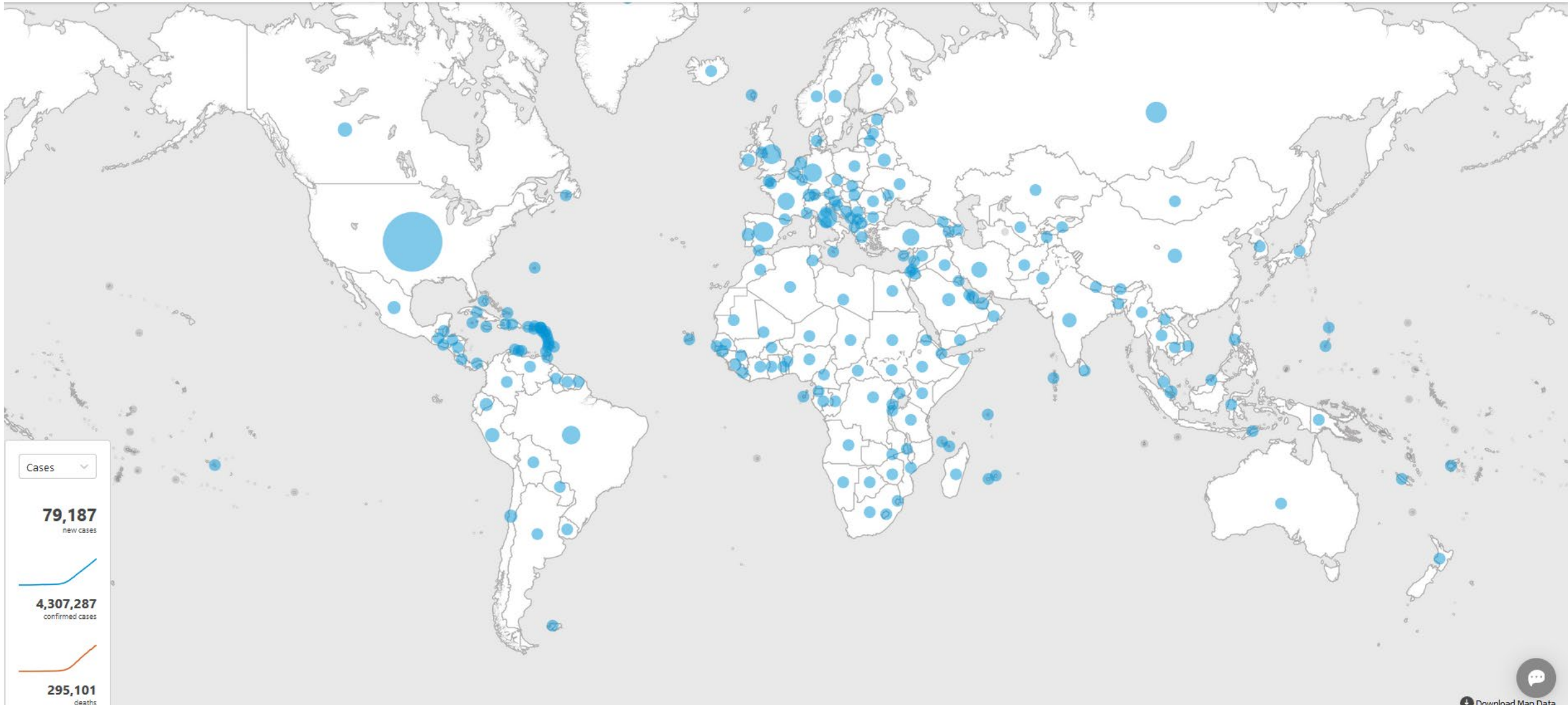
Overview

Explorer

WHO Coronavirus Disease (COVID-19) Dashboard

Data last updated: 2020/5/15, 9:28am CEST

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Coronavirus disease (COVID-19)

Situation Report – 115

Data as received by WHO from national authorities by 10:00 CEST, 14 May 2020

Situation in numbers (by WHO Region)

Total (new cases in last 24 hours)

Globally	4 248 389 cases (77 965)	292 046 deaths (4 647)
Africa	51 752 cases (2 323)	1 567 deaths (67)
Americas	1 819 553 cases (37 989)	109 121 deaths (2 617)
Eastern Mediterranean	293 805 cases (9 535)	9 389 deaths (130)
Europe	1 801 668 cases (21 352)	161 413 deaths (1 614)
South-East Asia	116 617 cases (5 685)	3 921 deaths (175)
Western Pacific	164 282 cases (1 081)	6 622 deaths (44)



Search by Country, Territory, or Area



Overview

Explorer

WHO Coronavirus Disease (COVID-19) Dashboard

Data last updated: 2020/5/15, 9:23am CEST

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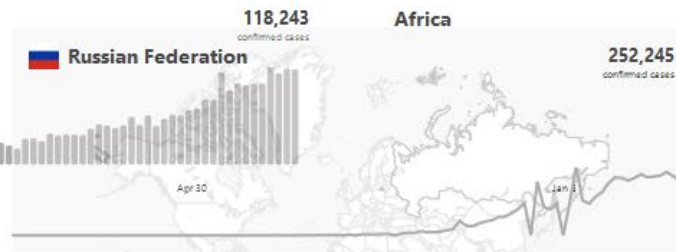
Source: World Health Organization

Highest Cases

By Country, Territory, or Area

Confirmed Cases

South-East Asia

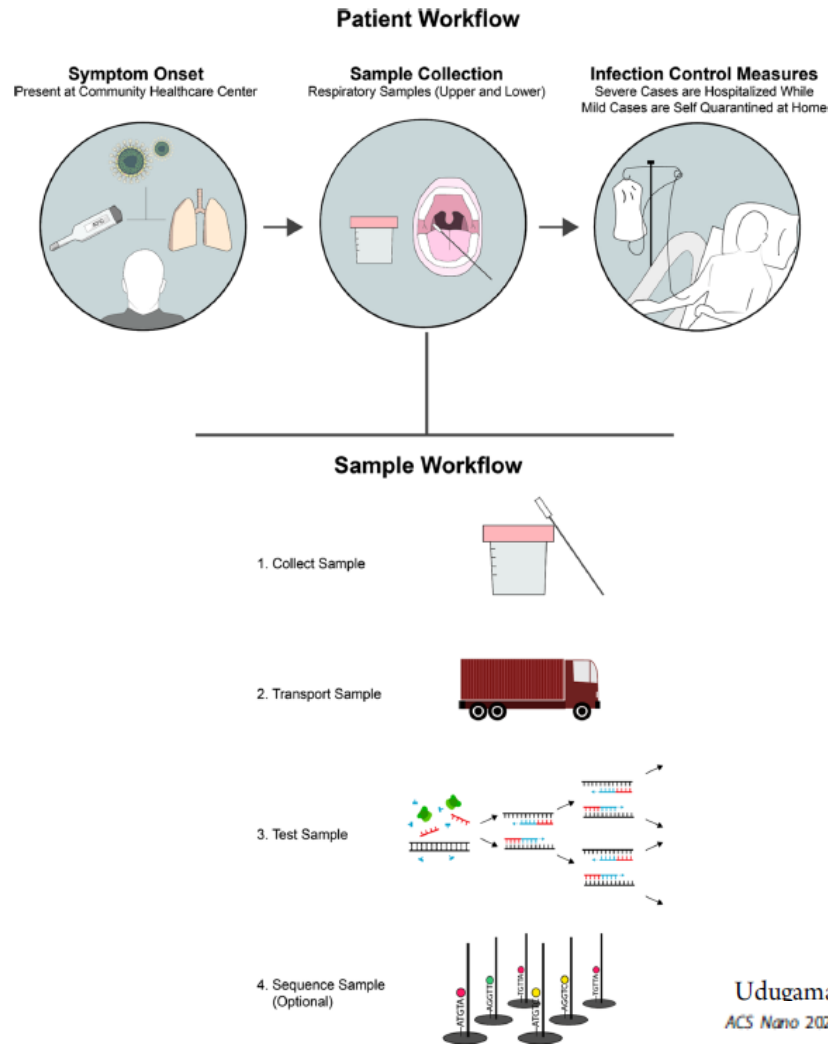


Tests for SARS-CoV-2/COVID-19 and Potential Uses

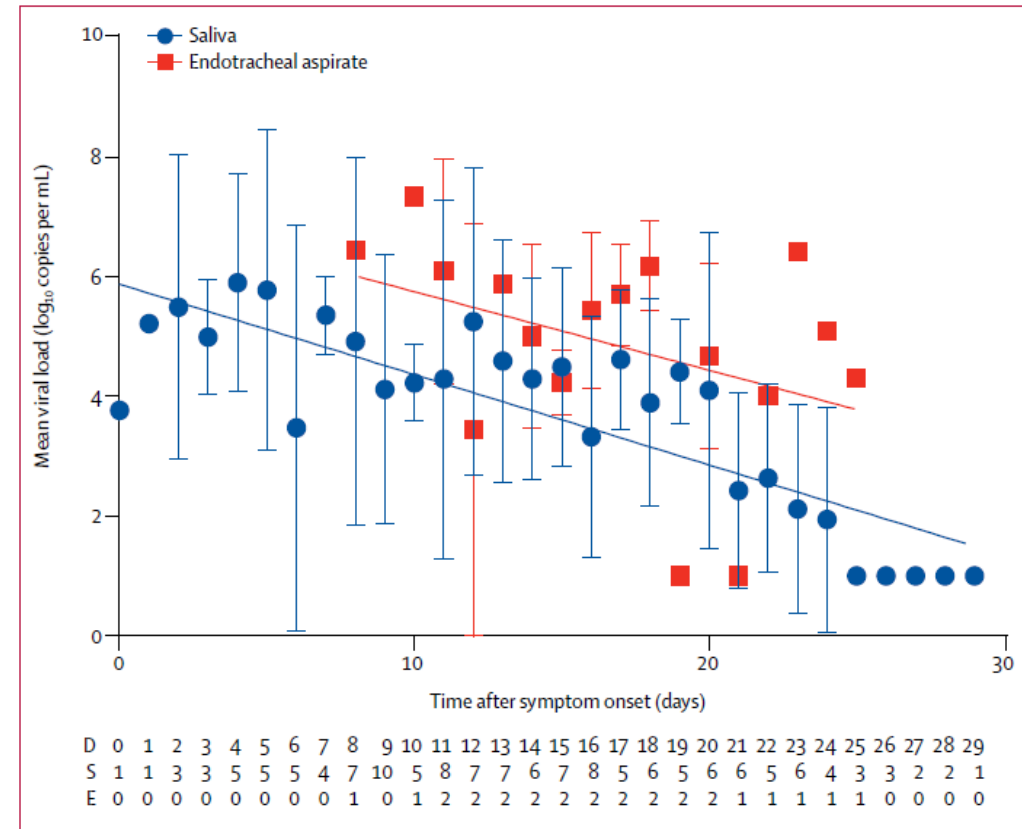
Type of Test	Measure	Value	Beneficiary
 Nucleic acid amplification test for viral RNA (nasopharyngeal swab, oropharyngeal swab, sputum, bronchoalveolar lavage fluid, others)	Current infection with SARS-CoV-2	- Inform individual of infection status so they can anticipate course of illness and take action to prevent transmission - Inform patient management and actions needed to prevent transmission - Inform actions needed to prevent transmission	- Individual - Healthcare or long-term care facility - Public health
 Antibody detection	Past exposure to SARS-CoV-2	- Detect susceptible individuals (antibody negative) and those previously infected - Identify individuals with neutralizing antibodies - Facilitate contact tracing and surveillance	- Identify those potentially immune to SARS-CoV-2 (if tests can detect protective immunity, individuals could be returned to work) - Healthcare facilities: Experimental therapy - Public health

American Society of Microbiology (Patel R, mBio. 2020)

Nucleic acid detection for respiratory viruses



SARS-2-CoV RNA last up to 30 days in respiratory samples



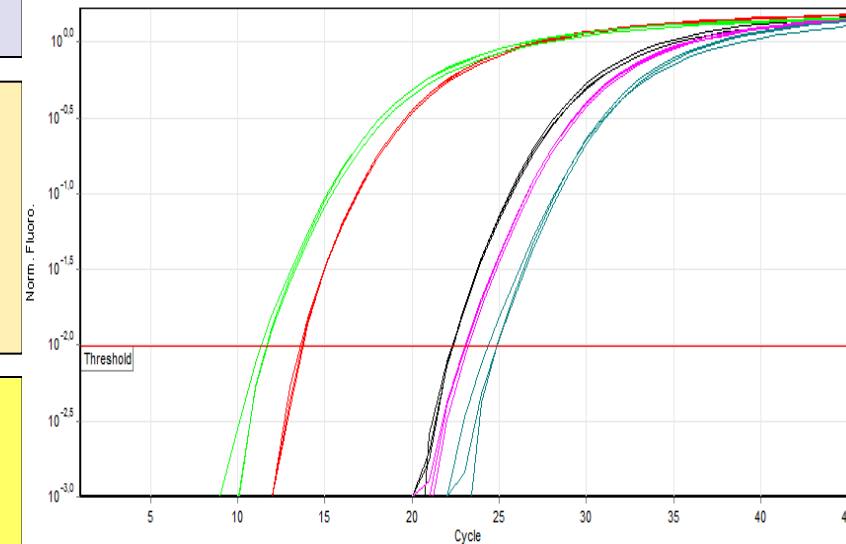
Kelvin Kai-Wang To* *Lancet Infect Dis* 2020;
20: 565–74

Multiplex Real Time PCR for respiratory viruses

5 ul Extracted N.A.; 25 ul final vol. (equivalent to 100 ul crude sample)

Quanta Thoughtmix mastermix

Mpx 1	Influenza A Influenza B	FAM HEX	Matrix Matrix
Mpx 2	HuCoV 229E/NL63 HuCoV OC43/HKU1 HMPV A/B hBoV	FAM FAM HEX TAMRA	1b gene 1b gene N gene NP1 gene
Mpx 3	Parainfluenza 1,2,3,4 AdV RSV A, B	FAM (4x) VIC Cy5 (2x)	HN gene Hexon NC
Mpx 4	Internal control Rhino/enterovirus	FAM HEX	human RNPgene 5'UTR



nCoV (RT)PCR Workflow overview

92 samples + 4 controls (pos, neg) per run (one PCR 96 mwp)



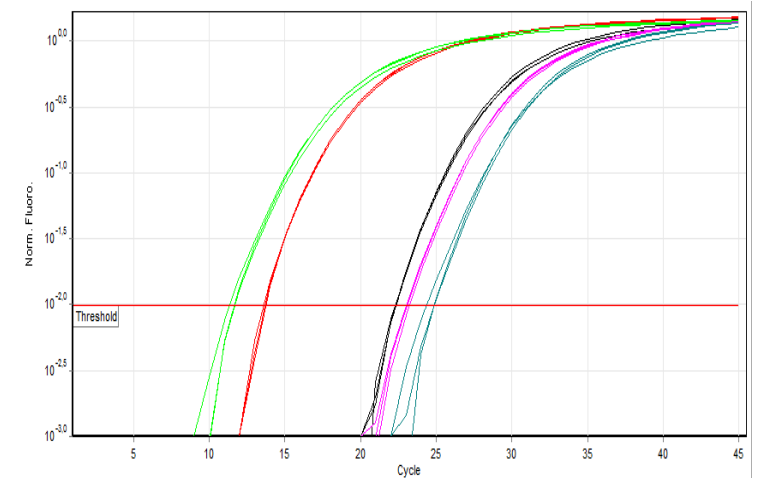
NA Extraction
EasyMag
1,5 hours
(30 min hands-on)



PCR setup
Epmotion
30 min
(15 min hands-on)



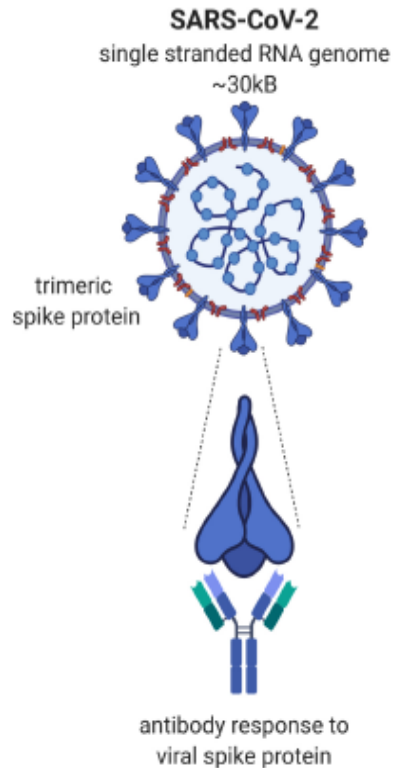
PCR
Lightcycler 480II
1,5 hours
(15 min hands-on)



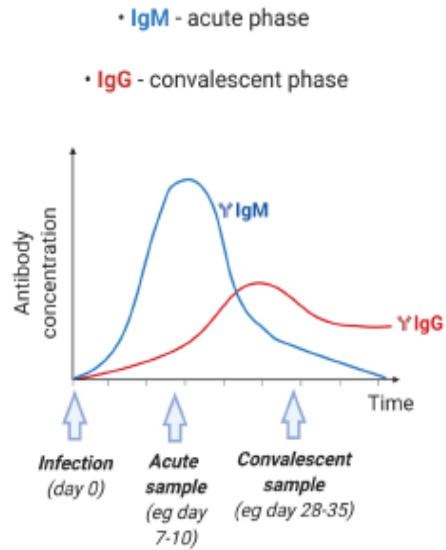
If N.A. extracts batched, up to 4-5 PCR rounds can be batched in one day: (368 - 460 samples throughput)

Antibody detection for SARS-CoV-2 (current)

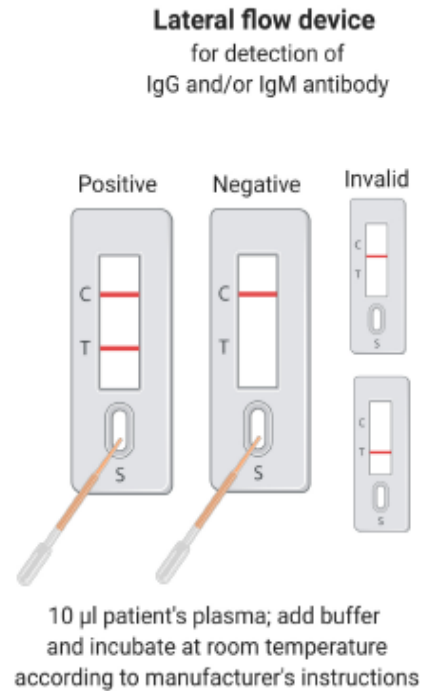
A: viral infection



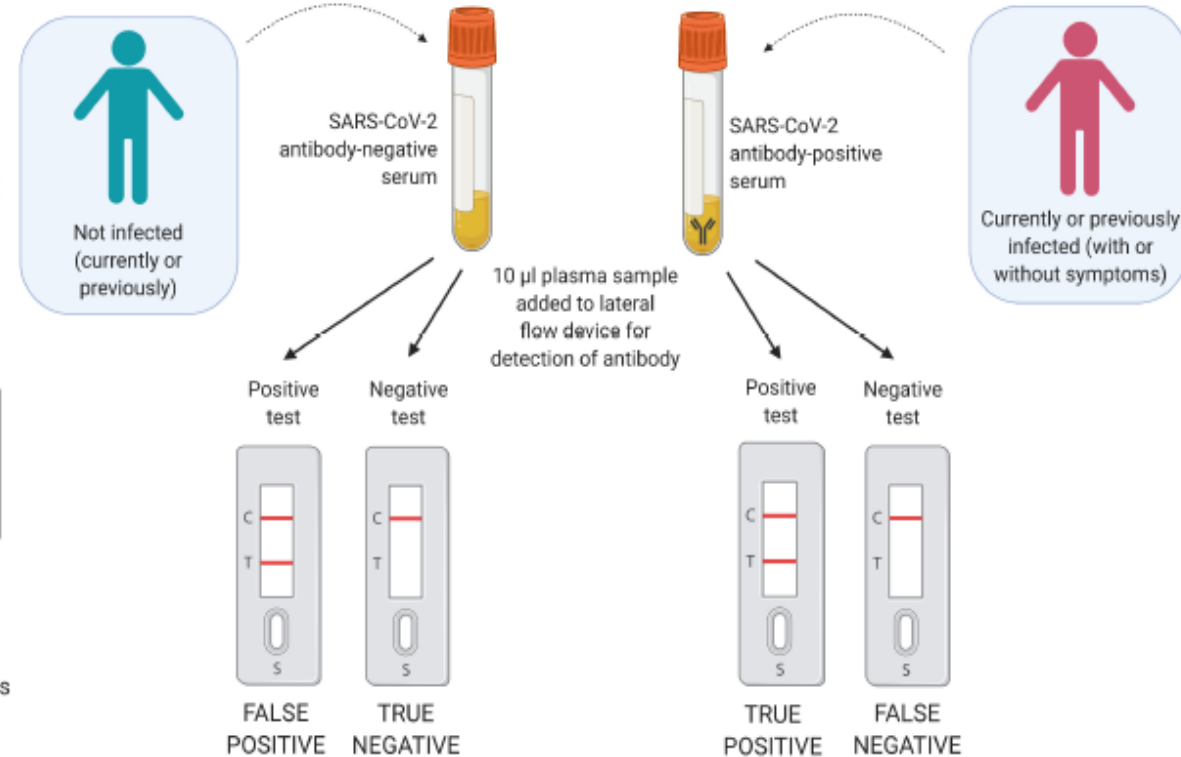
B: antibody response



C: antibody test



D: outcomes of lateral flow assays



UK National COVID Scientific Advisory Panel, Medrxiv 2020

Ens ha arribat el **SARS-CoV-2** de l'espai exterior ?



Directo La crisis del coronavirus: desescalada y fases en España

EMERGENCIA
SANITARIA

El Nobel francés Montagnier ve una manipulación del virus del sida



• Sostiene que el coronavirus causante de la Covid-19 es una fabricación humana, obra del laboratorio de Wuhan



El biólogo francés Luc Montagnier, en una imagen de archivo. (LV / David Airop)

EU SEBIO VAL | PARÍS, CORRESPONSAL 19/04/2020 08:42 | Actualizado a 19/04/2020 10:20

El **biólogo francés Luc Montagnier**, que ganó el Nobel de **Medicina** en el **2008** por participar en el descubrimiento del **virus del sida (VIH)**, sostiene que el **coronavirus** causante de la **Covid-19** es una **fabricación humana**, obra del **laboratorio de Wuhan** al que apuntan otras sospechas. Según Montagnier, se trató de una fuga accidental mientras investigaban una vacuna contra el sida.

Al minuto

Horóscopo de hoy para Escorpio, sábado 9 de mayo del 2020

Turistas y británicos que vuelvan al

El SARS-CoV-2 és una zoonosi



Wikipedia commons



Shao-Lun Zhai et al. *Veterinary Record* 2020;186:254

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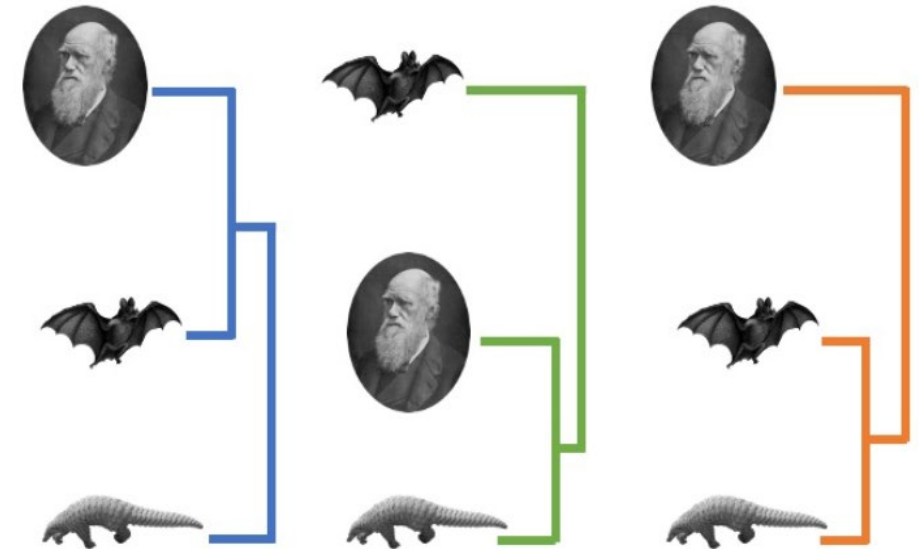
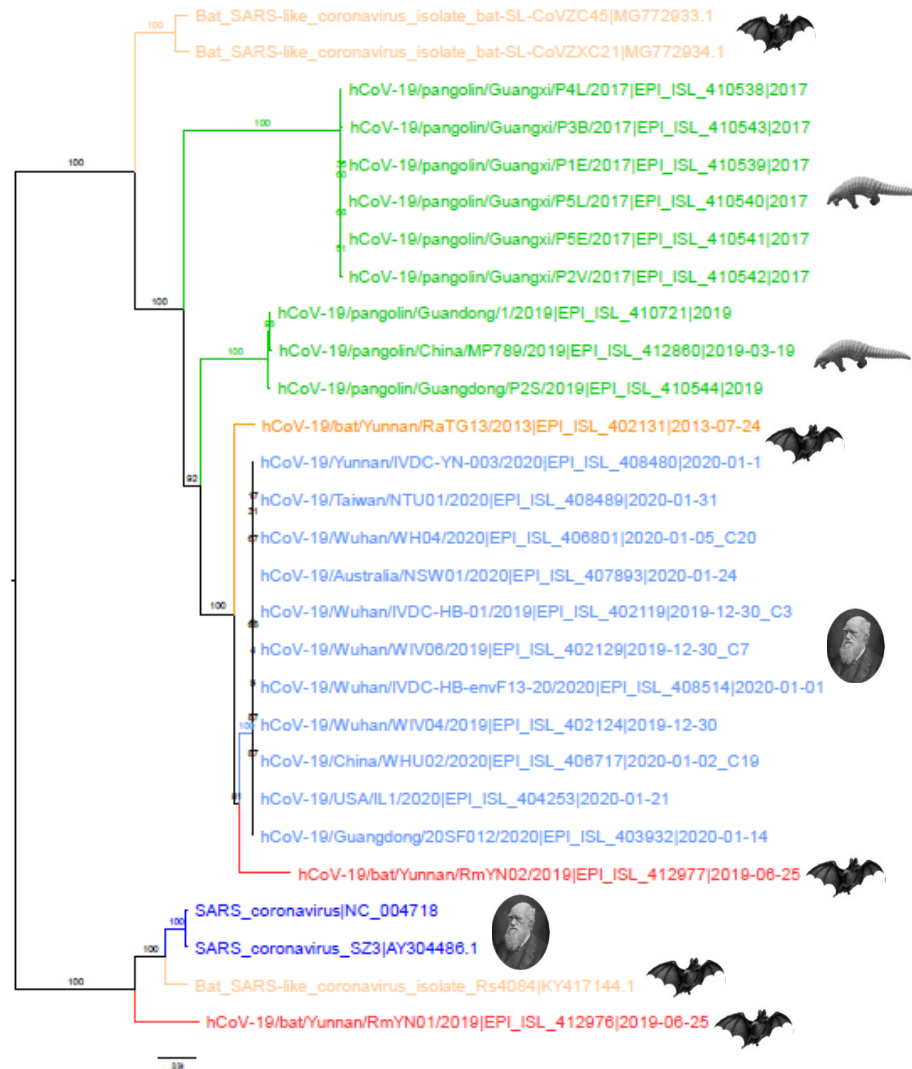


Figura adaptada de Zhang et al. (2020).

Full genome tree of hCoV-19-related precursors



- New nearest bat precursor from Yunnan 2019 (high identity in Orf1ab, greatest difference in Spike protein, recombination or mixed viruses in metagenomic sample, not yet peer-reviewed)
- Nearest pangolin precursors from Guangdong (Southern China)
- Previous closest bat precursor also from Yunnan (Southern China) but sample from 2013

Light Orange ... previous bat CoVs
 Orange ... previous closest bat precursor (Yunnan 2013)
 Red ... new bat CoVs (Yunnan 2019)
 Light blue ... hCoV-19 2019-2020
 Green ... pangolin CoV (Southern China 2019)
 Blue ... SARS CoV

We gratefully acknowledge the Authors from Originating and Submitting laboratories of sequence data on which the analysis is based.

Phylogenetic tree of full genome sequences using Maximum Likelihood method, gamma distributed rates, 200 bootstrap, raxml-ng)

2020-05-06 1600UTC

by BII/GIS, A*STAR Singapore



Global Influenza
 Hospital Surveillance
 Network

F. Xavier López

- Larger clades were named based on marker variants:
S ... ORF8-L84S
G ... S-D614G
V ... NS3-G251V

Full genome tree derived from all outbreak sequences 2020-05-06

G

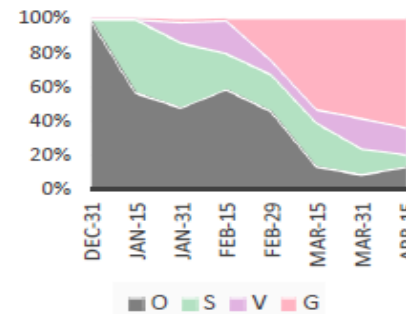
Notable changes:
15,290 full genomes (+326)
(excluding low coverage, out of 16,423 entries)

S clade 1,910 (+9):
3 USA/CT, 3 USA/UT, 3 USA/CA

G clade 9,725 (+248):
74 USA/NY, 58 USA/LA, 41 USA/UT, 28 Hungary, 16 USA/CT, 9 USA/WI, 8 USA/CA, 4 Canada, 3 Singapore, 3 USA/AK, 3 USA/NJ, 1 Poland

V clade 1,559 (+1):
1 Singapore

Other clades 2,096 (+68):
44 USA/CA, 19 Singapore, 4 Brunei, 1 Hungary



Blue ... new Asia
Green ... new Oceania
Magenta ... new Americas
Red ... new Europe
Gold ... new Africa
Black ... previous (until yesterday)

S

V

Neighbor-Joining tree with Maximum Composite Likelihood distance. Branch length in the units of the number of base substitutions per site. Uniform rates. Pairwise deletion.MEGA X and FigTree.

We gratefully acknowledge the Authors from Originating and Submitting laboratories of sequence data on which the analysis is based.

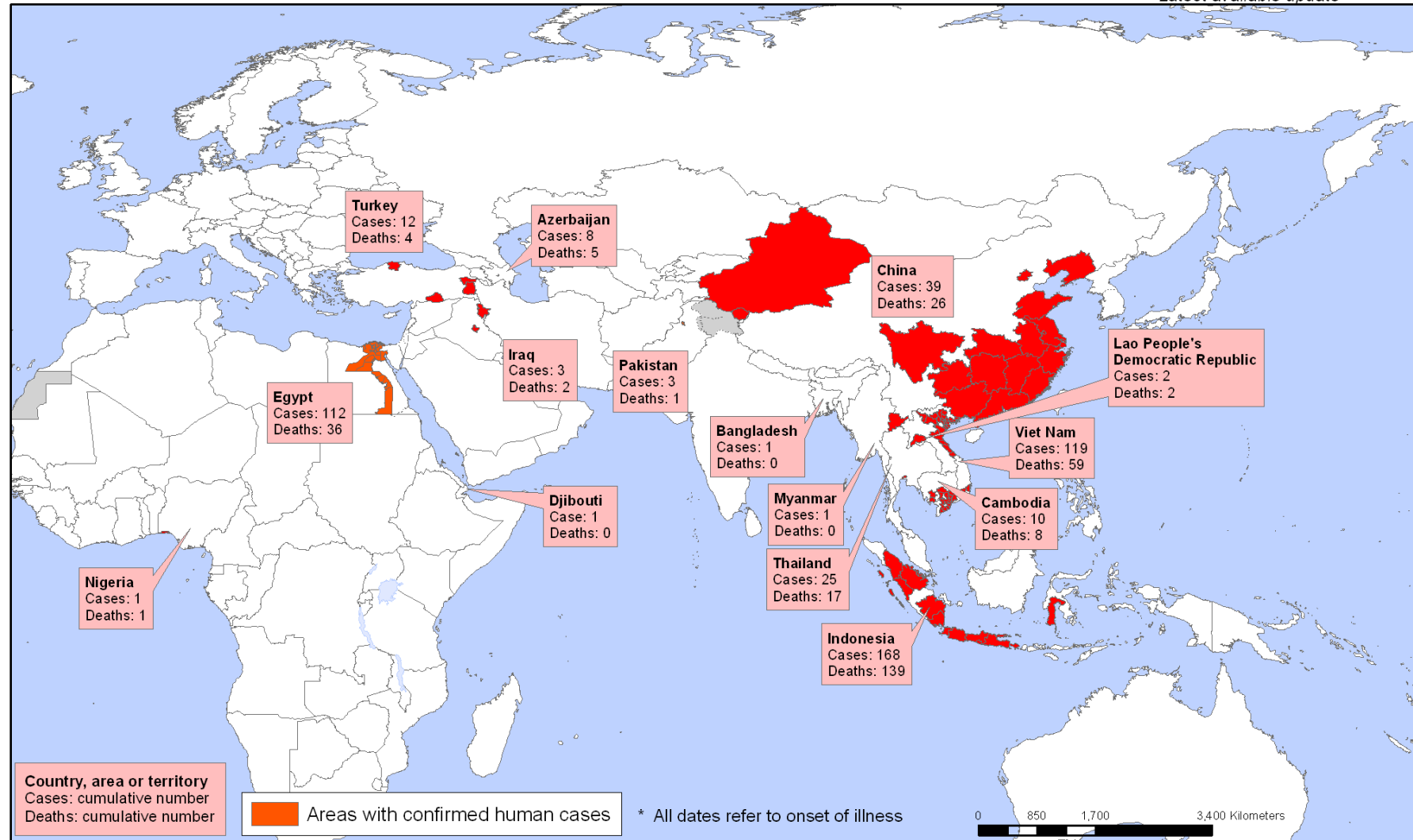


by BII/GIS, A*STAR Singapore



Areas with confirmed human cases of H5N1 avian influenza since 2003 *

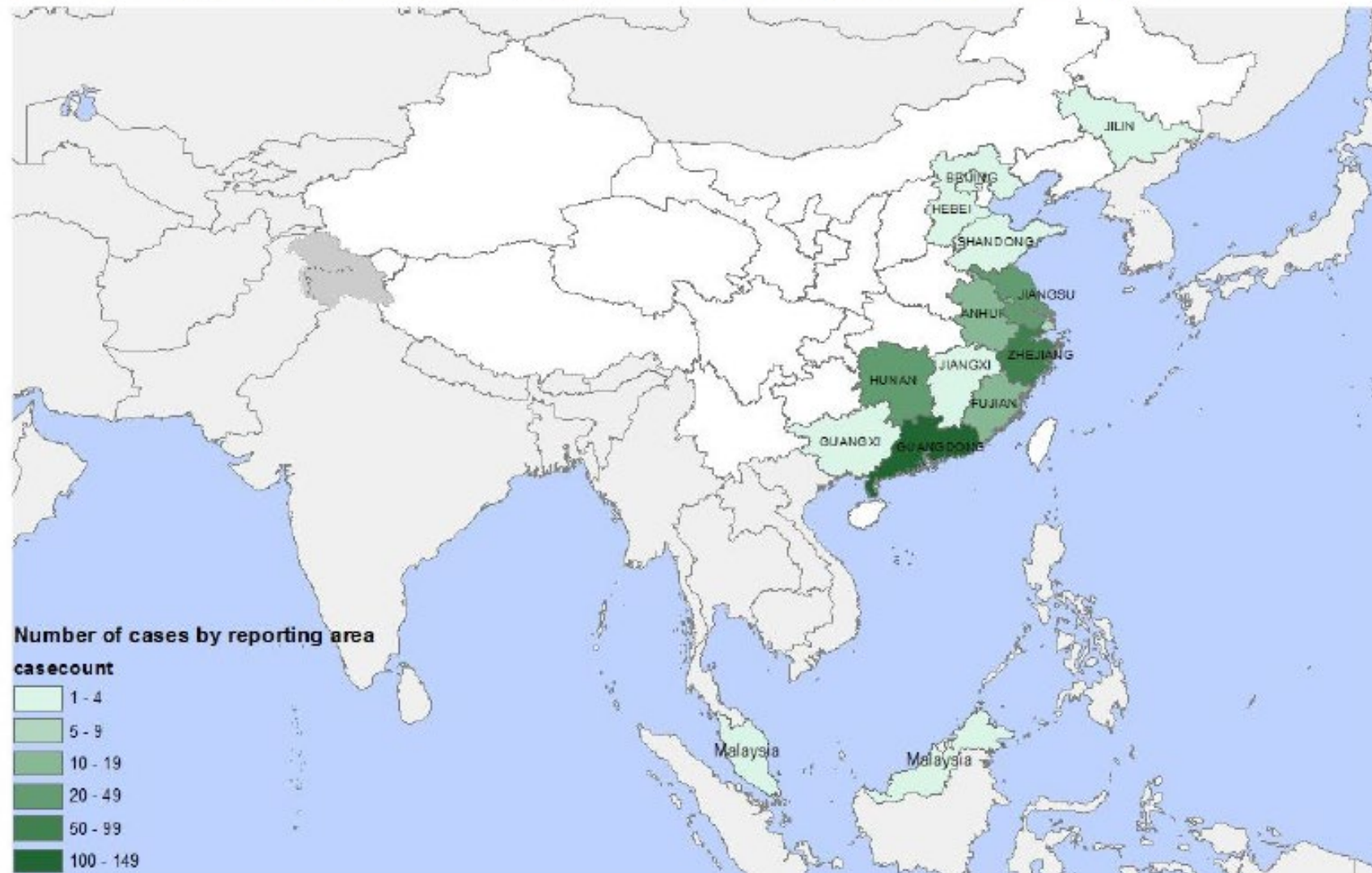
Status as of 31 August 2010
Latest available update



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 lines on maps represent approximate border lines for which there may not yet be full agreement. © WHO 2010. All rights reserved.

Data Source: WHO
Map Production: Public Health Information and Geographic Information System (GIS)
World Health Organization

Areas reporting confirmed human cases for influenza A(H7N9) to WHO from 2013-06-01 *



*All dates refer to onset of illness
Data as of 14/07/2014
Source: WHO

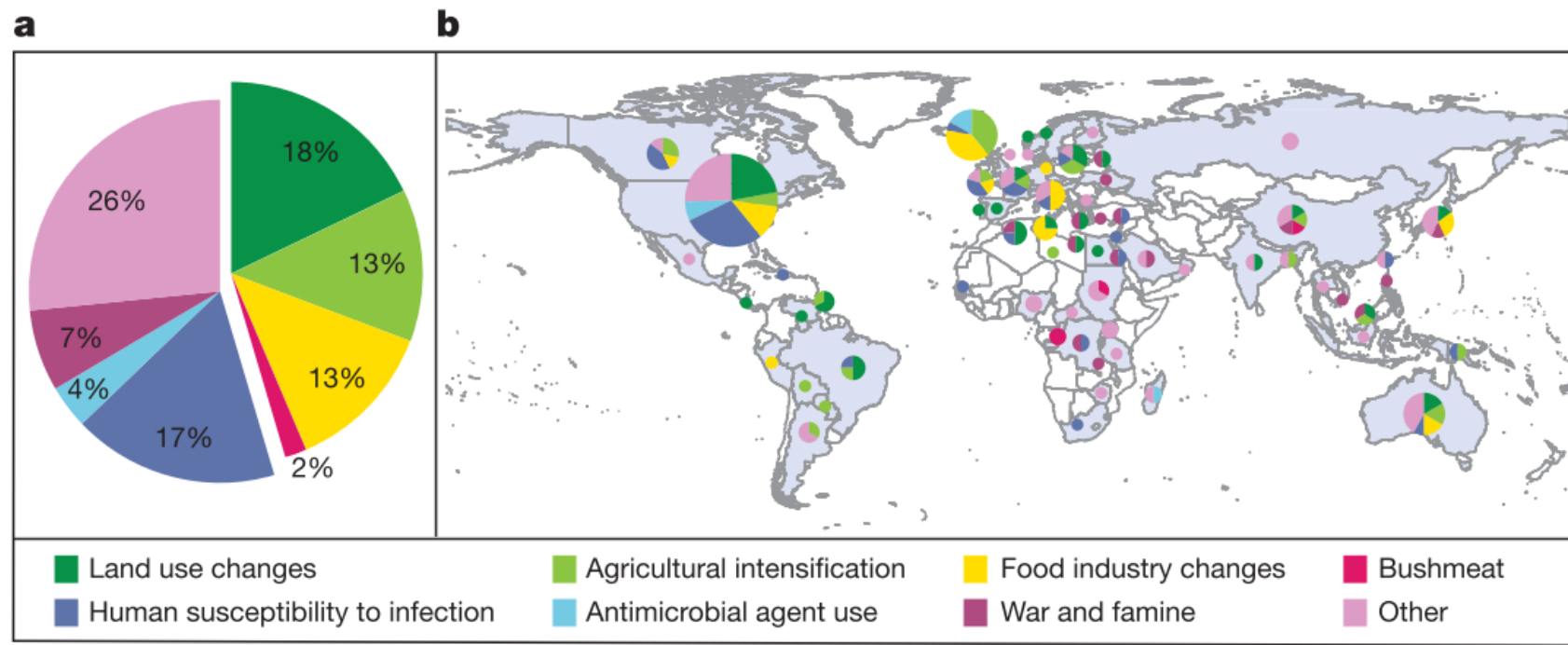
The information reported about the presentation of the situation in this publication does not imply the responsibility of the World Health Organization concerning the legal status of any country, territory, or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on the map represent approximate borderlines for which there may not yet be full agreement.
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Zoonosis

- **Viruela:** ¿Roedores?
 - **Sarampión:** Moquillo, Peste Bovina
 - **Rinovirus:** Caballos
 - **Gripe:** Aves
 - **Rabia:** Murciélagos, Cánidos
-
- **VIH:** Primates
 - **Hantavirus:** Ratones
 - **Virus Nipah:** Murciélagos
 - **Virus Nilo Occ.:** Aves
 - **SARS-CoV:** Murciélagos, Pequeños mamíferos

Drivers and locations of emergence events for zoonotic infectious diseases in humans since 1940



- Changes in land use, agricultural and other food production practices
- Wildlife hunting, increase in contact rates
- Changes in human susceptibility, demographics and behaviour, urbanization
- Breakdown of ecosystems and reduction in biodiversity
- International travel and commerce, “bioglobalization”, climate and weather

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“Quan una espècie augmenta desordenadament en un període curt, sovint apareixen epidèmies; i aquí tenim un filtre limitant, independent de la lluita per la vida.”

**Charles Darwin
On the Origin of Species**

