中国疾病预防控制中心
CHINESE CENTER FOR DISEASE CONTROL AND PREVENTION

中国科学院微生物研究所
INSTITUTE OF MICROBIOLOGY
CHINESE ACADEMY OF SCIENCES

What relevant knowledge did we have before the COVID-19 pandemic?

George Fu Gao
Institute of Microbiology, Chinese Academy of Sciences
Chinese Center for Disease Control and Prevention
Aug 29th, 2022

Black Swan or Grey Rhino?

GPMB 2019

Annual Reports:

Flu, Coronavirus

Not ready

We cannot work together

A global pandemic exercise

EVENT 201

A GLOBAL PANDEMIC EXERCISE

CAPS

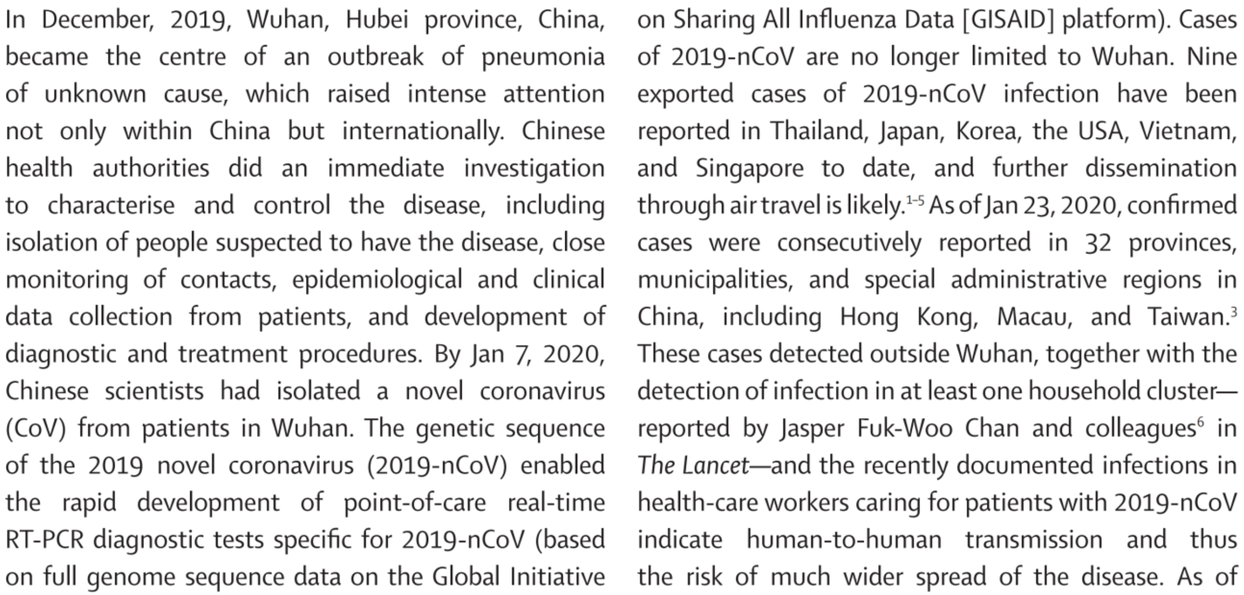
Coronavirus Associated Pneumonia Syndrome

- Event 201 was a pandemic tabletop exercise.
- October 18, 2019，Friday，New York, US
- https://www.centerforhealthsecurity.org/event201/about

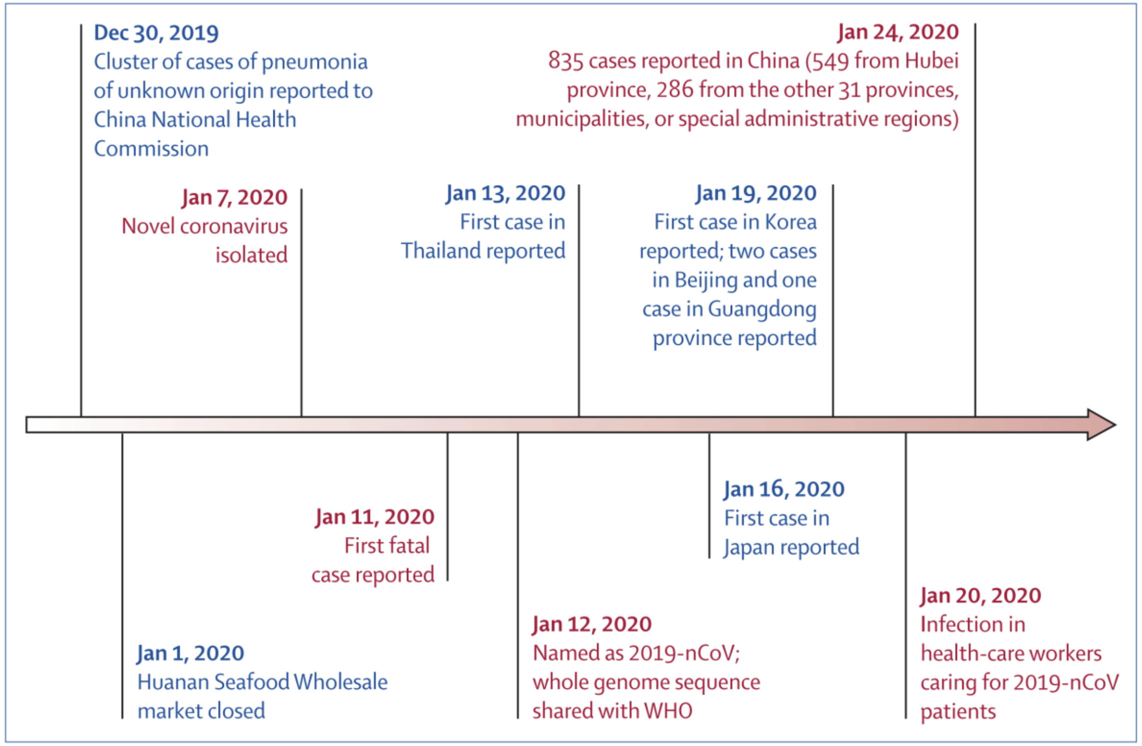
THE LANCET

A novel coronavirus outbreak of global health concern

Chen Wang, Peter W Horby, Frederick G Hayden, George F Gao



In December, 2019, Wuhan, Hubei province, China, became the centre of an outbreak of pneumonia of unknown cause, which raised intense attention not only within China but internationally. Chinese health authorities did an immediate investigation to characterise and control the disease, including isolation of people suspected to have the disease, close monitoring of contacts, epidemiological and clinical data collection from patients, and development of diagnostic and treatment procedures. By Jan 7, 2020, Chinese scientists had isolated a novel coronavirus (CoV) from patients in Wuhan. The genetic sequence of the 2019 novel coronavirus (2019-nCoV) enabled the rapid development of point-of-care real-time RT-PCR diagnostic tests specific for 2019-nCoV (based on full genome sequence data on the Global Initiative on Sharing All Influenza Data [GISAID] platform). Cases of 2019-nCoV are no longer limited to Wuhan. Nine exported cases of 2019-nCoV infection have been reported in Thailand, Japan, Korea, the USA, Vietnam, and Singapore to date, and further dissemination through air travel is likely.[1–5] As of Jan 23, 2020, confirmed cases were consecutively reported in 32 provinces, municipalities, and special administrative regions in China, including Hong Kong, Macau, and Taiwan.[3] These cases detected outside Wuhan, together with the detection of infection in at least one household cluster—reported by Jasper Fuk-Woo Chan and colleagues[6] in *The Lancet*—and the recently documented infections in health-care workers caring for patients with 2019-nCoV indicate human-to-human transmission and thus the risk of much wider spread of the disease. As of



Dec 30, 2019
Cluster of cases of pneumonia of unknown origin reported to China National Health Commission

Jan 1, 2020
Huanan Seafood Wholesale market closed

Jan 7, 2020
Novel coronavirus isolated

Jan 11, 2020
First fatal case reported

Jan 12, 2020
Named as 2019-nCoV; whole genome sequence shared with WHO

Jan 13, 2020
First case in Thailand reported

Jan 16, 2020
First case in Japan reported

Jan 19, 2020
First case in Korea reported; two cases in Beijing and one case in Guangdong province reported

Jan 20, 2020
Infection in health-care workers caring for 2019-nCoV patients

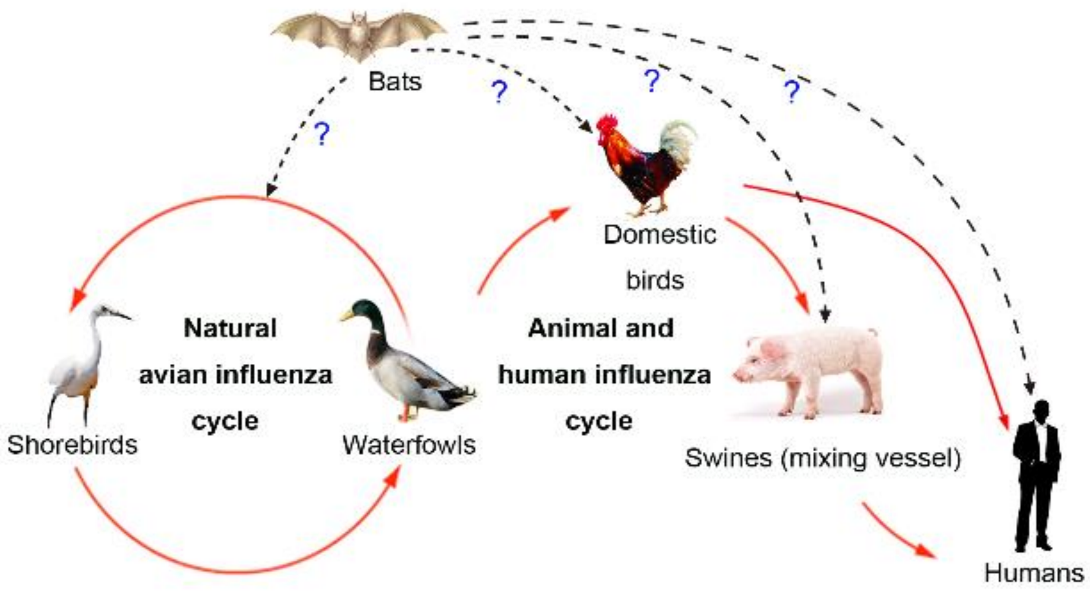
Jan 24, 2020
835 cases reported in China (549 from Hubei province, 286 from the other 31 provinces, municipalities, or special administrative regions)

Figure: Timeline of early stages of 2019-nCoV outbreak

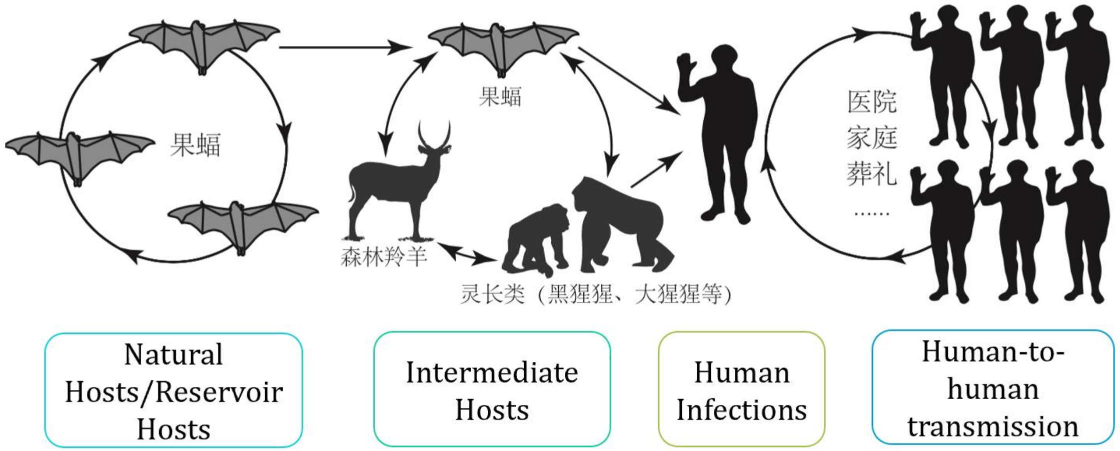
Global Concern

Published: January 24, 2020

Previous knowledge on the zoonotic viruses and spillover events



Natural Cycle of the Influenza viruses

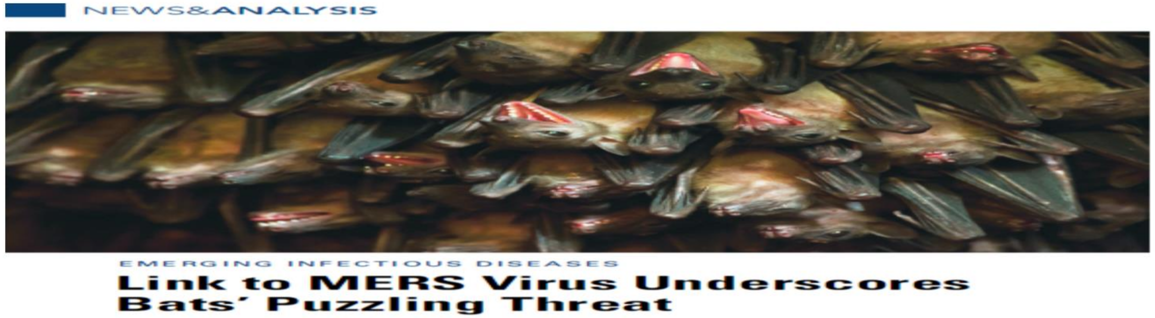


Natural Hosts/Reservoir Hosts

Intermediate Hosts

Human Infections

Human-to-human transmission



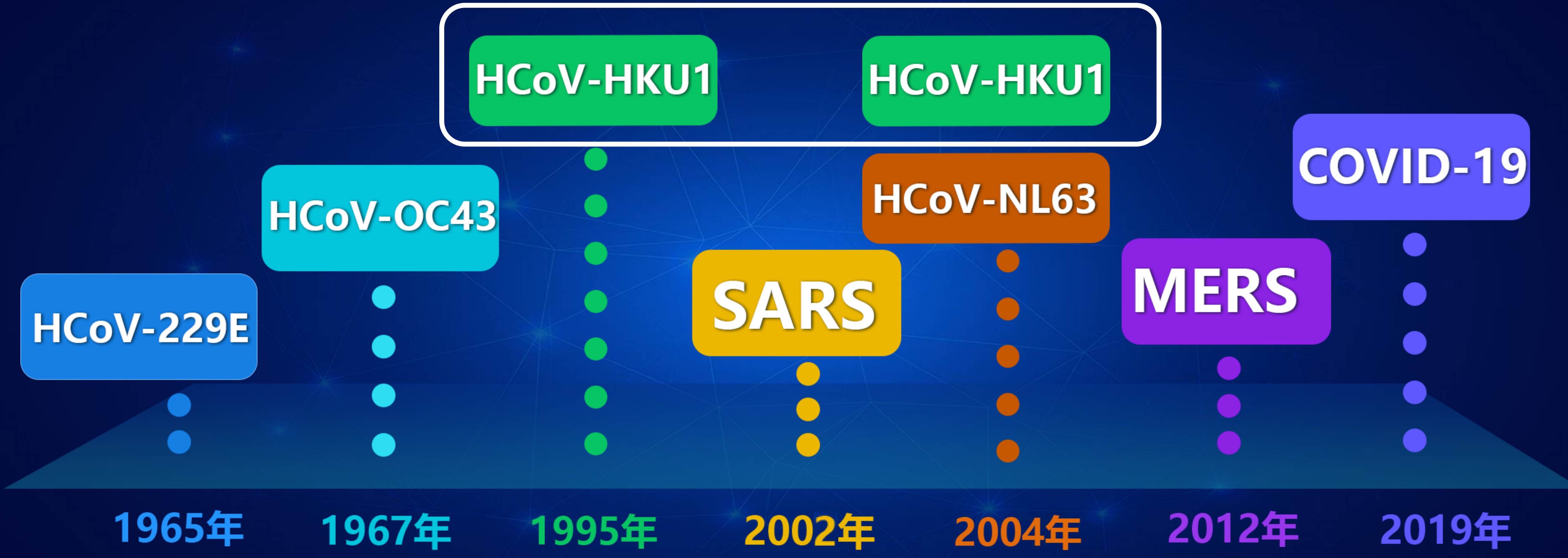
NEWS&ANALYSIS

EMERGING INFECTIOUS DISEASES

Link to MERS Virus Underscores Bats' Puzzling Threat

Ecology of Ebola

Seven coronaviruses can infect human beings
Two newly discovered



HCoV-229E
1965年

HCoV-OC43
1967年

HCoV-HKU1
1995年

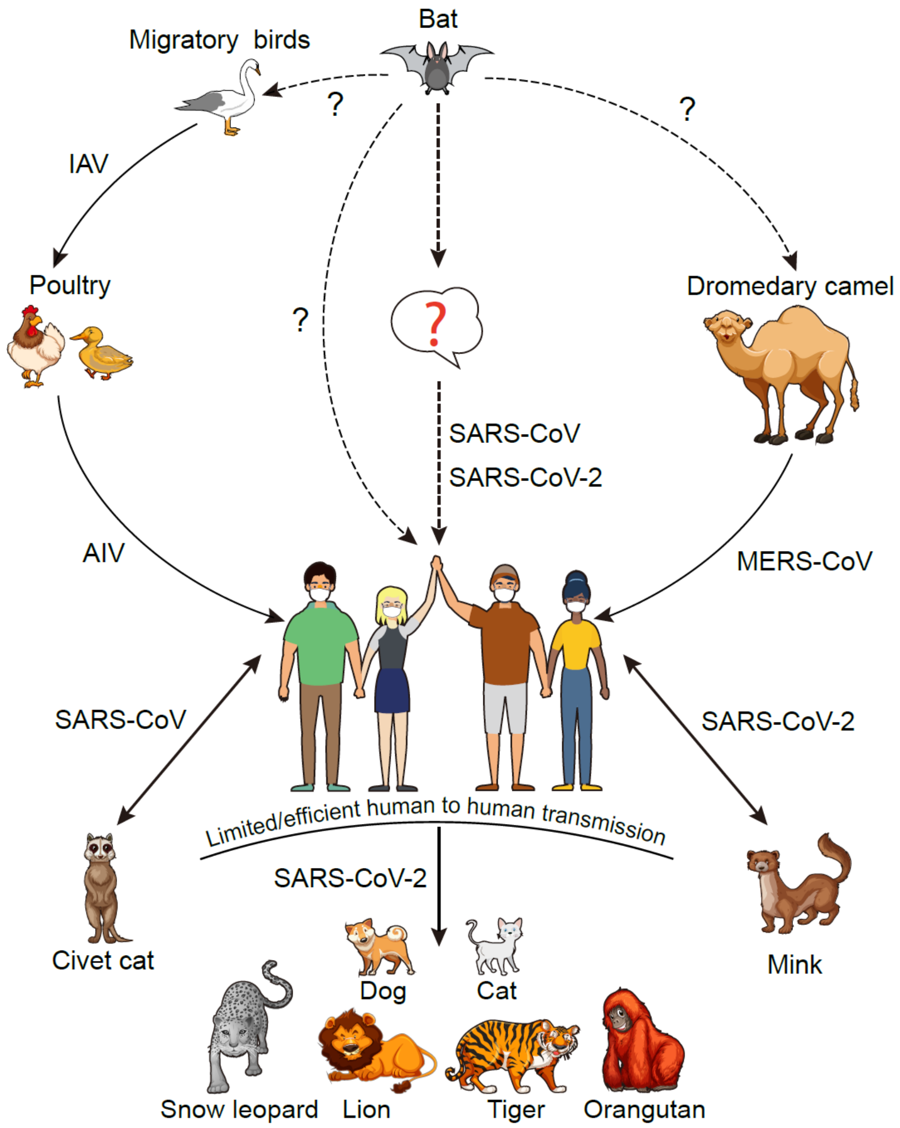
SARS
2002年

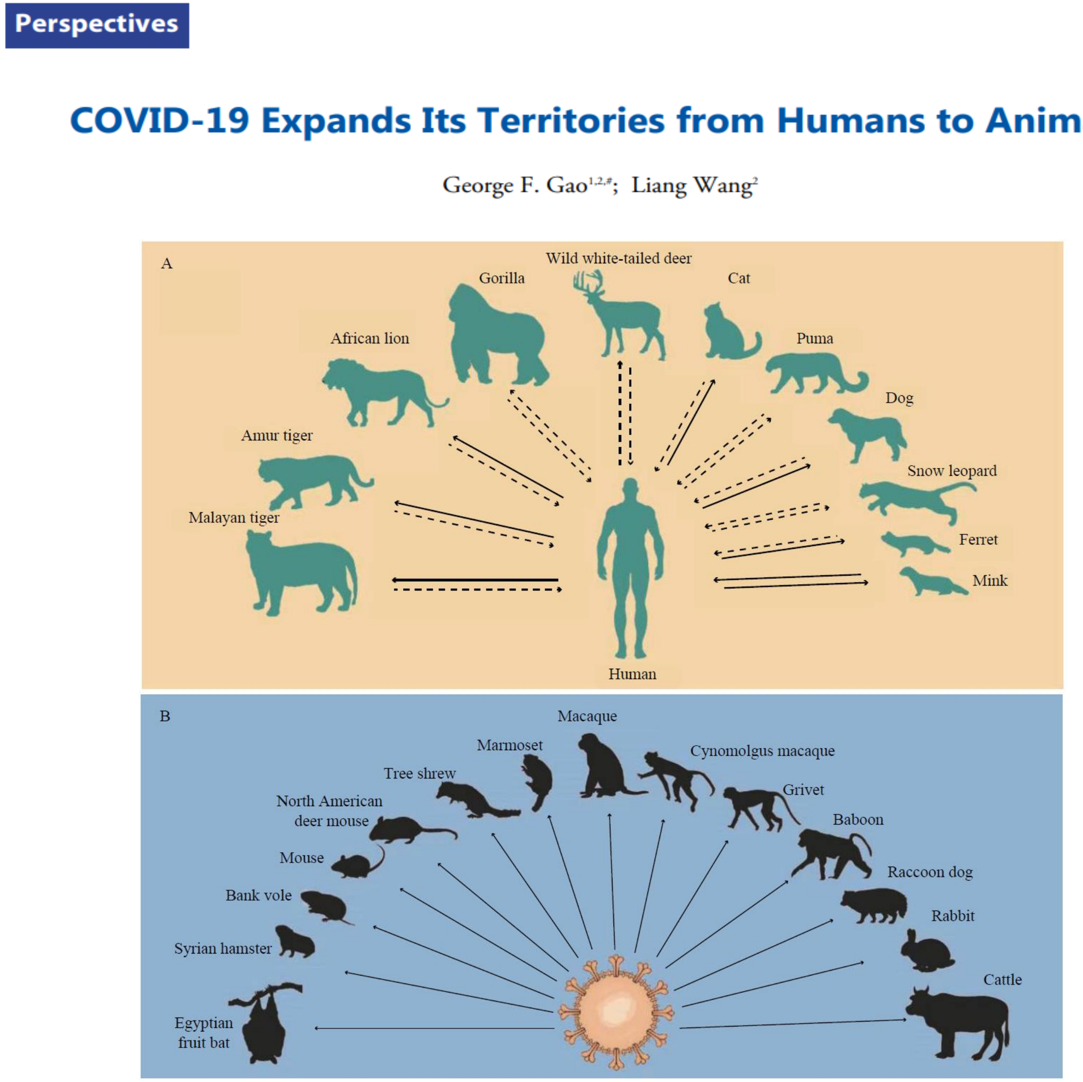
HCoV-HKU1
HCoV-NL63
2004年

MERS
2012年

COVID-19
2019年

Current SARS-CoV-2 is expanding the territories





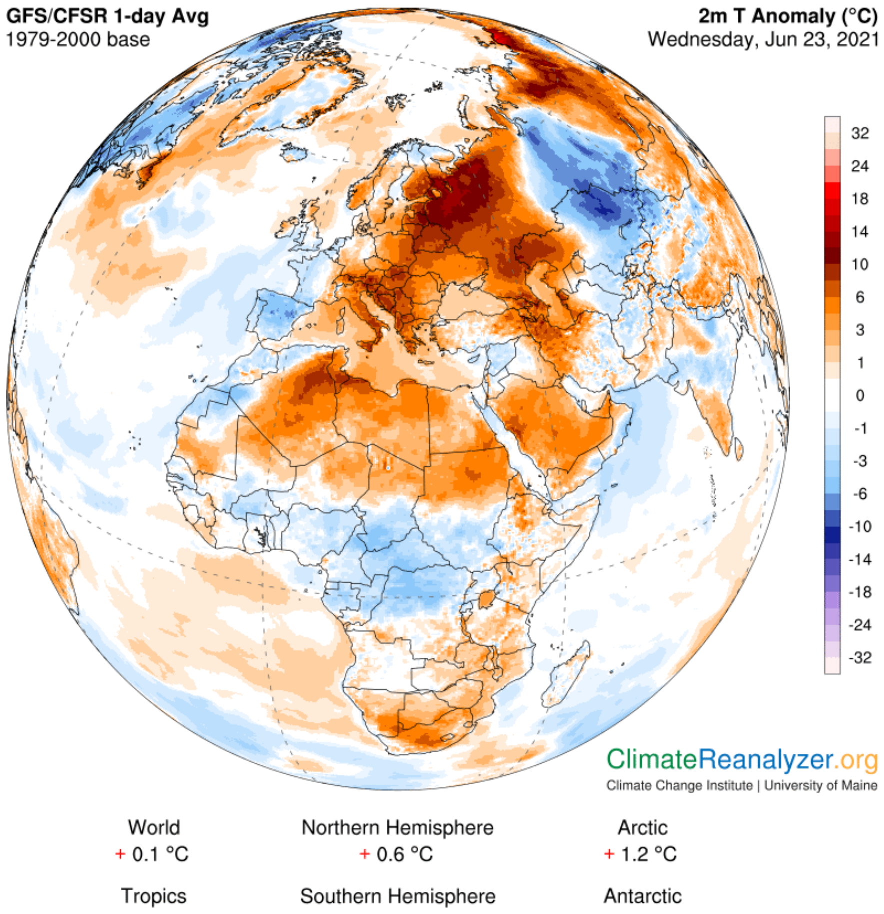
Perspectives

COVID-19 Expands Its Territories from Humans to Animals

George F. Gao[1,2,#]; Liang Wang[2]

Why do we have so many emerging viruses?

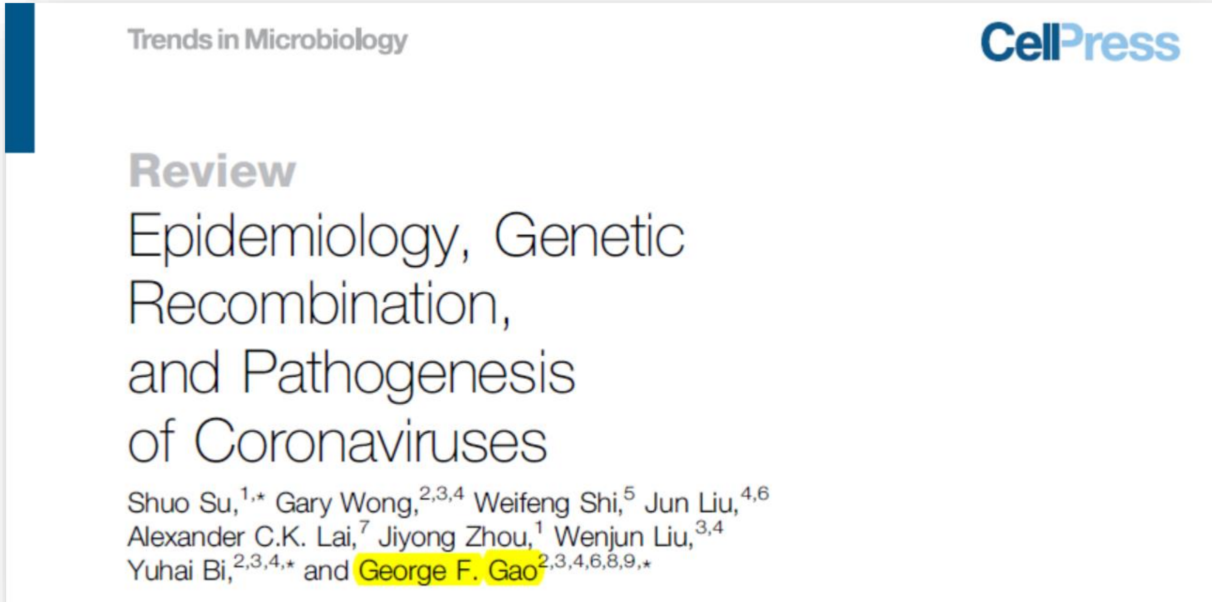
Climate and ecological changes



https://www.washingtonpost.com/weather/

Human behavior changes

It is likely not a matter of if, but when



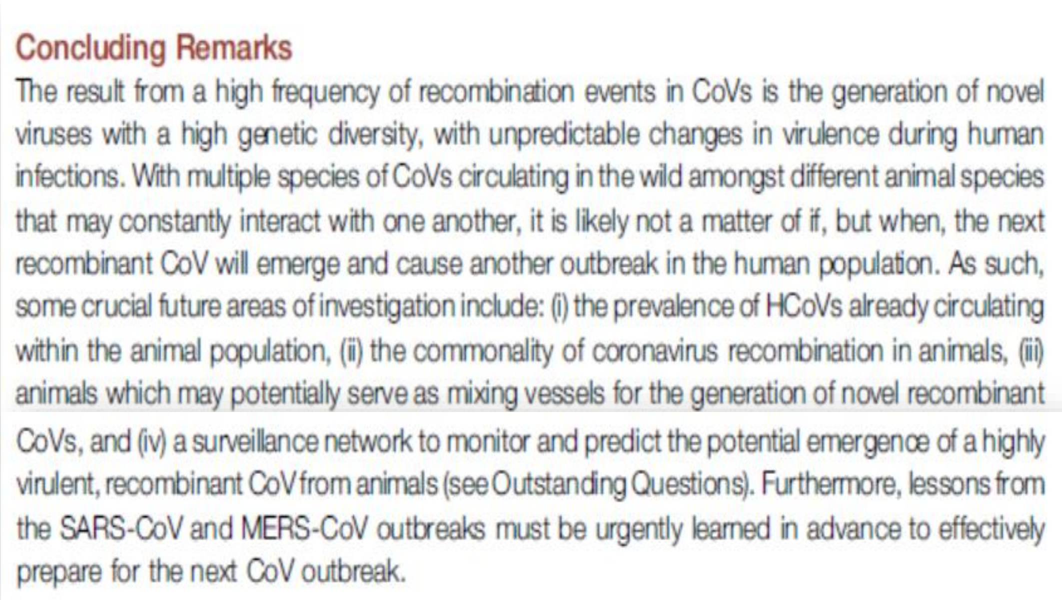
Trends in Microbiology

CellPress

Review

Epidemiology, Genetic Recombination, and Pathogenesis of Coronaviruses

Shuo Su,[1,*] Gary Wong,[2,3,4] Weifeng Shi,[5] Jun Liu,[4,6]
Alexander C.K. Lai,[7] Jiyong Zhou,[1] Wenjun Liu,[3,4]
Yuhai Bi,[2,3,4,*] and George F. Gao[2,3,4,6,8,9,*]



Concluding Remarks

The result from a high frequency of recombination events in CoVs is the generation of novel viruses with a high genetic diversity, with unpredictable changes in virulence during human infections. With multiple species of CoVs circulating in the wild amongst different animal species that may constantly interact with one another, it is likely not a matter of if, but when, the next recombinant CoV will emerge and cause another outbreak in the human population. As such, some crucial future areas of investigation include: (i) the prevalence of HCoVs already circulating within the animal population, (ii) the commonality of coronavirus recombination in animals, (iii) animals which may potentially serve as mixing vessels for the generation of novel recombinant CoVs, and (iv) a surveillance network to monitor and predict the potential emergence of a highly virulent, recombinant CoV from animals (see Outstanding Questions). Furthermore, lessons from the SARS-CoV and MERS-CoV outbreaks must be urgently learned in advance to effectively prepare for the next CoV outbreak.

…, it is likely not a matter of if, but when, the next recombinant CoV will emerge and cause another outbreak in the human population.

Trends in Microbiology
2016 June
Vol. 24, No 6: 490-502

Discovery of SARS-CoV-2

2nd Jan. 2020

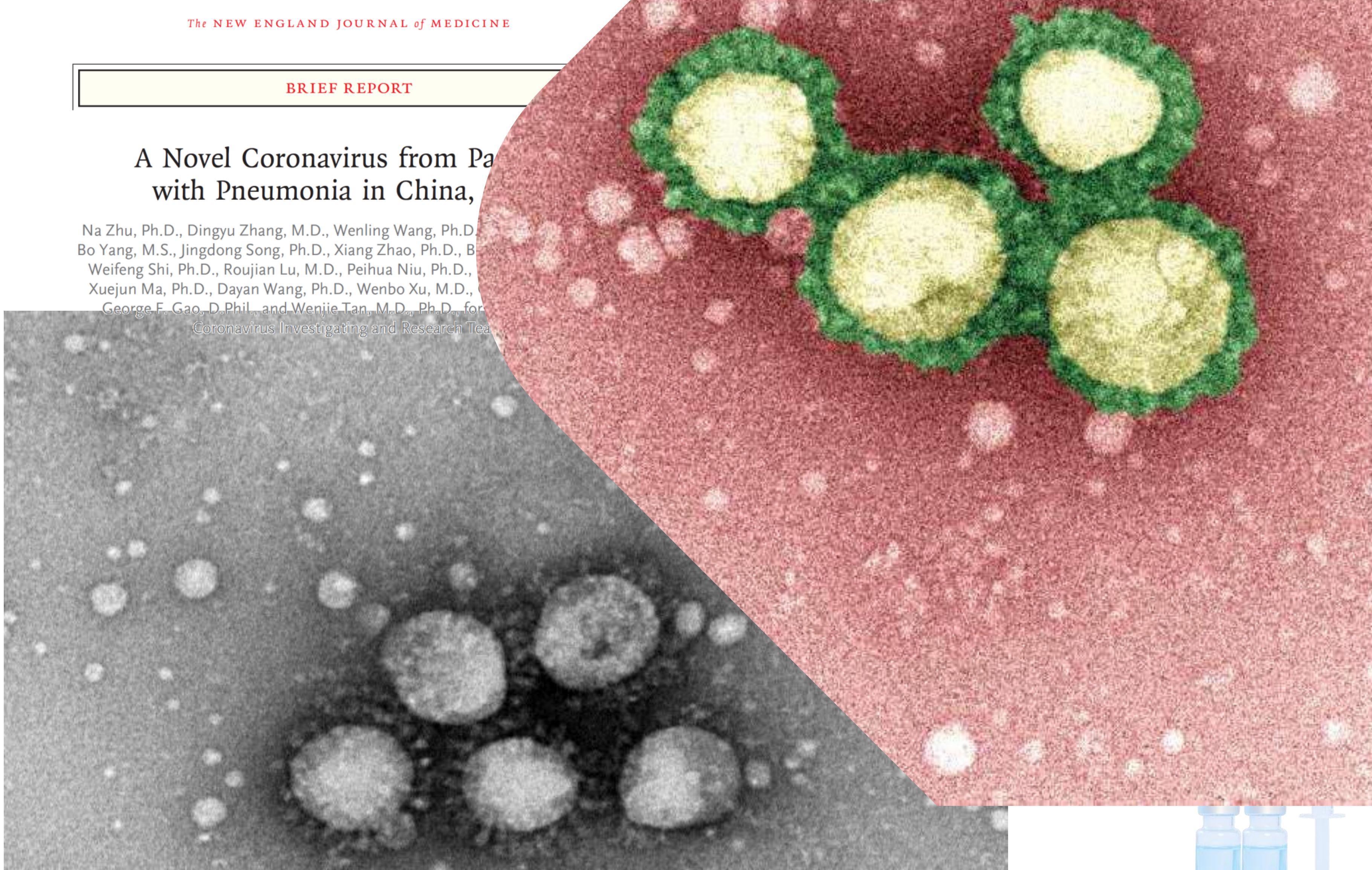
Obtaining the RT-PCR results 3 hours after receiving the samples.

3rd Jan. 2020

Obtaining the full genome sequences of SARS-CoV-2

7th Jan. 2020

Isolation of SARS-CoV-2



The NEW ENGLAND JOURNAL of MEDICINE

BRIEF REPORT

A Novel Coronavirus from Pa
with Pneumonia in China,

Na Zhu, Ph.D., Dingyu Zhang, M.D., Wenling Wang, Ph.D.
Bo Yang, M.S., Jingdong Song, Ph.D., Xiang Zhao, Ph.D., B
Weifeng Shi, Ph.D., Roujian Lu, M.D., Peihua Niu, Ph.D.,
Xuejun Ma, Ph.D., Dayan Wang, Ph.D., Wenbo Xu, M.D.,
George F. Gao, D.Phil., and Wenjie Tan, M.D., Ph.D., for
Coronavirus Investigating and Research Tea

Release the SARS-CoV-2 genome sequence

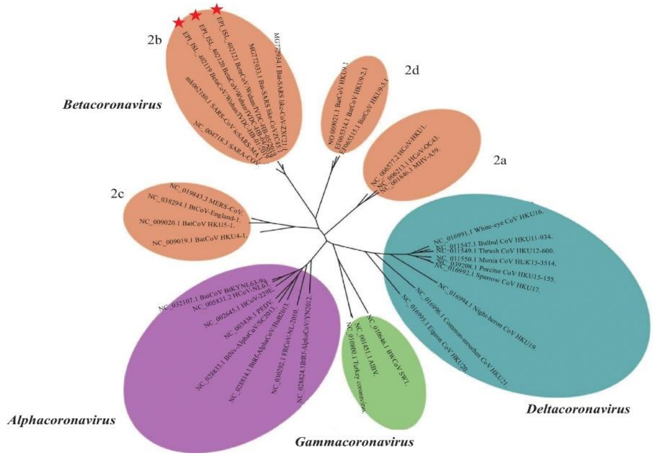
In 10th Jan. 2020, China CDC released the SARS-CoV-2 genome sequence in GISAID.

CHINA CDC WEEKLY

CCDC weekly

中国疾病预防控制中心周报

Notes from the Field: A Novel Coronavirus Genome Identified in a Cluster of Pneumonia Cases — Wuhan, China 2019–2020



In Focus

China releases genetic sequence of newly discovered coronavirus from Wuhan

The Chinese Center for Disease Control and Prevention, the Chinese Academy of Science and the Chinese Academy of Medical Science released through the GISAID Initiative the genome sequence of a newly discovered coronavirus. The virus was identified during an outbreak in the city of Wuhan, where patients were suffering from respiratory illnesses such as pneumonia since late December 2019.

The genome sequence of this betacoronavirus is crucial to develop specific diagnostic tests and to identify potential intervention options.

> read more and access the data

Courtesy: IVDC, China CDC

新型冠状病毒国家科技资源服务系统

毒种编号: CHPC 2020.00001; NPRC 2020.00001
中文名称: 新型冠状病毒武汉株01
英文名称: C-Tan-nCov Wuhan strain 01
分类学: 2019-nCoV, 冠状病毒β属
分离来源: 临床患者
采集地: 中国湖北武汉
分离时间: 2020年1月6日
生物危害程度: 二类
联系邮箱: ivdcolm@ivdc.chinacdc.cn; chpc@chinacdc.cn
照片来源: 国家病原微生物资源库（中国疾病预防控制中心病毒病预防控制所）

TABLE 1. Basic information for the first strain of 2019-nCoV.

Descriptors	Description
Code	CHPC 2020.00001, NPRC 2020.00001
Name in Chinese	新型冠状病毒武汉株01
Name in English	C-Tan-nCoV Wuhan Strain
Taxonomy	novel β genus coronavirus
Source of the Specimen	Clinical Patients
Source of Collection	Wuhan, Hubei Province, China
Isolation Date	Jan 6, 2020
Risk Level	BSL-3
Contact Info	ivdcolm@ivdc.chinacdc.cn, chpc@chinacdc.cn

Note: CHPC refers to the Center for Human Pathogen Collection of China CDC, and NPRC refers to the National Pathogen Resource Center of China.

TABLE 2. Real-time RT-PCR. The open reading frame 1ab (ORF1ab) was recommended. Primers and probes targeting the nucleoprotein gene region (nucleoprotein N) was used.

Item	Sequence
Target 1 (ORF1ab)	
Forward primer (F)	CCCTGTGGGTTTTACACTTAA
Reverse primer (R)	ACGATTGTGCATCAGCTGA
Fluorescent probes (P)	5'-FAM-CCGTCTGCGGTATGTGGAAAGGTTATGG-BHQ1-3'
Target 2 (N)	
Forward primer (F)	GGGGAACTTCTCCTGCTAGAAT
Reverse primer (R)	CAGACATTTTGCTCTCAAGCTG
Fluorescent probes (P)	5'-FAM-TTGCTGCTGCTTGACAGATT-TAMRA-3'

Note: Results reading: negative (no Ct value or Ct=40); positive (Ct value <37, considered positive); and suspicious (if Ct value is between 37 and 40, repeat testing is recommended). If Ct value <40 in repeat testing and distinctive peaks are observed in the amplification curve, the sample is considered positive; otherwise, the sample is considered negative.

4 Stages in China

Containment
Suppression
Accurate Mitigation/Suppresion
Local transmission again

China's Contribution to Modern Public Health


Spring


Wave

↕ ↕


Lake


Tsunami

Lancet Public Health

Zhongjie Li, *George F Gao

20tlph3669

PII

GOLD OA CC BY-NC-ND 4.0

Comment

Strengthening public health at the community-level in China

An unprecedented pandemic, COVID-19 is currently hitting the world.[1,2] After the initial outbreak in the city of Wuhan, Hubei province, COVID-19 is under control in China, with a few small waves caused by imported cases,[3,4] all of which have been stopped in China in 2–4 weeks, with between several cases and hundreds of cases per wave. We have seen clear peak-valley intervals with these small waves. It is crucial to understand why and how China has reached such success because it might help other countries. For COVID-19, we believe

CDC. Regional stations have been kept and renamed as local CDCs, from province to prefecture to county levels, which is different from the US CDC system. Since then, our four-level CDC system has been well built with large capacity and workforce. This system has proven to be the basis for the effective prevention and control of COVID-19. During the pandemic, community-level public health practice has supported health promotion and public understanding of science, leading to strong and intense public involvement in disease control and

Strethening Public Health
at Community-level!

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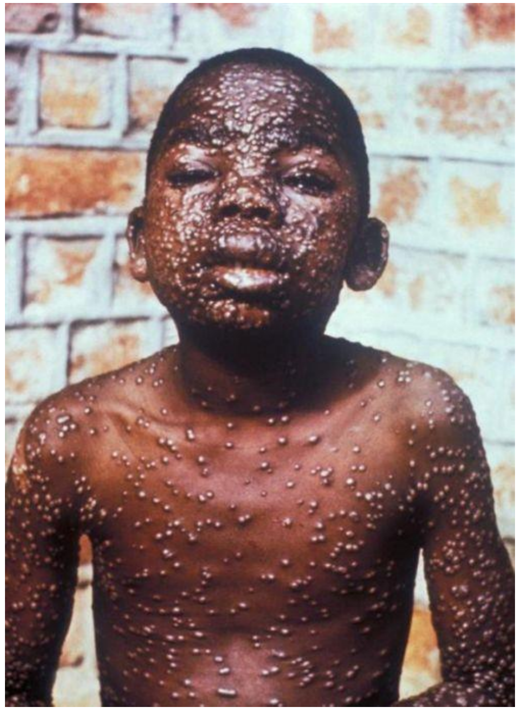
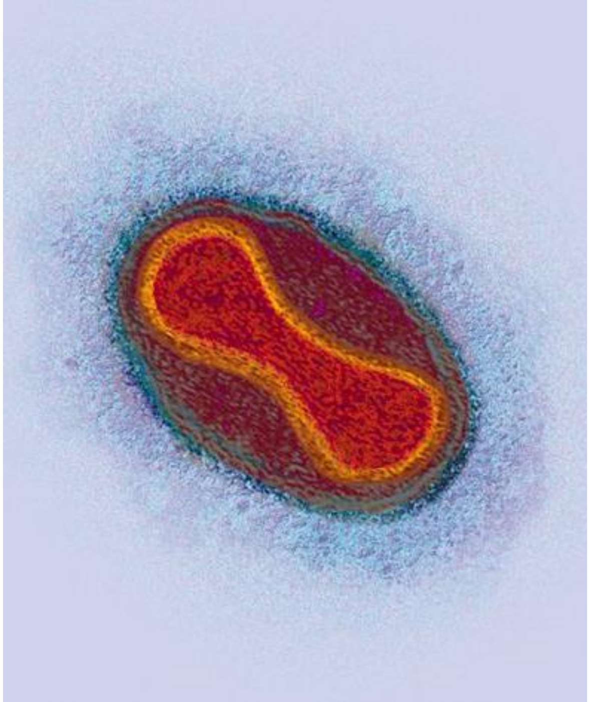
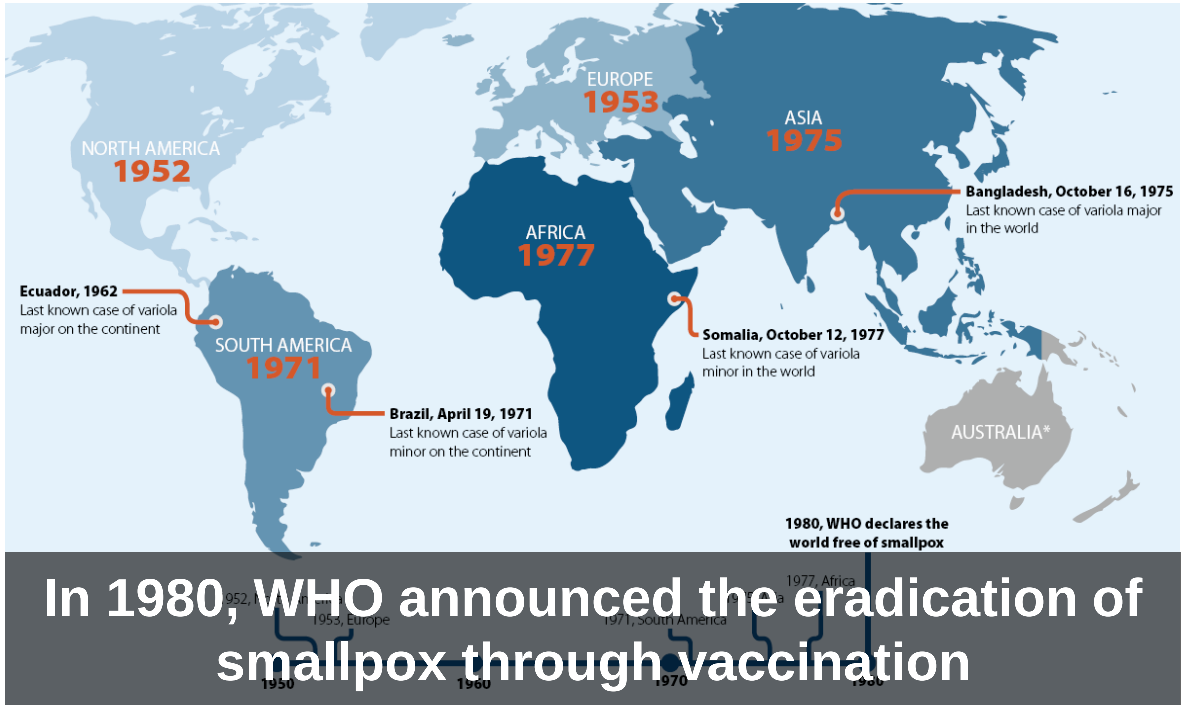
CHINESE ACADEMY OF SCIENCES

Saturated vaccine development Esp. in China

The vaccine:
Smallpox virus eradication



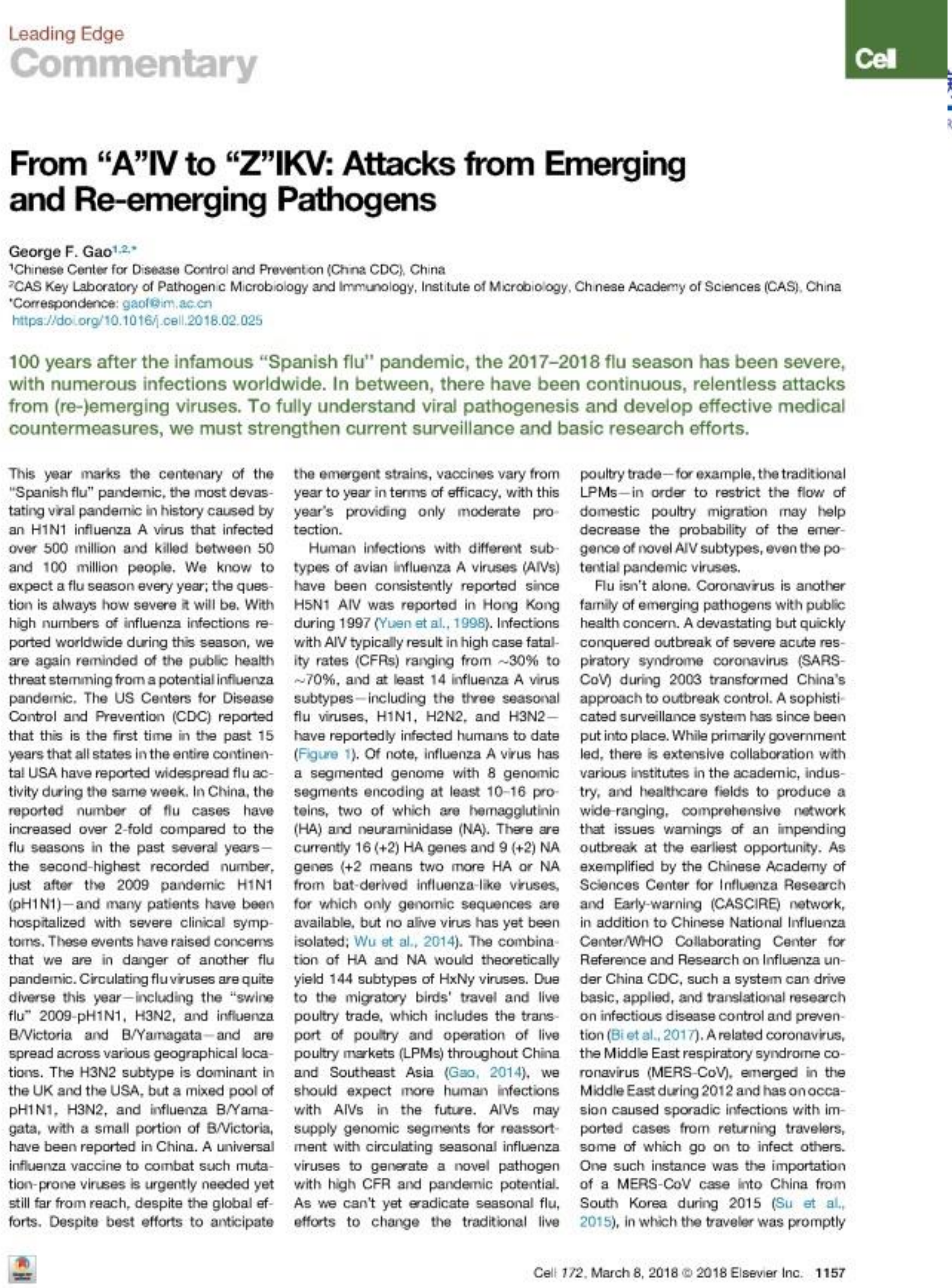




In 1980, WHO announced the eradication of smallpox through vaccination

Rinderpest is Another Virus that was Eradicated by vaccination

Disease X ???



Leading Edge
Commentary
Cell

From "A"IV to "Z"IKV: Attacks from Emerging and Re-emerging Pathogens

George F. Gao[1,2,*]
[1]Chinese Center for Disease Control and Prevention (China CDC), China
[2]CAS Key Laboratory of Pathogenic Microbiology and Immunology, Institute of Microbiology, Chinese Academy of Sciences (CAS), China
*Correspondence: gaof@im.ac.cn

https://doi.org/10.1016/j.cell.2018.02.025

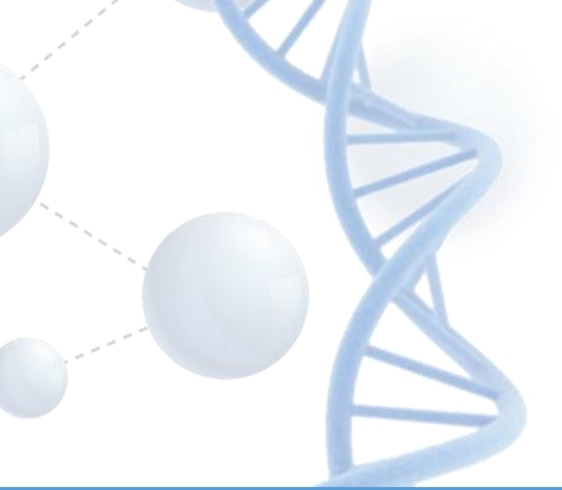
100 years after the infamous "Spanish flu" pandemic, the 2017–2018 flu season has been severe, with numerous infections worldwide. In between, there have been continuous, relentless attacks from (re-)emerging viruses. To fully understand viral pathogenesis and develop effective medical countermeasures, we must strengthen current surveillance and basic research efforts.

This year marks the centenary of the "Spanish flu" pandemic, the most devastating viral pandemic in history caused by an H1N1 influenza A virus that infected over 500 million and killed between 50 and 100 million people. We know to expect a flu season every year; the question is always how severe it will be. With high numbers of influenza infections reported worldwide during this season, we are again reminded of the public health threat stemming from a potential influenza pandemic. The US Centers for Disease Control and Prevention (CDC) reported that this is the first time in the past 15 years that all states in the entire continental USA have reported widespread flu activity during the same week. In China, the reported number of flu cases have increased over 2-fold compared to the flu seasons in the past several years—the second-highest recorded number, just after the 2009 pandemic H1N1 (pH1N1)—and many patients have been hospitalized with severe clinical symptoms. These events have raised concerns that we are in danger of another flu pandemic. Circulating flu viruses are quite diverse this year—including the "swine flu" 2009-pH1N1, H3N2, and influenza B/Victoria and B/Yamagata—and are spread across various geographical locations. The H3N2 subtype is dominant in the UK and the USA, but a mixed pool of pH1N1, H3N2, and influenza B/Yamagata, with a small portion of B/Victoria, have been reported in China. A universal influenza vaccine to combat such mutation-prone viruses is urgently needed yet still far from reach, despite the global efforts. Despite best efforts to anticipate the emergent strains, vaccines vary from year to year in terms of efficacy, with this year's providing only moderate protection.

Human infections with different subtypes of avian influenza A viruses (AIVs) have been consistently reported since H5N1 AIV was reported in Hong Kong during 1997 (Yuen et al., 1998). Infections with AIV typically result in high case fatality rates (CFRs) ranging from ~30% to ~70%, and at least 14 influenza A virus subtypes—including the three seasonal flu viruses, H1N1, H2N2, and H3N2—have reportedly infected humans to date (Figure 1). Of note, influenza A virus has a segmented genome with 8 genomic segments encoding at least 10–16 proteins, two of which are hemagglutinin (HA) and neuraminidase (NA). There are currently 16 (+2) HA genes and 9 (+2) NA genes (+2 means two more HA or NA from bat-derived influenza-like viruses, for which only genomic sequences are available, but no alive virus has yet been isolated; Wu et al., 2014). The combination of HA and NA would theoretically yield 144 subtypes of HxNy viruses. Due to the migratory birds' travel and live poultry trade, which includes the transport of poultry and operation of live poultry markets (LPMs) throughout China and Southeast Asia (Gao, 2014), we should expect more human infections with AIVs in the future. AIVs may supply genomic segments for reassortment with circulating seasonal influenza viruses to generate a novel pathogen with high CFR and pandemic potential. As we can't yet eradicate seasonal flu, efforts to change the traditional live poultry trade—for example, the traditional LPMs—in order to restrict the flow of domestic poultry migration may help decrease the probability of the emergence of novel AIV subtypes, even the potential pandemic viruses.

Flu isn't alone. Coronavirus is another family of emerging pathogens with public health concern. A devastating but quickly conquered outbreak of severe acute respiratory syndrome coronavirus (SARS-CoV) during 2003 transformed China's approach to outbreak control. A sophisticated surveillance system has since been put into place. While primarily government led, there is extensive collaboration with various institutes in the academic, industry, and healthcare fields to produce a wide-ranging, comprehensive network that issues warnings of an impending outbreak at the earliest opportunity. As exemplified by the Chinese Academy of Sciences Center for Influenza Research and Early-warning (CASCIRE) network, in addition to Chinese National Influenza Center/WHO Collaborating Center for Reference and Research on Influenza under China CDC, such a system can drive basic, applied, and translational research on infectious disease control and prevention (Bi et al., 2017). A related coronavirus, the Middle East respiratory syndrome coronavirus (MERS-CoV), emerged in the Middle East during 2012 and has on occasion caused sporadic infections with imported cases from returning travelers, some of which go on to infect others. One such instance was the importation of a MERS-CoV case into China from South Korea during 2015 (Su et al., 2015), in which the traveler was promptly

Attacks by EID Gao, Cell, 2018



THANK YOU!