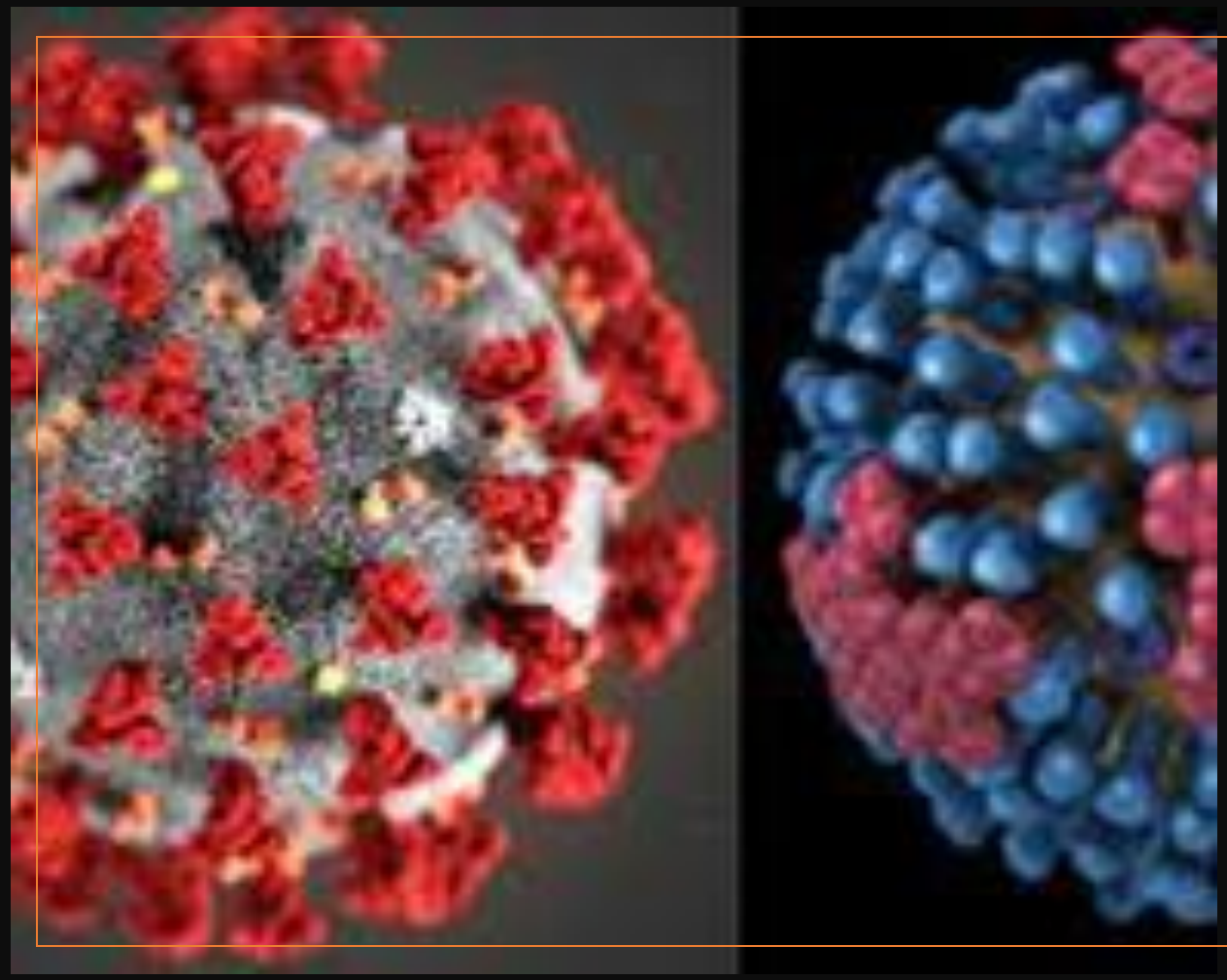


The Coming Flu Season: COVID and Influenza Converge

Kimberly Shriner, M.D., F.A.C.P.

September 1, 2020

The COVID Situation

COVID-19 Cases

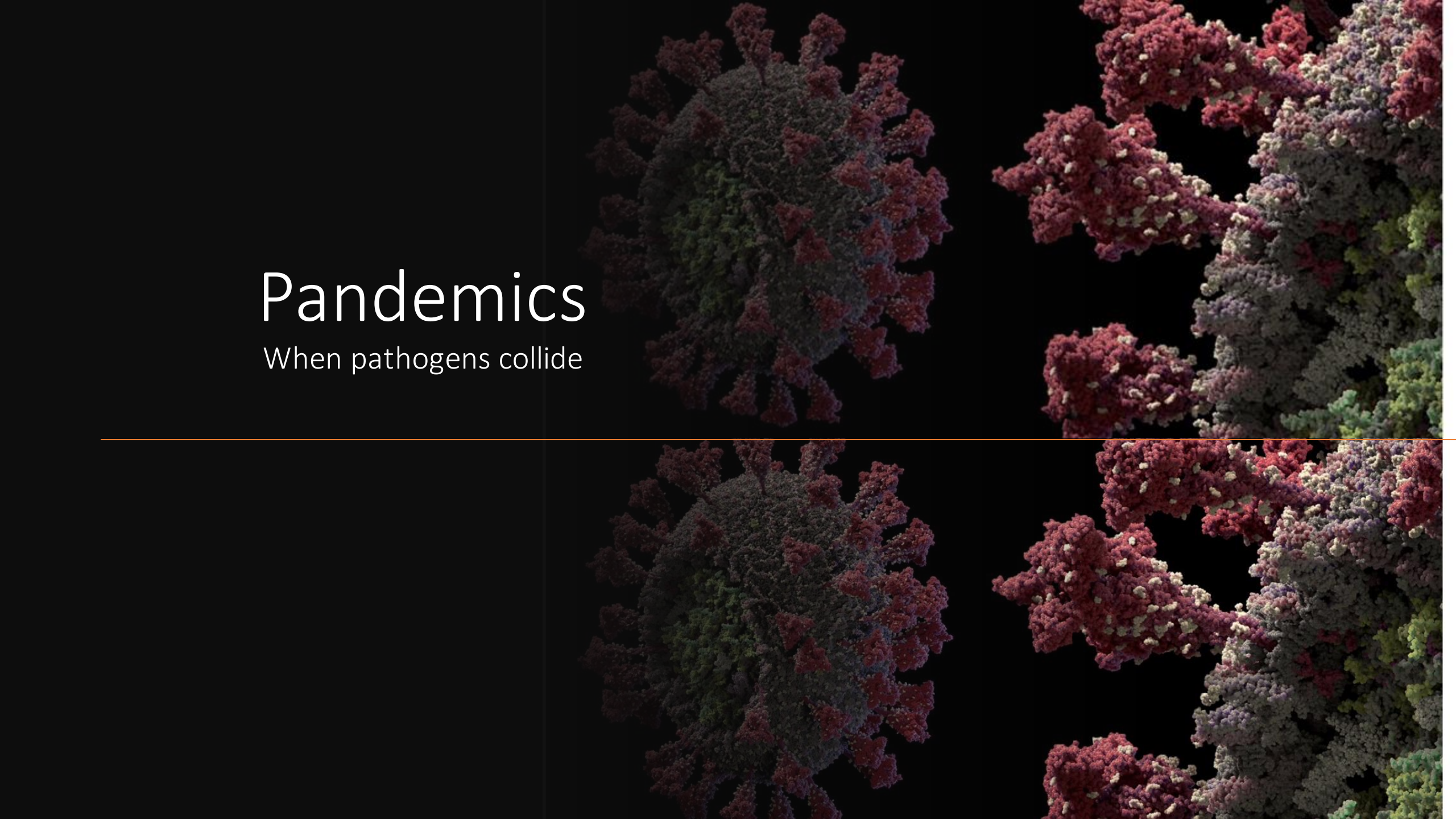
- Global
  - 25, 405, 845 confirmed cases
  - 849, 349 deaths
- US
  - 6, 029, 695 cases confirmed
  - 183, 585 deaths
- LA County
  - 241, 768 confirmed cases
  - 5769 deaths

8.30.20
coronavirus.jhu.edu.

publichealth.lacounty.gov
//media

Pandemics

When pathogens collide



Influenza as a Pandemic Pathogen

- 1918-1919 Spanish Flu : H1N1; 1/3 of world's population infected
- 1957 H2N2 pandemic
- 1968 H3N2 pandemic
- H1N1 pdm o9 virus pandemic

Mortality

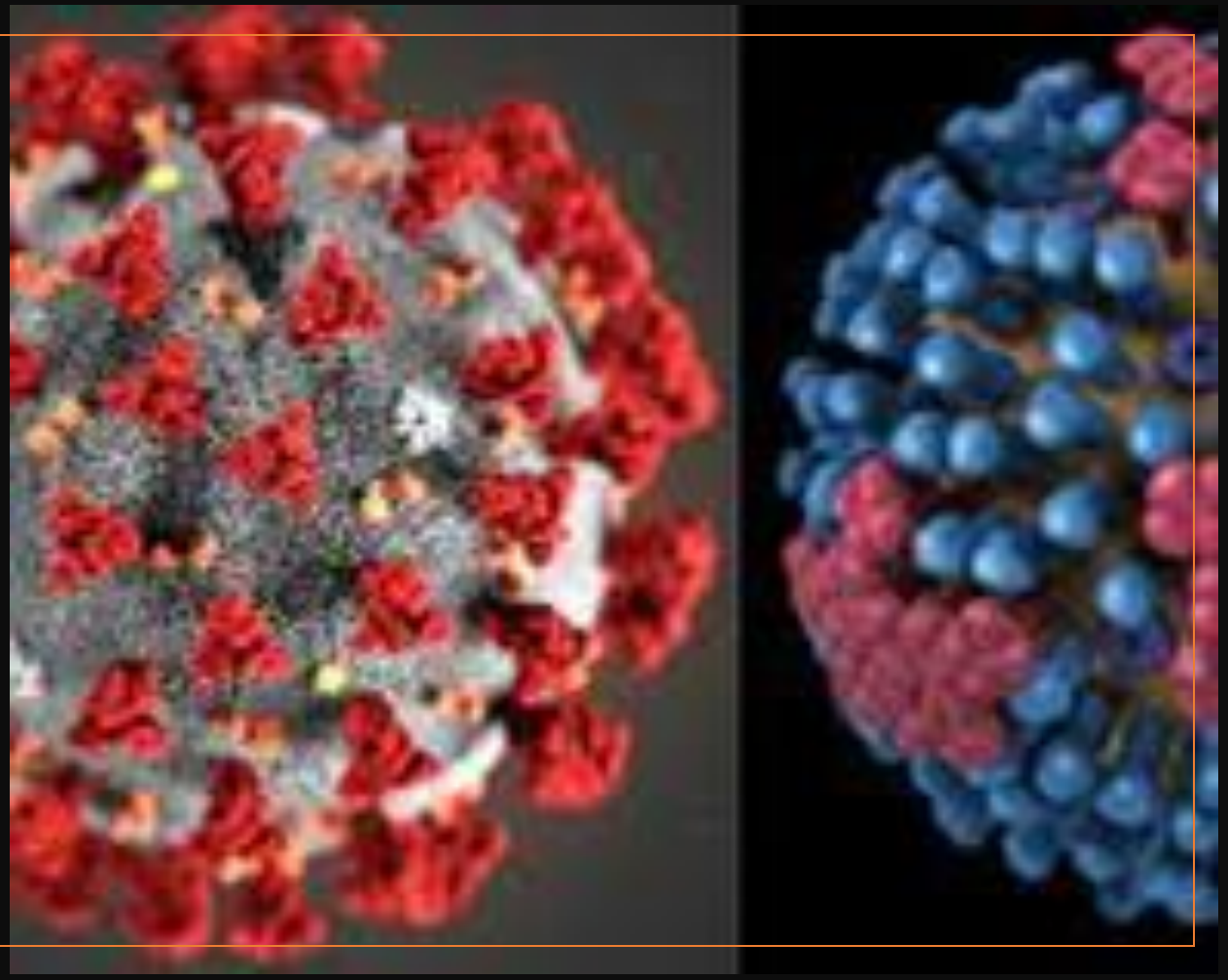
Influenza

- US 2018-2019 Season
- 35 million illnesses
- 16.5 million medical visits
- 490, 600 hospitalizations
- 34, 200 deaths

COVID 19

- January-August “season” US
- 6, 029, 695 cases
- 183, 585 deaths

The Pathogens

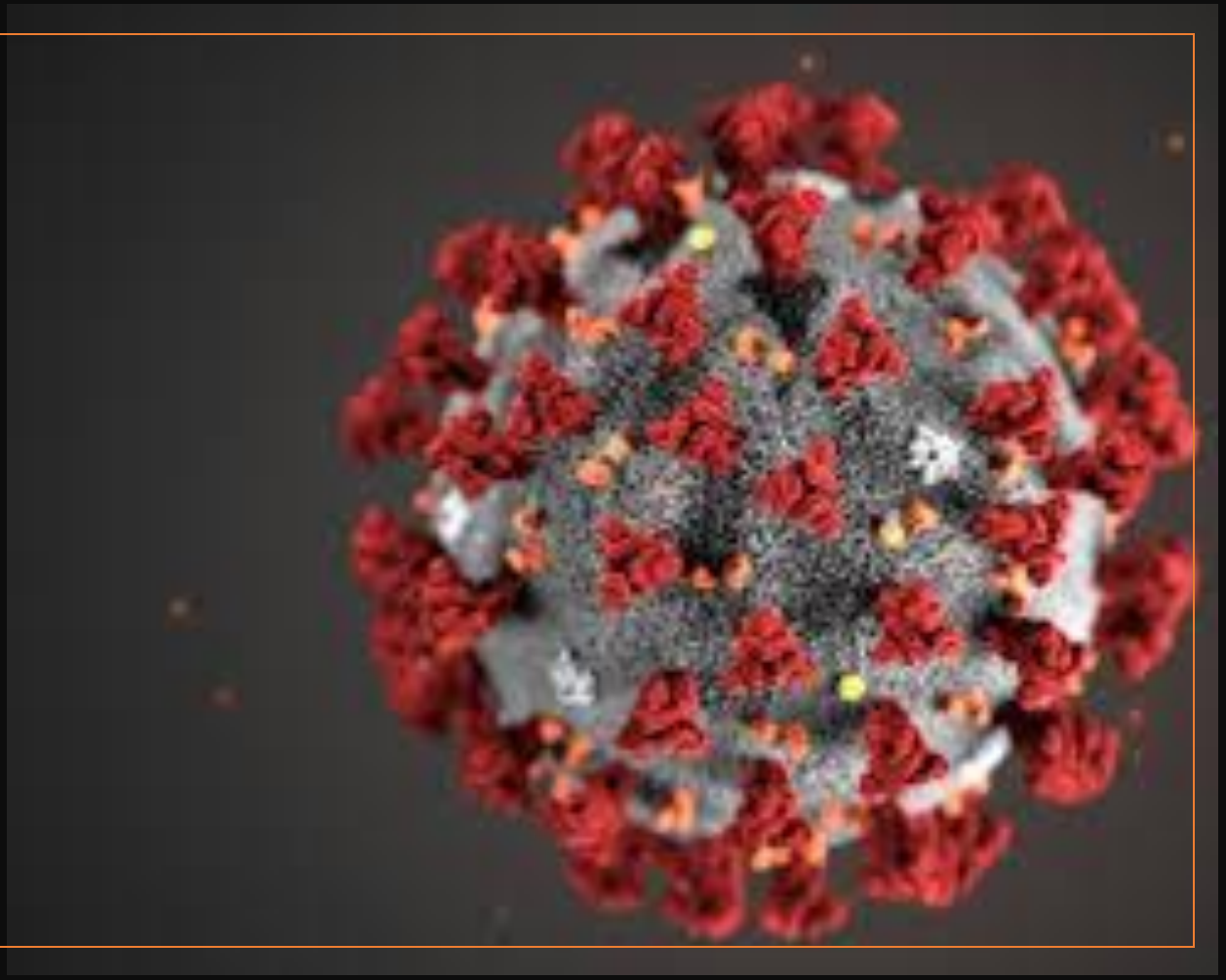


Reporter to Dr. Anthony Fauci: “ What is your nightmare scenario?”

Dr. Fauci: ”This is it.”

Fauci said the virus met all four criteria for a nightmare scenario — it is new, respiratory-borne, easily transmissible and has a significant degree of illness or mortality.

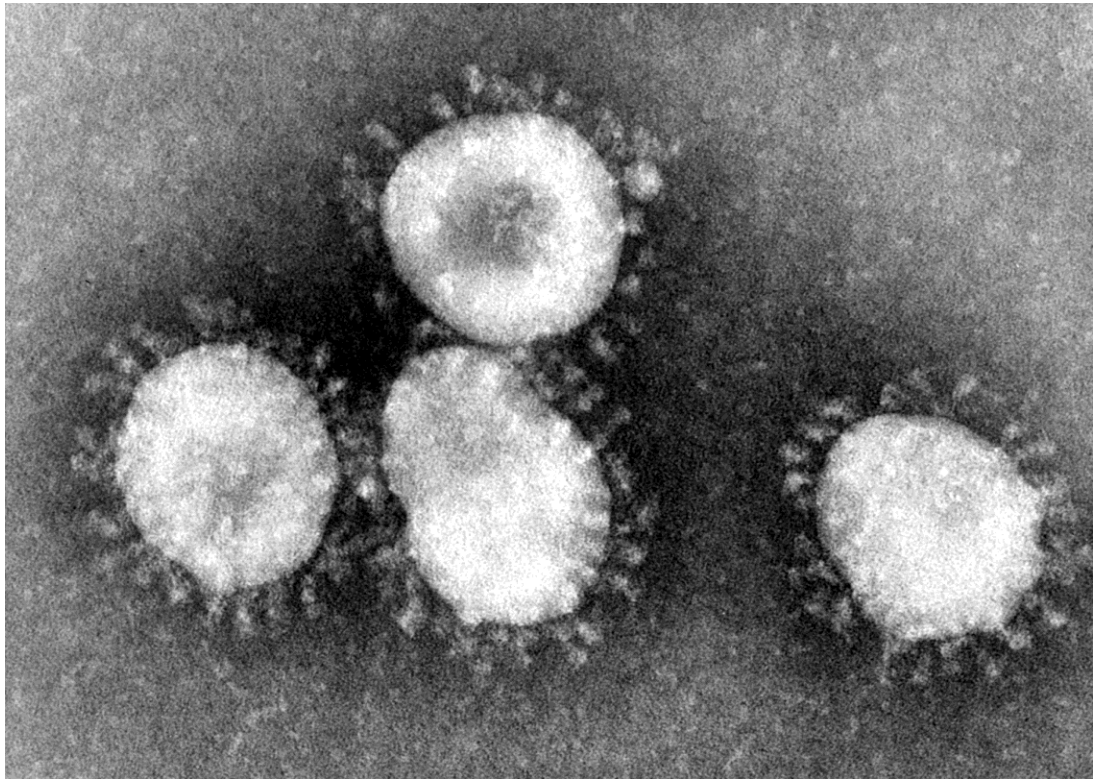
SARS CoV-2



SARS CoV-2

- Highly infectious pathogen,
- Rapid and wide global spread; No country immune
- High density of disease
- Causes very serious illness and frequently death
- Transmitted through even casual human interaction/behaviors
- No one has immunity
- No robust therapies
- No vaccine as yet

Coronaviruses (*Coronavirinae*)

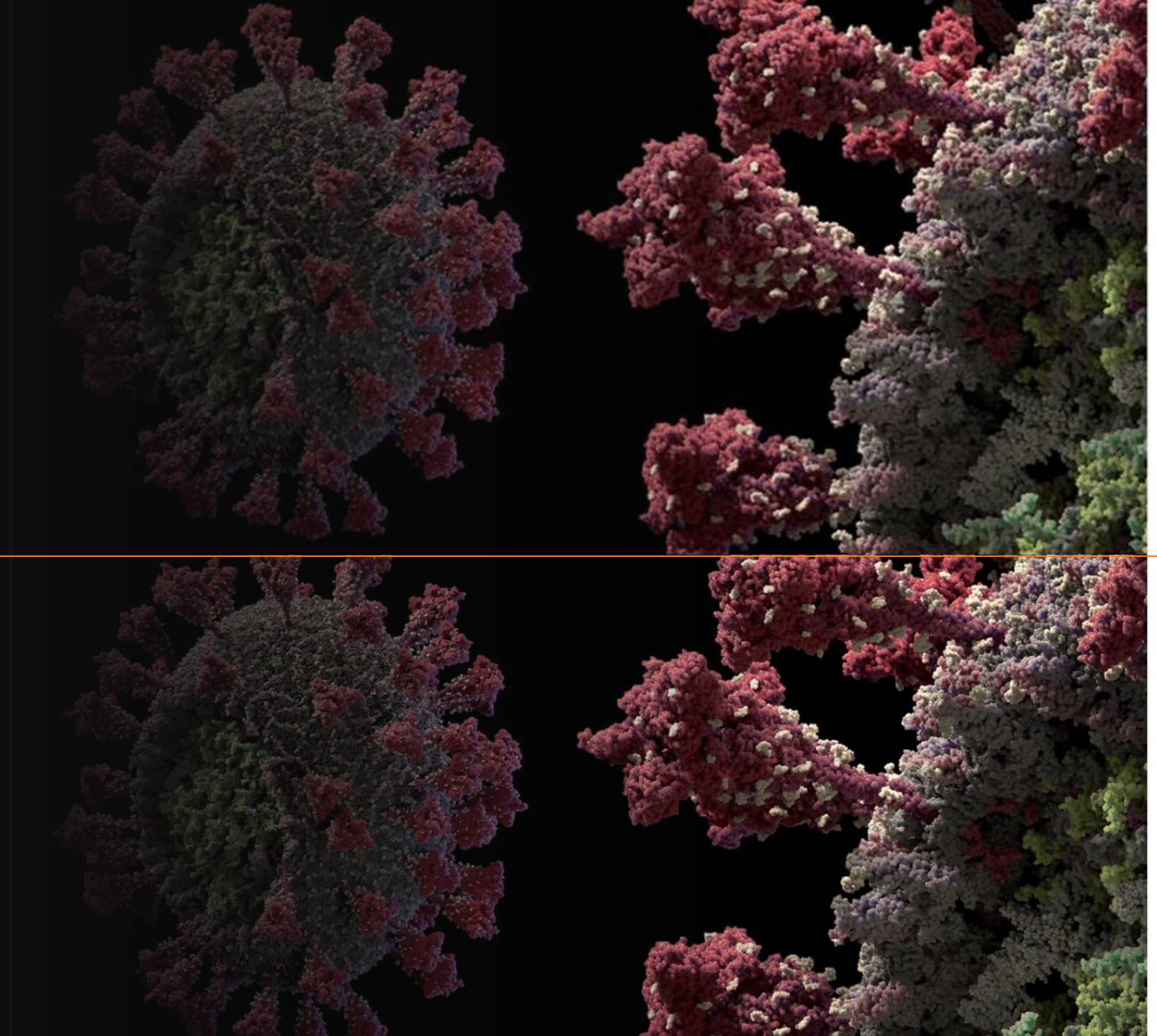


- RNA virus
- Largest genome of any RNA virus
- Usually affect birds and mammals (not reptiles)
- Common cause of upper respiratory infections, lower respiratory infections (bronchitis and pneumonia) and ARDS.

Coronaviruses and their hosts

Genus	Species
Alphacoronavirus	Bat coronavirus CDPHE15
	Bat coronavirus HKU10
	Human coronavirus 229E
	Human coronavirus NL63
	Miniopterus bat coronavirus 1
	Miniopterus bat coronavirus HKU8
	Mink coronavirus 1
	Porcine epidemic diarrhoea virus
	Rhinolophus bat coronavirus HKU2
	Scotophilus bat coronavirus 512
Betacoronavirus	Betacoronavirus 1
	Hedgehog coronavirus 1
	Human coronavirus HKU1
	Middle East respiratory syndrome-related coronavirus
	Murine coronavirus
	Pipistrellus bat coronavirus HKU5
	Rousettus bat coronavirus HKU9
	Severe acute respiratory syndrome-related coronavirus
	Tylonycteris bat coronavirus HKU4
Deltacoronavirus	Bulbul coronavirus HKU11
	Common moorhen coronavirus HKU21
	Coronavirus HKU15
	Munia coronavirus HKU13
	Night heron coronavirus HKU19
	Thrush coronavirus HKU12
	White-eye coronavirus HKU16
	Wigeon coronavirus HKU20
Gammacoronavirus	Avian coronavirus
	Beluga whale coronavirus SW1

Origins



- Not a hoax
- Not a laboratory experiment gone wrong
- Not a bioterrorist weapon

Zoonotic Infection

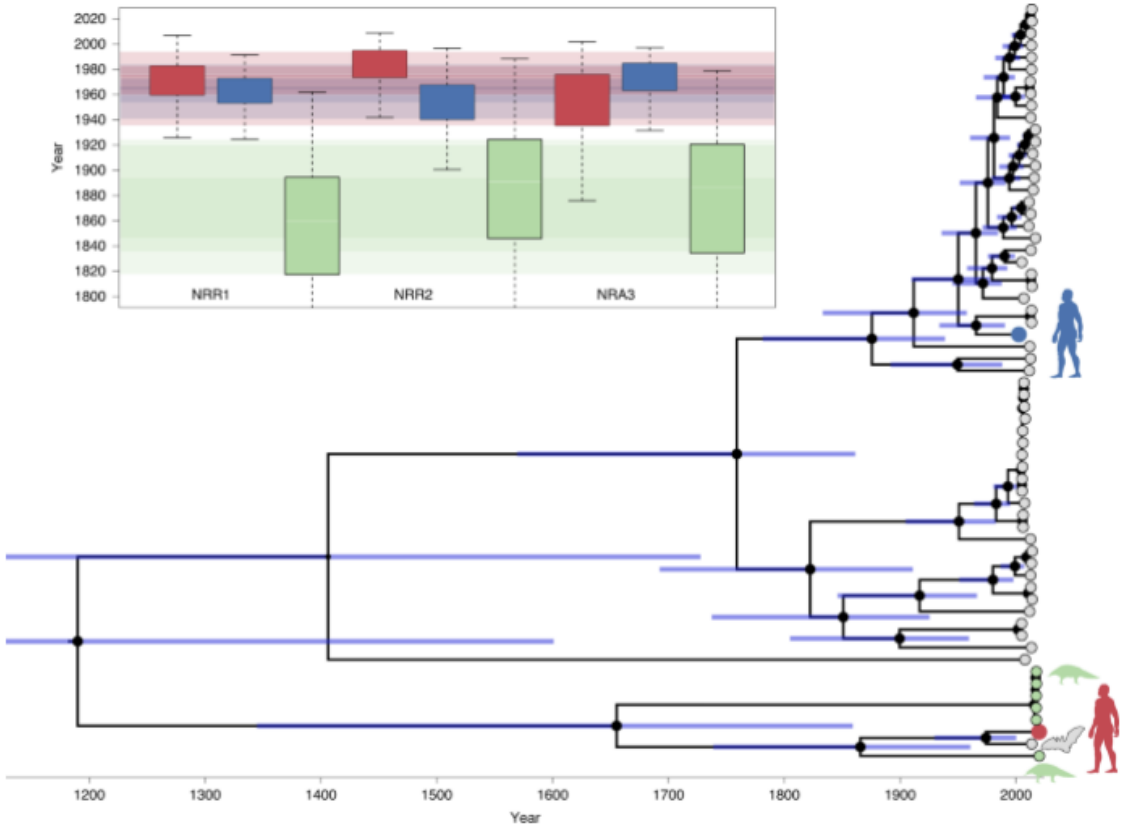
- Anderson et al. *Nature Medicine* April 2020:

- Thorough evaluation of genome of SARS CoV2
- Attention to the unique adaptation of the receptor binding domain (RBD) of the spike protein
- Apparent genetic mutation that allowed avid attachment to human ACE 2 receptors
- Affinity of human ACE 2 binding product of natural selection in animal host *before* zoonotic transfer
- Harbored in bats, but pangolin ACE2 similarity to human ACE 2 receptors may have promoted the natural selection

Evolutionary rates and divergence data show that SARS CoV-2 has been circulating in bats for decades.

Rhinophilus affinis

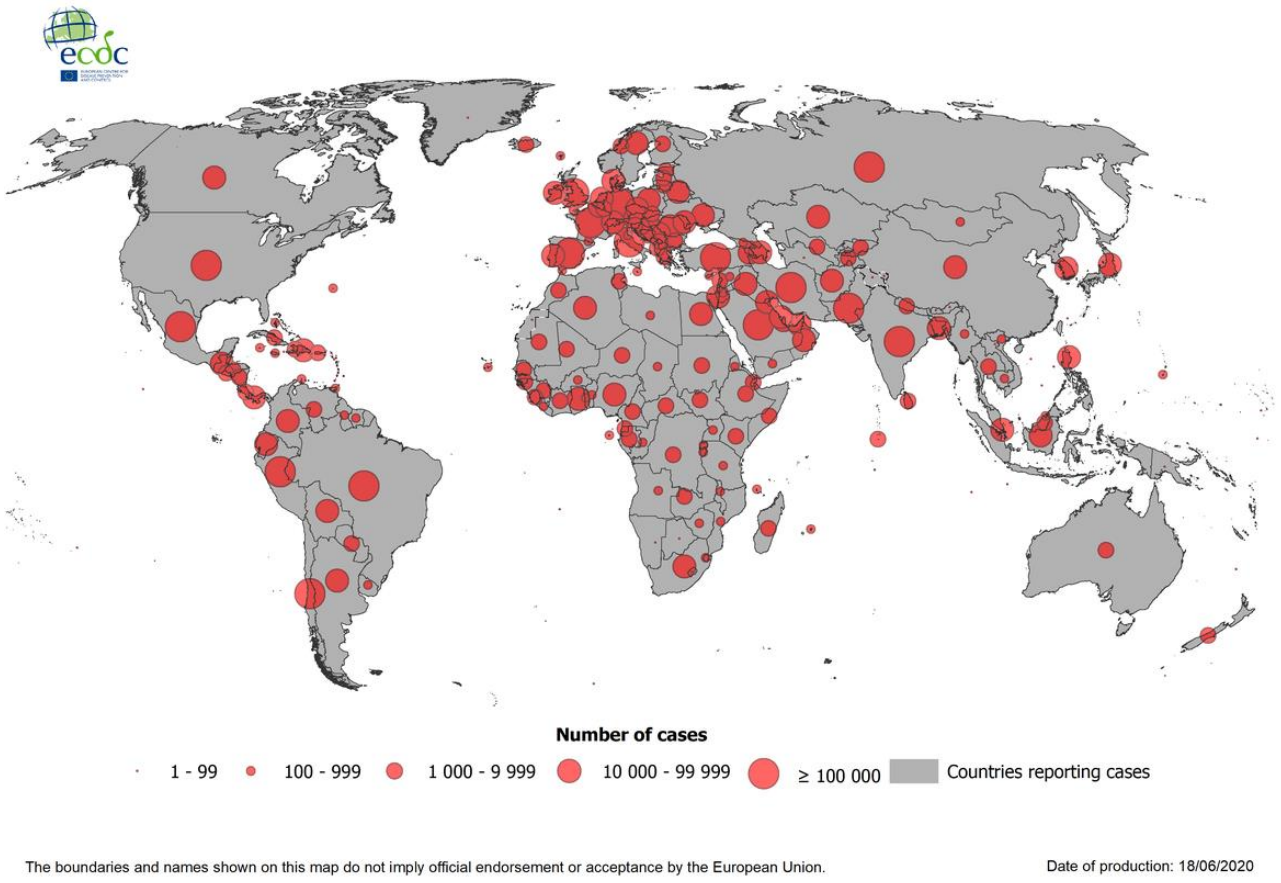
Fig. 5: Time-measured phylogenetic estimates and divergence times for sarbecovirus lineages using an HCoV-OC43-centred rate prior.

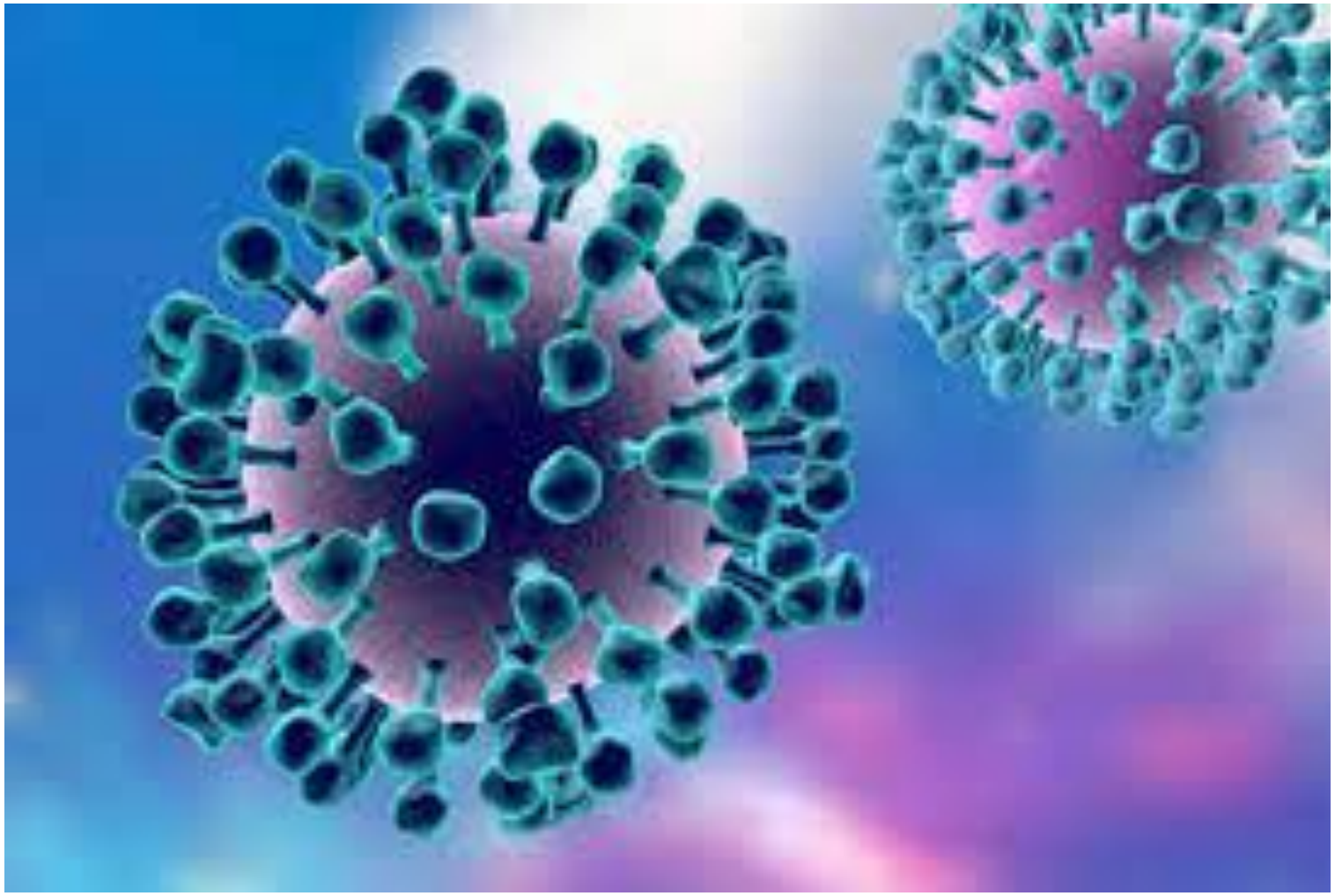


Boni et al. Nature Microbiology 2020

SARS-Co-V2

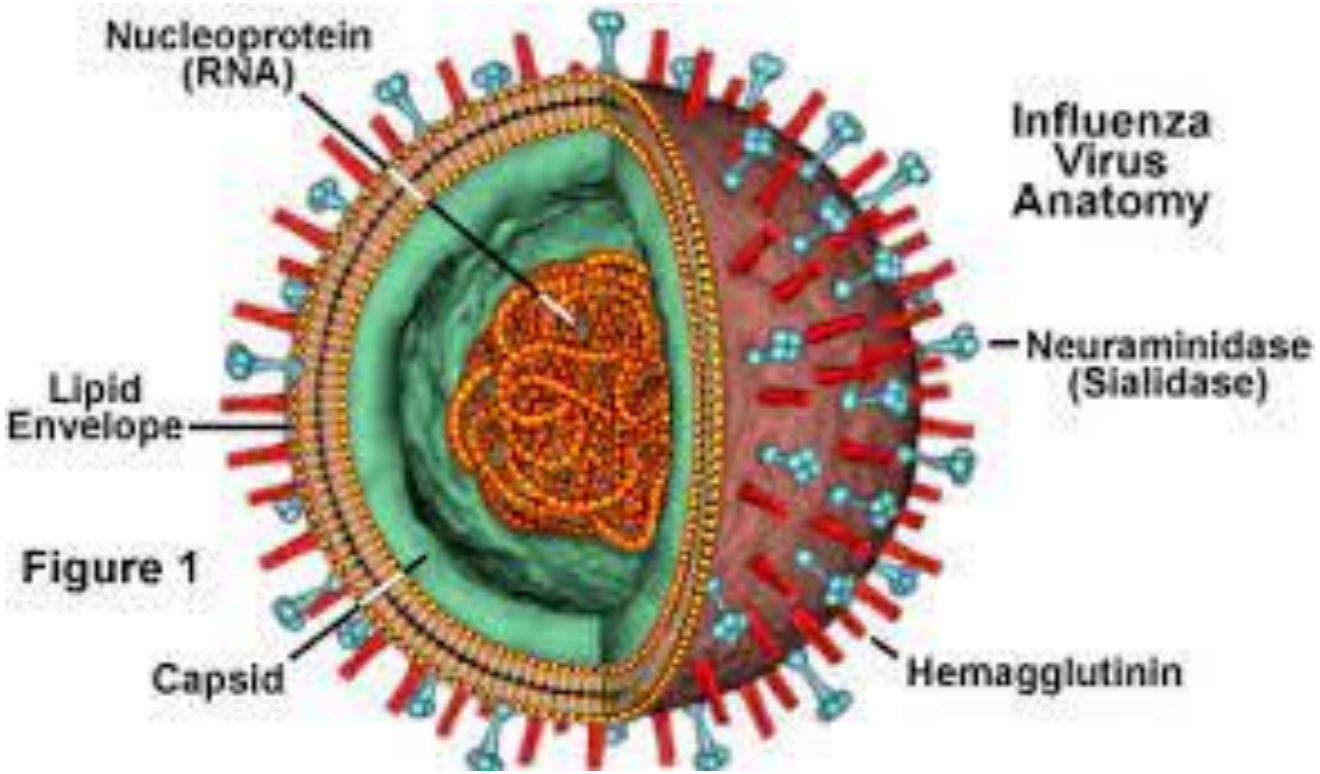
From a Wuhan Wet Market to the rest of the world



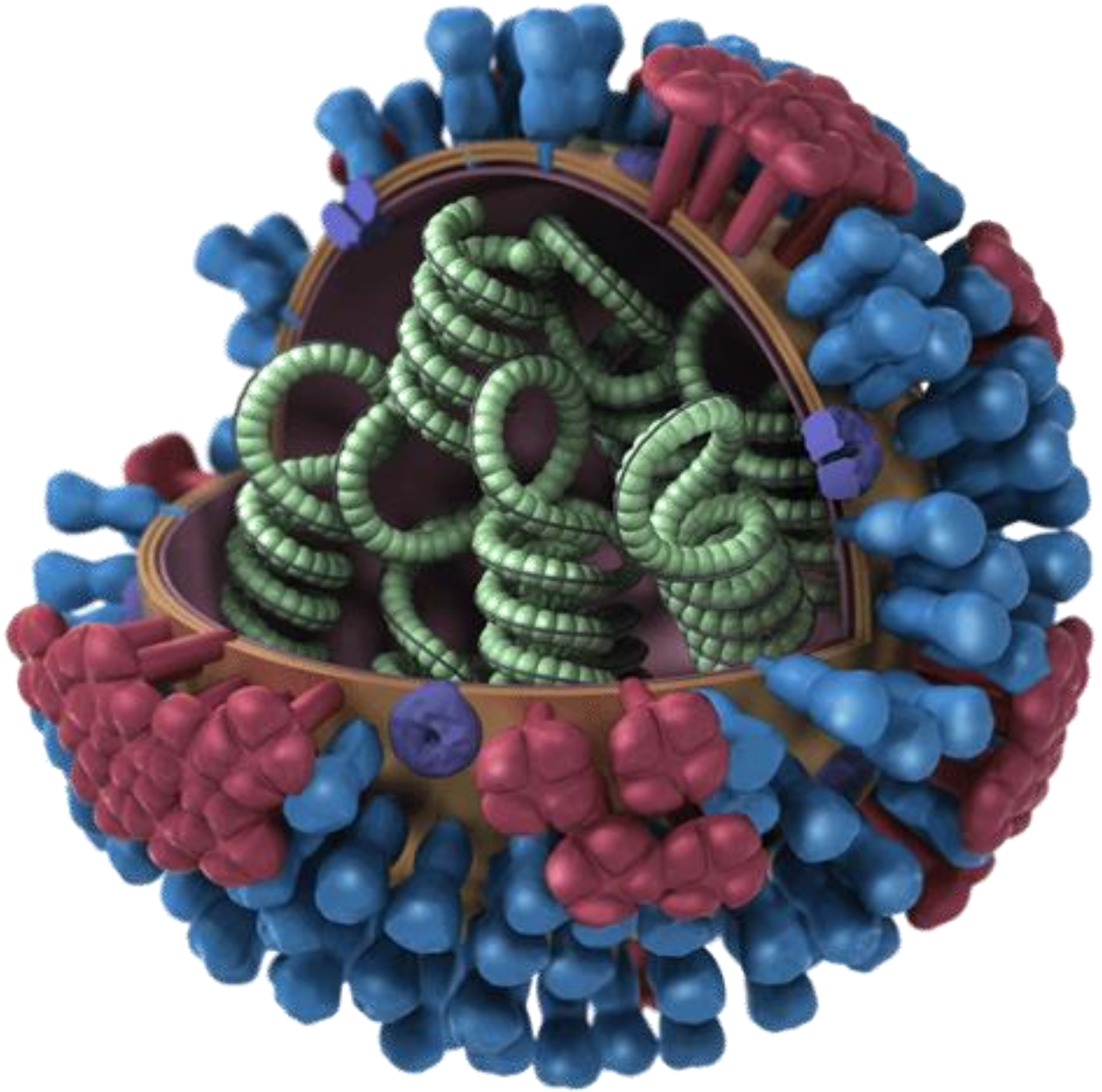


Influenza

Influenza

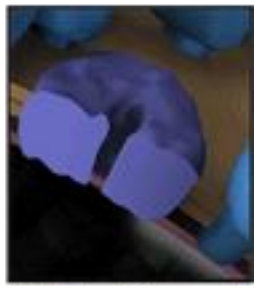


- 4 types: Influenza A, B, C, D
- Human Influenza A and B cause seasonal epidemics
- Influenza A only type that is known to cause flu pandemics.
- INFLUENZA A:
- 18 different hemagglutinin subtypes and 11 different neuraminidase subtypes



Hemagglutinin

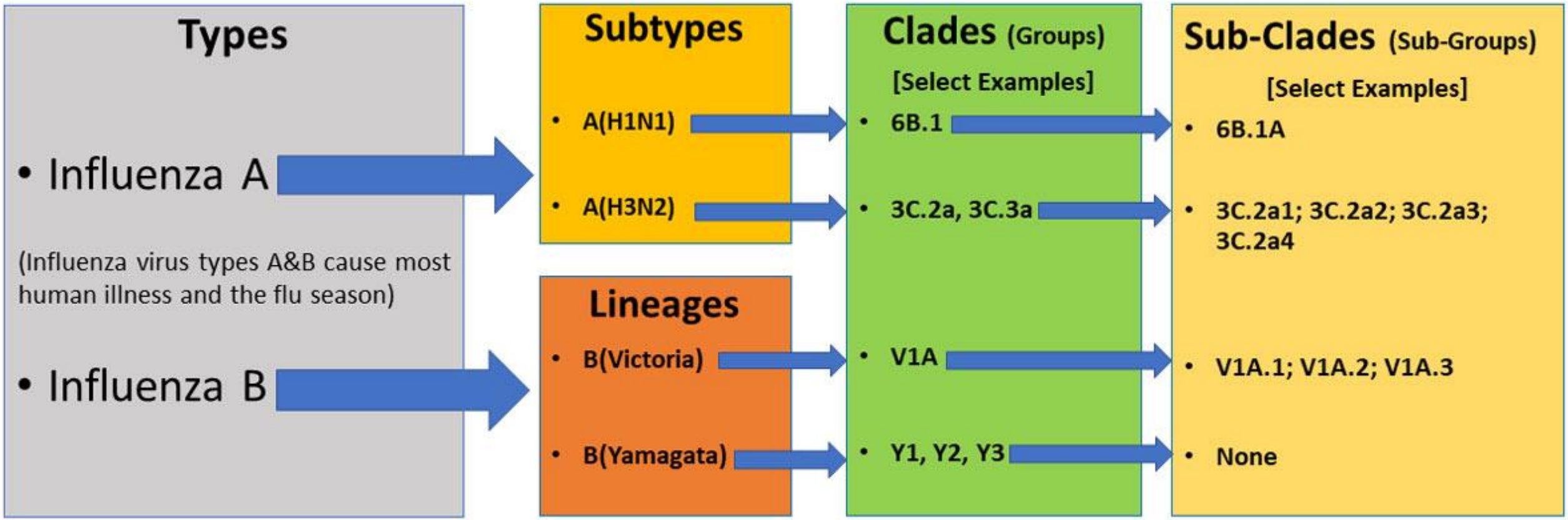
Neuraminidase



M2 Ion Channel

RNP

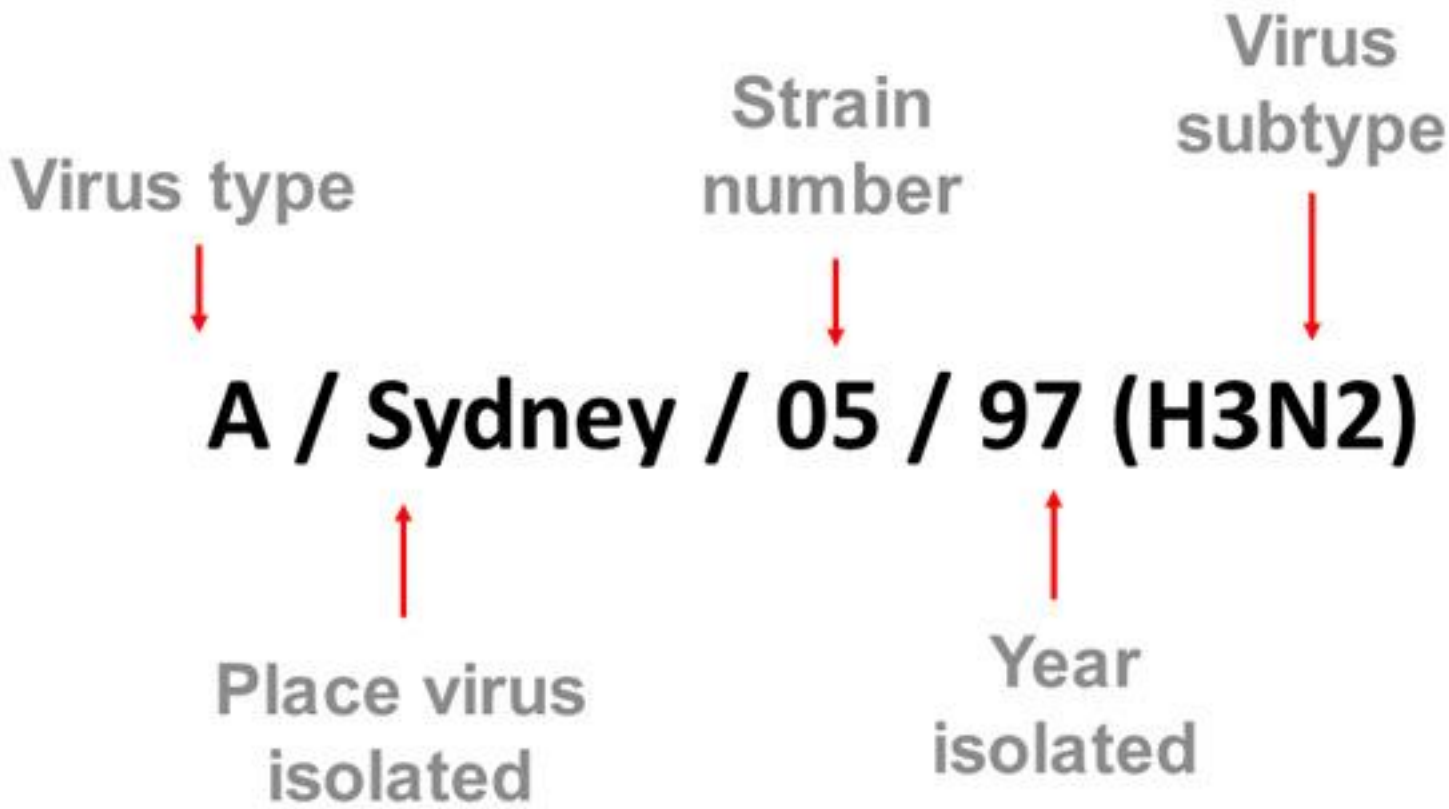
Human Seasonal Influenza Viruses



Influenza Viruses

- Currently circulating H1N1 influenza viruses are related to the previous 2009 H1N1 virus that emerged in 2009 and caused a pandemic
- H3N2 tend to be more virulent and change more rapidly, both antigenically (related to receptors on the surface of the virus) or genetically
- Influenza antigens are the molecules that trigger an immune response and are the targets for annual vaccine production

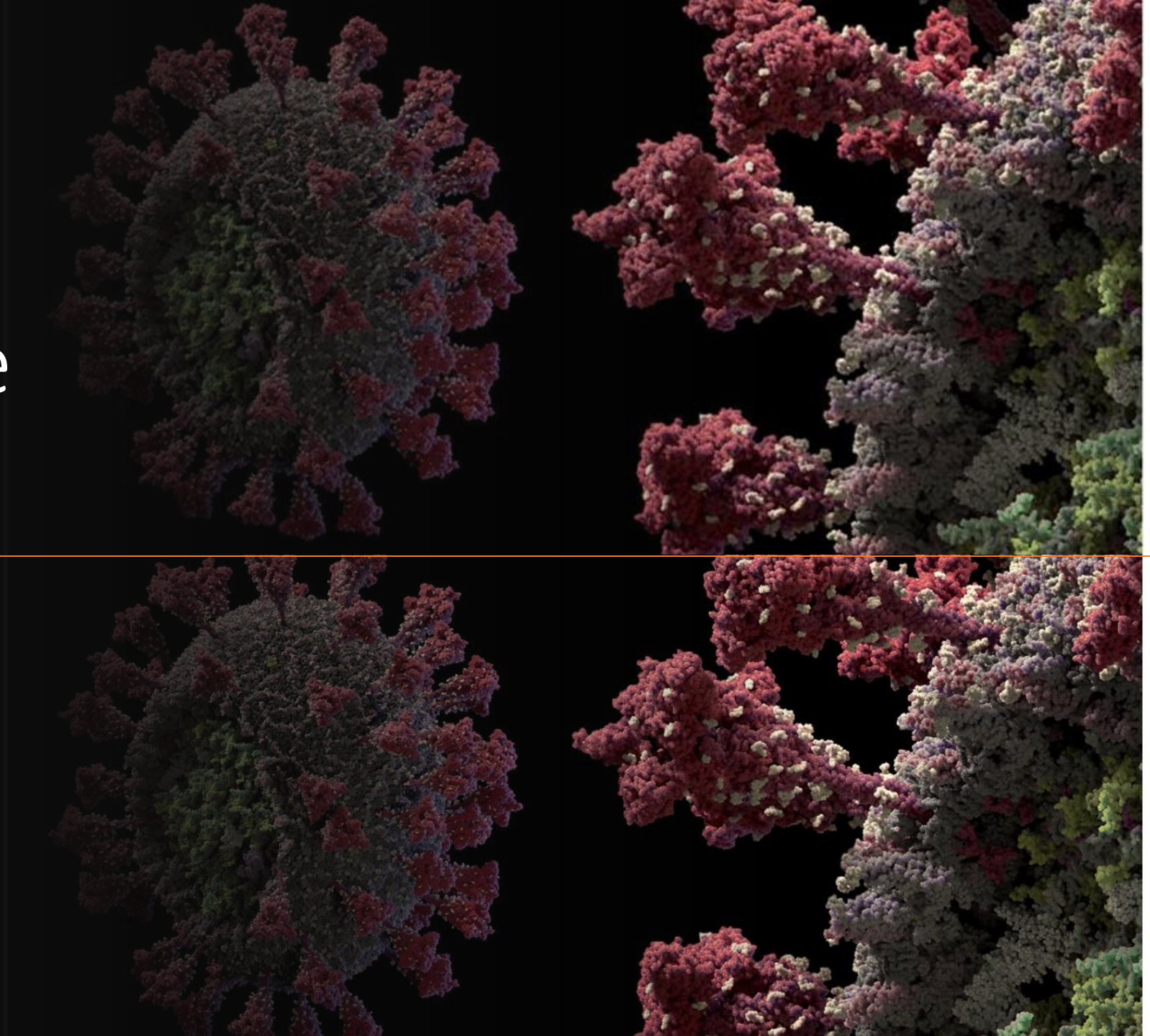
Understanding the naming of flu viruses



Influenza in other animals

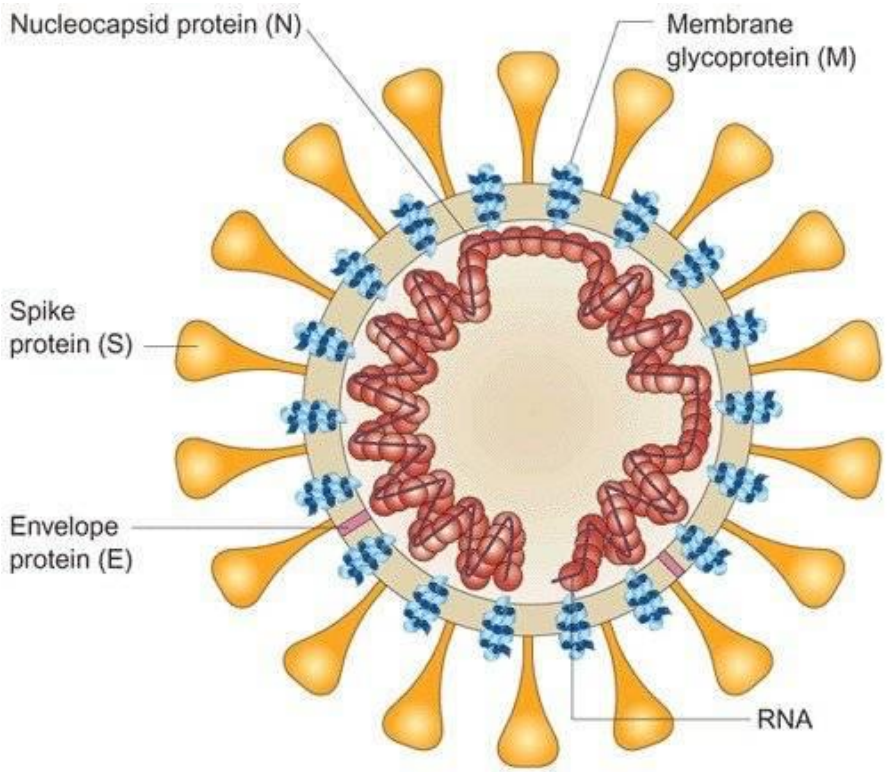
Viral Structure

SARS CoV-2

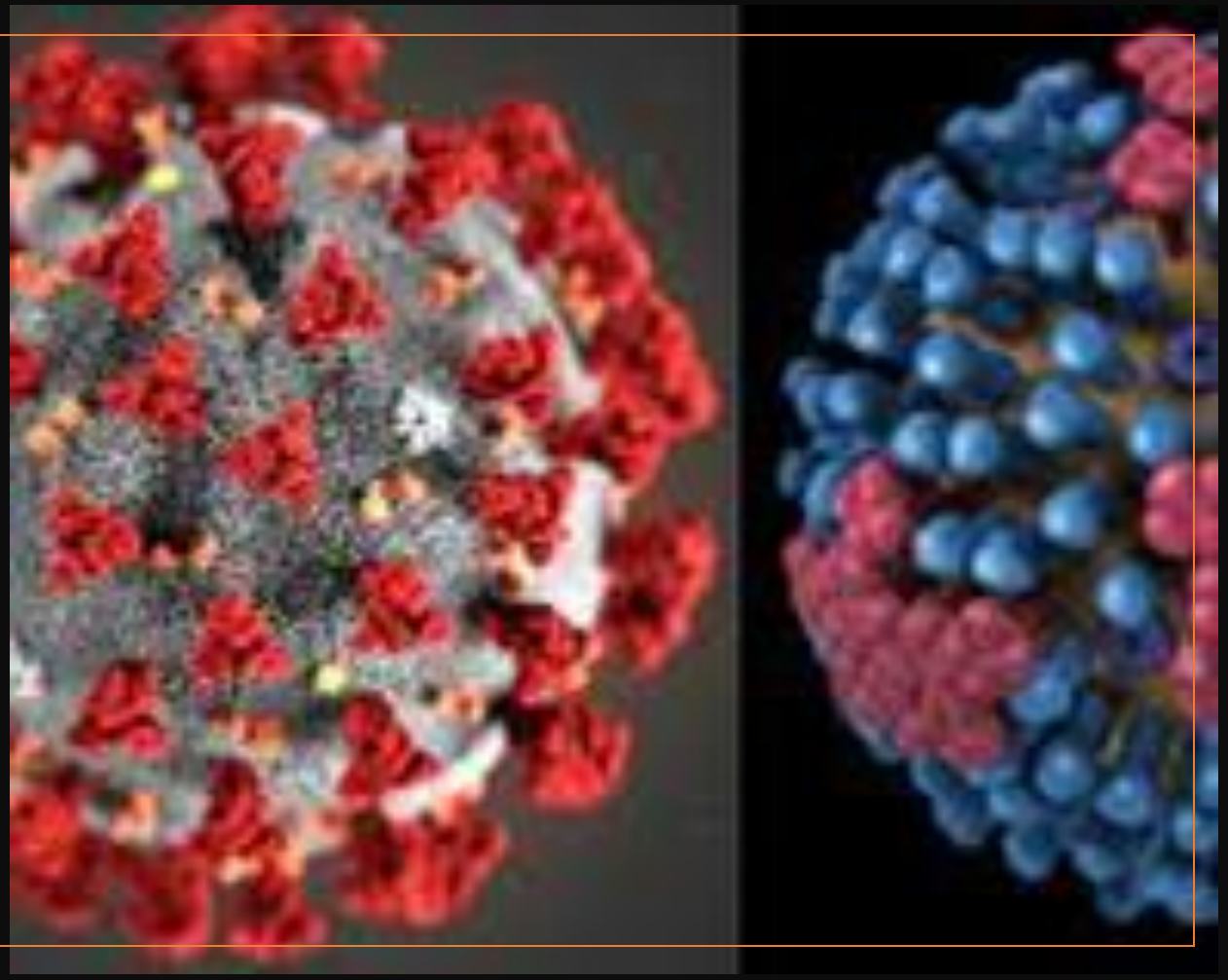


Coronaviruses (CoV)

- 4 major structural proteins:
  - 1)Spike protein (S)
  - 2)Nucleocapsid protein (N)
  - 3)Membrane protein (M)
  - 4)Envelope protein (E)

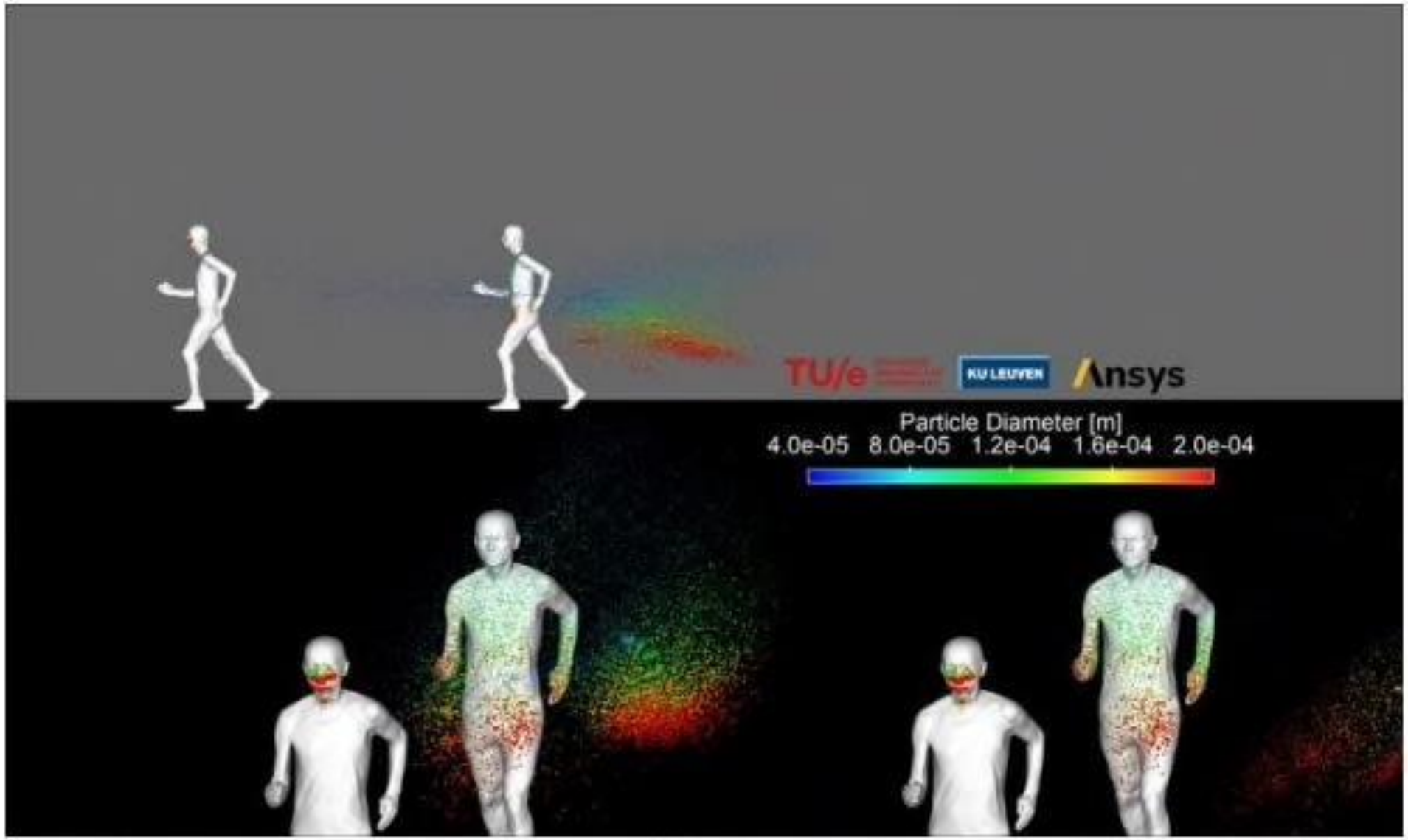


Transmission



Highly Infectious

- Droplet borne usually
- Aerosolized occasionally
- Contaminated surfaces to mucus membranes
- Viral load/inoculum at time of exposure important
- Length of time of exposure important



TU Eindhoven and KU Leuven CFD simulation of the slipstream with microdroplets for running (fast) at 14.4 km/h. Snapshot at given moment in time.

Spike Protein Mutation and Circulating SARS CoV-2

New Results

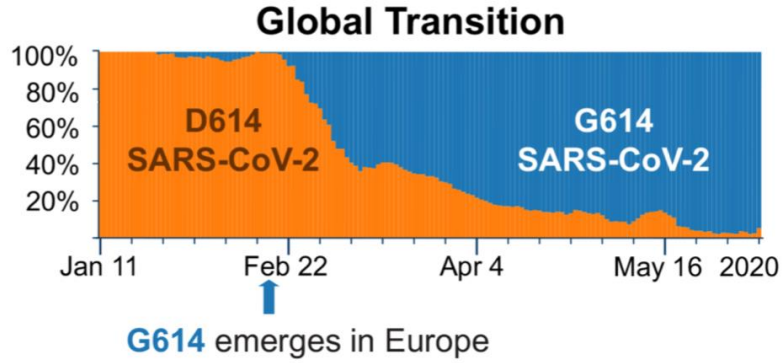
Previous Next

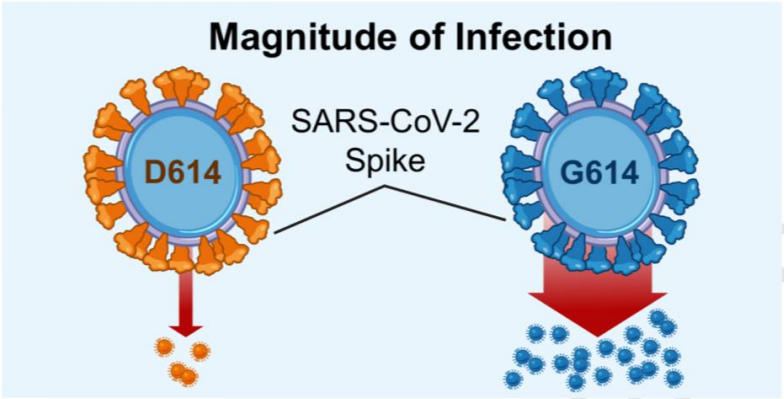
Spike mutation pipeline reveals the emergence of a more transmissible form of SARS-CoV-2

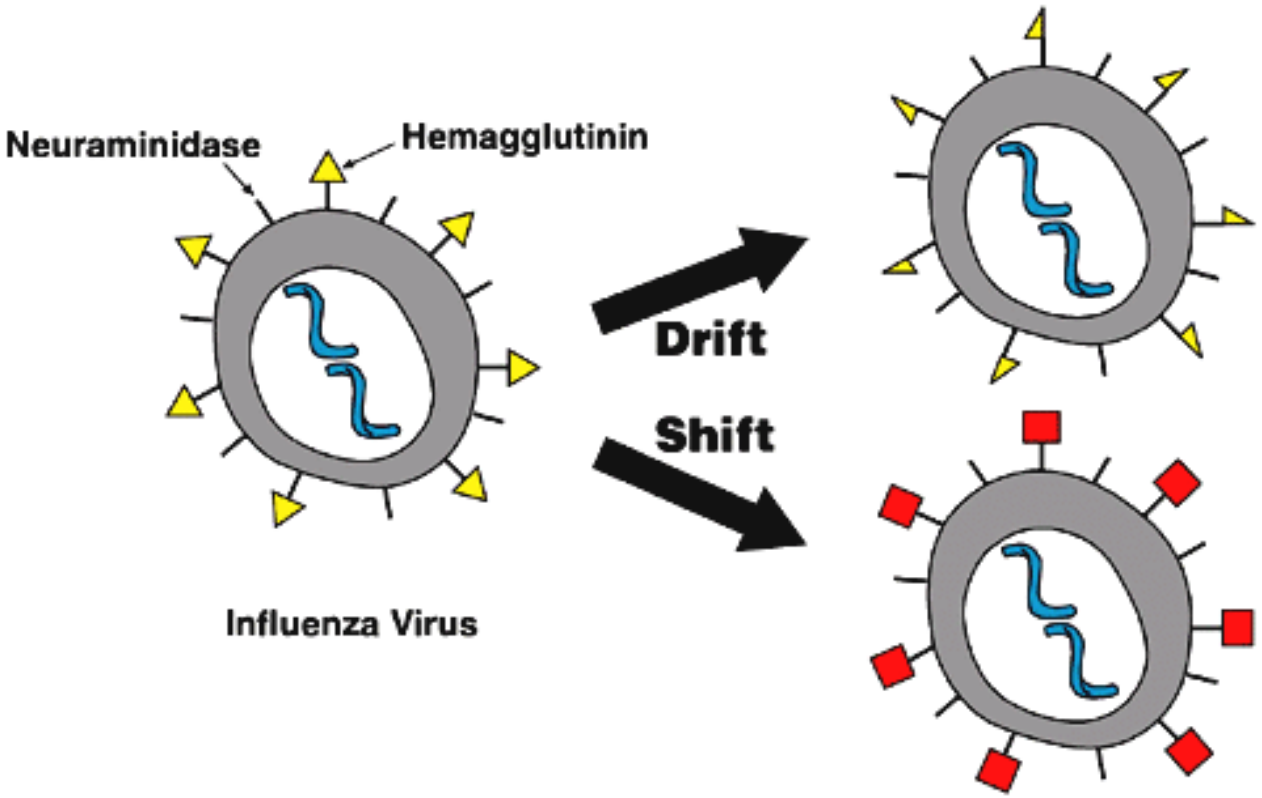
B Korber, WM Fischer, S Gnanakaran, H Yoon, J Theiler, W Abfalterer, B Foley, EE Giorgi, T Bhattacharya, MD Parker, DG Partridge, CM Evans, TI de Silva, on behalf of the Sheffield COVID-19 Genomics Group, CC LaBranche, DC Montefiori

doi: https://doi.org/10.1101/2020.04.29.069054

Posted April 30, 2020.







Antigenic Drift vs Antigenic Shift

Infectivity

- Ro (R naught) value
  - Term from demographic data; refers to “reproduction” and “zeroth generation” or patient zero. Basic reproduction number
  - For pandemics, represents the number of new infections estimated to stem from a single case
  - For SARVSCoV2 around 2-5 but 2-2.5 more realistic
  - Influenza 1.3 vs measles 5
- Serial Interval: how fast does it spread?
  - SARVSCoV2 estimates 4-4.5 days (faster than SARS 1)

Infectivity

- Highly infectious: Basic reproductive number, R naught value 2.5-5, depending on studies
- Higher Ro value means more of the population needs to have antibodies to the disease to achieve herd immunity
- Ro value less than one may dictate loosening of social distancing

Importance of Household Transmission SARS CoV -2

- Contact tracing study in South Korea
- 59, 073 contacts of 5,706 index COVID 19 patients
- Household contacts: 11.8%
- Nonhousehold contacts: 1.9%
- Highest COVID rate for household contacts of school aged children attending school (18.6%) and lowest rate during school closure children 0-9 yrs (5.3%)
- Concurrent findings other studies in China, France and Hong Kong:
  - Estimated rates of seconday infection within household 35%

Park et al. Emerging Inf Dis. Oct 2020

Risk Factors for Transmission

Situation

- Encounter infected individual
- Congregant living situations
- Crowds
- Duration of exposure
- Inoculum size of exposure

Host

- Age
- Occupation
- Socioeconomic status
- Comorbidities

Aerosolization of SARS CoV2

medRxiv

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Comments (14)

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Viable SARS-CoV-2 in the air of a hospital room with COVID-19 patients

Posted August 04, 2020.

John A Lednicky, Michael Lauzardo, Z. Hugh Fan, Antarpreet S Jutla, Trevor B Tilly, Mayank Gangwar, Moiz Usmani, Sripriya N Shankar, Karim Mohamed, Arantza Eiguren-Fernandez, Caroline J Stephenson, Md. Mahbubul Alam, Maha A Elbadry, Julia C Loeb, Kuttichantran Subramaniam, Thomas B Waltzek, Kartikeya Cherabuddi, John Glenn Morris Jr., Chang-Yu Wu

doi: https://doi.org/10.1101/2020.08.03.20167395

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Supplementary Material

Data/Code

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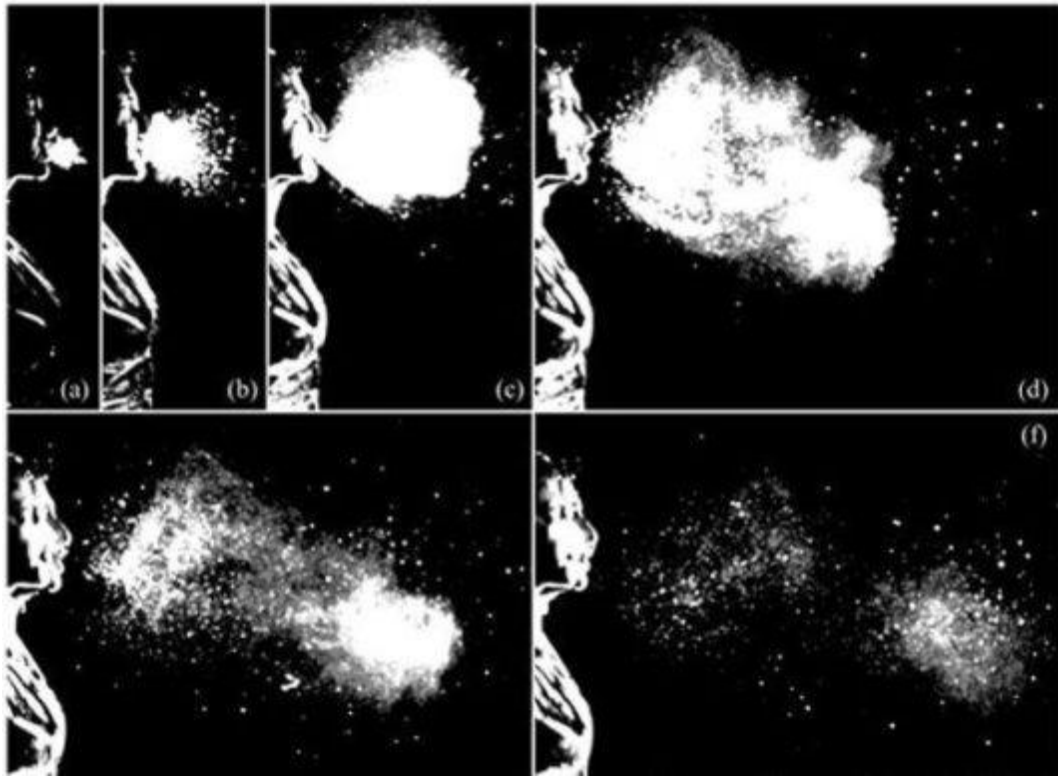
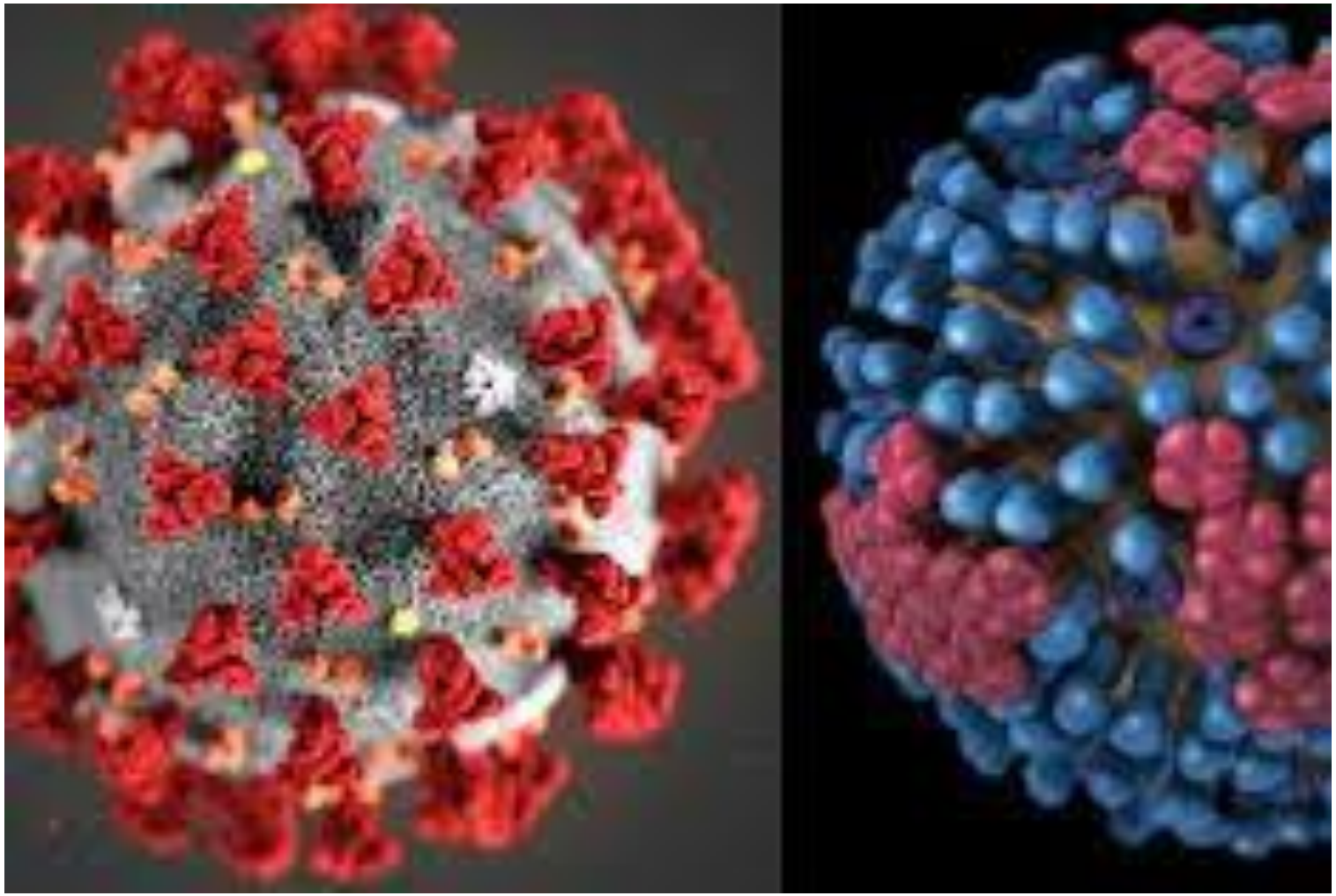
Citation Tools

This article is a preprint and has not been peer-reviewed [what does this mean?]. It reports new medical research that has yet to be evaluated and so should *not* be used to guide clinical practice.

Tweet Like 18K





Reducing Transmission

Influenza Vaccine 2020-21 Composition

- The egg-based vaccines for the 2020-2021 Northern Hemisphere vaccine season contain the following components:
- A/Guangdong-Maonan/SWL1536/2019 (H1N1)pdm09–like virus (new for 2020-2021)
- A/Hong Kong/2671/2019 (H3N2)–like virus (new for 2020-2021)
- B/Washington/02/2019 (B/Victoria lineage)–like virus (new for 2020-2021)
- The quadrivalent egg-culture influenza vaccines contain an additional B strain, B/Phuket/3073/2013-like virus (B/Yamagata lineage) (no change from prior season), in addition to the 3 viral strains listed above.
- The recombinant or cell-culture quadrivalent vaccine composition is as follows:
- A/Hawaii/70/2019 (H1N1)pdm09–like virus (new for 2020-2021)
- A/Hong Kong/45/2019 (H3N2)–like virus (new for 2020-2021)
- B/Washington/02/2019 (B/Victoria lineage)–like virus (new for 2020-2021)
- B/Phuket/3073/2013–like (Yamagata lineage) virus (no change from the prior season)

WHO 2020

U.S. INFLUENZA VACCINES FOR THE 2020-21 SEASON

INACTIVATED INFLUENZA VACCINES (IIVs) and RECOMBINANT INFLUENZA VACCINE (RIV4)

Trade name *Manufacturer*	Presentation	Age indication	HA, µg/dose (each virus)	Thimerosal Yes/No (If yes, Mercury, µg/0.5mL)
Quadrivalent IIVs (IIV4s)—Standard-dose—Egg-based				
Afluria Quadrivalent *Seqirus*	0.25 mL prefilled syringe* 0.5 mL prefilled syringe 5.0 mL multidose vial*	6 through 35 mos ≥3 yrs ≥6 mos (needle/syringe) 18 through 64 yrs (jet injector)	7.5/0.25 mL 15/0.5 mL See note for dosing*	No No Yes (24.5)
Fluarix Quadrivalent *GlaxoSmithKline*	0.5 mL prefilled syringe	≥6 mos	15/0.5mL	No
FluLaval Quadrivalent *GlaxoSmithKline*	0.5 mL prefilled syringe	≥6 mos	15/0.5mL	No
Fluzone Quadrivalent *Sanofi Pasteur*	0.5 mL prefilled syringe† 0.5 mL single-dose vial 5.0 mL multidose vial	≥6 mos ≥6 mos ≥6 mos	15/0.5 mL See note for dosing†	No No Yes (25)
Quadrivalent IIV (IIV4)—Standard-dose—Cell culture-based (ccIIV4)				
Flucelvax Quadrivalent *Seqirus*	0.5 mL prefilled syringe 5.0 mL multidose vial	≥4 yrs ≥4 yrs	15/0.5mL	No Yes (25)
Quadrivalent IIV (IIV4)—High-dose—Egg-based (HD-IIV4)				
Fluzone High-Dose Quadrivalent *Sanofi Pasteur*	0.7 mL prefilled syringe	≥65 yrs	60/0.7mL	No
Quadrivalent IIV (IIV4)—Standard-dose—Adjuvanted—Egg-based (aIIV4)				
Fluad Quadrivalent *Seqirus*	0.5 mL prefilled syringe	≥65 yrs	15/0.5mL	No
Trivalent IIV (IIV3)—Standard-dose—Adjuvanted—Egg-based (aIIV3)				
Fluad *Seqirus*	0.5 mL prefilled syringe	≥65 yrs	15/0.5mL	No
Quadrivalent RIV (RIV4)—Recombinant HA				
Flublok Quadrivalent *Sanofi Pasteur*	0.5 mL prefilled syringe	≥18 yrs	45/0.5mL	No

Abbreviations: IIV=inactivated influenza vaccine; RIV=recombinant influenza vaccine; HA=hemagglutinin; mos=months; yrs=years.

** For Afluria Quadrivalent, children aged 6 through 35 mos should receive 0.25mL per dose. Persons ≥36 mos (≥3 yrs) should receive 0.5mL per dose.*

† For Fluzone Quadrivalent, persons ≥36 mos (≥3 yrs) should receive 0.5mL per dose. Children aged 6 through 35 mos may receive either 0.25mL or 0.5mL per dose per

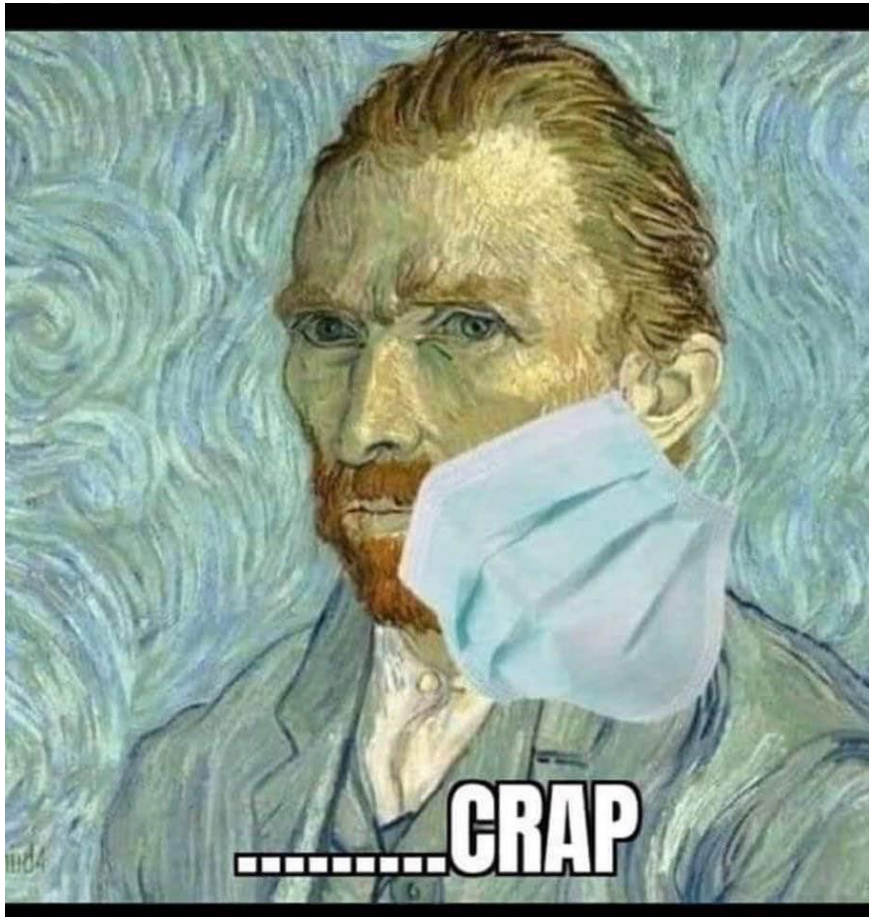
Influenza Vaccination

- All individuals > 6 months in age
- Should be administered by end of October, but can be given throughout the season (not too early as may wane in effectiveness)
- High dose quadrivalent vaccine may be of benefit in adults > 65 years
- Healthy, non immune compromised individuals ages 2-49 may receive the live attenuated intranasal spray

SARS CoV0-2

How to prevent transmission

Personal Protection



- Hand Hygiene
- Social Distancing
- Masks
- Gloves
- Gowns
- PAPRs

PPE

- Droplet

- Airborne

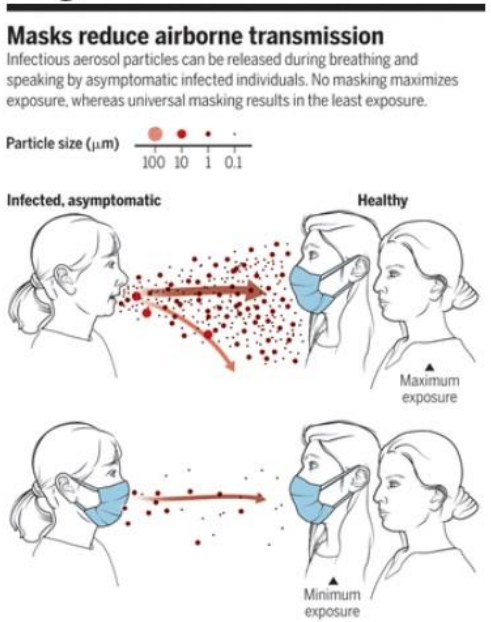
Reducing transmission of SARS-CoV-2

Kimberly A. Prather[1], **Chia C. Wang**[2,3], **Robert T. Schooley**[4]

+ See all authors and affiliations

Science 27 May 2020:
eabc6197
DOI: 10.1126/science.abc6197

Figures



Masks reduce airborne transmission.

Infectious aerosol particles can be released during breathing and speaking by asymptomatic infected individuals. No masking maximizes exposure, whereas universal masking results in the least exposure.

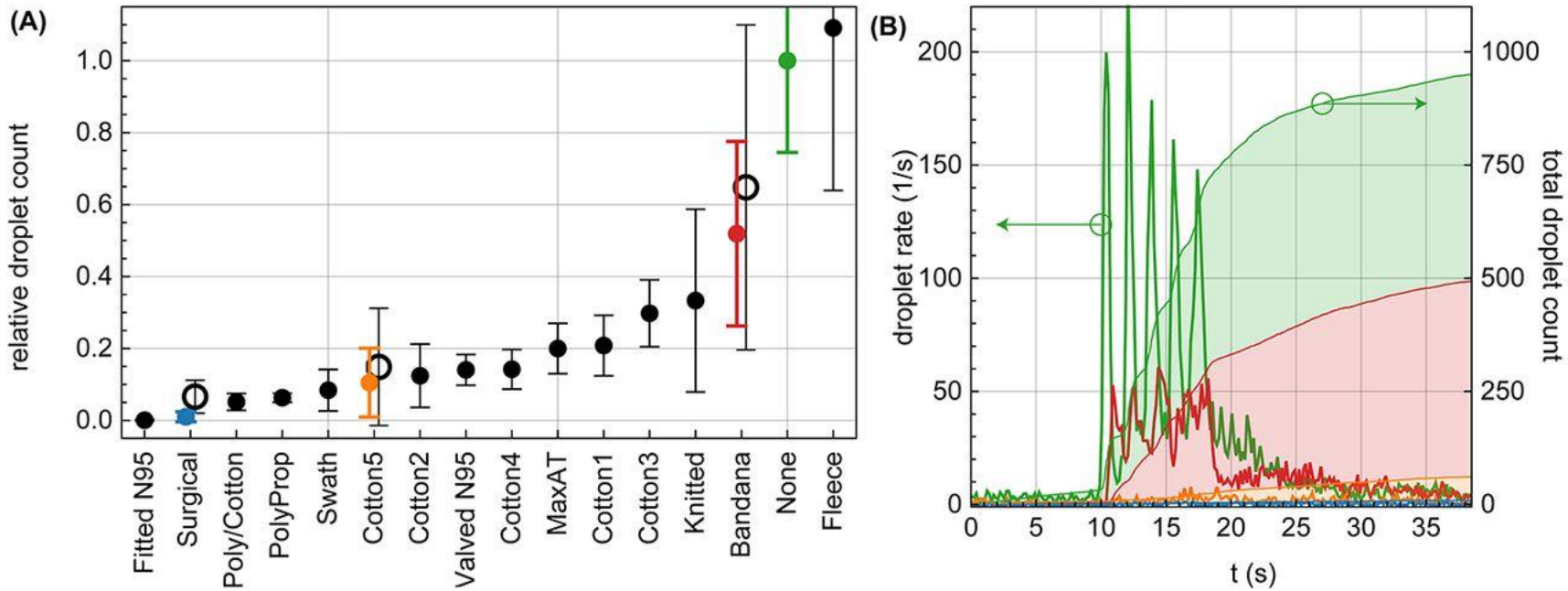
GRAPHIC: V. ALTOUNIAN/*SCIENCE*

COVID-19

By Wei Lyu and George L. Wehby

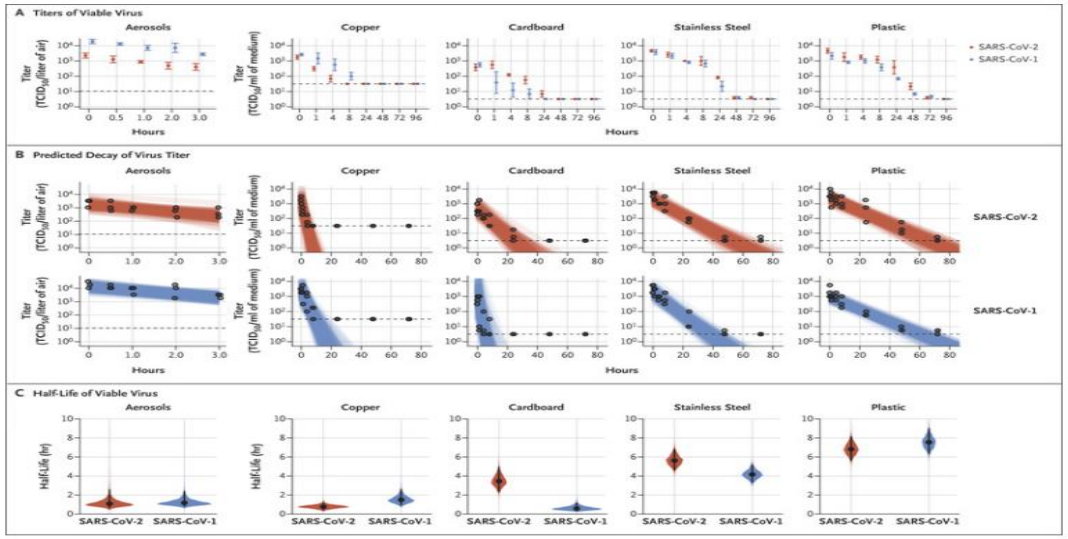
Community Use Of Face Masks And COVID-19: Evidence From A Natural Experiment Of State Mandates In The US

DOI: 10.1377/hlthaff.2020.00818
HEALTH AFFAIRS 39,
NO. 8 (2020): 1–7



Fischer et al. Sciences Advances. 7 Aug 2020.

Good Hand Hygeine



Viability of SARS-CoV-1 and SARS-CoV-2 in Aerosols and on Various Surfaces.

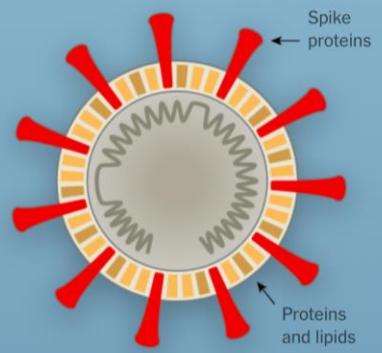
SARS-CoV-2 remained viable in aerosols throughout the duration of our experiment (3 hours), with a reduction in infectious titer from $10^{3.5}$ to $10^{2.7}$ $TCID_{50}$ per liter of air. This reduction was similar to that observed with SARS-CoV-1, from $10^{4.3}$ to $10^{3.5}$ $TCID_{50}$ per milliliter (Figure 1A).

SARS-CoV-2 was more stable on plastic and stainless steel than on copper and cardboard, and viable virus was detected up to 72 hours after application to these surfaces (Figure 1A), although the virus titer was

If you feel sick, stay home

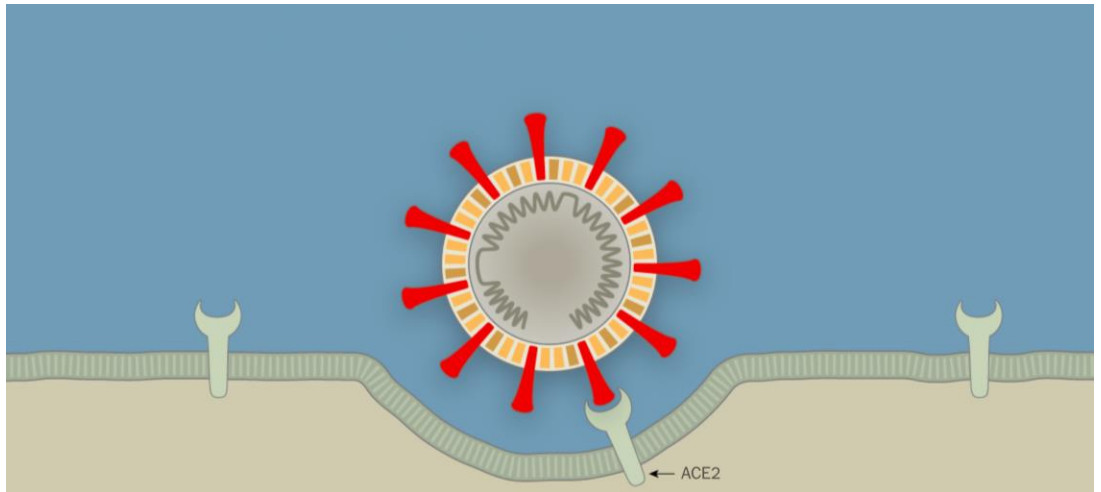
Outdoors is safer than indoors

Pathophysiology



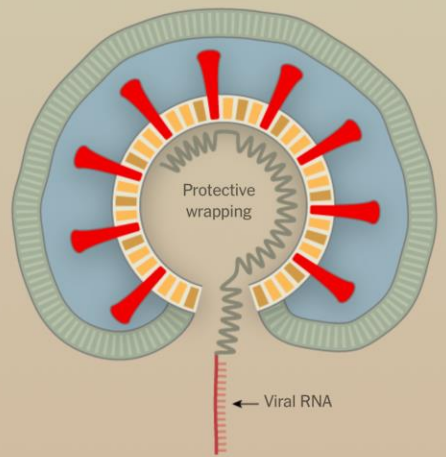
Covered With Spikes

The coronavirus is named after the crownlike spikes that protrude from its surface. The virus is enveloped in a bubble of oily lipid molecules, which falls apart on contact with soap.



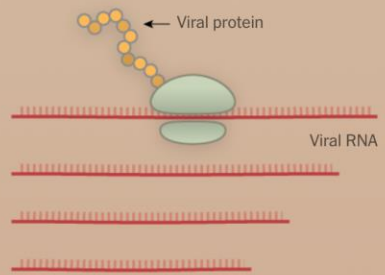
Entering a Vulnerable Cell

The virus enters the body through the nose, mouth or eyes, then attaches to cells in the airway that produce a protein called ACE2. The virus is believed to have originated in bats, where it may have attached to a similar protein.



Releasing Viral RNA

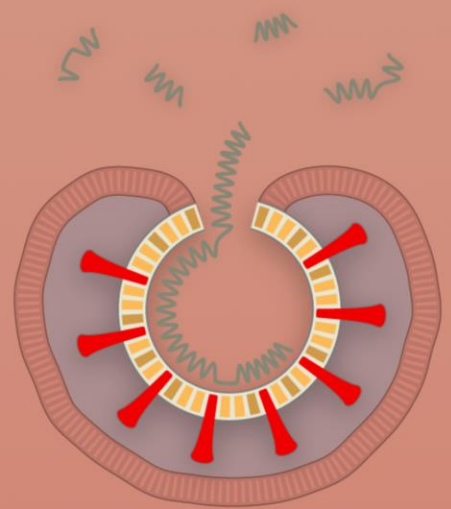
The virus infects the cell by fusing its oily membrane with the membrane of the cell. Once inside, the coronavirus releases a snippet of genetic material called RNA.



Hijacking the Cell

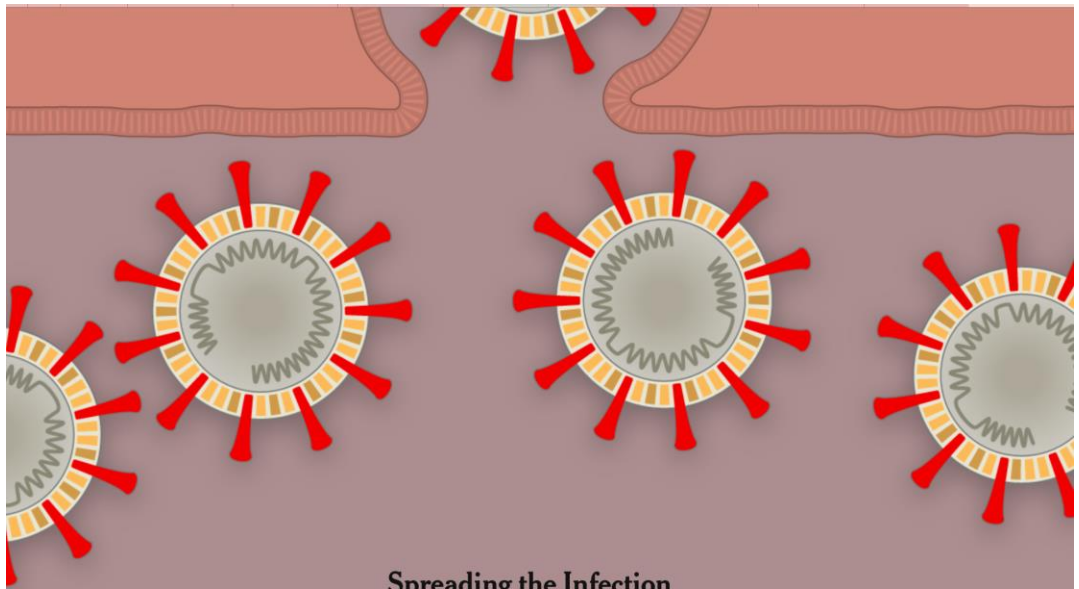
The virus's genome is less than 30,000 genetic "letters" long. (Ours is over 3 billion.) The infected cell reads the RNA and begins making proteins that will keep the immune system at bay and help assemble new copies of the virus.

Antibiotics kill bacteria and do not work against viruses. But researchers are testing antiviral drugs that might disrupt viral proteins and stop the infection.



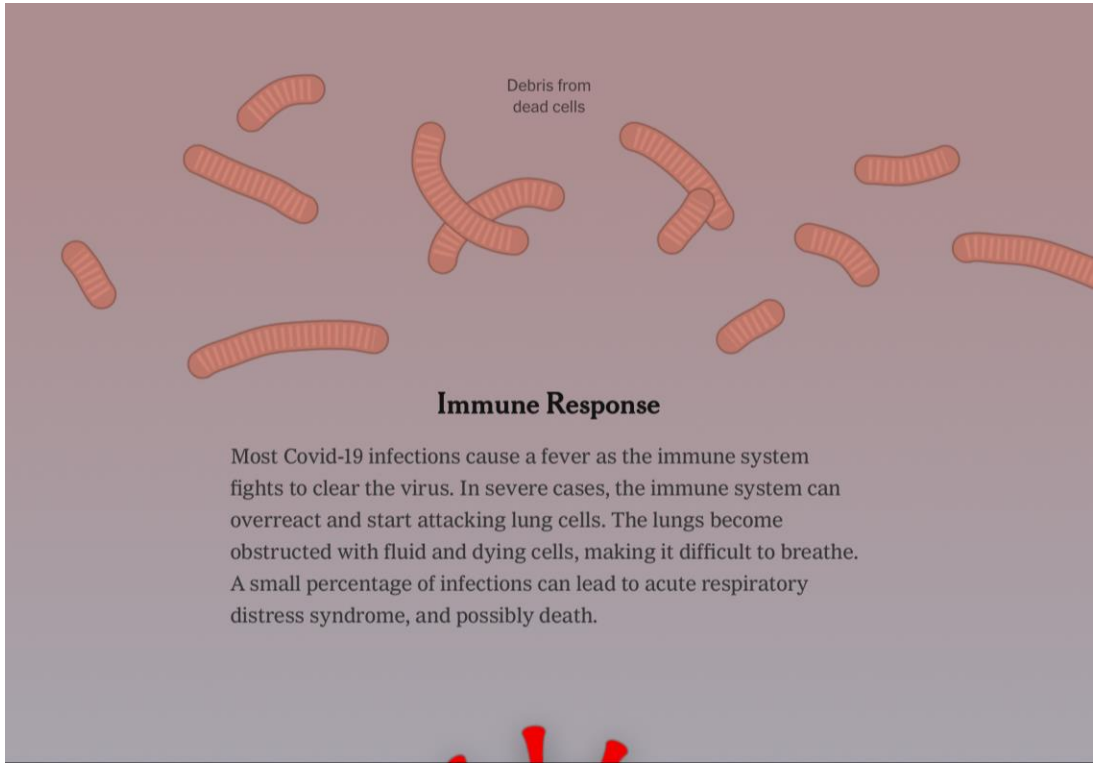
Assembling New Copies

New copies of the virus are assembled and carried to the outer edges of the cell.



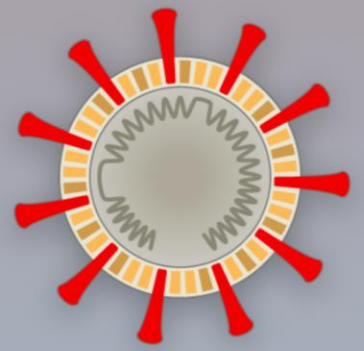
Spreading the Infection

Each infected cell can release millions of copies of the virus before the cell finally breaks down and dies. The viruses may infect nearby cells, or end up in droplets that escape the lungs.



Immune Response

Most Covid-19 infections cause a fever as the immune system fights to clear the virus. In severe cases, the immune system can overreact and start attacking lung cells. The lungs become obstructed with fluid and dying cells, making it difficult to breathe. A small percentage of infections can lead to acute respiratory distress syndrome, and possibly death.



Leaving the Body

Coughing and sneezing can expel virus-laden droplets onto nearby people and surfaces, where the virus can remain infectious for several hours to several days. The C.D.C. recommends that people diagnosed with Covid-19 wear masks to reduce the release of viruses. Health care workers and others who care for infected people should wear masks, too.

Inflammatory Response

- Profound immune activation and dysregulation
- Clear association with excessive morbidity and mortality
- High levels of circulating inflammatory chemicals
- Profound reduction in protective lymphocytes
- Cell infiltration of multiple organs
- Hyperactivation of monocytes/macrophages increasing cytopathologic effects in end organs
- Presence of fibrosis inducing macrophages
- Microemboli

Merad. Nature Reviews Immunology. May 6, 2020

Risk Factors

- Age
- Congregant Living Situations
- Occupation
- Gender
- Socioeconomic
- Duration of virus exposure
- Comorbidities: DM, HTN, cardiopulmonary disease, obesity
- Blood type?

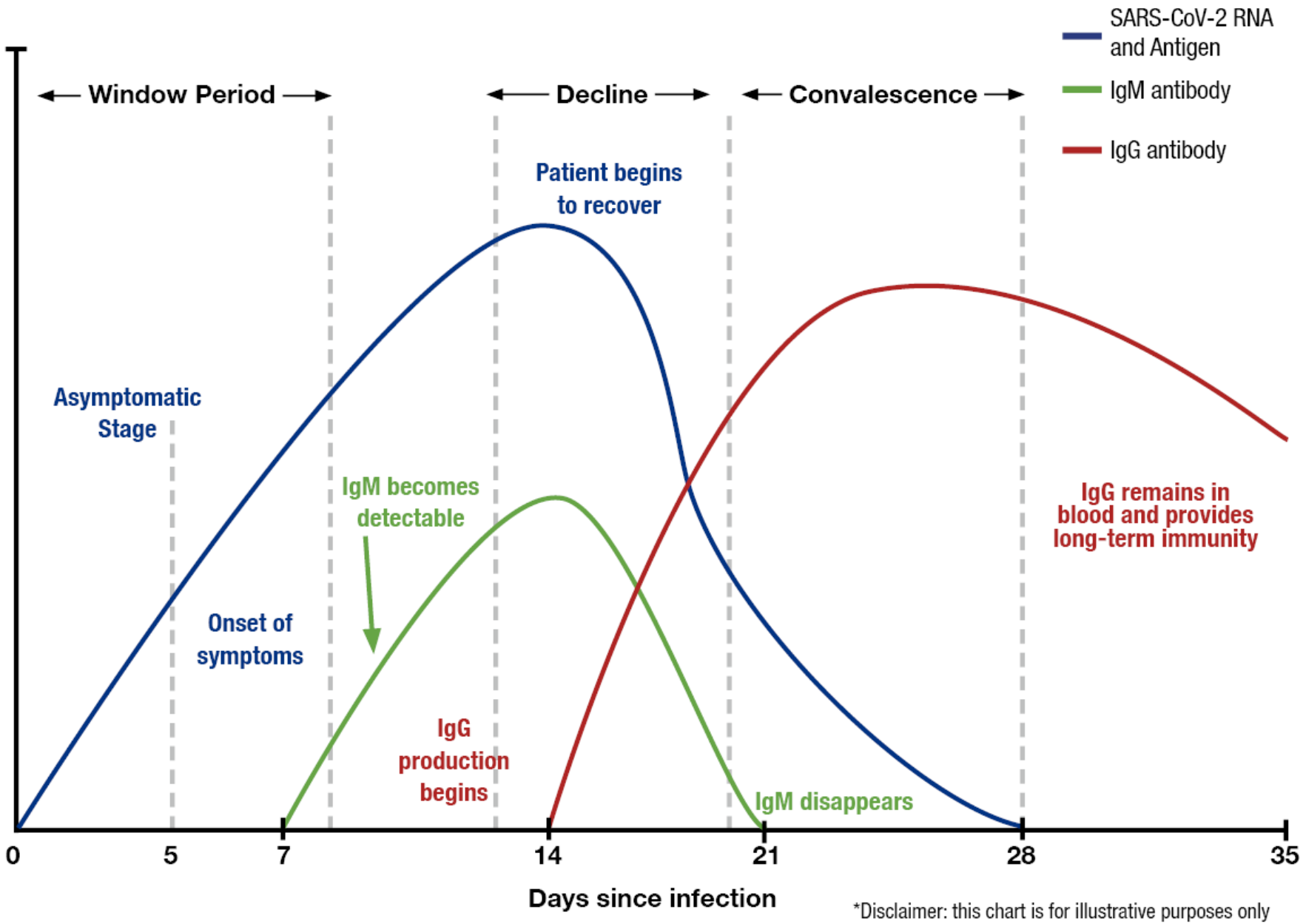
The End Result

Organ Systems infected and affected

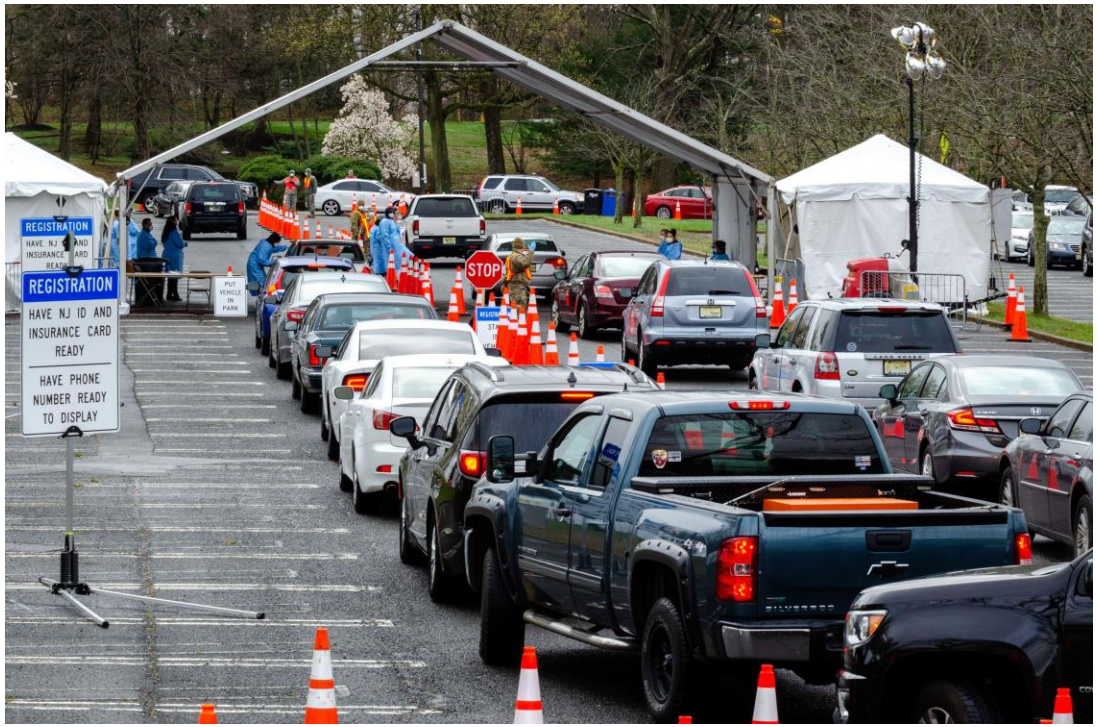
- Lungs
- Heart
- Kidneys
- Brain
- Immune System
- Coagulation System
- Reproductive? Testes as sanctuary for virus

One of the lungs removed from the patient. The surgeon said the damage was among the worst he'd seen.

Northwestern Medicine


SARS-CoV-2 RNA and Antigen
IgM antibody
IgG antibody
Window Period
Decline
Convalescence
Patient begins to recover
Asymptomatic Stage
IgM becomes detectable
Onset of symptoms
IgG production begins
IgM disappears
IgG remains in blood and provides long-term immunity
0
5
7
14
21
28
35
Days since infection
*Disclaimer: this chart is for illustrative purposes only

Testing


REGISTRATION
HAVE NJ ID AND INSURANCE CARD READY
HAVE PHONE NUMBER READY TO DISPLAY
STOP

Testing

What we need

- Essential to control pandemic and assess disease density
- Needs to be highly accurate
- Need plenty of supplies
  - Swabs
  - Testing platforms
- Inexpensive
- No transmission risk to collector
- FAST RESULTS

What we have

- Many different companies making accurate tests
- Still not available in the numbers needed
- Some not accurate
- Require skill and PPE for collection
- Turnaround time often delayed

Testing

- Molecular
  - Active Infection
    - Nasopharyngeal swabs: PCR
    - Good specificity
    - Reasonable sensitivity
    - Collection dependent
    - Many providers now
    - Includes influenza and other respiratory viruses
    - Yale Saliva Test
      - Promising
      - Inexpensive
      - No PPE for collector
      - Rapid
      - Acceptable Sensitivity /Specificity
    - Antigen/Antibody Tests
      - Poor performance
      - False negatives
- Serologic
  - Presence of antibodies

Management and Therapies


Here you may be Cured

Treatments and Management

- Supplemental oxygen/delay ventilation
- Antivirals
- Antiinflammatory drugs
- Convalescent Plasma
- Supplemental medications
- Neutralizing antibodies
- Novel agents

Remdesivir

- Gilead Pharmaceuticals
- Novel antiviral: nucleotide analogue
- Interrupts viral replication
- Broad spectrum activity against RNA viruses, including MERS and SARS
- Intravenous (200 mg day 1 then 100 mg daily for 5 days)
- FDA fast track approved

Remdesivir for the Treatment of Covid-19- Preliminary Report - NEJM

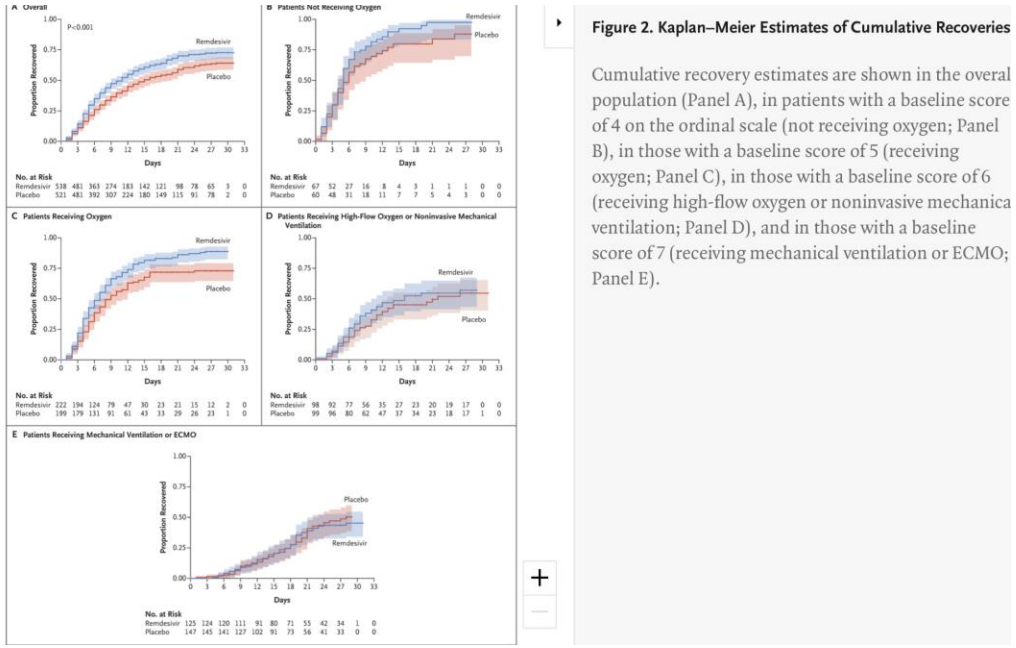


Figure 2. Kaplan–Meier Estimates of Cumulative Recoveries

Cumulative recovery estimates are shown in the overal population (Panel A), in patients with a baseline score of 4 on the ordinal scale (not receiving oxygen; Panel B), in those with a baseline score of 5 (receiving oxygen; Panel C), in those with a baseline score of 6 (receiving high-flow oxygen or noninvasive mechanica ventilation; Panel D), and in those with a baseline score of 7 (receiving mechanical ventilation or ECMO; Panel E).

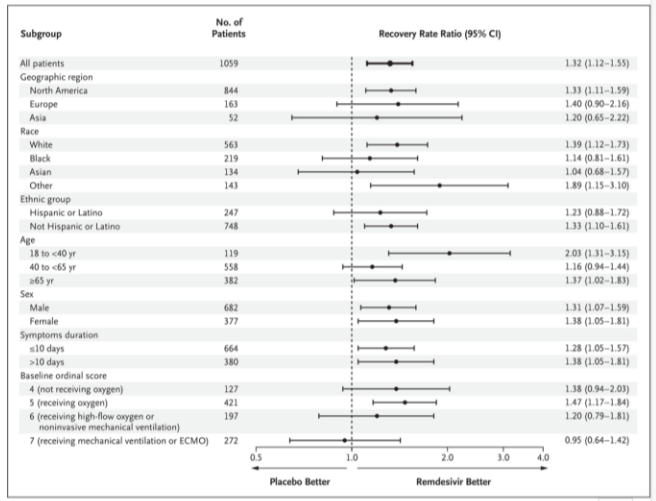
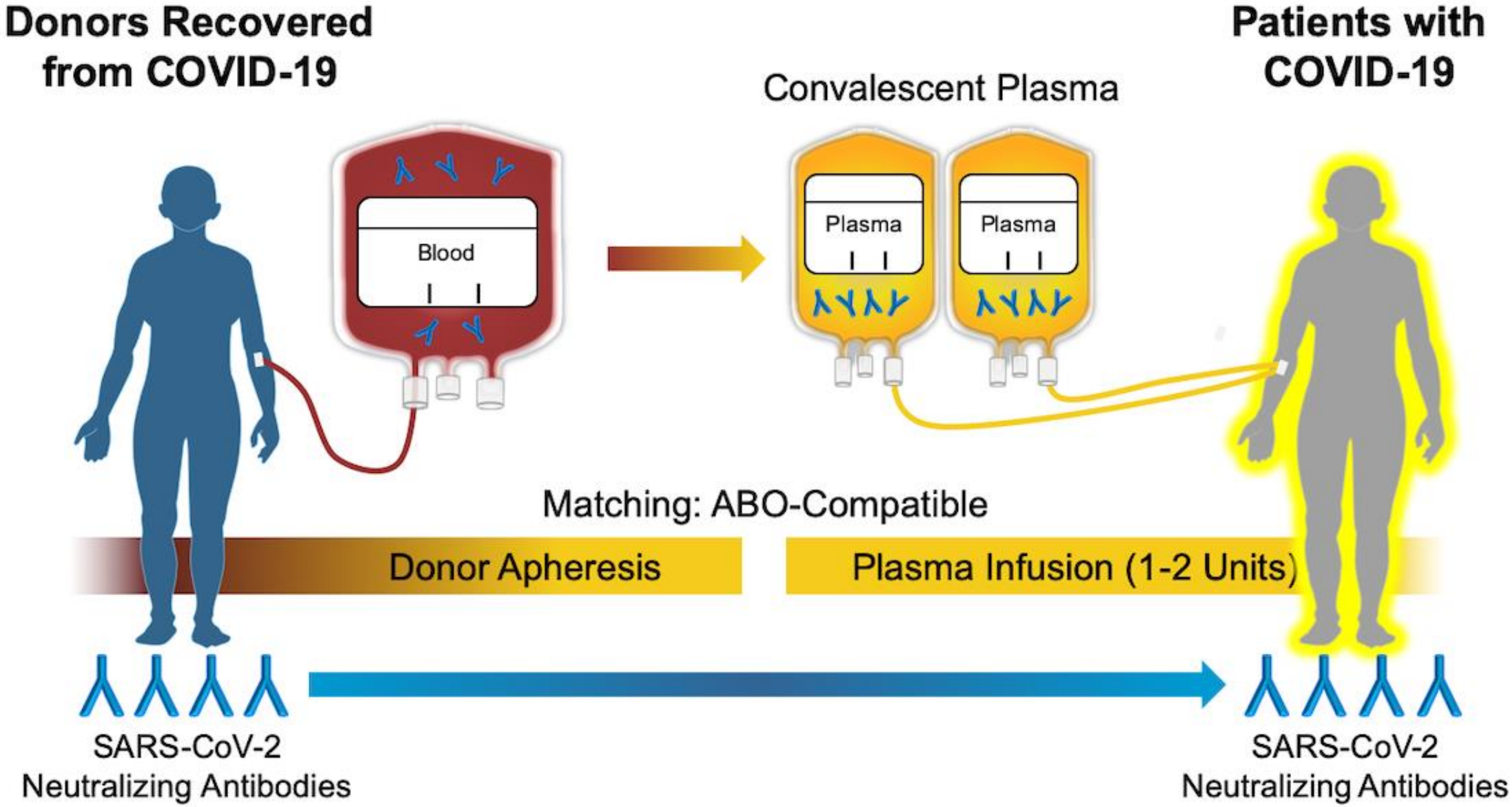


Figure 3. Time to Recovery According to Subgroup.

The widths of the confidence intervals have not been adjusted for multiplicity and therefore cannot be used to infer treatment effects. Race and ethnic group were reported by the patients.

Beigel et al. NEJM: May 22. 2020

Convalescent Plasma


Donors Recovered from COVID-19
Patients with COVID-19
Convalescent Plasma
Blood
Plasma
Plasma
Matching: ABO-Compatible
Donor Apheresis
Plasma Infusion (1-2 Units)
SARS-CoV-2 Neutralizing Antibodies
SARS-CoV-2 Neutralizing Antibodies

Convalescent Plasma

Convalescent plasma treatment of severe COVID-19: A matched control study

Sean T. H. Liu, Hung-Mo Lin, Ian Baine, Ania Wajnberg, Jeffrey P. Gumprecht, Farah Rahman, Denise Rodriguez, Pranai Tandon, Adel Bassily-Marcus, Jeffrey Bander, Charles Sanky, Amy Dupper, Allen Zheng, Deena R. Altman, Benjamin K. Chen, Florian Krammer, Damodara Rao Mendu, Adolfo Firpo-Betancourt, Matthew A. Levin, Emilia Bagiella, Arturo Casadevall, Carlos Cordon-Cardo, Jeffrey S. Jhang, Suzanne A. Arinsburg, David L. Reich, Judith A. Aberg, Nicole M. Bouvier

doi: https://doi.org/10.1101/2020.05.20.20102236

- 39 patients
- Matched control patients identified in retrospective cohort
- CP recipients more likely to have steady or improved oxygenation
- CP recipients had improved survival compared to controls (p.039)
- Covariates adjusted cox model-CP showed better survival for non-intubated patients than intubated patients.
- CURRENTLY UNDER REVIEW AS TO EFFICACY
- PERHAPS MORE EFFECTIVE EARLIER IN DISEASE

Novel Therapies

- EIDD 2108
  - Novel antiviral causes terminal mutation in SARSCoV2 replication
  - Oral
  - Could be used as therapy and PROPHYLAXIS
  - Studied in mouse model; on to primates

Immunotherapy

- Dexamethasone
  - RECOVERY TRIAL IN UK
    - 2100 enrolled-6 mg /d for 10 days
    - Compared to 4300 patients with “standard care”
    - Marked reduction in death in critically ill patients on ventilators or with moderate disease
    - No effect with mild disease
    - Not yet published/peer reviewed
    - ?timing of initiation of steroid.
- Anti-inflammatories
  - Il-6 inhibitors
- Cytokine inhibitors

Anticoagulation

- ASA
- Low molecular weight heparin
- ?therapeutic intensity anticoagulation
  - Studies in progress

  - Recurrent Clotting
    - Consider increased intensity of anticoagulation
    - Switch anticoagulants

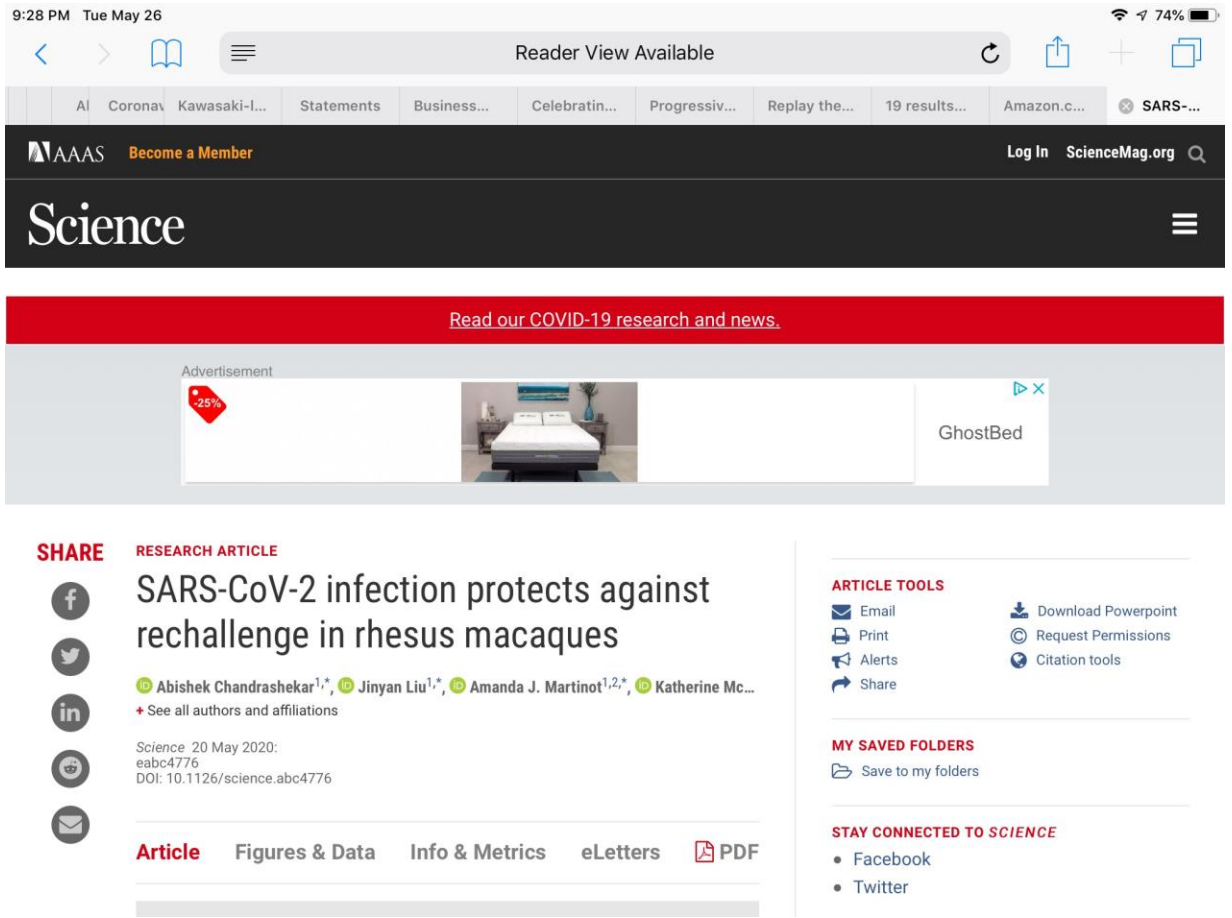
    - **HAVE TO ASSESS THE BLEEDING RISK WITH ALL OF THE ABOVE.**

Hydroxychloroquine (plaquenil)

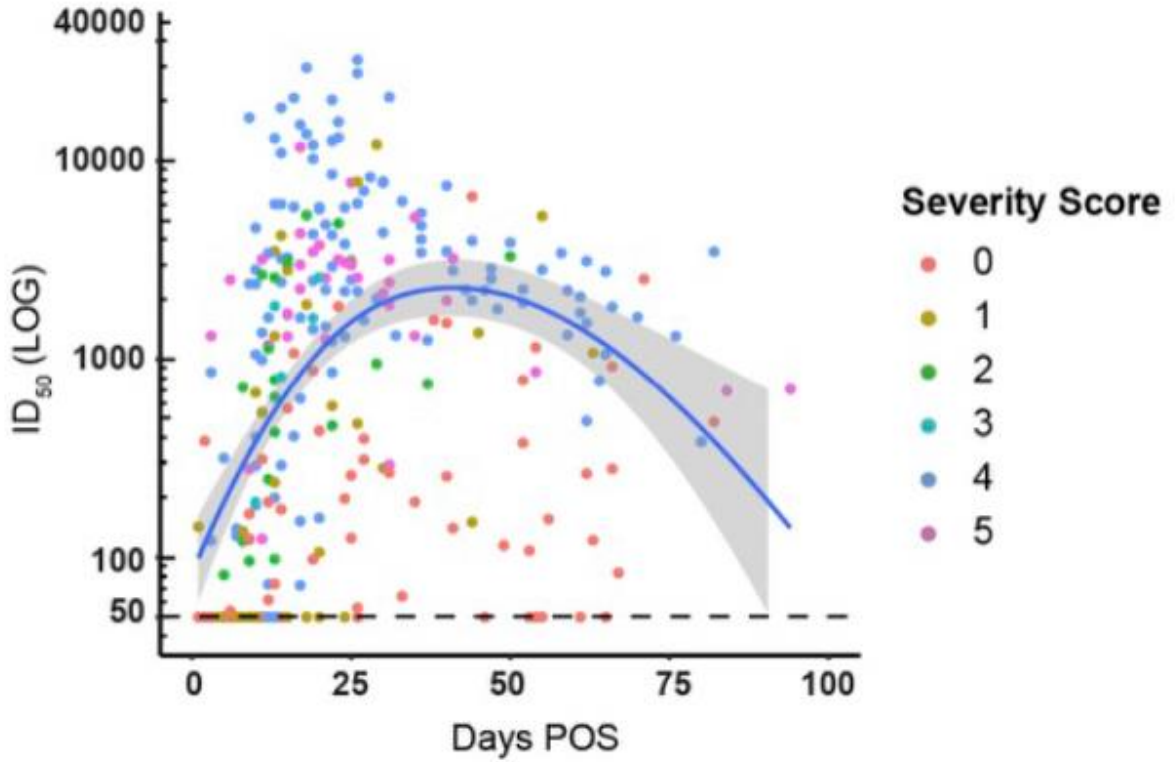
- <u>Multinational Registry Study</u>
- 96,032 patients
- No benefit of hydroxychloroquine; decreased in hospital outcomes and decreased survival in hydroxy recipients
- Published in Lancet
- Subsequent critique about how data gathered and track record of principal investigator (NY Times 7.27.20)
- VA Study
  - Retrospective analysis of 368 patients
  - Patients receiving hydroxychloroquine had higher rates of death

  - DON'T USE IT

Neutralizing Antibodies may be protective



SARS-CoV-2 Neutralization titers post-infection



From Seow et al; medRxiv preprint doi: https://doi.org/10.1101/2020.07.09.20148429

Monoclonal Antibodies-Investigational Regeneron

- Promising data based on humanized mouse studies and observation of convalescent humans
- Spike protein antibodies generated through mouse immunization and B cell clonal proliferation
- Humanized mouse model and genetic engineering can lead to large array of potentially effective neutralizing antibodies creating an antibody cocktail while minimizing odds of viral escape
- UCLA study participant

Do some people have some immunity to SARS-CoV2?

Comment | Published: 07 July 2020

Pre-existing immunity to SARS-CoV-2: the knowns and unknowns

Alessandro Sette & Shane Crotty

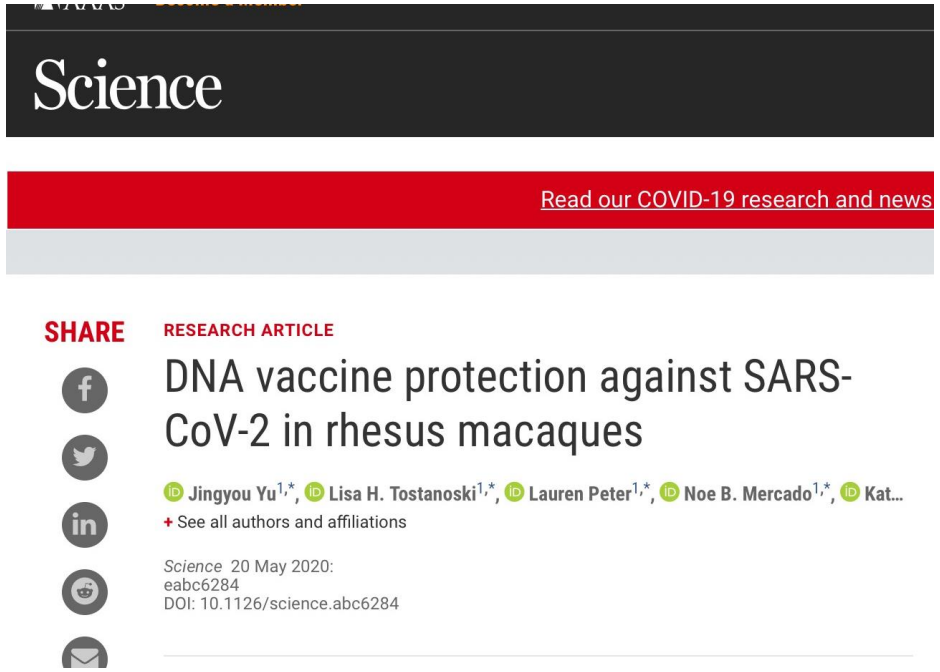
Nature Reviews Immunology

20, 457–458(2020) | Cite this article

Post COVID considerations

- Plasma donation
  - Durability/longevity of convalescent antibodies
- Long term sequelae
  - Clinical
  - psychological
- Can a recovered patient have a second infection?

Vaccines



Science

Read our COVID-19 research and news

SHARE

RESEARCH ARTICLE

DNA vaccine protection against SARS-CoV-2 in rhesus macaques

Jingyou Yu[1,*], Lisa H. Tostanoski[1,*], Lauren Peter[1,*], Noe B. Mercado[1,*], Kat…

+ See all authors and affiliations

Science 20 May 2020:
eabc6284
DOI: 10.1126/science.abc6284

Vaccine candidates-importance of spike protein

Moderna-

mRNA 1273

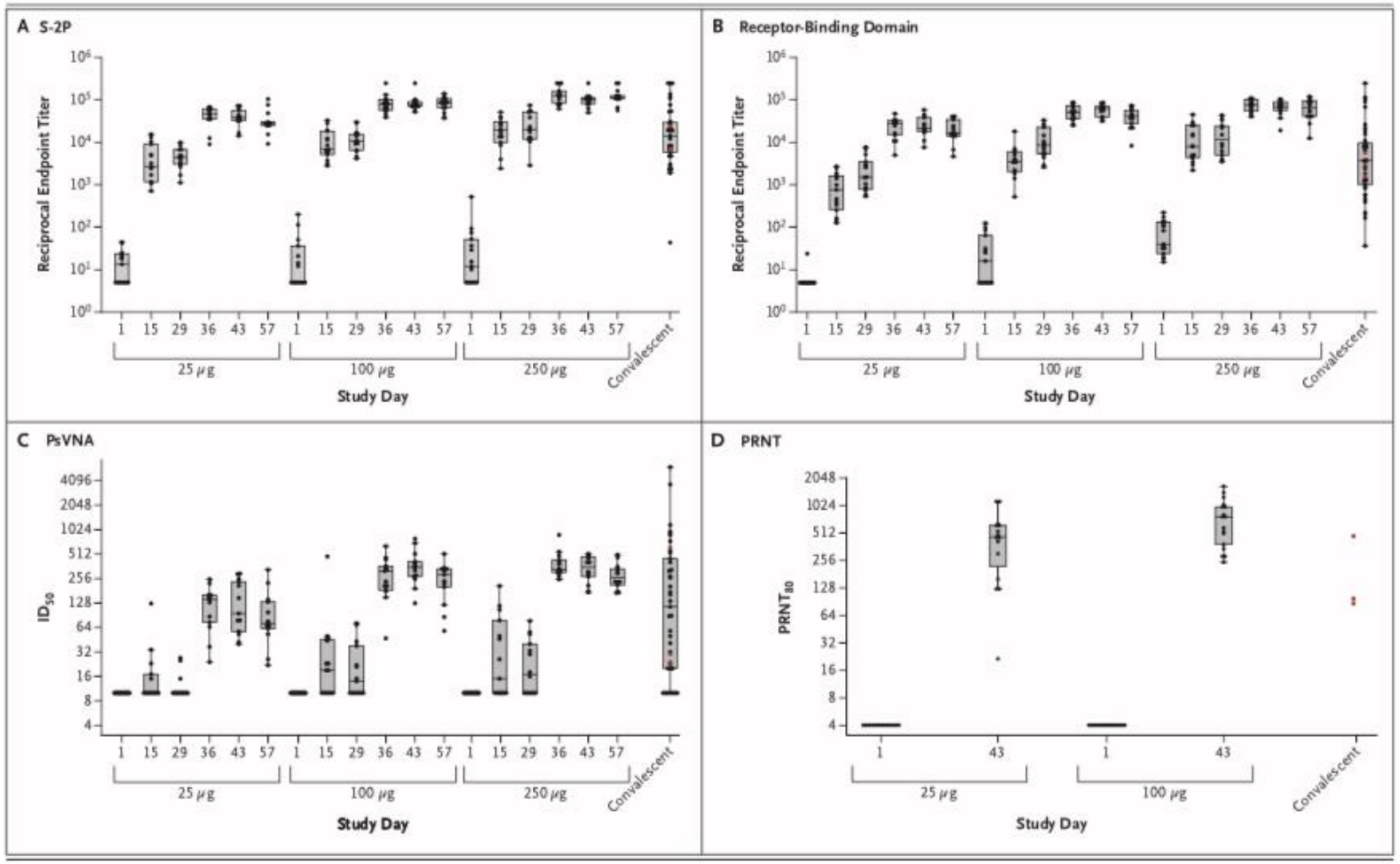
AstraZeneca/Univ of OxfordChAdOx1nCov-19

Novavax NVX-CoV2373-nanotechnology

Sanofi/GSK-recombinant protein adjuvant vaccine

Pfizer BNT 162-mRNA

Moderna mRNA vaccine
Prelim results



The NEW ENGLAND JOURNAL of MEDICINE

NEJM: Jul 15.2020

“Mild to moderate side effects”

- Associated with higher dose or second dose
- Fever > 103 degrees
- Severe myalgias
- Injection site pain
- syncope

Oxford/AstraZeneca: ChAdox1nCoV-19 vaccine

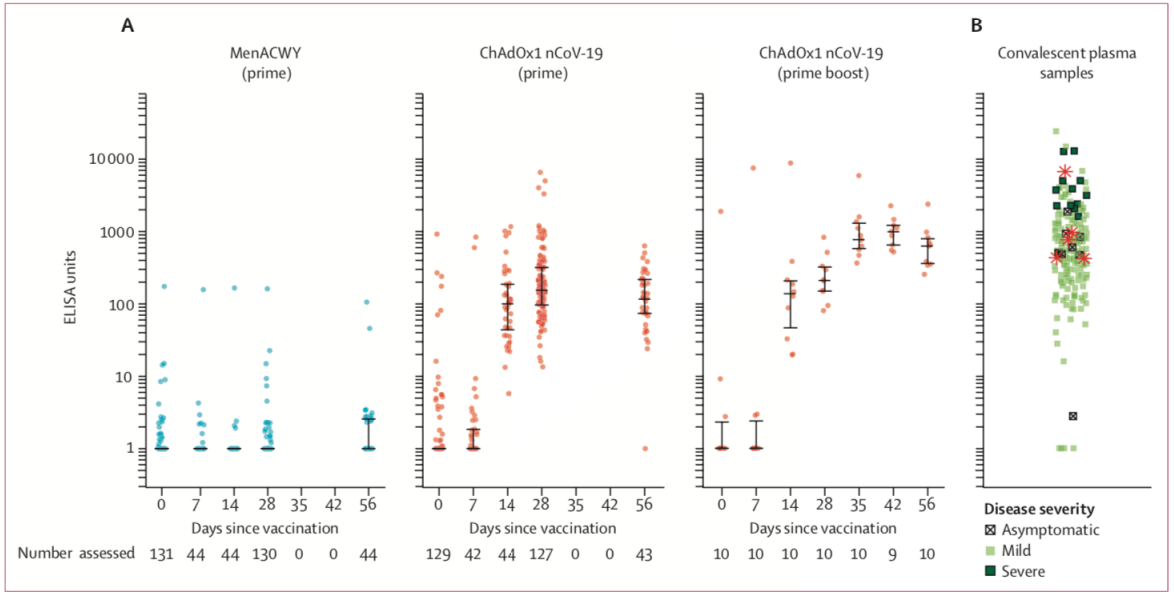


Figure 3: **SARS-CoV-2 IgG response by standardised ELISA to spike protein in trial participants (A) and in 180 convalescent plasma samples from 172 patients with PCR-confirmed COVID-19 and eight asymptomatic health-care workers (B)**
Error bars show median (IQR). Participants in the prime boost group received their second dose at day 28. Lower limit of quantification is 1 ELISA unit. Red stars in panel B show five samples also tested on the Marburg VN assay (see figure 4). MenACWY=meningococcal group A, C, W-135, and Y conjugate vaccine. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2.

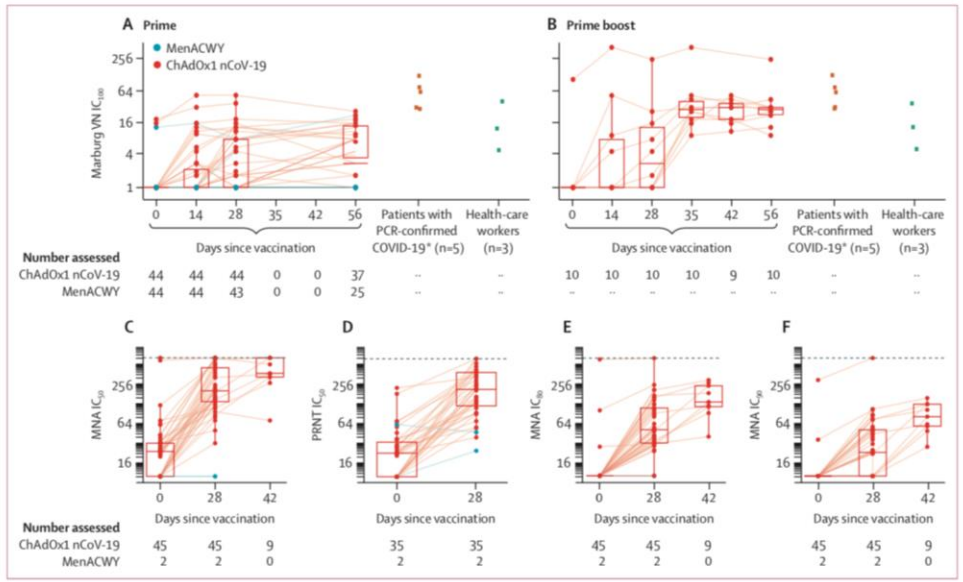


Figure 4: **Live SARS-CoV-2 neutralisation assays (Marburg VN and PHE PRNT$_{90}$) and microneutralisation assays (PHE MNA)**
Panels A and B show live SARS-CoV-2 neutralisation (Marburg VN) in prime (A) and prime boost (B) trial participants (boosted at day 28) and convalescent plasma from patients with PCR-confirmed COVID-19 and asymptomatic health-care workers. Panels C, E, and F show the PHE MNA (at IC$_{50}$, IC$_{80}$, and IC$_{90}$, respectively) and panel D the PHE PRNT$_{90}$. The day 42 timepoint was only measured in participants who received a booster dose at day 28. Solid lines connect samples from the same participant. Boxes show median (IQR). Dotted lines show upper limits of detection. MenACWY=meningococcal group A, C, W-135, and Y conjugate vaccine. PHE=Public Health England. MNA=microneutralisation assay. PRNT=plaque reduction neutralisation test. VN=virus neutralisation. IC=inhibitory concentration. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. *ELISA results for these five convalescent plasma samples are shown in figure 3 as red stars.

Folegatti et al. The Lancet:
July 20, 2020

Going Forward

Recommendations for staying healthy during the winter of 2020-2021

- Get a flu shot
- Wear a mask
- Practice social distancing
- Weigh your risks
- Stay informed and follow the science
- Be creative
- Be thoughtful
- Be patient, we will get through this


INFLUENZA
WEAR
YOUR
MASK
It May Save Your Life!


However long the night,
the dawn will break.
~ African proverb

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Questions?