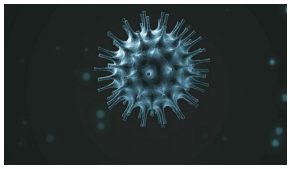
An update on COVID-19 - including vaccines


Dr Julian W Tang, Honorary Associate Professor/Clinical Virologist
Respiratory Sciences, University of Leicester, Leicester, UK

Hosted by Martin Kiernan
martin@webbertraining.com

www.webbertraining.com **December 17, 2020**

Dr Julian W Tang BA MBChB MA PhD MRCP FRCPath FHKCPath FHKAM
Consultant Virologist/Honorary Associate Professor
Clinical Microbiology, University Hospitals of Leicester NHS Trust/ Respiratory Sciences, University of Leicester, Leicester, UK

- I trained in Medicine and Zoology at Cambridge, before completing a Zoology PhD in biological fluid dynamics in Aberdeen. I then finished my medical training in Sheffield. After my general medical training, I completed my specialist clinical virology training at University College London in 2005.
- Later the same year, I moved to Hong Kong after the SARS 2003 outbreaks, as an Assistant Professor, developing a clinical and research interest in respiratory viruses, particularly on influenza and its transmission.
- I moved to Singapore in 2008 as a Consultant/ Virologist, arriving there just in time for the 2009 A/H1N1 influenza pandemic. There, we built a 1 m diameter schlieren imaging system to visualise human exhaled airflows such as breathing, talking, coughing, sneezing, singing – to aid aerosol infection control guidance.
- After several years in Singapore, I spent a couple of years working in Edmonton, AB, Canada - where we described the first imported, fatal human case of avian A/H5N1 influenza into North America in 2013.
- I returned to the UK in 2014, settling in Leicester, UK, where I have been running the diagnostic virology laboratory and advising on the clinical management and infection control of viral infections, particularly respiratory viruses, like influenza and SARS-CoV-2 that is causing the current COVID-19 pandemic.

Research interests:

Aerosol transmission and infection control of viruses

Viral phylogenetics and molecular epidemiology

Respiratory viruses and emerging infections

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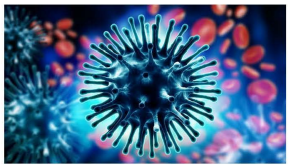
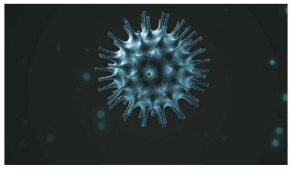
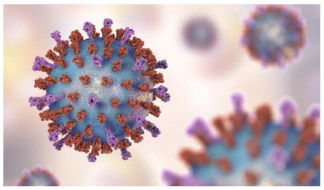
Some context: respiratory virus infections

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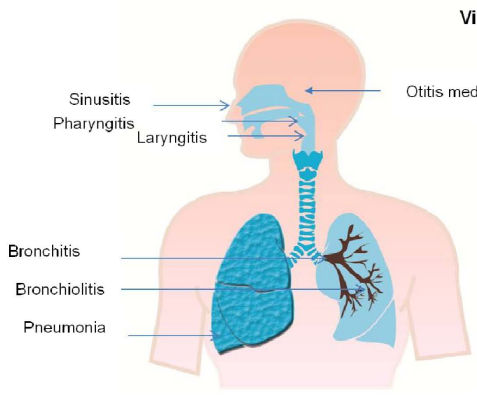

Viruses that infect the upper respiratory tract

Rhinovirus
Coronavirus
Influenza virus
Parainfluenza virus
Respiratory Syncytial virus
Herpesvirus
Adenovirus
Bocavirus
Coxsackivirus

Viruses that infect the lower respiratory tract

Influenza virus
Parainfluenza virus
Respiratory Syncytial virus
Adenovirus
Bocavirus
Metapneumovirus

https://www.intechopen.com/books/respiratory-disease-and-infection-a-new-insight/pathogenesis-of-viral-respiratory-infection

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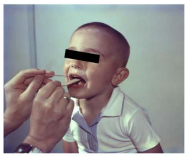
Respiratory Viruses (AusDiagnostics, 16-WELL (Ref 20602))
Influenza A
Influenza B
Influenza A typing H1/H3
Parainfluenza 1, 2, 3 & 4
Respiratory Syncytial Virus A & B
Adenovirus groups B, C, E, some A, D
Rhinovirus & Enterovirus
Enterovirus
Metapneumovirus
Coronavirus 229E, HKU-1, NL63 & OC43
Bocavirus

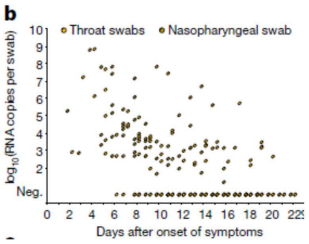
http://www.ausdiagnostics.com/uploads/6/9/8/2/69822307/9150r05_easy-plex_384_system__high-plex__ifu_160803.pdf



https://phil.cdc.gov/Details.aspx?pid=10188

Diagnostic nose/ throat swabs can detect all these respiratory viruses – exhalation activities will naturally aerosolise these viruses from the oral cavity –

Typical viral loads have been reported as 10^2-10^9 cop/swab



https://www.nature.com/articles/s41586-020-2196-x.pdf

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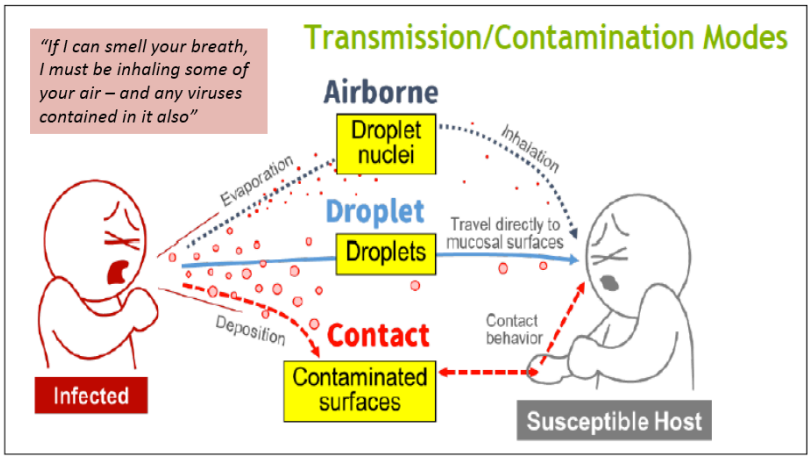

There is a continuum of droplet sizes moving from larger to smaller droplets in aerosols that are airborne – viruses (and other pathogens) can be carried in all of them and be transmitted via breathing, talking, laughing, coughing, sneezing, etc.

https://www.rehva.eu/fileadmin/user_upload/2020.04.28_COVID-19_BuildUp_webinar_by_REHVA.pdf

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What about the virus?
What is it and where did it come from?

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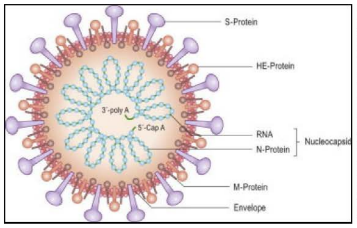
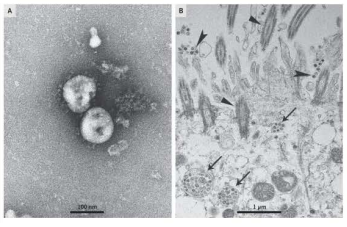
VIROLOGY: Coronaviruses (CoV) are a large family of lipid-enveloped, positive-sense, single-stranded RNA viruses that cause illness ranging from the common cold to more severe diseases such as Middle East Respiratory Syndrome (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV). A novel coronavirus (nCoV) is a new strain that has not been previously identified in humans.

Coronaviruses are zoonotic, meaning they are transmitted between animals and people. Detailed investigations found that SARS-CoV was transmitted from civet cats to humans and MERS-CoV from dromedary camels to humans. Several known coronaviruses are circulating in animals that have not yet infected humans.

Common signs of infection include respiratory symptoms, fever, cough, shortness of breath and breathing difficulties. In more severe cases, infection can cause pneumonia, severe acute respiratory syndrome, kidney failure and even death.

https://www.who.int/health-topics/coronavirus





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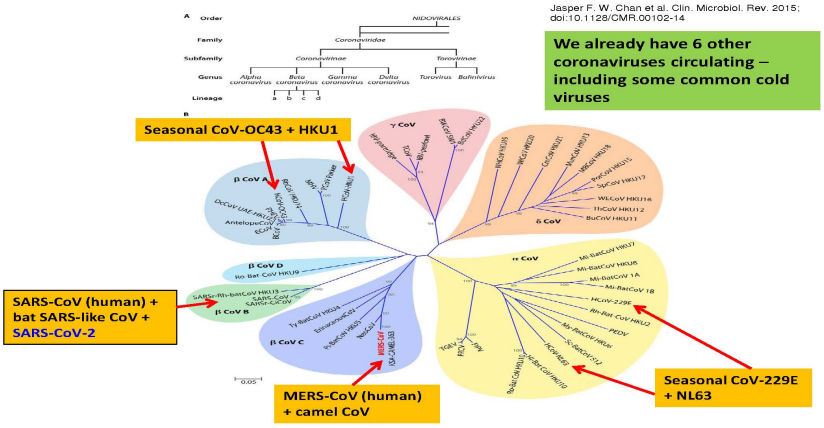
(A) Taxonomy of Coronaviridae according to the International Committee on Taxonomy of Viruses.

Jasper F. W. Chan et al. Clin. Microbiol. Rev. 2015; doi:10.1128/CMR.00102-14



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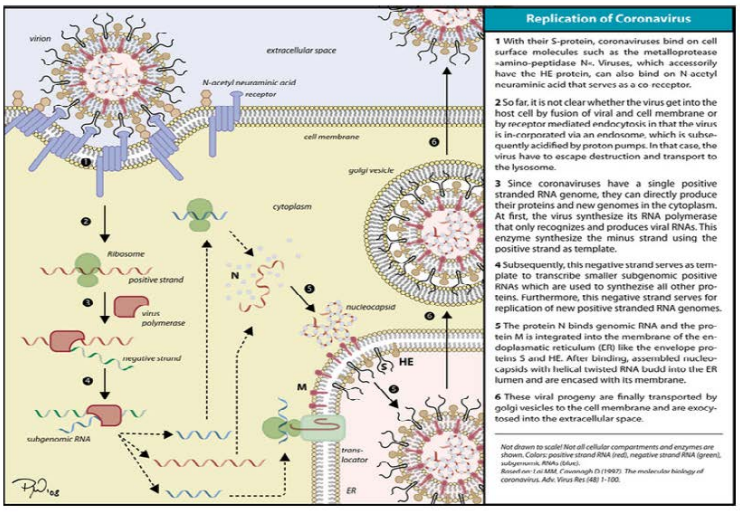

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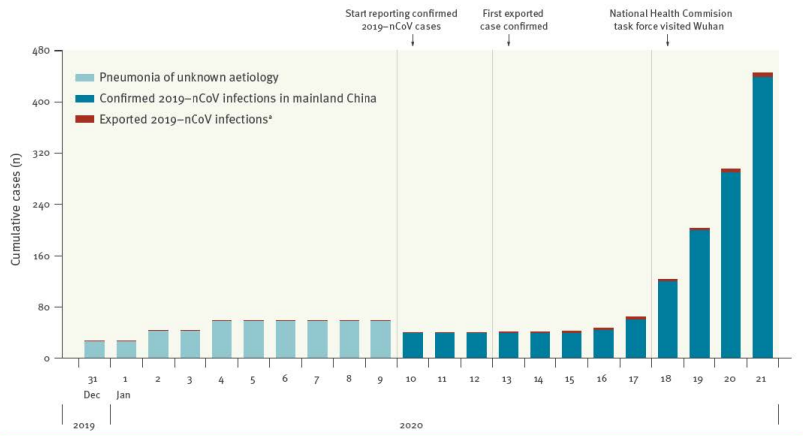
FIGURE 1

Increase in laboratory-confirmed cases of 2019-nCoV infection over time, as at 21 January 2020



Initially fairly low key reporting (e.g. on ProMed) during late Dec 2019 and early Jan 2020... sudden increase in case numbers – likely due to increased case finding/ ascertainment effect by local authorities after 17 Jan 2020.

https://eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.3.2000044#r20

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Possible reservoir?

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Bats – again!

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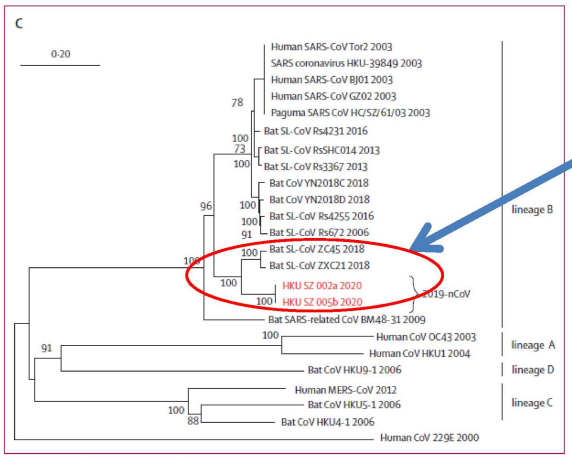

Closest phylogenetically to bat SARS-like CoVs – initially – but more recently, the pangolin is thought to be the intermediate host

Figure 3: **Phylogenetic trees of genetic sequences**
(A) Amplicon fragments of RNA-dependent RNA polymerase of patients 1, 2, 4, 5, and 7. (B) Amplicon fragments of Spike gene of patients 1, 2, 4, 5, and 7. (C) The full genome sequences of strains from patients 2 and 5. Red text indicates the coronavirus (CoV) strains detected in the patients in the present study. 2019-nCoV is 2019 novel coronavirus. HKU-SZ-001 refers to the strain detected in the nasopharyngeal swab of patient 1; HKU-SZ-002a refers to strain detected in the nasopharyngeal swab of patient 2; HKU-SZ-002b refers to strain detected in the serum sample of patient 2; HKU-SZ-004 refers to the strain detected in the nasopharyngeal swab of patient 4; HKU-SZ-005 refers to the strain detected in the throat swab of patient 5; HKU-SZ-005b refers to the strain detected in the sputum sample of patient 5; HKU-SZ-007a refers to the strain detected in the nasopharyngeal swab of

https://www.nejm.org/doi/full/10.1056/NEJMoa2001017

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Estimates of animal to human introduction for SARS-CoV-2:

between 28/10/19 to 20/12/19

– possibly 29/11/19

So just 2-3 months ago – likely from the seafood market in Wuhan.

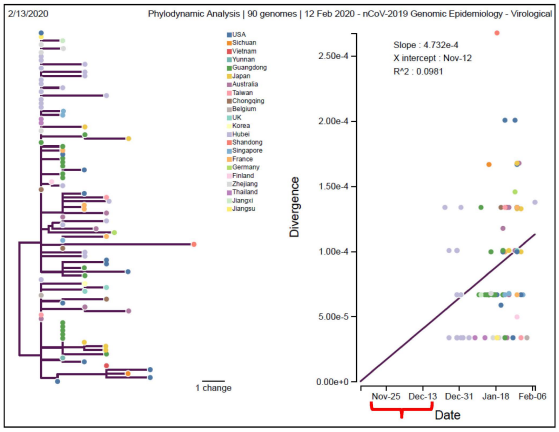

Figure 1 | Maximum likelihood tree of nCoV2019 genomes constructed using PhyML [1]. The tree is rooted using the oldest sequence but this is an arbitrary choice. Interactive tree figure by @john.mccrone using figtree.js.

Coalescent model	Estimated TMRCA	95% interval
Constant sizeNA		
Exponential growth29-Nov-2019		28-Oct-2019 – 20-Dec-2019

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Aspects of viral shedding and transmission

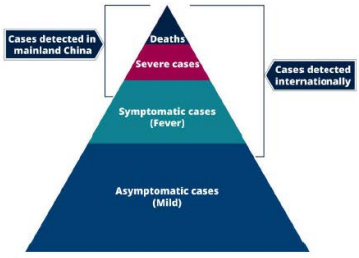

Figure 1: Spectrum of cases for 2019-nCoV, illustrating imputed sensitivity of surveillance in mainland China and in travellers arriving in other countries or territories from mainland China.

https://www.imperial.ac.uk/media/imperial-college/medicine/sph/ide/gida-fellowships/imperial-College-2019-nCoV-severity-10-02-2020.pdf

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Table 1: Best-case, central and worst-case estimates of 2019-nCoV human-to-human R_0 compatible with either 4000 (top half of table) or 1000 (bottom half of table) total cases by 18/01/2020. Values of R_0 >1 represent self-sustaining human-to-human and are highlighted in red. Baseline estimates highlighted in bold.

Number of cases caused by zoonotic exposure	Assumed total number of cases by 18/01/2020	Best-case R_0	Central (median) R_0	Worst-case R_0
40	**4000**	**2.1**	**2.6**	**3.5**
80	4000	1.8	2.2	2.7
120	4000	1.7	2.0	2.4
160	4000	1.6	1.8	2.2
200	4000	1.5	1.7	2.0
40	1000	1.4	1.9	2.7
80	1000	1.2	1.5	2.0
120	1000	1.1	1.3	1.7
160	1000	1.0	1.2	1.5
200	1000	0.9	1.1	1.3

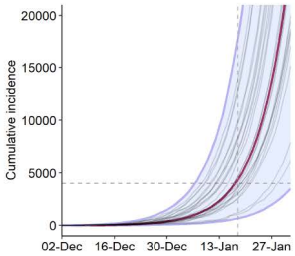

Figure 1: Illustration of estimation method for central estimate of R_0=2.6. Red curve represents median cumulative case numbers over time, calculated from 5000 simulated trajectories of the epidemic, assuming zoonotic exposure of 40 cases in December 2019 and the generation time and variability in infectiousness of SARS. The grey region indicates the 95 percentile range of trajectories – individual simulated epidemics (a random subset of which are shown as light grey curves) are highly variable, reflecting the random nature of disease transmission. Dotted lines indicate January 18th (vertical) and 4000 cumulative cases (horizontal).

Results from Imperial College modelling team also agree with recent study from Hong Kong University team that doubling time for these cases is around 6 days

- though recent figures suggest that the doubling time may be even shorter than this
- R_0 ~2-4 still holds – but may vary during outbreak
- https://www.jiidonline.com/action/showPdf?pii=S1201-9712%2820%2930053-9

https://www.imperial.ac.uk/media/imperial-college/medicine/sph/ide/gida-fellowships/Imperial-2019-nCoV-transmissibility.pdf

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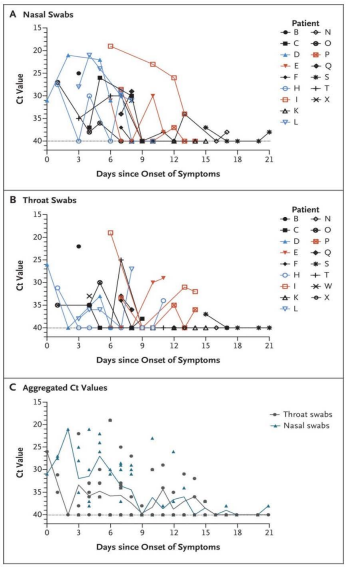

Figure 1. Viral Load Detected in Nasal and Throat Swabs Obtained from Patients Infected with SARS-CoV-2.

Panel A shows cycle threshold (Ct) values of Orf1b on reverse-transcriptase–polymerase-chain-reaction (RT-PCR) assay that were detected in nasal swabs obtained from 14 patients with imported cases and 3 patients with secondary cases, and

Panel B shows the Ct values in throat swabs. Patient Z did not have clinical symptoms and is not included in the figure. Patients with imported cases who had severe illness (Patients E, I, and P) are labeled in red, patients with imported cases who had mild-to-moderate illness are labeled in black, and patients with secondary cases (Patients D, H, and L) are labeled in blue. A linear mixed-effects model was used to test the Ct values from nasal and throat swabs among severe as compared with mild-to-moderate imported cases, which allowed for within-patient correlation and a time trend of Ct change. The mean Ct values in nasal and throat swabs obtained from patients with severe cases were lower by 2.8 (95% confidence interval [CI], −2.4 to 8.0) and 2.5 (95% CI, −0.8 to 5.7), respectively, than the values in swabs obtained from patients with mild-to-moderate cases.

Panel C shows the aggregated Ct values of Orf1b on RT-PCR assay in 14 patients with imported cases and 3 patients with secondary cases, according to day after symptom onset. Ct values are inversely related to viral RNA copy number, with Ct values of 30.76, 27.67, 24.56, and 21.48 corresponding to 1.5×10^4, 1.5×10^5, 1.5×10^6, and 1.5×10^7 copies per milliliter. Negative samples are denoted with a Ct of 40, which was the limit of detection.

Zou et al. N Engl J Med 2020. DOI: 10.1056/NEJMc2001737

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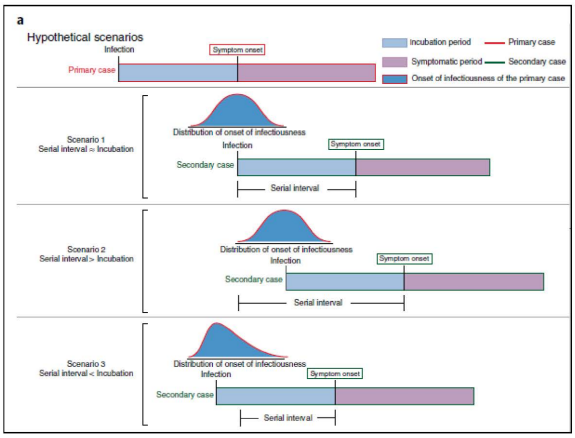
BRIEF COMMUNICATION
https://doi.org/10.1038/s41591-020-0869-5
nature medicine

Temporal dynamics in viral shedding and transmissibility of COVID-19

Xi He[1,3], Eric H. Y. Lau[2,3]✉, Peng Wu[2], Xilong Deng[1], Jian Wang[1], Xinxin Hao[2], Yiu Chung Lau[2], Jessica Y. Wong[2], Yujuan Guan[1], Xinghua Tan[1], Xiaoneng Mo[1], Yanqing Chen[1], Baolin Liao[1], Weilie Chen[1], Fengyu Hu[1], Qing Zhang[1], Mingqiu Zhong[1], Yanrong Wu[1], Lingzhai Zhao[1], Fuchun Zhang[1], Benjamin J. Cowling[2,4], Fang Li[1,4] and Gabriel M. Leung[2,4]



There is some speculation that the peak of live virus shedding may occur just before or around the onset of symptoms for SARS-CoV-2

– which is why it has been so difficult to air-sample and culture live virus from the environments around COVID-19 patients

– despite high levels of SARS-CoV-2 RNA on their nose/throat swabs.

Most transmission may actually occur just before symptom onset for this virus

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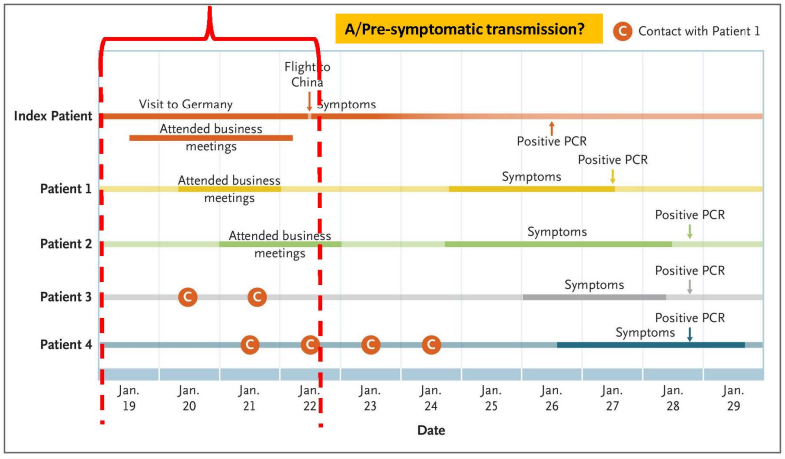

"This case of 2019-nCoV infection was diagnosed in Germany and transmitted outside Asia. However, it is notable that the infection appears to have been transmitted during the incubation period of the index patient, in whom the illness was brief and nonspecific.[3]"

The fact that asymptomatic persons are potential sources of 2019-nCoV infection may warrant a reassessment of transmission dynamics of the current outbreak.

https://www.nejm.org/doi/full/10.1056/NEJMc2001468?query=recirc_mostViewed_railB_article

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Presymptomatic SARS-CoV-2 Infections and Transmission in a Skilled Nursing Facility

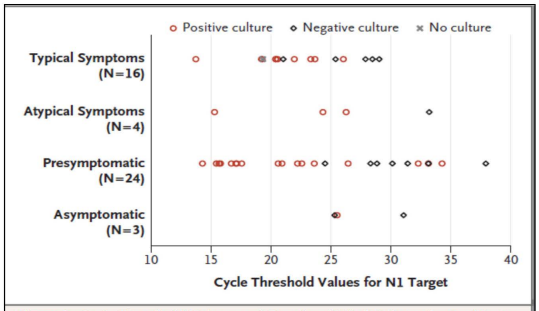

Figure 2. Cycle Threshold Values and Results of Viral Culture for Residents with Positive SARS-CoV-2 Tests According to Their Symptom Status.
Shown are N1 target cycle threshold values and viral culture results for 47 residents' first positive test for SARS-CoV-2 stratified by the resident's symptom status at the time of the test. One positive test was not assessed for culture growth. Typical symptoms include fever, cough, and shortness of breath; atypical symptoms include chills, malaise, increased confusion, rhinorrhea or nasal congestion, myalgia, dizziness, headache, nausea, and diarrhea.

https://www.nejm.org/doi/pdf/10.1056/NEJMoa2008457

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Presymptomatic SARS-CoV-2 Infections and Transmission in a Skilled Nursing Facility

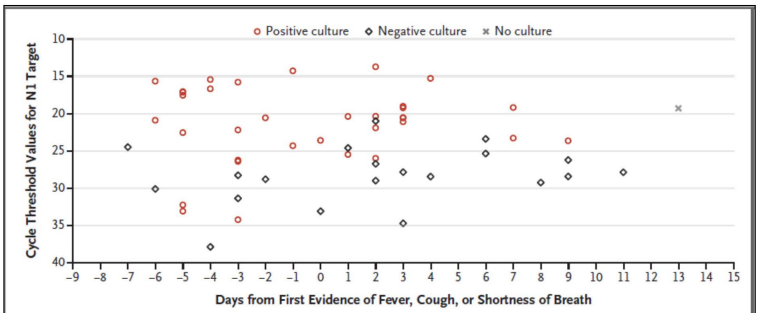

Figure 3. Cycle Threshold Values Relative to First Evidence of Fever, Cough, or Shortness of Breath.
Shown are N1 target cycle threshold values and viral culture results for each resident's positive tests for SARS-CoV-2 shown by day since the first evidence of fever, cough, or shortness of breath (N=55). Dates of onset of typical symptoms were known for 43 residents; 12 residents with two specimens that were positive for SARS-CoV-2 are also included. One positive test was not assessed for culture growth. The relationship between the first test and the second test for residents who had two positive tests is shown in Figure S2.

https://www.nejm.org/doi/pdf/10.1056/NEJMoa2008457

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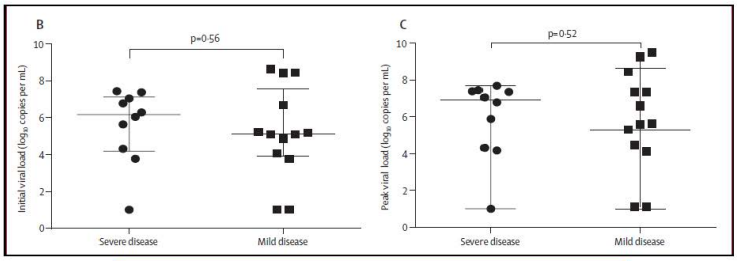
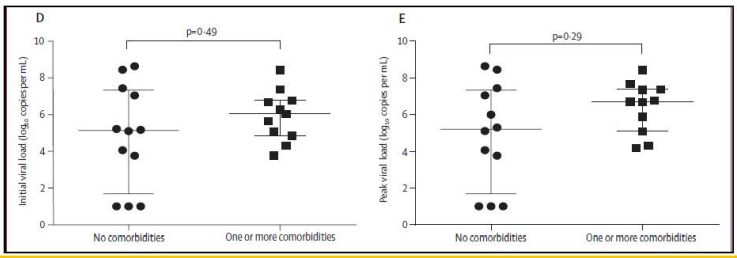


No difference in initial and peak viral loads in severe vs mild disease



No difference in initial and peak viral loads in patients without any and those with one or more comorbidities

https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30196-1/fulltext

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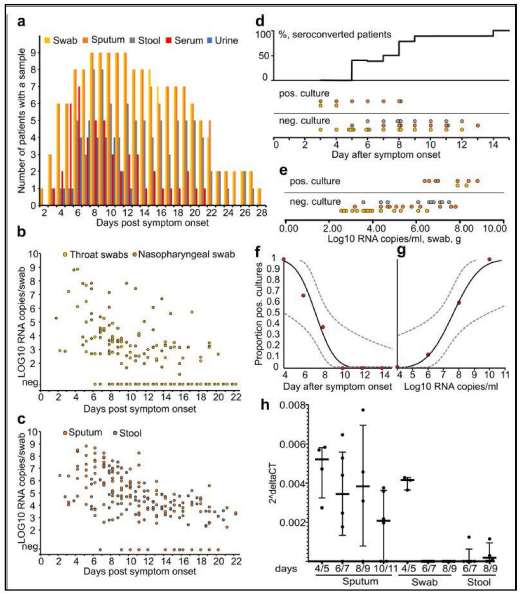

Viable virus – remains detectable for up to Day 8 post-illness onset

Throat/nasal swabs just as sensitive as sputum for PCR testing

Neutralising antibodies arise around Day 8 post-illness onset

https://www.nature.com/articles/s41586-020-2196-x

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How is the virus transmitted and how can we control it?

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How COVID-19 Spreads

The virus is thought to spread mainly from person-to-person.
•Between people who are in close contact with one another (within about 6 feet).
•Through respiratory droplets produced when an infected person coughs, sneezes, or talks.
•These droplets can land in the mouths or noses of people who are nearby or possibly be inhaled into the lungs.
•COVID-19 may be spread by people who are not showing symptoms.
The virus spreads easily between people

The virus that causes COVID-19 is spreading very easily and sustainably between people. Information from the ongoing COVID-19 pandemic suggest that this virus is spreading more efficiently than influenza, but not as efficiently as measles, which is highly contagious. The virus does not spread easily in other ways

COVID-19 is a new disease and we are still learning about how it spreads. It may be possible for COVID-19 to spread in other ways, but these are not thought to be the main ways the virus spreads.

•**From touching surfaces or objects**. It may be possible that a person can get COVID-19 by touching a surface or object that has the virus on it and then touching their own mouth, nose, or possibly their eyes. This is not thought to be the main way the virus spreads, but we are still learning more about this virus.

https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/how-covid-spreads.html

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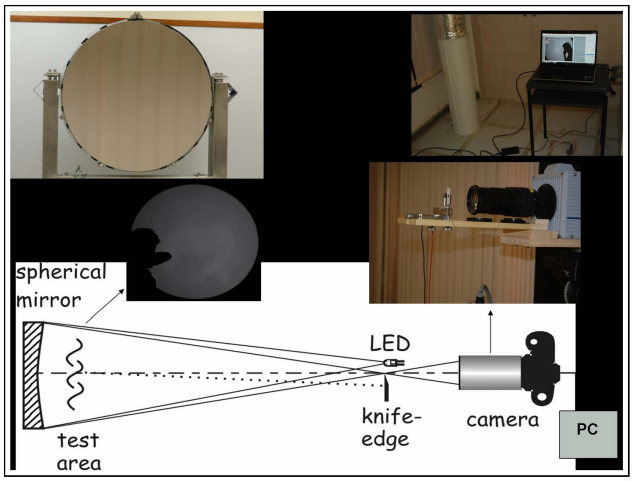

Visualisation of exhaled airflows in real-time from human volunteers using schlieren/shadowgraph mirror-camera set-up
– across a 1 m distance (= mirror diameter)

https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0034818

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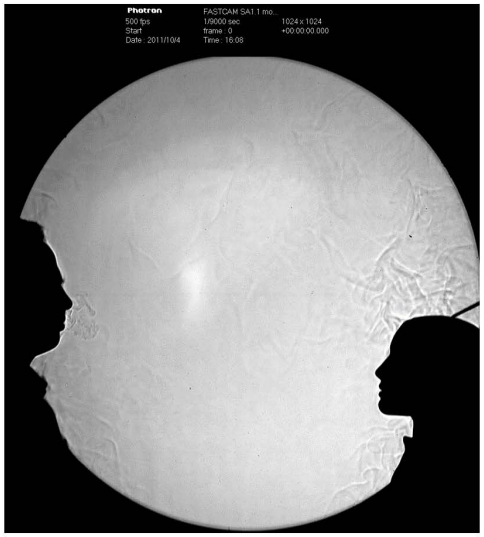
Talking – exhalation flows – and garlic breath…

Online video at: https://www.youtube.com/watch?v=OsBGaWdHHyg

28

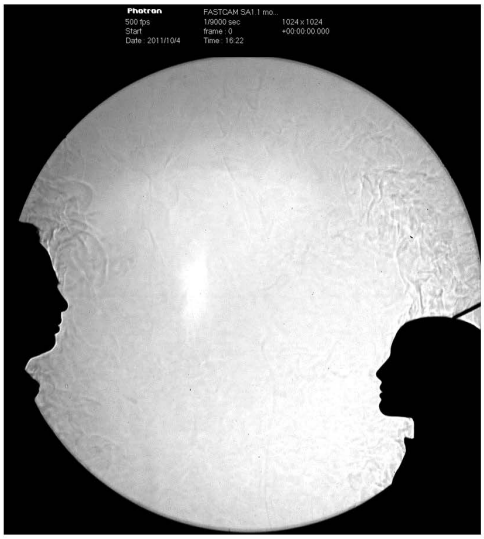
Nose breathing – exhalation flows – during conversation…



Online video at: https://www.youtube.com/watch?v=g9oQzqTPnu8

29

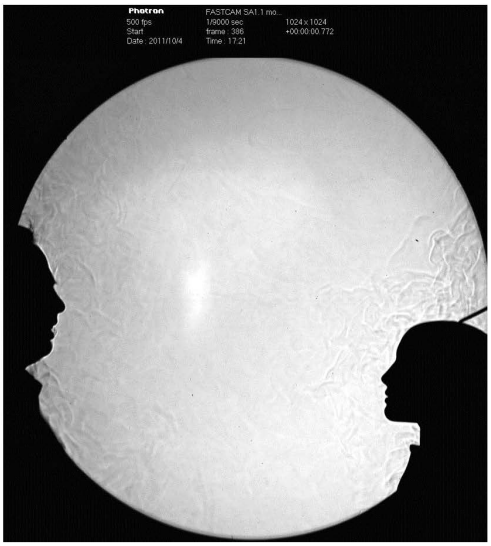
Mouth breathing – exhalation flows – during conversation…



Online video at: https://www.youtube.com/watch?v=IHUMdhBGt1c

30

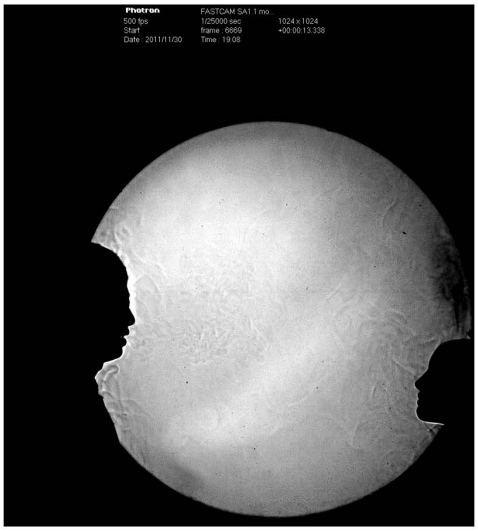
Laughing – exhalation flows – the joke may be on you…



Online video at: https://www.youtube.com/watch?v=Eue9f73SB6E&list=PL8pE_CuHoXJXZExcWwk_0tsqjT2Ydwsxg&index=10&t=0s

31

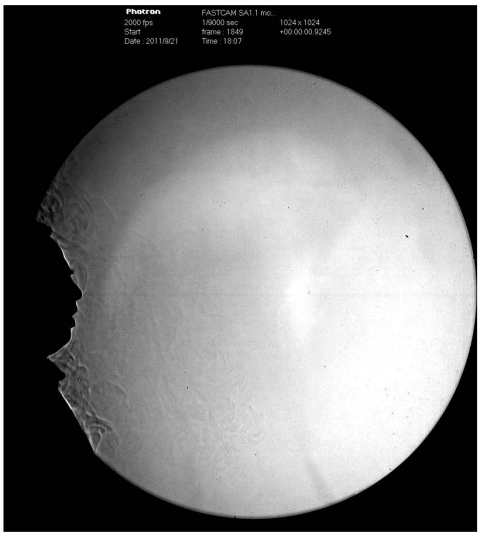
Singing (Happy Birthday) – possibly enhanced exhalation flows…



Online video at: https://www.youtube.com/watch?v=suN_GAE03fk&list=PL8pE_CuHoXJXZExcWwk_0tsqjT2Ydwsxg&index=5

32

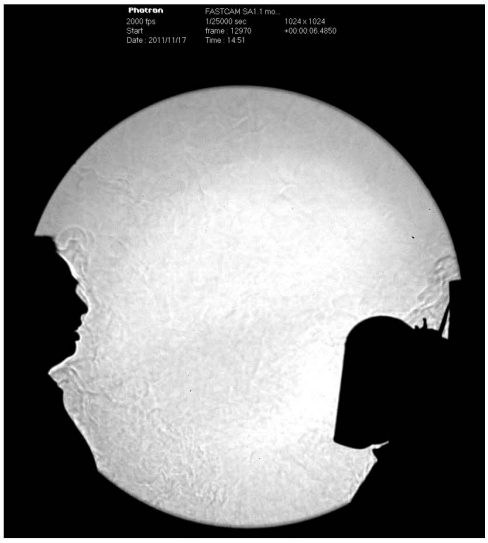
Coughing – enhanced exhalation flows…



Online video at: https://www.youtube.com/watch?v=KOkE4jjsXWY&list=PL8pE_CuHoXJXZExcWwk_0tsqjT2Ydwsxg&index=10

33

Sneezing – enhanced exhalation flows…



Online video at: https://www.youtube.com/watch?v=ZDiLsu8hipI

34

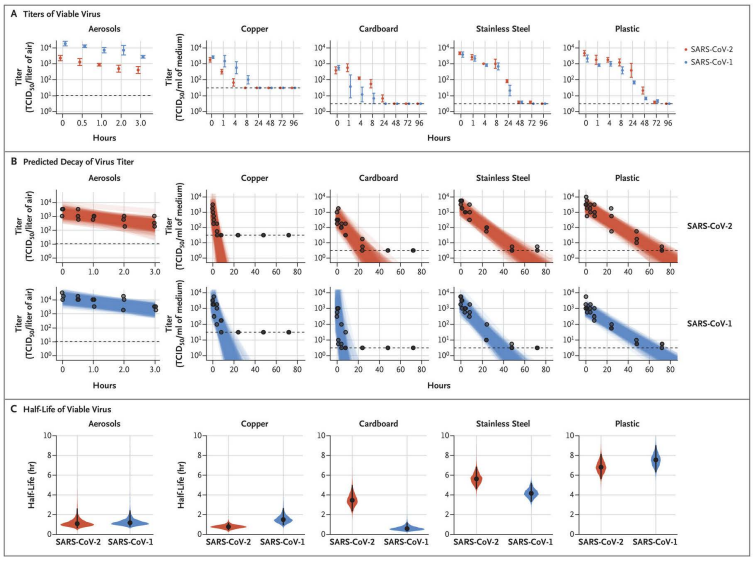


Figure 1. Viability of SARS-CoV-1 and SARS-CoV-2 in Aerosols and on Various Surfaces.

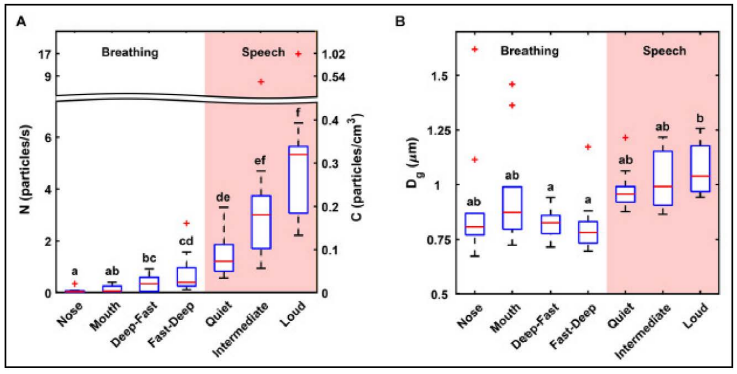
https://www.nejm.org/doi/full/10.1056/NEJMc2004973

35

Aerosol emission and superemission during human speech increase with voice loudness

Sima Asadi[1], Anthony S. Wexler[2,3,4,5], Christopher D. Cappa[6], Santiago Barreda[6], Nicole M. Bouvier[7,8] & William D. Ristenpart[1]

Figure 5. Comparison of (A) emission rate/concentration and (B) corresponding geometric mean diameters of particles emitted during various modes of breathing versus speech at different loudness levels. "Nose" denotes normal nasal breathing; "Mouth" denotes normal mouth breathing; "Deep-Fast" denotes deep, slow nasal inhalation followed by fast mouth exhalation; "Fast-Deep" denotes fast nasal inhalation followed by deep (i.e., slow and prolonged) mouth exhalation. "Quiet", "Intermediate", and "Loud" denote loudness levels while reading aloud a passage of text ("Rainbow" passage) at respective amplitudes. Red lines indicate medians, while bottom and top of blue boxes indicate the 25th and 75th percentiles respectively; sample size is n = 10. Outliers (defined as values that exceed 2.7 standard deviations) are indicated with red plus signs. Note that the 2 outliers for speech in (A) are a different individual (F4) than the two outliers observed for nose and fast-deep breathing (M24 and M5 respectively). Scheffe groups are indicated with letters; groups with no common letter are considered significantly different with $p < 0.05$; cf. Supplementary Table S1. Note that (A) has different scales above and below the break.



Number, concentration and sizes of droplets (<5 um) produced by different breathing and talking modes

https://www.nature.com/articles/s41598-019-38808-z

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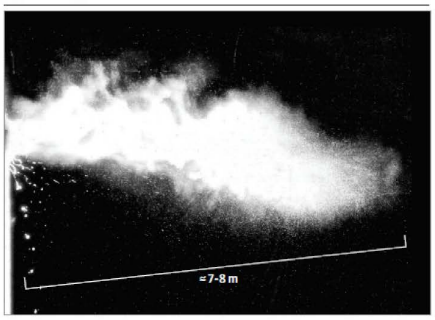
JAMA Insights

Turbulent Gas Clouds and Respiratory Pathogen Emissions
Potential Implications for Reducing Transmission of COVID-19

Lydia Bourouiba, PhD

Figure. Multiphase Turbulent Gas Cloud From a Human Sneeze



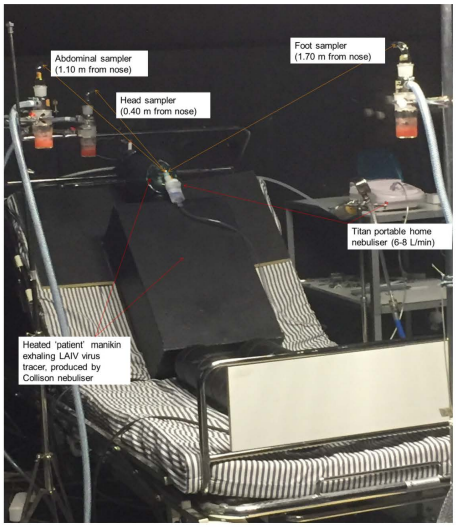
The dichotomy of large vs small droplets remains at the core of the classification systems of routes of respiratory disease transmission adopted by the World Health Organization and other agencies, such as the Centers for Disease Control and Prevention. These classification systems employ various arbitrary droplet diameter cutoffs, from 5 to 10 µm, to categorize host-to-host transmission as droplets or aerosol routes.[1] Such dichotomies continue to underly current risk management, major recommendations, and allocation of resources for response management associated with infection control, including for COVID-19. Even when maximum containment policies were enforced, the rapid international spread of COVID-19 suggests that using arbitrary droplet size cutoffs may not accurately reflect what actually occurs with respiratory emissions, possibly contributing to the ineffectiveness of some procedures used to limit the spread of respiratory disease.

Droplet vs aerosols – can physically travel further than 1-2 m depending on the initial exhalation force and ambient airflows; can range in diameter from 1-100 um within exhale breath, coughs, sneezes, and may carry differing numbers of viruses

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

https://www.nejm.org/doi/full/10.1056/NEJMc2004973

37



The experiment was run a total of 5 times over two days to give average viral loads at each of the SKC sampling locations: 7.34±0.28x104 copies/ml VTM (head), 2.09±0.41x104 copies/ml VTM (abdomen), and 1.41±0.23x104 copies/ml VTM (feet).

Converting these averaged viral loads in copies/ml VTM to copies/L air (given that each air sample was obtained from a total air volume collection of 120 L), this gives approximately: 612 viruses/L (head), 174 viruses/L (abdomen), 118 viruses/L (feet).

These results show that aerosols from a nebulizer mask can spread throughout the room at a decreasing concentration with increasing distance from the source. This experiment was performed within a ventilated experimental chamber with 12 ACH.

Tang et al. Nebulisers as a potential source of airborne virus.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7227527/

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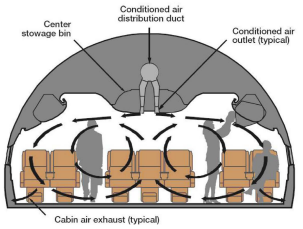
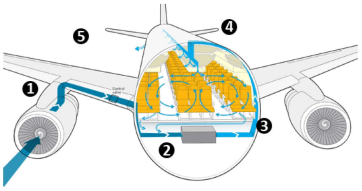
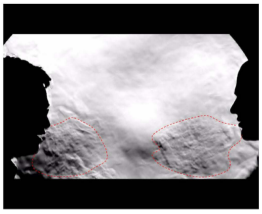


https://aviation.stackexchange.com/questions/26105/where-does-the-air-enter-the-passenger-cabin



https://www.quora.com/What-are-some-things-that-airline-cabin-crews-know-but-wont-tell-you

Plane ventilation systems will not prevent short-range aerosol transmission during conversational situations with nearest neighbors
– but will reduce the build-up of airborne virus in the passenger cabin to reduce/prevent longer-range airborne transmission
– so masking on planes is important still



https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0021392

https://www.techbyn.com/researchers-conduct-a-reassuring-study-on-coronavirus-transmission-risks-involved-on-planes/

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nature

https://doi.org/10.1038/s41586-020-2271-3

Accelerated Article Preview

Aerodynamic analysis of SARS-CoV-2 in two Wuhan hospitals

Received: 14 March 2020
Accepted: 20 April 2020

Yuan Liu, Zhi Ning, Yu Chen, Ming Guo, Yingle Liu, Nirmal Kumar Gali, Li Sun, Yuxian Duan, Jing Cai, Dane Westerdahl, Xinjin Liu, Ke Xu, Kin-fai Ho, Haidong Kan, Qingyan Fu & Ke Lan

Although we have not established the infectivity of the virus detected in these hospital areas, we propose that SARS-CoV-2 may have the potential to be transmitted via aerosols. Our results indicate that room ventilation, open space, sanitization of protective apparel, and proper use and disinfection of toilet areas can effectively limit the concentration of SARS-CoV-2 RNA in aerosols. Future work should explore the infectivity of aerosolized virus.

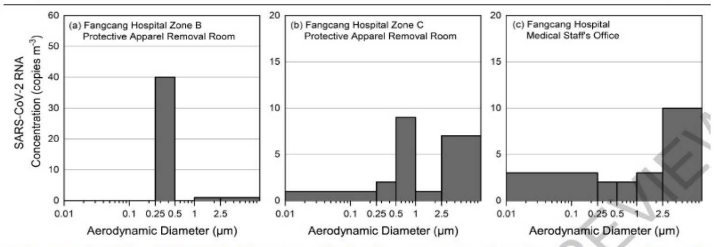

Fig. 1 | Concentration of airborne SARS-CoV-2 RNA in different aerosol size bins. The x axis represents aerodynamic diameter in logarithmic scale to cover the multiple magnitude of measured aerosol diameter..

https://www.nature.com/articles/s41586-020-2271-3_reference.pdf

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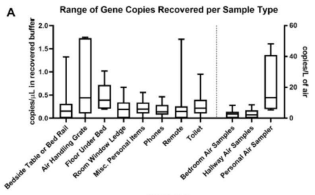
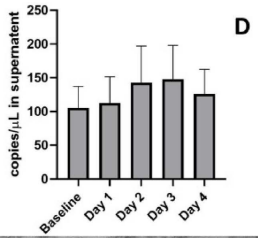
OPEN

Aerosol and surface contamination of SARS-CoV-2 observed in quarantine and isolation care

Joshua L. Santarpia[1,2✉], Danielle N. Rivera[2], Vicki L. Herrera[2], M. Jane Morwitzer[1], Hannah M. Creager[2], George W. Santarpia[3], Kevin K. Crown[2], David M. Brett-Major[1], Elizabeth R. Schnaubelt[1,2], M. Jana Broadhurst[2], James V. Lawler[1,2], St. Patrick Reid[4] & John J. Lowe[1,2]

The first study to demonstrate viable SARS-CoV-2 in air-samplers collected from a healthcare setting.





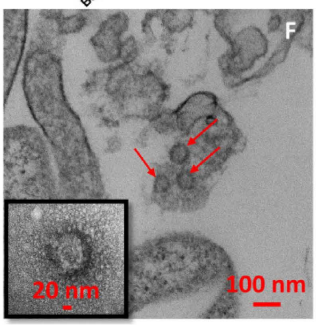


Figure 2. Results of SARS-CoV-2 cell culture experiments. Images and graphs describe the results of cell culture of two environmental samples. The two samples are shown: an air sample from the NQU hallway on day 8 (A,C,E), the windowsill from NQU A on day 1 (B,D,F). Cytopathic effect observed in these samples (A,B) is generally mild, compared to the control (top center) which had no environmental sample added. RT-qPCR from daily withdrawals of 100 μL of supernatant from the cell culture of each sample indicates changes in viral RNA in the supernatant throughout cultivation. The hallway air sample indicates a decrease in RNA concentration in the supernatant over the first 2 days, consistent with the withdrawal of supernatant for analysis. Increase in concentration is observed on both days 3 and 4 (C). The windowsill sample showed stable and possible increasing viral concentrations for the first 3 days, despite the withdrawal of supernatant for analysis (D). Immunofluorescent staining of the hallway air sample indicates the presence of SARS-CoV-2, after 3 days of cell culture (E), as compared to control cells (inset), which were not exposed to any environmental sample. TEM images of the lysates from the windowsill culture (F) clearly indicate the presence of intact SARS-CoV-2 virions, after 3 days of cell culture.

https://www.nature.com/articles/s41598-020-69286-3.pdf

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International Journal of Infectious Diseases 100 (2020) 476–482
Contents lists available at ScienceDirect
International Journal of Infectious Diseases
journal homepage: www.elsevier.com/locate/ijid

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

John A. Lednicky[a,b,*], Michael Lauzardo[b,c], Z. Hugh Fan[d,e], Antarpreet Jutla[f], Trevor B. Tilly[f], Mayank Gangwar[f], Moiz Usmani[f], Sripriya Nannu Shankar[f], Karim Mohamed[g], Arantza Eiguren-Fernandez[g], Caroline J. Stephenson[a,b], Md. Mahbubul Alam[a,b], Maha A. Elbadry[a,b], Julia C. Loeb[a,b], Kuttichantran Subramaniam[b,h], Thomas B. Waltzek[b,h], Kartikeya Cherabuddi[c], J. Glenn Morris Jr.[b,c], Chang-Yu Wu[f]

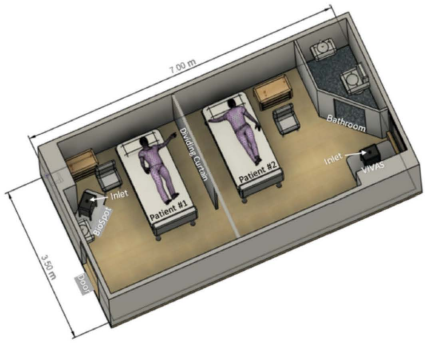

Figure 1. A schematic diagram of room with the depiction of patient bed and air sampler locations.

Table 4
Estimate of viable virus counts based on $TCID_{50}$ tests.

Sample ID	Virus genome equivalents/L of air[a]	$TCID_{50}$/100 μl	Viable virus count/L air
1-1 BioSpot	94	2.68E+04	74
1-2 BioSpot + HEPA	-	0	0
1-3 BioSpot	30	6.31E+03	18
2-1 VIVAS	44	1.00E+04	27
2-2 VIVA S+ HEPA	-	0	0
2-3 VIVAS	16	2.15E+03	6

[a] From Table 2.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7493737/pdf/main.pdf

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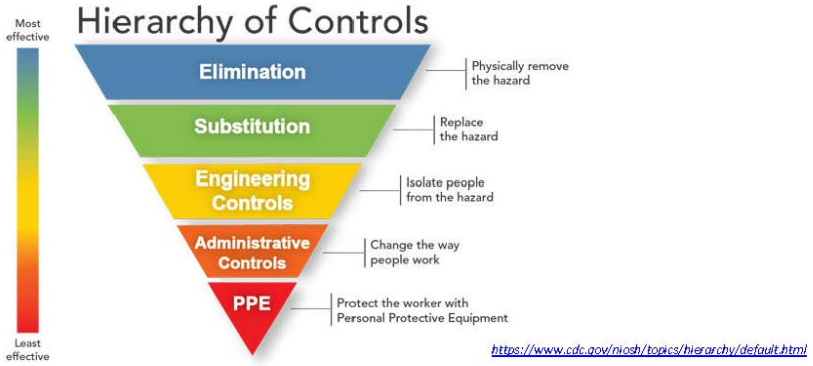

https://www.cdc.gov/niosh/topics/hierarchy/default.html

Dealing with airborne transmission of SARS-CoV-2 – ASHRAE and REHVA:

"Such small virus particles stay airborne and can travel long distances carried by airflows in the rooms or in the extract air ducts of ventilation systems. Airborne transmission has caused infections of SARS-CoV-1 in the pastxiii,xiv. For Corona disease (COVID-19) it is likely but not yet documented. There is also no reported data or studies to rule out the possibility of the airborne-particle route."

https://www.rehva.eu/fileadmin/user_upload/REHVA_COVID-19_guidance_document_ver2_20200403_1.pdf

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Perspective

MAY 21, 2020

Universal Masking in Hospitals in the Covid-19 Era

Michael Klompas, M.D., M.P.H., Charles A. Morris, M.D., M.P.H., Julia Sinclair, M.B.A., Madelyn Pearson, D.N.P., R.N., and Erica S. Shenoy, M.D., Ph.D.

The first is during the care of a patient with unrecognized Covid-19. A mask alone in this setting will reduce risk only slightly, however, since it does not provide protection from droplets that may enter the eyes or from fomites on the patient or in the environment that providers may pick up on their hands and carry to their mucous membranes (particularly given the concern that mask wearers may have an increased tendency to touch their faces).

More compelling is the possibility that wearing a mask may reduce the likelihood of transmission from asymptomatic and minimally symptomatic health care workers with Covid-19 to other providers and patients. This concern increases as Covid-19 becomes more widespread in the community. We face a constant

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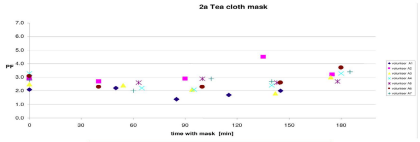
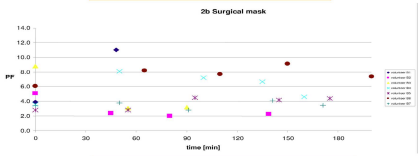
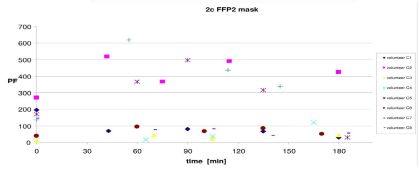
~2-4-fold reduction of incoming aerosol



~2-10-fold reduction of incoming aerosol



~50-500-fold reduction of incoming aerosol



Home-made cloth masks (made out of ?1-layer tea cloth in this study) can reduce the exposure from incoming aerosols (produced by lighted candles) by up to 2-4-fold (i.e. ~50-75%) though this will depend on how the mask is made, what it is made from, and the nature of the aerosols to which it is exposed. (2008)

https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0002618

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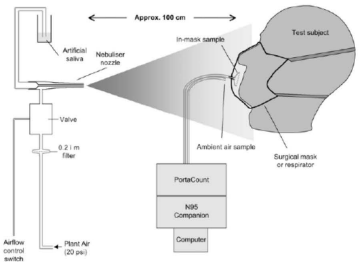

Figure 2.1. Schematic diagram of the inert aerosol test arrangement

HSE Health and Safety Executive

Evaluating the protection afforded by surgical masks against influenza bioaerosols

Gross protection of surgical masks compared to filtering facepiece respirators

Prepared by the **Health and Safety Laboratory** for the Health and Safety Executive 2008

Surgical masks can also protect the wearer to some degree by reducing the exposure to incoming droplets and aerosols by up to 6-fold (i.e. ~83%), from others who are ill. (2008)

https://www.hse.gov.uk/research/rrpdf/rr619.pdf

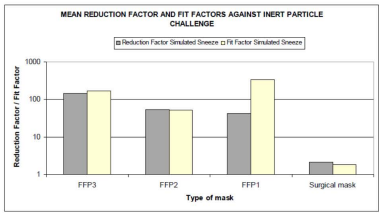

Figure 3.6 Mean values of the reduction factors and fit factor results for the grouped range of filtering facepieces and surgical masks tested against the inert simulated sneeze

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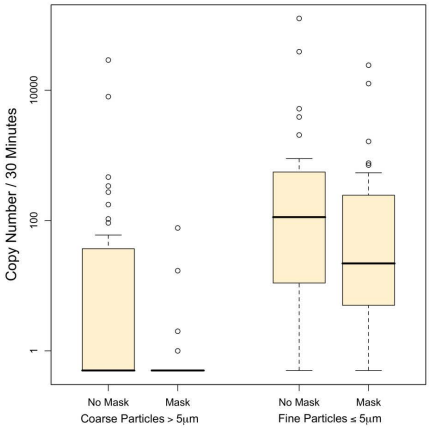
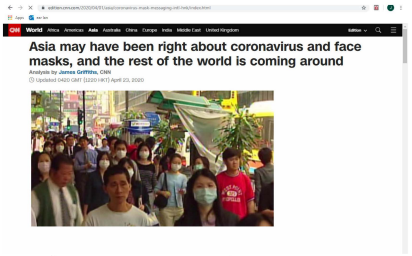
Surgical masks can contain and therefore reduce the dissemination of droplets and aerosols produced by a sick wearer by up to 3-4-fold (i.e. ~67-75%) to protect others. (2013)



https://journals.plos.org/plospathogens/article?id=10.1371/journal.ppat.1003205

https://sph.umd.edu/news-item/flu-may-be-spread-just-breathing-new-study-shows-coughing-and-sneezing-not-required

47



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Returning to school – safely!

Taiwan

https://www.cbc.ca/news/business/taiwan-covid-19-lessons-1.5505031

Vietnam

https://www.vox.com/21270817/coronavirus-schools-reopen-germany-vietnam-new-zealand

Thailand

https://www.dailymail.co.uk/news/article-8611385/Thai-kindergartners-sealed-perspex-boxes-playtime-fight-against-coronavirus.html

Japan

https://www.newsbreak.com/news/1579287266593/japanese-students-go-back-to-school-with-face-shields

China

https://www.sciencemag.org/news/2020/07/school-openings-across-globe-suggest-ways-keep-coronavirus-buy-despite-outbreaks#

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Immunological considerations for COVID-19 vaccine strategies

Mangalakumari Jeyanathan[1,2,3,5], Sam Afkhami[1,2,3,5], Fiona Smaill[2,3], Matthew S. Miller[1,3,4], Brian D. Lichty[1,2] and Zhou Xing[1,2,3]

https://www.nature.com/articles/s41577-020-00434-6#Tab1

Moderna: mRNA - SARS-CoV-2 S protein
Pfizer-BionTech: mRNA - SARS-CoV-2 S protein

Russian Sputnik V: AdV5/AdV26 - SARS-CoV-2 S protein
Oxford-AstraZeneca: ChpzAdV – SARS-CoV-2 S protein
Janssen/Johnson&Johnson: Ad26 - SARS-CoV-2 S protein

GSK/Sanofi: protein S subunit, similar to flu
Novavax: NVXCoV2373, S protein subunit

Chinese-SinoVac: whole inactivated SARS-CoV-2
Valneva: whole inactivated virus

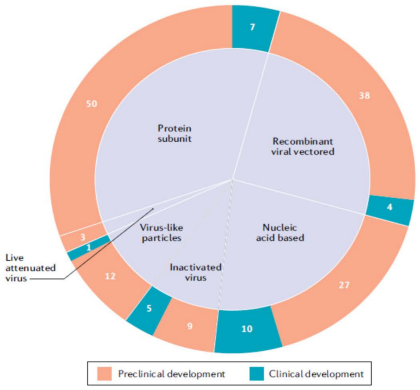

Fig. 1 | **The global COVID-19 vaccine landscape.** The six major types of candidate vaccine for coronavirus disease 2019 (COVID-19) are illustrated (live attenuated virus, recombinant viral vectored, inactivated virus, protein subunit, virus-like particles and nucleic acid based), showing the number of candidate vaccines that are currently under clinical and preclinical development. The nucleic acid-based platform includes both mRNA vaccines (6 clinical and 16 preclinical) and plasmid DNA vaccines (4 clinical and 11 preclinical). Data obtained from REF[5].

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Which COVID-19 vaccines has the UK pre-ordered:

Moderna (mRNA-1273): 5 million doses (2 dose/person) – *Phase 3*

Pfizer-BioNTech (mRNA-BNT162b2): 40 million doses (2 dose/person) – *Phase 3*

Oxford AstraZeneca (ChAdOx1 nCoV-19): 100 million doses (2 dose/person) – *Phase 2/3*

Novavax (NVXCoV2373, S protein subunit): 60 million doses (2 dose/person) – *starting Phase 3 in UK*

Janssen/Johnson&Johnson Ad26.COV2-S: 30 million doses (2 dose/person)) – *starting Phase 3 in UK*

GSK/Sanofi (protein S subunit, similar to flu): 60 million (2 dose/person) – *Phase 1/2 USA*

Valneva (whole inactivated virus): 60 million doses (2 dose/person) – *Phase 1 clinical trials to start end 2020*

https://www.cityam.com/which-covid-vaccines-has-the-uk-government-ordered/
https://www.nature.com/articles/s41577-020-00434-6
(+various other company, media, government online sources)

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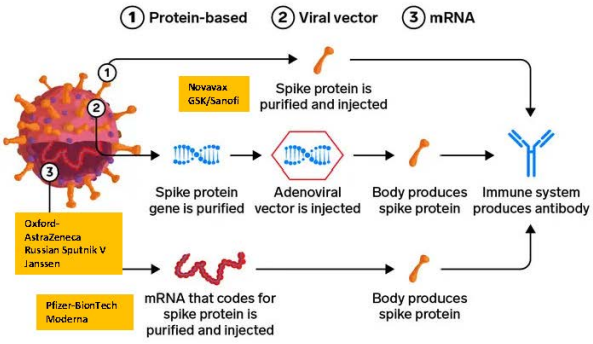
Three types of coronavirus vaccines in development



Source: National Institutes of Health presentation at Senate hearing on September 9, 2020 INSIDER

https://www.businessinsider.com/leading-us-coronavirus-vaccines-how-they-work-compare-2020-10?r=US&IR=T

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REVIEW ARTICLE OPEN

The promise of mRNA vaccines: a biotech and industrial perspective

Nicholas A. C. Jackson[1*], Kent E. Kester[2], Danilo Casimiro[2], Sanjay Gurunathan[2] and Frank DeRosa[2]

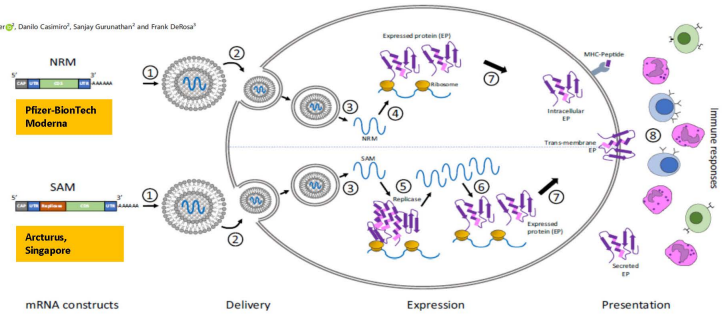

Fig. 1 Two categories of mRNA constructs are being actively evaluated. Non-replicating mRNA (NRM) constructs encode the coding sequence (CDS), and are flanked by 5′ and 3′ untranslated regions (UTRs), a 5′-cap structure and a 3′-poly-(A) tail. The self-amplifying mRNA (SAM) construct encodes additional replicase components able to direct intracellular mRNA amplification. (1) NRM and SAM are formulated in this illustration in lipid nanoparticles (LNPs) that encapsulate the mRNA constructs to protect them from degradation and promote cellular uptake. (2) Cellular uptake of the mRNA with its delivery system typically exploits membrane-derived endocytic pathways. (3) Endosomal escape allows release of the mRNA into the cytosol. (4) Cytosol-located NRM constructs are immediately translated by ribosomes to produce the protein of interest, which undergoes subsequent post-translational modification. (5) SAM constructs can also be immediately translated by ribosomes to produce the replicase machinery necessary for self-amplification of the mRNA. (6) Self-amplified mRNA constructs are translated by ribosomes to produce the protein of interest, which undergoes subsequent post-translational modification. (7) The expressed proteins of interest are generated as secreted, *trans*-membrane, or intracellular protein. (8) The innate and adaptive immune responses detect the protein of interest.

https://www.nature.com/articles/s41541-020-0159-8

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Table 1 | **Immunological properties of major COVID-19 candidate vaccine platforms**

Vaccine platform	SARS-CoV-2 antigens	Neutralizing antibody response	T cell response			Pre-existing antivector immunity	Route of vaccination	Overall immunogenicity	Other attributes
			$CD4^+$ T_H cells	$CD8^+$ T cells	Lung T_{RM} cells				
Viral-vectored vaccines									
Ad5 (non-replicating) Russian Sputnik V	S protein	Quality and durability affected by pre-existing antivector immunity	T_H1 cell	Potent response; negative effects from pre-existing antivector immunity	Induced by RM but not IM route	High, age-dependent, prevalence in blood; low prevalence in respiratory tract	Parenteral (IM) in clinical trials	Strong with single delivery but hindered by pre-existing antivector immunity	Ample human safety data; RM delivery helps bypass antivector immunity; can be delivered by inhaled aerosol
Ad26 (non-replicating) Russian Sputnik V Janssen	S protein	Quality and durability affected by pre-existing antivector immunity	T_H1 cell	Moderate response; negative effects from pre-existing antivector immunity	Induced by RM but not IM route	Medium prevalence	Parenteral (IM) in planned clinical trials	Weak; requires repeated or heterologous boost vaccination	Established human safety from HIV and Ebola vaccine trials; RM delivery helps bypass antivector immunity
ChAd (non-replicating) Oxford-AstraZeneca	S protein	Unimpeded owing to lack of pre-existing antivector immunity	T_H1 cell	Potent response	Induced by RM but not IM route	Very low prevalence	Parenteral (IM) in clinical trials	Strong with single delivery	Well-established human safety data; amenable to RM delivery; can be used as a stand-alone vaccine or in prime–boost regimens

https://www.nature.com/articles/s41577-020-00434-6#Tab1

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Vaccine platform	SARS-CoV-2 antigens	Neutralizing antibody response	T cell response			Pre-existing antivector immunity	Route of vaccination	Overall immunogenicity	Other attributes
			$CD4^+$ T_H cells	$CD8^+$ T cells	Lung T_{RM} cells				
Other vaccines									
mRNA-based vaccine Pfizer-BioNTech Moderna	S protein or RBD encapsulated in lipid nanoparticle	Unimpeded owing to lack of pre-existing antivector immunity	T_H1 cell or T_H2 cell depending on adjuvant	Depends on choice of adjuvant and formulation	Not induced by parenteral route	None	Parenteral (IM) in clinical trials	Requires repeated delivery	Adjuvant required; unclear whether it is amenable to RM vaccination
DNA-based vaccine	S protein	Unimpeded owing to lack of pre-existing antivector immunity	T_H1 cell	Response not as strong as for some of the viral vectors	Not induced	None	Parenteral (IM) in clinical trials	Weaker than mRNA-based vaccine; requires repeated delivery	Adjuvant required; not amenable to RM vaccination
Live attenuated virus	Multiple viral antigens	Strong induction	T_H1 cell	Strong response	Induced by RM but not IM route	No cross-reactive antibodies; cross-reactive T cells from seasonal coronavirus infections	Parenteral (SC)	Requires only a single delivery	Extensive safety testing required for potential recombination with wild-type virus

https://www.nature.com/articles/s41577-020-00434-6#Tab1

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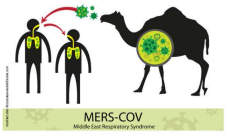
The question now is whether it will:

- *disappear from the human population completely like SARS-CoV has thus far, to return and remain within the confines of its zoonotic origins*

- *continue to infect humans sporadically like MERS-CoV, avian A(H5N1) and A(H7N9) influenza viruses, which continue to cause significant morbidity and mortality though to relatively few people*



- *become a truly seasonal human respiratory virus, like the former pandemic influenza virus A(H1N1)pdm09, and the other seasonal coronaviruses, which circulate annually with less severe morbidity and mortality*

https://www.id-hub.com/2020/02/10/the-emergence-and-spread-of-the-2019-novel-coronavirus-2019-ncov/

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