

The Daily COVID-19 Literature Surveillance Summary

November 04, 2020



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COVID-19 Daily Literature Surveillance

COVID19LST



Bringing you real time, distilled information for guiding best practices during the COVID-19 pandemic

LEVEL OF EVIDENCE

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

Question	Step 1 (Level 1*)	Step 2 (Level 2*)	Step 3 (Level 3*)	Step 4 (Level 4*)	Step 5 (Level 5)
How common is the problem?	Local and current random sample surveys (or censuses)	Systematic review of surveys that allow matching to local circumstances**	Local non-random sample**	Case-series**	n/a
Is this diagnostic or monitoring test accurate? (Diagnosis)	Systematic review of cross sectional studies with consistently applied reference standard and blinding	Individual cross sectional studies with consistently applied reference standard and blinding	Non-consecutive studies, or studies without consistently applied reference standards**	Case-control studies, or "poor or non-independent reference standard"**	Mechanism-based reasoning
What will happen if we do not add a therapy? (Prognosis)	Systematic review of inception cohort studies	Inception cohort studies	Cohort study or control arm of randomized trial*	Case-series or case-control studies, or poor quality prognostic cohort study**	n/a
Does this intervention help? (Treatment Benefits)	Systematic review of randomized trials or n-of-1 trials	Randomized trial or observational study with dramatic effect	Non-randomized controlled cohort/follow-up study**	Case-series, case-control studies, or historically controlled studies**	Mechanism-based reasoning
What are the COMMON harms? (Treatment Harms)	Systematic review of randomized trials, systematic review of nested case-control studies, n-of-1 trial with the patient you are raising the question about, or observational study with dramatic effect	Individual randomized trial or (exceptionally) observational study with dramatic effect	Non-randomized controlled cohort/follow-up study (post-marketing surveillance) provided there are sufficient numbers to rule out a common harm. (For long-term harms the duration of follow-up must be sufficient.)*	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning
What are the RARE harms? (Treatment Harms)	Systematic review of randomized trials or n-of-1 trial	Randomized trial or (exceptionally) observational study with dramatic effect			
Is this (early detection) test worthwhile? (Screening)	Systematic review of randomized trials	Randomized trial	Non-randomized controlled cohort/follow-up study**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning

* Level may be graded down on the basis of study quality, imprecision, indirectness (study PICO does not match questions PICO), because of inconsistency between studies, or because the absolute effect size is very small; Level may be graded up if there is a large or very large effect size.

** As always, a systematic review is generally better than an individual study.

How to cite the Levels of Evidence Table

OCEBM Levels of Evidence Working Group*. "The Oxford 2011 Levels of Evidence". Oxford Centre for Evidence-Based Medicine. <http://www.cebm.net/index.aspx?o=5653>

* OCEBM Table of Evidence Working Group = Jeremy Howick, Iain Chalmers (James Lind Library), Paul Glasziou, Trish Greenhalgh, Carl Heneghan, Alessandro Liberati, Ivan Moschetti, Bob Phillips, Hazel Thornton, Olive Goddard and Mary Hodgkinson

EXECUTIVE SUMMARY

Understanding the Pathology

- Should we be testing for more than SARS-CoV-2 antibodies? Microbiologists, pathologists, and public health experts associated with Mount Sinai Hospital analyzed 3277 blood specimens from recovered COVID-19 patients and found that [neutralizing antibody level is the highest 31-35 days post symptom onset](#), even though general SARS-CoV-2 antibody levels had been high (well above the 160 titer range cutoff) long before this, suggesting the importance of also testing for neutralizing antibodies.

Transmission & Prevention

- How do close contact and aerosol transmission risks compare? Swiss environmental engineers applied a Quantitative Microbial Risk Assessment (QMRA) to evaluate SARS-CoV-2 infection risk via aerosol transmission and close indoor contact using dose-response mice models and infection risk data from meta-analyses and found [lower infection transmission risk via aerosol exposure](#) within one hour (10^{-6} to 10^{-4}) compared to close contact (10^{-1} ; 12.8% risk within 1m) in a typically ventilated room (10-400 square-meters) with one infected person. Close contact may pose higher infection risk than aerosol transmission, but suggest real-life circumstances (i.e. prolonged exposure, higher density) could heighten risk of aerosol transmission not accounted for in this analysis.
- Are transmission precautions in schools beneficial? Infectious Disease physicians from the US and UK reviewed data on transmission and detection of SARS-CoV-2 infection and found that children under 10 years old are less susceptible to contracting SARS-CoV-2, transmission of the virus is more robust in high schools compared to primary schools, and schools with transmission prevention measures in place have seen less viral spread compared to schools with no preventative measures, [supporting the implementation of transmission prevention measures in schools](#) (high schools in particular) to slow viral spread in the community.

R&D: Diagnosis & Treatments

- Polyester or foam nasal swabs: which is better? A comparative analysis investigated sensitivity of polyester and foam nasal swabs stored in viral transport media (VTM), saline, or dry tubes from 126 convalescent COVID-19 patients and found polyester and foam swabs had sensitivities of 87.3% versus 94.5% in VTM, 87.5% versus 93.8% in saline, and 75.0% versus 90.6% in dry tubes, respectively. [Polyester swabs had higher cycle threshold values and decreased performance compared to foam swabs](#) when viral loads were near detection threshold, but because estimated sensitivity above 87% was deemed sufficient for times of public health emergency, polyester swabs stored in VTM or saline may suffice in settings where swab shortages exist.

Mental Health & Resilience Needs

- How do science literacy and neurological mechanisms contribute to false beliefs? A Behavioral Neurologist from University of California, San Francisco describes that the neural mechanism behind false beliefs in COVID-19 conspiracy theories and science denial in healthy individuals is similar to those that have Lewy body dementia or Fronto-temporal dementia, concluding that [“developing frontal circuitry to support the process of reasoning is part of education and science literacy and stands at the core of a healthy democracy.”](#) Establishing this is the responsibility of the medical and scientific community through changes in the education system and working with political officials.

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EPIDEMIOLOGY

SYMPTOMS AND CLINICAL PRESENTATION

ADULTS

REINFECTION OF COVID-19 AFTER 3 MONTHS WITH A DISTINCT AND MORE AGGRESSIVE CLINICAL PRESENTATION: CASE REPORT

Torres DA, Ribeiro LDCB, Riello APFL, Horovitz DDG, Pinto LFR, Croda J.. J Med Virol. 2020 Oct 28. doi: 10.1002/jmv.26637. Online ahead of print.

Level of Evidence: 5 - Case Report

BLUF

This case report describes a previously healthy 36-year-old physician without comorbidities who contracted a mild case of COVID-19 in Rio de Janeiro, Brazil of March 2020 and was reinfected three months later with a stronger, more symptomatic COVID-19 course (including severe respiratory and gastrointestinal manifestations) (Figure 1-2). The authors suggest this could be a case of possible reinfection by a different strain and lack of prolonged immunity after initial infection, highlighting the importance of continued proper PPE and COVID-19 precautions even after someone has already been infected.

ABSTRACT

The sudden pandemic caused by SARS-CoV-2 exposed healthcare professionals worldwide to high viral loads, in an early epidemiological moment, often without the recommended personal protective equipment. We report the case of a Brazilian doctor who, after presenting a mild clinical episode of COVID-19 with molecular confirmation by RT-PCR in March 2020, appeared with a new acute infection by SARS-CoV-2 three months later. In middle of June, she had significant and very specific symptoms of COVID-19 with tomographic and serological confirmation of reinfection. There is a strong probability that these two episodes of infection were caused by different viral strains and that each genetic variation is related to specific clinical manifestations. We observed that, in addition to the different symptoms presented in the reinfections' episode, there was a more intense organic inflammatory response to the virus, with clinical repercussion. This clinical case should be an alert regarding the maintenance of individual protection among health cares, even in individuals who have already had COVID-19, since there is still no guarantee of prolonged immunity. This article is protected by copyright. All rights reserved.

FIGURES

Fig 1. Chronology of clinical and laboratory events in the reported case.

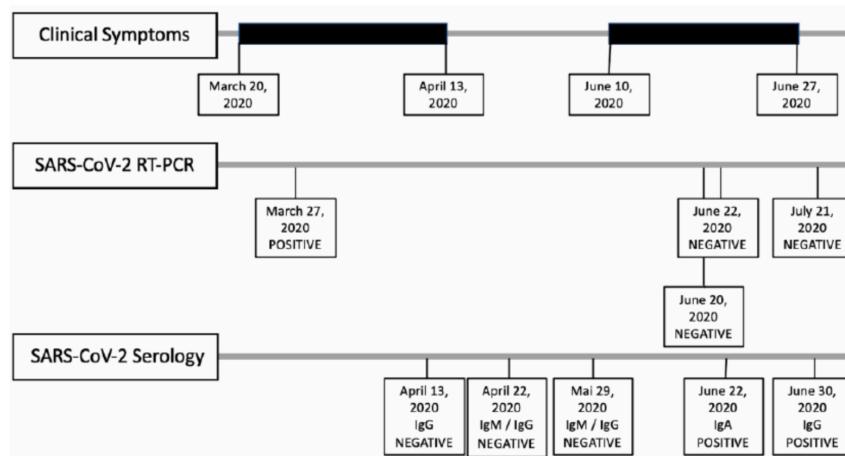
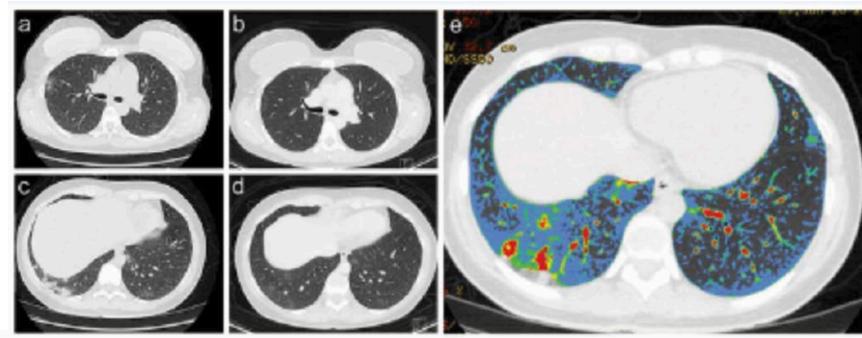


Fig 2. CT chest scans performed on the 11th day of symptoms (a, c and e) and 24th day of symptoms (b and d) of the second clinical episode. (a) and (c) Ground-glass opacities associated with bilateral and multilobar consolidation foci, predominantly peripheral, sometimes with a rounded aspect, some with areas of septal thickening, more evident in the lower right lobe. (b) and (d) Almost complete resolution of the alterations found in the previous exam, with discrete areas of attenuation in ground glass persisting. (e) Graphical demonstration with color map overlay. The areas in blue represent mild impairment, in green a little greater impairment, in yellow greater impairment and in red consolidations.



UNDERSTANDING THE PATHOLOGY

IN SILICO

STRUCTURE OF THE SARS-COV-2 NSP1/5'-UNTRANSLATED REGION COMPLEX AND IMPLICATIONS FOR POTENTIAL THERAPEUTIC TARGETS, A VACCINE, AND VIRULENCE

Vankadari N, Jeyasankar NN, Lopes WJ.. J Phys Chem Lett. 2020 Nov 2:9659-9668. doi: 10.1021/acs.jpclett.0c02818. Online ahead of print.

Level of Evidence: Other - Mechanism-based reasoning

BLUF

Physical chemists from Monash University in Australia conducted a computational study on the kinetic and structural characteristics of the SARS-CoV-2 leader protein Nsp1 and the stem-loop (SL1) region of 5'UTR of SARS-CoV-2 (Figure 1). The findings explore a potential mechanism behind Nsp1 protein altering the human's innate immune system to permit viral replication, and identifies potential drugs to impede the Nsp1/SL1 complex (Figures 4, 5). The authors call for more structural, functional, and molecular dynamics studies to further the development of vaccines and therapies against COVID-19.

ABSTRACT

SARS-CoV-2 is the cause of the ongoing Coronavirus disease 19 (COVID-19) pandemic around the world causing pneumonia and lower respiratory tract infections. In understanding the SARS-CoV-2 pathogenicity and mechanism of action, it is essential to depict the full repertoire of expressed viral proteins. The recent biological studies have highlighted the leader protein Nsp1 of SARS-CoV-2 importance in shutting down the host protein production. Besides, it still enigmatic how Nsp1 regulates for translation. Here we report the novel structure of Nsp1 from SARS-CoV-2 in complex with the SL1 region of 5'UTR of SARS-CoV-2, and its factual interaction is corroborated with enzyme kinetics and experimental binding affinity studies. The studies also address how leader protein Nsp1 of SARS-CoV-2 recognizes its self RNA toward translational regulation by further recruitment of the 40S ribosome. With the aid of molecular dynamics and simulations, we also demonstrated the real-time stability and functional dynamics of the Nsp1/SL1 complex. The studies also report the potential inhibitors and their mode of action to block viral protein/RNA complex formation. This enhance our understanding of the mechanism of the first viral protein Nsp1 synthesized in the human cell to regulate the translation of self and host. Understanding the structure and mechanism of SARS-CoV-2 Nsp1 and its interplay with the viral RNA and ribosome will open the arena for exploring the development of live attenuated vaccines and effective therapeutic targets for this disease.

FIGURES

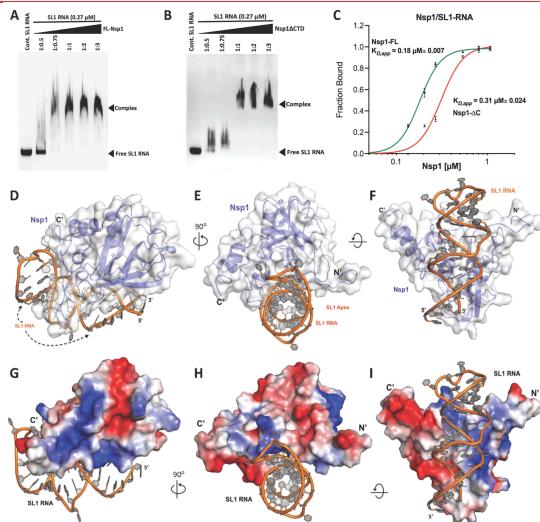


Figure 1. (A-C) EMSA measurement of Nsp1 affinity for SL1 of 5'UTR. Unlabeled SL1 RNA was tracked in native PAGE after incubation with increasing amounts of (A) Nsp1-FL or (B) Nsp1 Δ CTD to compare their binding affinities. The $K_{D,app}$ values were determined as the protein concentration to affect half of the maximal binding to the SL1 RNA. (C) The binding curves showing a higher binding affinity of $K_{D,app} = 0.18 \mu\text{M}$ was observed for Nsp1-FL, and a lower affinity of $K_{D,app} = 0.31 \mu\text{M}$ was observed for Nsp1 Δ C. The positions of free SL1 RNA and the respective Nsp1/SL1 complex are indicated. (D-F) Surface (white) and cartoon (blue) diagram showing the structure of the Nsp1/SL1 RNA complex from SARS-CoV-2. The bound RNA is shown in gray nucleotide base pairs with an orange phosphate backbone. The N- and C-terminal regions of Nsp1 and 5' and 3' of SL1 RNA are labeled accordingly. (G-I) Surface charge distribution of the Nsp1/SL1 RNA complex from SARS-CoV-2 (blue, negatively charged area; red, positively charged area). Front, orthogonal, and bottom views of the complex structure are shown for both the cartoon representation and the surface charge distribution.

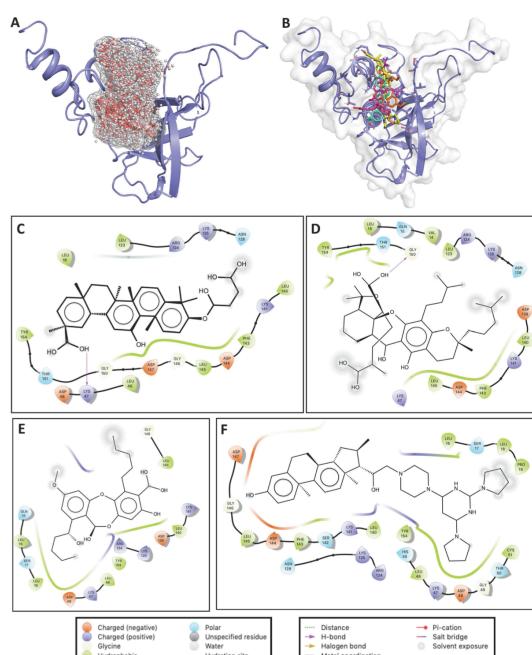


Figure 4. Potential drugs that could block Nsp1/SL1 complex formation. Detailed structural interaction view of potential drugs interacting with Nsp1, which potentially could block the viral RNA binding. (A) Overall clusters of individual Nsp1 inhibitors and the drug-binding pocket of Nsp1 are illustrated. (B) Virtual binding and positioning of four potential inhibitors of Nsp1. (C) Glycyrrhetic acid. (D) Garcinolic acid. (E) Lobaric acid. (F) Tirilazad. The binding affinities are -9.24, -9.53, -8.6, and -10.4 kcal/mol, respectively. The position and residue names are labeled accordingly, and the type of interaction between the individual drug and amino acids is marked as shown in the legend.

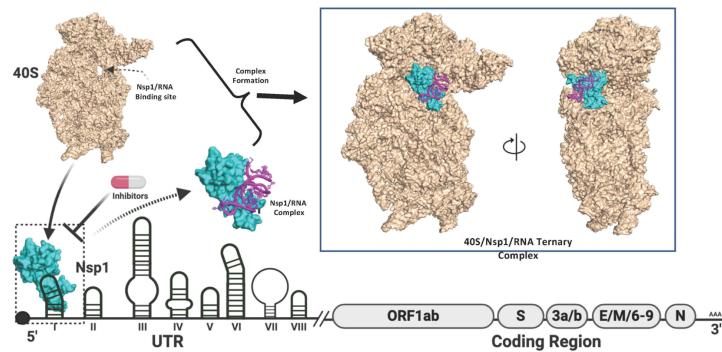


Figure 5. Schematic representation of the potential role of the Nsp1/SL1 complex. The Nsp1 of SARS-CoV-2 interacts with SL1 occurs at the start of the SARS-CoV-2 5' UTR/IRES, which is followed by neighboring SL2-S8 involved in the recruitment of various viral and host translational regulation proteins (eIF4G, 4A/B, etc.). The Nsp1 binds to SL1 at higher affinity and may recruit or augment the 40S ribosomal subunit through direct interaction in the presence or absence of bound viral RNA. The entire SARS-CoV-2 genome containing the 5' UTR region (stem-loops) and the coding region (codes for viral proteins) are depicted in the cartoon diagram. The recruitment process of 40S over Nsp1 or in the absence of RNA is shown with arrows.

Virtually modeled and docked ternary-complex structure of the 40S/Nsp1/SL1 is shown in the boxed area (front and orthogonal view, with Nsp1 shown in the cyan surface model and bound SL1 RNA shown in the pink helical cartoon), thus structurally demonstrating the dual role of Nsp1 in viral RNA translation regulation and effective blocking of the 40S host mRNA binding cleft independently and the recruitment of 40S over viral RNA via Nsp1 binding.

IN VITRO

NEUTRALIZING ANTIBODY RESPONSES IN COVID-19 CONVALESCENT SERA

Lee WT, Girardin RC, Dupuis Ii AP, Kulas KE, Payne AF, Wong SJ, Arinsburg S, Nguyen FT, Mendum DR, Firpo-Betancourt A, Jhang J, Wajnberg A, Krammer F, Cordon-Cardo C, Amher S, Montecalvo M, Hutton B, Taylor J, McDonough KA.. J Infect Dis. 2020 Oct 26:jiaa673. doi: 10.1093/infdis/jiaa673. Online ahead of print.

Level of Evidence: 4 - Local non-random sample

BLUF

Microbiologists, pathologists, and public health experts associated with Mount Sinai Hospital (MSH) analyzed 3277 blood specimens from recovered COVID-19 patients to test for antibody levels and percentage of neutralizing antibodies. They found that neutralizing antibody level is the highest 31-35 days post symptom onset, even though general SARS-CoV-2 antibody levels had been high (well above the 160 titer range cutoff) long before this. The authors suggest the importance of not only testing for antibodies to SARS-CoV-2, but also testing for neutralizing antibodies.

ABSTRACT

Passive transfer of antibodies from COVID-19 convalescent patients is being used as an experimental treatment for eligible patients with SARS-CoV-2 infections. The United States Food and Drug Administration's (FDA) guidelines for convalescent plasma initially recommended target antibody titers of 160. We evaluated SARS-CoV-2 neutralizing antibodies in sera from recovered COVID-19 patients using plaque reduction neutralization tests (PRNT) at moderate (PRNT50) and high (PRNT90) stringency thresholds. We found that neutralizing activity significantly increased with time post symptom onset (PSO), reaching a peak at 31-35 days PSO. At this point, the number of sera having neutralizing titers of at least 160 was ~93% (PRNT50) and ~54% (PRNT90). Sera with high SARS-CoV-2 antibody levels (>960 ELISA titers) showed maximal activity, but not all high titer sera contained neutralizing antibody at FDA recommended levels, particularly at high stringency. These results underscore the value of serum characterization for neutralization activity.

TRANSCRIPTOMIC ANALYSIS REVEALS NOVEL MECHANISMS OF SARS-COV-2 INFECTION IN HUMAN LUNG CELLS

Yang S, Wu S, Yu Z, Huang J, Zhong X, Liu X, Zhu H, Xiao L, Deng Q, Sun W.. Immun Inflamm Dis. 2020 Oct 30. doi: 10.1002/iid3.366. Online ahead of print.

Level of Evidence: Other - Mechanism-based reasoning

BLUF

Investigators primarily from The 6th Affiliated Hospital of Shenzhen University Health Science Center (China) explored the mechanism of infection and progression of disease caused by SARS-CoV-2 in lung cells through the use of transcriptome analysis of 4 human lung-derived cell lines (A549, NHBE, Calu3, and ACE2 over expressing A549) and 4 human lung biopsies (2 SARS-CoV-2 positive and 2 negative). Given this study's findings (illustrated below), this transcriptome information may be utilized to scan for drug therapeutics that limit inflammatory immune responses and aberrant metabolic pathways.

SUMMARY

Several findings from this study included:

- 1) 14 differentially expressed genes (DEGs) upon SARS-CoV-2 infection that were primarily interferon-stimulated genes (Figure 1)
- 2) upregulation of genes related to nucleotide, amino acid, and lipid metabolism that are unique to SARS-CoV-2 infection when compared to RSV, IAV, and HPIV3 infections (Figure 3)
- 3) increased ACE-2 expression (in ACE-2 overexpressing A549 cells) allowed for increased SARS-CoV-2 infection, but lack of ACE-2 expression (in A549 cells) did not prevent infection (Figure 4).

ABSTRACT

BACKGROUND: Severe acute respiratory syndrome coronavirus clade 2 (SARS-CoV-2) is a single-stranded RNA virus responsible for the global pandemic of the coronavirus disease-2019 (COVID-19). To date, there are still no effective approaches for the prevention and treatment of COVID-19. **OBJECTIVE:** The present study aims to explore the possible mechanisms of SARS-CoV-2 infection in human lung cells. **METHODS:** Data interpretation was conducted by recruiting bioinformatics analysis, including Gene Ontology and Kyoto Encyclopedia of Genes and Genomes pathways analysis using downloaded data from the NCBI Gene Expression Omnibus database. **RESULTS:** The present study demonstrated that SARS-CoV-2 infection induces the upregulation of 14 interferon-stimulated genes, indicative of immune, and interferon responses to the virus. Notably, genes for pyrimidine metabolism and steroid hormone biosynthesis are selectively enriched in human lung cells after SARS-CoV-2 infection, suggesting that altered pyrimidine metabolism and steroid biosynthesis are remarkable, and perhaps druggable features after SARS-CoV-2 infection. Besides, there is a strong positive correlation between viral ORF1ab, ORF6, and angiotensin-converting enzyme 2 (ACE2) expression in human lung cells, implying that ACE2 facilitates SARS-CoV-2 infection and replication in host cells probably through the induction of ORF1ab and ORF6.

FIGURES

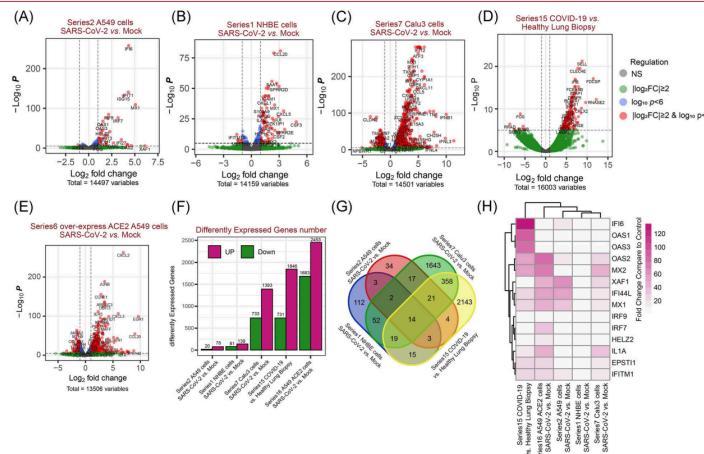


Figure 1 Many differentially expressed genes in a variety of types of human lung cells. (A-E) Volcano plot for the cells with mRNA expression differences in each paired group. Log2 (fold change) is plotted as the abscissa, and log10 (p value) is plotted as the ordinate. Differentially expressed genes (DEGs) are indicated in red. (F) The total up- or downregulated DEGs in each paired group. (G) A Venn diagram presents the number of unique or shared DEGs in each paired group. (H) A fold-change heatmap of the shared 14 genes from each human lung cells with SARS-CoV-2 infection. mRNA, messenger RNA; SARS-CoV-2, severe acute respiratory syndrome coronavirus clade 2

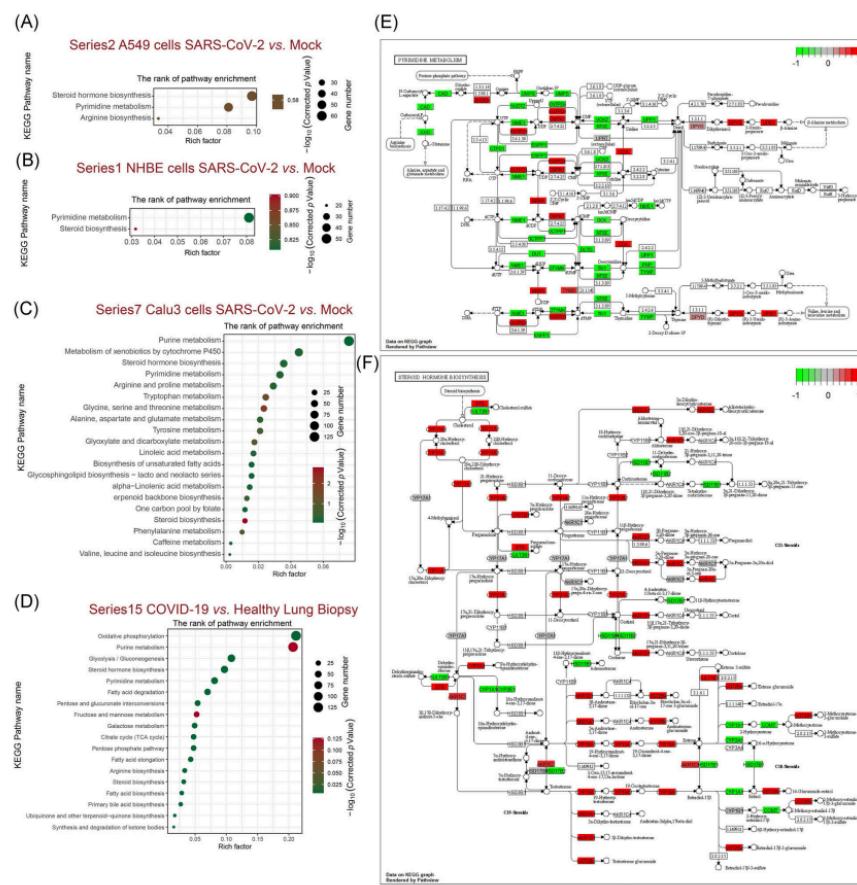


Figure 3 Kyoto Encyclopedia of Genes and Genomes (KEGG) classifications of DEGs in varies types of human lung cells. The comparison of pathway enrichment in A549 cells (A), NHBE cells (B), Calu3 cells (C), and COVID-19 lung biopsy (D) after SARS-CoV-2 infection. It showed the top 20 significantly enriched KEGG pathways. The rich factor as the abscissa and KEGG terms is plotted as the ordinate. The functional analysis of the DEGs enriched in the pathways of pyrimidine metabolism (E) and steroid hormone biosynthesis (F) were shown. DEG, differentially expressed gene; NHBE, normal human bronchial epithelial; SARS-CoV-2, severe acute respiratory syndrome coronavirus clade 2

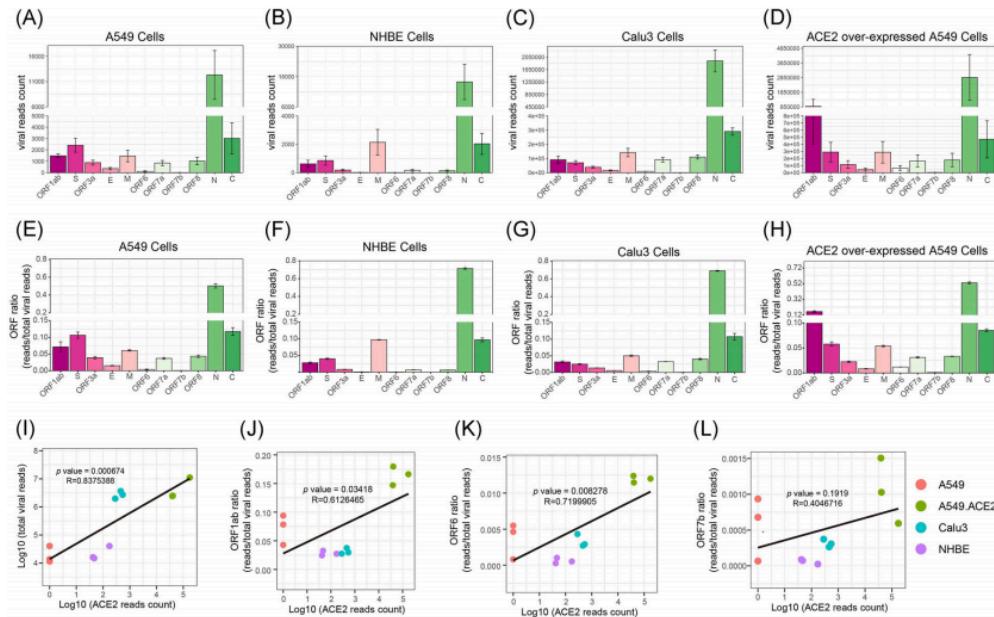


Figure 4 Quantitation of viral gene expression of SARS-CoV-2 in varies types of human lung cells after infection. The read-count of each open read frame (ORF) in A549 cells (A), NHBE cells (B), Calu3 cells (C), and ACE2 over-expressing A549 cells (D) after SARS-CoV-2 infection. The read-count ratio of each ORF in A549 cells (E), NHBE cells (F), Calu3 cells (G), and ACE2 over-expressing A549 cells (H) after SARS-CoV-2 infection. (I) The regression analysis of total viral read-count and the expression of ACE2. The regression analysis of ORF1ab (J), ORF6 (K), and ORF7b (L) read-count ratio and the expression of ACE2. Pearson's product-moment correlation. ACE2, angiotensin-converting enzyme 2; NHBE, normal human bronchial epithelial; SARS-CoV-2, severe acute respiratory syndrome coronavirus clade 2

TRANSMISSION & PREVENTION

INFORMED CONSENT DISCLOSURE TO VACCINE TRIAL SUBJECTS OF RISK OF COVID-19 VACCINES WORSENING CLINICAL DISEASE

Cardozo T, Veazey R.. Int J Clin Pract. 2020 Oct 28:e13795. doi: 10.1111/ijcp.13795. Online ahead of print.

Level of Evidence: Other - Review / Literature Review

BLUF

Investigators from Tulane University and New York University Lang Health review current published literature on COVID-19 vaccines in order to determine if there is enough evidence for clinicians to adequately inform patients on possible vaccine risks. Their review relates harmful side effects of failed vaccines against MERS and SARS, which are structurally similar to SARS-CoV-2, suggesting that these adverse reactions could occur in COVID-19 vaccine trials. One of these side effects is antibody-dependent enhancement (ADE), which is an adverse immune response to a minimally modified viral material. The authors suggest a risk of ADE occurring in vaccine recipients with COVID-19 and worsening the disease course, emphasizing a need for complete and specific disclosure to vaccine trial participants and future vaccine recipients on this possible side effect.

ABSTRACT

AIMS OF THE STUDY: Patient comprehension is a critical part of meeting medical ethics standards of informed consent in study designs. The aim of the study was to determine if sufficient literature exists to require clinicians to disclose the specific risk that COVID-19 vaccines could worsen disease upon exposure to challenge or circulating virus. **METHODS USED TO CONDUCT THE STUDY:** Published literature was reviewed to identify preclinical and clinical evidence that COVID-19 vaccines could worsen disease upon exposure to challenge or circulating virus. Clinical trial protocols for COVID-19 vaccines were reviewed to determine if risks were properly disclosed. **RESULTS OF THE STUDY:** COVID-19 vaccines designed to elicit neutralizing antibodies may sensitize vaccine recipients to more severe disease than if they were not vaccinated. Vaccines for SARS, MERS and RSV have never been approved, and the data generated in the development and testing of these vaccines suggest a serious mechanistic concern: that vaccines designed empirically using the traditional approach (consisting of the unmodified or minimally modified coronavirus viral spike to elicit neutralizing antibodies), be they composed of protein, viral vector, DNA or RNA and irrespective of delivery method, may worsen COVID-19 disease via antibody-dependent enhancement (ADE). This risk is sufficiently obscured in clinical trial protocols and consent forms for ongoing COVID-19 vaccine trials that adequate patient comprehension of this risk is unlikely to occur, obviating truly informed consent by subjects in these trials. **CONCLUSIONS DRAWN FROM THE STUDY AND CLINICAL IMPLICATIONS:** The specific and significant COVID-19 risk of ADE should have been and should be prominently and independently disclosed to research subjects currently in vaccine trials, as well as those being recruited for the trials and future patients after vaccine approval, in order to meet the medical ethics standard of patient comprehension for informed consent.

DEVELOPMENTS IN TRANSMISSION & PREVENTION

DOSE-RESPONSE RELATION DEDUCED FOR CORONAVIRUSES FROM COVID-19, SARS AND MERS META-ANALYSIS RESULTS AND ITS APPLICATION FOR INFECTION RISK ASSESSMENT OF AEROSOL TRANSMISSION

Zhang X, Wang J.. Clin Infect Dis. 2020 Oct 29:ciaa1675. doi: 10.1093/cid/ciaa1675. Online ahead of print.

Level of Evidence: Other - Mechanism-based reasoning

BLUF

Swiss environmental engineers applied a Quantitative Microbial Risk Assessment (QMRA) to evaluate SARS-CoV-2 infection risk via aerosol transmission and close indoor contact (Figure 1) using dose-response mice models and infection risk data from meta-analyses. Authors observed lower infection transmission risk via aerosol exposure within one hour (10^{-6} to 10^{-4}) compared to close contact (10^{-1} ; 12.8% risk within 1m) in a typically ventilated room (10-400 square-meters) with one infected person (Figures 2,3). Authors state close contact may pose higher infection risk than aerosol transmission, but suggest real-life circumstances (i.e. prolonged exposure, higher density) could heighten risk of aerosol transmission not accounted for in this analysis.

ABSTRACT

BACKGROUND: A comprehensive understanding of the transmission routes of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is of great importance for the effective control of the spread of Corona Virus Disease 2019 (COVID-19). However, the fundamental dose-response relation is still missing for better evaluating and controlling the infection risk. **METHODS:** We developed a simple framework to integrate the a priori dose-response relation for SARS-CoV based on mice experiments, the recent data on infection risk from a meta-analysis and the respiratory virus shedding in exhaled breath, to shed light on the dose-response relation for human. The aerosol transmission infection risk was evaluated based on the dose-response model for typical indoor environment. **RESULTS:** The developed dose-response relation is an exponential function with a constant k in the range of about 6.4×10^{-4} to 9.8×10^{-5} virus copies, which means that the infection risk caused by one virus copy in viral shedding is on the order of 10^{-6} to 10^{-5} . The median infection risk via aerosol transmission with one-hour exposure (10^{-6} to 10^{-4}) was significantly lower than the risk caused by close contact (10^{-1}) in a room of the area from 10 to 400 m² with one infected individual in it and with typical ventilation rate 1 ACH (Air Changes per Hour). **CONCLUSIONS:** The infection risk caused by aerosol transmission was significantly lower than the risk caused by close contact. It is still necessary to be cautious for the potential aerosol transmission risk in small rooms with prolonged exposure duration.

FIGURES

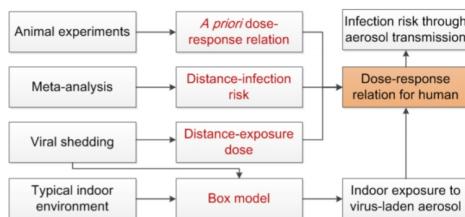


Figure 1: "Schematic diagram for deducing the dose-response relation and Quantitative Microbial Risk Assessment (QMRA) for typical indoor environment".

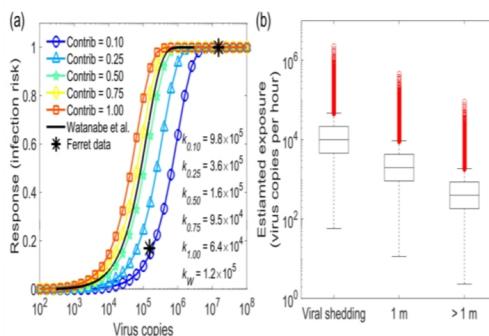


Figure 2: "Results under the assumption of log-normal distribution of viral shedding $\log_{10}(\text{Evirus}) \sim \text{Normal}(4, 0.5)$, with 40% positive viral shedding. (a) The estimated dose-response relations based on the different contribution levels (0.1, 0.25, 0.5, 0.75 and 1) of the airborne virus-laden particles to the total dose from both exposure to airborne viruses and contact transmission. The solid line is the dose-response relation for SARS-CoV based on mice experiments 3. The stars are the dose-dependent response to infection with SARS-CoV-2 from the ferret model 19. A conversion factor of 300 from plaque-forming units (PFU) to virus copies was utilized based on the previous study on SARS-CoV 18. (b) viral shedding and exposure dose for 1 hour duration, zero values are not shown in the figure".

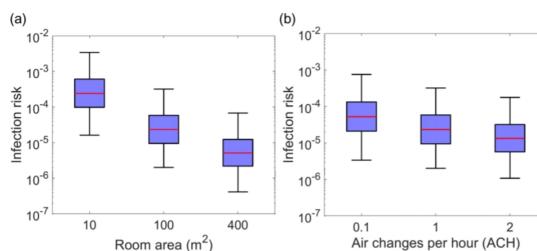


Figure 3: "Influences of the room size and ventilation on the infection risk via aerosol transmission. (a) Infection risk via aerosol transmission in rooms of various sizes with ventilation rates of 1 ACH and one infected individual for one hour exposure; (b) Infection risk via aerosol transmission in a 100 m² room with different ventilation rates for one hour exposure".

PREVENTION IN THE COMMUNITY

ON THE EFFECT OF AGE ON THE TRANSMISSION OF SARS-COV-2 IN HOUSEHOLDS, SCHOOLS AND THE COMMUNITY

Goldstein E, Lipsitch M, Cevik M.. J Infect Dis. 2020 Oct 29:jiaa691. doi: 10.1093/infdis/jiaa691. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

Infectious Disease physicians from the US and UK reviewed data on transmission and detection of SARS-CoV-2 infection and found the following:

- 1) Children under 10 years old are less susceptible to contracting SARS-CoV-2.
- 2) Transmission of the virus is more robust in high schools compared to primary schools.
- 3) Schools with transmission prevention measures in place have seen less viral spread compared to schools with no preventative measures.

The authors support the implementation of transmission prevention measures in schools (high schools in particular) to slow viral spread in the community.

ABSTRACT

BACKGROUND: There is limited information on the effect of age on the transmission of SARS-CoV-2 infection in different settings. **METHODS:** We reviewed published studies/data on detection of SARS-CoV-2 infection in contacts of COVID-19 cases, serological studies, and studies of infections in schools. **RESULTS:** Compared to younger/middle aged adults, susceptibility to infection for children aged under 10y is estimated to be significantly lower, while estimated susceptibility to infection in adults aged over 60y is higher. Serological studies suggest that younger adults (particularly those aged under 35y) often have high cumulative incidence of SARS-CoV-2 infection in the community. There is some evidence that given limited control measures, SARS-CoV-2 may spread robustly in secondary/high schools, and to a lesser degree in primary schools, with class size possibly affecting that spread. There is also evidence of more limited spread in schools when some mitigation measures are implemented. Several potential biases that may affect these studies are discussed. **CONCLUSIONS:** Mitigation measures should be implemented when opening schools, particularly secondary/high schools. Efforts should be undertaken to diminish mixing in younger adults, particularly individuals aged 18-35y to mitigate the spread of the epidemic in the community.

MANAGEMENT

ACUTE CARE

IS NEWLY DIAGNOSED DIABETES A STRONGER RISK FACTOR THAN PRE-EXISTING DIABETES FOR COVID-19 SEVERITY?

Sathish T, de Mello GT, Cao Y.. J Diabetes. 2020 Oct 27. doi: 10.1111/1753-0407.13125. Online ahead of print.

Level of Evidence: Other - Expert Opinion

BLUF

In a letter to the editor published in October of 2020, a team of epidemiologists from Canada, Brazil, and Australia discuss emerging data suggesting risk for poor prognosis in COVID-19 patients may be greater in patients with newly-diagnosed diabetes than those with pre-existing diabetes. Authors advocate for diabetes screening in all COVID-19 patients to better identify those who should be monitored closely for complications.

NEONATAL/PEDIATRIC INTENSIVE CARE

BILATERAL PULMONARY EMBOLI IN A TEENAGER WITH POSITIVE SARS-COV-2 ANTIBODY

Kotula JJ, Balakumar N, Khan D, Patel B.. Pediatr Pulmonol. 2020 Oct 23. doi: 10.1002/ppul.25132. Online ahead of print.

Level of Evidence: Other - Case Report

BLUF

Pediatricians from Nicklaus Children's Hospital in Miami, Florida discussed the case of a 15 year old female with positive SARS-CoV-2 IgM admitted for appendectomy who, on post-operative day three, developed bilateral pulmonary emboli leading to cardiac arrest and neurological devastation. Her neurologic status did not improve after successful catheter directed thrombolysis and she was ultimately discharged to inpatient rehabilitation. Authors argue this case highlights the thrombotic risk of SARS-CoV-2 infection, suggesting catheter directed thrombolysis can be safely considered to treat pulmonary emboli in pediatric patients with SARS-CoV-2.

ABSTRACT

Thromboembolic phenomena, particularly pulmonary emboli, have been described in adult patients with SARS-CoV-2 infection, but have been less evident in children. We describe a case of a teenager with bilateral pulmonary emboli leading to cardiovascular collapse in the setting of a positive SARS-CoV-2 IgM antibody. This article is protected by copyright. All rights reserved.

SURGICAL SUBSPECIALTIES

GENERAL SURGERY

MODELING THE IMPACT OF DELAYING BARIATRIC SURGERY DUE TO COVID-19: A DECISION ANALYSIS

Shipe ME, Beeghly-Fadiel A, Deppen SA, English W, Grogan EL.. Obes Surg. 2020 Oct 26. doi: 10.1007/s11695-020-05054-6. Online ahead of print.

Level of Evidence: Other - Modeling

BLUF

Surgeons from Vanderbilt University developed a decision analysis model for determining whether or not to postpone bariatric surgery amidst fluctuating SARS-CoV-2 infection rates (Table 1, Figure 1). Based on a 45-year-old female with diabetes and BMI of 45, the model showed no difference in 20-year overall survival rate with immediate versus delayed surgery; however, with infection rate >4%, delaying 6 months improved long-term survival. Authors suggest local transmission rates should inform surgeons' decisions to resume bariatric surgery.

ABSTRACT

We developed a decision analysis model to evaluate risks and benefits of delaying scheduled bariatric surgery during the novel coronavirus disease (COVID-19) pandemic. Our base case was a 45-year-old female with diabetes and a body mass index of 45 kg/m². We compared immediate with delayed surgery after 6 months to allow for COVID-19 prevalence to decrease. We found that immediate and delayed bariatric surgeries after 6 months resulted in similar 20-year overall survival. When the probability of COVID-19 infection exceeded 4%, then delayed surgery improved survival. If future COVID-19 infection rates were at least half those in the immediate scenario, then immediate surgery was favored and local infection rates had to exceed 9% before surgical delay improved survival. Surgeons should consider local disease prevalence and patient comorbidities associated with increased mortality before resuming bariatric surgery programs.

FIGURES

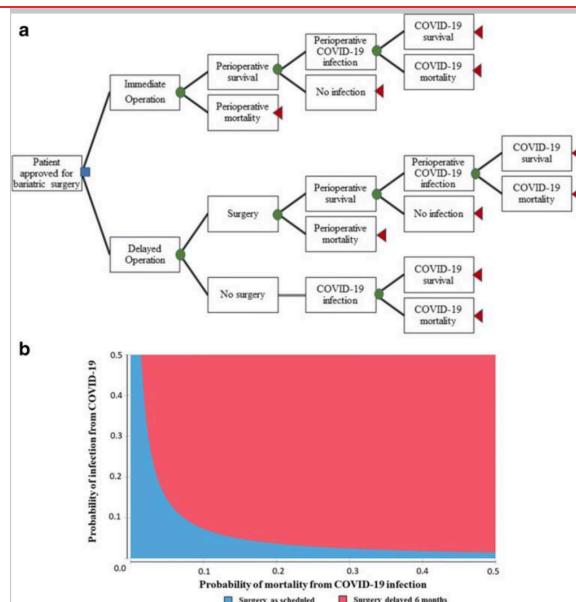


Fig. 1: a. Decision analysis tree for resuming bariatric surgery during COVID-19 pandemic. Blue square: decision node, whether to choose immediate or delayed surgery. Green circles: chance nodes. Red triangles: terminal nodes. b. Two-way sensitivity analysis for probability of infection and mortality from COVID-19. Graph displays the favored strategy (immediate or delayed surgery) across a range of possible hospital-acquired COVID-19 infection and COVID-19-related mortality probabilities while holding all other model variables constant at baseline values

	Probability	Values for sensitivity analysis	Reference(s)
Operative mortality	0.0058	0.00001–0.011	[1, 7]
COVID-19 mortality	0.25	0.1–0.5	[3–5]
Immediate surgery			
Perioperative COVID-19	0.014	0–0.05	*
Delayed surgery			
Undergoes surgery	0.99	-	-
No surgery	0.01	0.00001–0.05	[1, 8]
Perioperative COVID-19	0.00001	0.001–0.009	*
20-year overall survival			
Immediate surgery	0.847	0.8–0.95	[2]
Delayed surgery	0.842	0.78–0.93	[2]
No surgery	0.725	0.65–0.85	[2]

COVID-19 novel coronavirus disease discovered in 2019

*Parameters set by research team based on local data

Table 1. Model parameters

ADJUSTING PRACTICE DURING COVID-19

FOR HEALTHCARE PROFESSIONALS

IMPACT OF WEARING A SURGICAL MASK ON RESPIRATORY FUNCTION IN VIEW OF A WIDESPREAD USE DURING COVID-19 OUTBREAK. A CASE-SERIES STUDY

Ciocan C, Clari M, Fabbro D, De Piano ML, Garzaro G, Godono A, Gullino A, Romano C.. Med Lav. 2020 Oct 31;111(5):354-364. doi: 10.23749/mdl.v111i5.9766.

Level of Evidence: 4 - Case-series

BLUF

This case series from the University of Torino, Italy examines how surgical mask use affects respiratory function in 10 healthcare workers, including 3 smokers and 3 asthmatics. Using respiratory function testing throughout a 4-hour period of continuous mask use and arterial blood gas sampling, authors found no significant respiratory impairment in healthy patients, smokers, or those with asthma (Figure 2). While acknowledging the study's small sample size, authors endorse the safety of mask usage for healthcare workers based on these findings but note further research is needed for evaluation of those with respiratory and cardiac conditions.

ABSTRACT

BACKGROUND: Because of the COVID-19 outbreak, the widespread use of Respiratory Protective Devices (RPD) is recommended to prevent the spread of infection. This recommendation involves not only healthcare workers but other category of workers and the general population as well, in public places, especially where social distancing is difficult to maintain. The use of facemasks should not cause physical impairment to individuals, especially for people suffering from lung and heart diseases. **OBJECTIVES:** To evaluate the impact of RPDs on the respiratory function in healthy and asthmatic subjects, in order to identify the fitness for use mainly, but not only for, occupational purposes during COVID-19 outbreak. **METHODS:** Ten individuals were included, three of which affected by asthma and three current smokers. A Respiratory Functional Test (RFT) was performed at three times: at the beginning of the work shift 1) without wearing and 2) wearing surgical masks, and 3) after 4 hours of usual working activities wearing the masks. Arterial Blood Gas (ABG) samples were also tested before the first test and the third test. **RESULTS:** Observed RFTs and ABG parameters did not suffer significant variations, but for Maximal Voluntary Ventilation ($P=0.002$). Data on asthmatic subjects and smokers were comparable to healthy subjects. **DISCUSSION:** Our results suggest that wearing a surgical mask does not produce significant respiratory impairment in healthy subjects nor in subjects with asthma. Four hours of continuing mask-wearing do not cause a reduction in breathing parameters. Fitness for use in subjects with more severe conditions has to be evaluated individually. Our adapted technique for RFTs could be adopted for the individual RPDs fitness evaluation.

FIGURES

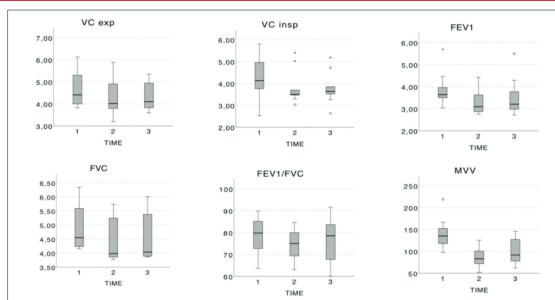


Figure 2 - Respiratory Function Test values at basal (1), mask-basal (2), and mask-active (3) times. Circles and asterisks represent outlier values

SURGICAL SUBSPECIALTIES

THORACIC SURGERY

TRIAGE AND MANAGEMENT OF AORTIC EMERGENCIES DURING THE CORONAVIRUS DISEASE 2019 (COVID-19) PANDEMIC: A CONSENSUS DOCUMENT SUPPORTED BY THE AMERICAN ASSOCIATION FOR THORACIC SURGERY (AATS) AND ASIAN SOCIETY FOR CARDIOVASCULAR AND THORACIC SURGERY (ASCVTS)

Mehta CK, Malaisrie SC, Budd AN, Okita Y, Matsuda H, Fleischman F, Ueda Y, Bavaria JE, Moon MR.. Asian Cardiovasc Thorac Ann. 2020 Oct 30;218492320974505. doi: 10.1177/0218492320974505. Online ahead of print.

Level of Evidence: Other - Guidelines and Recommendations

BLUF

Surgeons associated with the American Association for Thoracic Surgery and the Asian Society for Cardiovascular and Thoracic Surgery provide interim evidence-based recommendations for triage and management of aortic emergencies during the COVID-19 pandemic (Table 1, Figures 1 and 3). These guidelines may facilitate efforts in redirecting resources (i.e., personnel, equipment, and operating room) during aortic emergencies while minimizing the risk of nosocomial transmission of COVID-19.

FIGURES

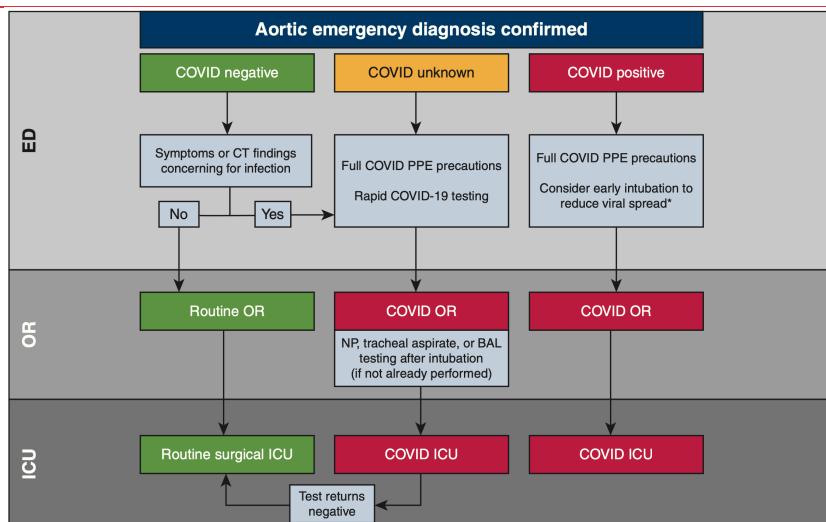


Figure 1. Algorithm for triaging patients from the emergency room based on COVID testing status.

*Patients requiring high flow oxygen, non-invasive ventilation, or other oxygen source with high potential for aerosol-generation should be considered for early intubation in the ER in order to reduce viral spread during transport. ED, Emergency department; COVID-19, coronavirus disease 2019; CT, computed tomography; PPE, personal protective equipment; OR, operating room; NP, nasopharyngeal; BAL, bronchoalveolar lavage; ICU, intensive care unit.

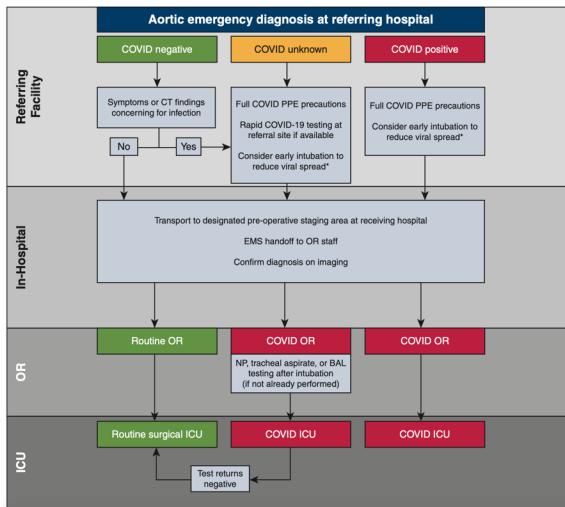


Figure 3. Algorithm for triaging patients from an external hospital.

*Patients requiring high-flow oxygen, noninvasive ventilation, or other oxygen source with high potential for aerosol-generation should be considered for early intubation before transport to reduce viral spread during transport. COVID-19, Coronavirus disease 2019; CT, computed tomography; PPE, personal protective equipment; EMS, emergency medical services; OR, operating room; NP, nasopharyngeal; BAL, bronchoalveolar lavage; ICU, intensive care unit.

Preoperative considerations
Preoperative evaluation should be performed before transport to OR
A preoperative surgical staging area should be identified (for direct-to-OR protocols)
Appropriate PPE measures should be strictly followed for all personnel
Surgical procedures should ideally be performed in COVID-19–designated ORs that have the capability of providing negative pressure airflow
The minimum number of personnel required should be directly involved in patient care
Anesthetic considerations
All precautions should be taken to minimize exposure to aerosol- generating procedures
Recommendations for endotracheal intubation include rapid sequence intubation, an experienced provider performing the procedure, and elective use of a video laryngoscope
If testing for COVID-19 was not yet achieved, a sample should be collected once in the operating room
Ventilation of patients should follow ARDS protocols
Care should be taken during TEE examination, including appropriate PPE
Procedural considerations
Prepping and draping in usual sterile fashion with emphasis on an appropriate drape barrier between anesthesia and surgical teams
Expedited repairs should be favored over complex repairs
Consider blood-conservation management strategies
Chest tubes should be checked for air leaks and secure connections
Postoperative care
Ideal postoperative care in a COVID-19–designated ICU
Extubation criteria should be carefully considered to mitigate risk of reintubation

Table 1. Suggested approach for the management of aortic emergencies during the COVID-19 pandemic.

OR, Operating room; COVID-19, coronavirus 2019; ARDS, acute respiratory distress syndrome; TEE, transesophageal echocardiogram; PPE, personal protective equipment; ICU, intensive care unit.

R&D: DIAGNOSIS & TREATMENTS

CURRENT DIAGNOSTICS

A COMPARISON OF HEALTH CARE WORKER-COLLECTED FOAM AND POLYESTER NASAL SWABS IN CONVALESCENT COVID-19 PATIENTS

Hart B, Tu YP, Jennings R, Verma P, Padgett LR, Rains D, Vojta D, Berke EM.. PLoS One. 2020 Oct 27;15(10):e0241100. doi: 10.1371/journal.pone.0241100. eCollection 2020.

Level of Evidence: 2 - Individual cross sectional studies with consistently applied reference standard and blinding

BLUF

A comparative analysis by several US research institutions investigated sensitivity of polyester and foam nasal swabs stored in viral transport media (VTM), saline, or dry tubes from convalescent COVID-19 patients ($n=126$). They found polyester and foam swabs had sensitivities of 87.3% versus 94.5% in VTM, 87.5% versus 93.8% in saline, and 75.0% versus 90.6% in dry tubes, respectively (Figures 1,2,3). Authors determined polyester swabs had higher cycle threshold values and decreased performance compared to foam swabs when viral loads were near detection threshold, but estimated sensitivity above 87% was deemed sufficient for times of public health emergency, so although foam swabs may be superior, polyester swabs stored in VTM or saline may suffice in settings where swab shortages exist.

ABSTRACT

Both polyester and foam nasal swabs were collected from convalescent COVID-19 patients at a single visit and stored in viral transport media (VTM), saline or dry. Sensitivity of each swab material and media combination were estimated, three by three tables were constructed to measure polyester and foam concordance, and cycle threshold (C_t) values were compared. 126 visits had polyester and foam swabs stored in viral transport media (VTM), 51 had swabs stored in saline, and 63 had a foam swab in VTM and a polyester swab stored in a dry tube. Polyester and foam swabs had an estimated sensitivity of 87.3% and 94.5% respectively in VTM, 87.5% and 93.8% respectively in saline, and 75.0% and 90.6% respectively for dry polyester and foam VTM. Polyester and foam C_t values were correlated, but polyester showed decreased performance for cases with a viral load near the detection threshold and higher C_t values on average.

FIGURES

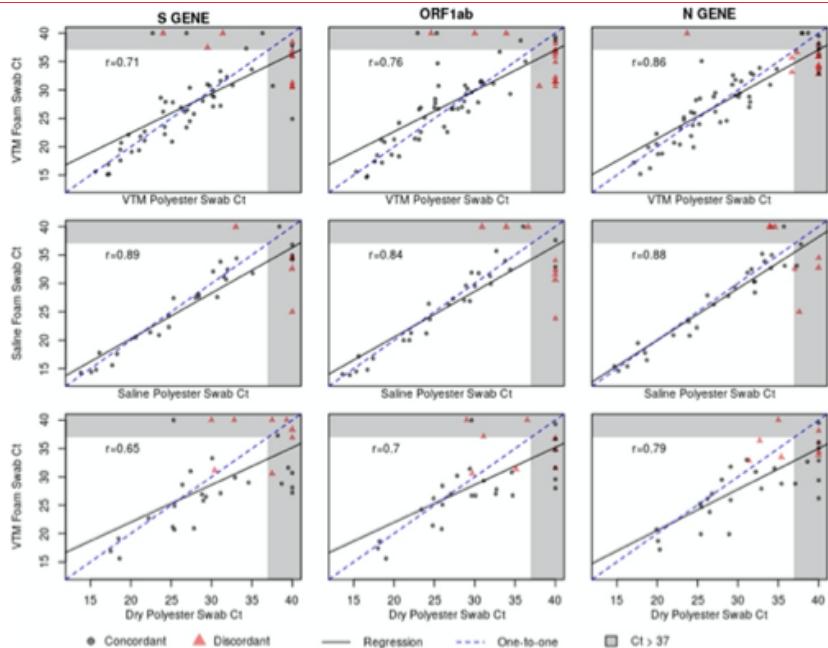


Fig 1. Ct correlation plots. Plots showing the cycle threshold (Ct) values for each of the three RNA targets and three transport media. The black line represents the best fitting linear regression, the dashed blue line represents a perfect one-to-one relationship.

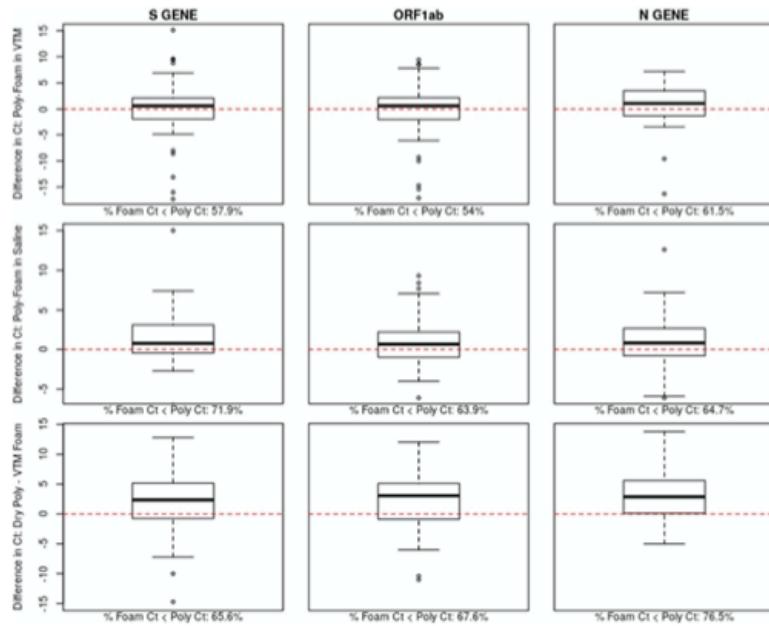


Fig 2. Ct difference boxplots. Plots showing the difference in cycle threshold (Ct) of the polyester and foam swabs collected at the same visits. Positive values represent higher Ct values in the polyester swab. The dashed red line represents equivalent Ct values. The percentage of samples for which the foam swab has a lower Ct value is shown below each sub-plot.

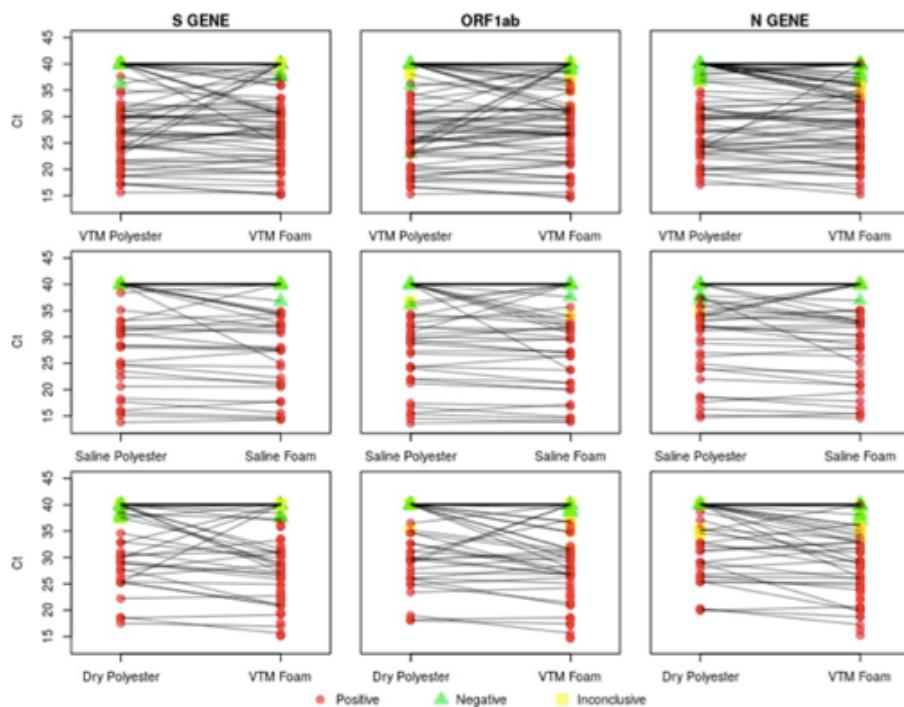


Fig 3. Paired Ct plots. Paired Ct plots showing the polyester and foam Ct values for each transport media and target gene combination considered. Swabs collected at the same visit are connected by a black line.

EVALUATION OF SARS-COV-2 IgG ANTIBODY RESPONSE IN PCR POSITIVE PATIENTS: COMPARISON OF NINE TESTS IN RELATION TO CLINICAL DATA

Naaber P, Hunt K, Pesukova J, Haljasmägi L, Rumm P, Peterson P, Hololejenko J, Eero I, Jõgi P, Toompere K, Sepp E.. PLoS One. 2020 Oct 27;15(10):e0237548. doi: 10.1371/journal.pone.0237548. eCollection 2020.

Level of Evidence: 4 - Case-series, case-control, or historically controlled studies

BLUF

Researchers from the University of Tartu and SYNLAB in Estonia compared the sensitivity and specificity of nine SARS-CoV-2 IgG/total antibody tests (listed below) from serum samples of 97 COVID-19 patients and 100 controls April 28 to May 7, 2020 in Kuressaare Hospital. They found that the overall agreement between tests was 71-95% and the specificity was within 98-100% (Table 2, 3, 4). The range of these results suggest that some antibody tests are more sensitive than others and symptoms, time of the test, and use of more than one antigen in testing should be considered for obtaining the most accurate results.

SUMMARY

The SARS-CoV-2 antibody (Ab) tests evaluated in this study include:

- 5 laboratory tests for IgG (SNIBE, Euroimmun, Abbott, Epitope, DiaSorin)
- 1 laboratory total Ab (Roche) test
- 1 rapid IgG test (SD Biosensor)
- 2 in-house IgG tests (LIPS N and LIPS S-RDB) were compared.

ABSTRACT

SARS-CoV-2 antibody tests are available in various formats, detecting different viral target proteins and antibody subclasses. The specificity and sensitivity of SARS-CoV-2 antibody tests are known to vary and very few studies have addressed the performance of these tests in COVID-19 patient groups at different time points. We here compared the sensitivity and specificity of seven commercial (SNIBE, Epitope, Euroimmun, Roche, Abbott, DiaSorin, Biosensor) and two in-house LIPS assays (LIPS N and LIPS S-RBD) IgG/total Ab tests in serum samples from 97 COVID-19 patients and 100 controls, and correlated the results with the patients' clinical data and the time-point the test was performed. We found a remarkable variation in the sensitivity of antibody tests with the following performance: LIPS N (91.8%), Epitope (85.6%), Abbott and in-house LIPS S-RBD (both 84.5%), Roche (83.5%), Euroimmun (82.5%), DiaSorin (81.4%), SNIBE (70.1%), and Biosensor (64.9%). The overall agreement between the tests was between 71-95%, whereas the specificity of all tests was within 98-100%. The correlation with patients' clinical symptoms score ranged from strongest in LIPS N ($\rho = 0.41$; $p < 0.001$) to nonsignificant in LIPS S-RBD. Furthermore, the time of testing since symptom onset had an impact on the sensitivity of some tests. Our study highlights the importance to consider clinical symptoms, time of testing, and using more than one viral antigen in SARS-CoV-2 antibody testing. Our results suggest that some antibody tests are more sensitive for the detection of antibodies in early stage and asymptomatic patients, which may explain the contradictory results of previous studies and should be taken into consideration in clinical practice and epidemiological studies.

FIGURES

Tests	Agreement between qualitative results, %							
	Correlation between quantitative values, p ($p < 0.001$ in all significant cases)							
SNIBE	Epitope	85	77	85	86	80	84	76
		0.91	0.64	0.68	0.84	0.70	0.6	0.56
Epitope		82	90	93	84	91	86	77
		0.56	0.59	0.80	0.65	0.53	0.46	NA ^a
Euroimmun			87	81	95	88	85	74
			0.66	0.65	0.95	0.73	0.50	NA ^a
Roche				89	88	91	88	79
				0.78	0.71	0.67	0.51	NA ^a
Abbott					82	90	87	78
					0.71	0.59	0.51	NA ^a
DiaSorin						87	84	77
						0.78	0.53	NA ^a
LIPS S-RBD							80	76
							NS ^b	NA ^a
LIPS N								71
								NA ^a

^a NA—not applicable. Only qualitative interpretation (absence or presence of test line).

^b NS—no significant correlation ($p > 0.05$).

<https://doi.org/10.1371/journal.pone.0237548.t003>

Table 3. Agreement between qualitative results (positive or negative) and correlation between quantitative values of different tests in COVID-19 patients' samples ($n = 97$).

Tests	Quantitative test value median (25%; 75% percentiles) % of positive tests in subgroup		
	Asymptomatic $n = 20$	Symptoms score 1–6 $n = 43$	Symptoms score 7–14 $n = 34$
SNIBE	0.79 (0.16; 12.6) ¹ 40 ^{c,d}	2.39 (0.97; 12.11) 74 ^a	9.05 (2.00; 21.7) ¹ 82 ^b
Epitope	0.47 (0.26; 0.90) ² 80	0.61 (0.35; 0.83) 86	0.81 (0.45; 1.05) ² 88
Euroimmun	0.32 (0.65; 5.21) 65	4.60 (1.92; 7.25) 86	6.19 (2.45; 7.29) 88
Roche	2.94 (0.45; 12.27) ^{3,4} 60 ^{c,d}	12.55 (3.02; 39.2) ³ 88 ^c	34.17 (6.34; 43.26) ⁴ 91 ^d
Abbott	3.02 (1.99; 5.21) ⁵ 80	5.61 (2.01; 7.65) ⁶ 81	6.82 (4.75; 7.98) ^{5,6} 91
DiaSorin	37.00 (5.99; 67.80) ^{7,8} 65	70.40 (26.5; 134) ⁸ 83	86.1 (35.9; 154) ⁸ 88
LIPS S-RBD	4.78 (2.14; 22.03) 75	14.19 (4.63; 58.10) 83	14.36 (6.03; 30.86) 91
LIPS N	5.20 (2.83; 10.49) ^{9,10} 80	11.33 (6.24; 24.74) ^{9,11} 95	19.49 (9.12; 80.20) ^{10,11} 94
Biosensor	NA ^g 40 ^{e,f}	NA ^g 65 ^e	NA ^g 79 ^f

Statistical difference between quantitative data

¹ $p = 0.01$

² $p = 0.026$

³ $p = 0.006$

⁴ $p < 0.001$

⁵ $p = 0.004$

⁶ $p = 0.04$

⁷ $p = 0.017$

⁸ $p = 0.008$

⁹ $p = 0.018$

¹⁰ $p < 0.001$

¹¹ $p = 0.029$, and between percentage of positive results

¹ $p = 0.01$

² $p = 0.002$

³ $p = 0.02$

⁴ $p = 0.01$

⁵ $p = 0.002$

⁶ $p = 0.007$

⁸NA—not applicable. Only qualitative interpretation (absence or presence of test line).

<https://doi.org/10.1371/journal.pone.0237548.t004>

Table 4. Antibody detection by tests in COVID-19 patients ($n = 97$) with different symptoms scores.

Test, manufacturer ^a	Antibody class and protein	Sensitivity ^b	Specificity ^c
MAGLUMI 2019-nCoV IgG, SNIBE (Shenzhen New Industries Biomedical Engineering Co)	IgG, not specified	70.1%	98%
SARS-CoV-2 ELISA IgG, EUROIMMUN AG	IgG, S1	82.5%	98%
SARS-CoV-2 IgG, Abbott Laboratories	IgG, N	84.5%	100%
Elecys® Anti-SARS-CoV-2, Roche Diagnostics GmbH	Total Ab, N	83.5%	100%
EDI® Novel Coronavirus COVID-19 IgG ELISA, Epitope Diagnostics Inc	IgG, N and S	85.6%	98%
LIAISON® SARS-CoV-2 S1/S2 IgG, DiaSorin S.p.A.	IgG, S1 and S2	81.4%	99%
STANDARD™ Q COVID-19 IgM/IgG Duo Test, SD Biosensor Inc	IgG, N	64.9%	100%
LIPS S-RBD IgG, in-house	IgG, S-RBD	84.5% ^d	98% ^d
LIPS N IgG, in-house	IgG, N	91.8% ^d	98% ^d

^aShort names used in the text are indicated in bold.
^bBased on testing of 97 serum samples from COVID-19 patients' in present study.
^cBased on testing of 100 pre COVID-19 sera in present study.
^dIn LIPS tests statistical (not clinically validated) cut-offs were applied.

<https://doi.org/10.1371/journal.pone.0237548.t002>

Table 2. Sensitivity and specificity of tests according to present study.

DEVELOPMENTS IN TREATMENTS

TARGETING COMPLEMENT ACTIVATION IN COVID-19

Kulkarni HS, Atkinson JP.. Blood. 2020 Oct 29;136(18):2000-2001. doi: 10.1182/blood.2020008925.

Level of Evidence: Other - Expert Opinion

BLUF

Two physicians at Washington University School of Medicine (U.S.) comment on Yu et al.'s (2020) study, which illustrated that COVID-19 may activate the alternative complement pathway and that factor D and an anti-C5 monoclonal antibody can prevent this activation in vitro (Figure 1). Although the authors relate the high therapeutic potential of this pathway, they express several concerns about the study (illustrated below), suggesting that further investigation is needed before this intervention may aid COVID-19 patients.

SUMMARY

The authors relate the following concerns regarding Yu et al.'s (2020) study:

- 1) C3, factor B, or properdin may be better to use than factor D, as factor D is known to cause alternative pathway (AP) activation in vivo
- 2) the study did not rule out the important role of the lectin pathway,
- 3) AP activation, while possibly detrimental in the long-term, likely plays an important role in initial defense against viral invasion
- 4) the study was conducted completely in vitro, and critical examination of results will need to be conducted in vivo.

FIGURES

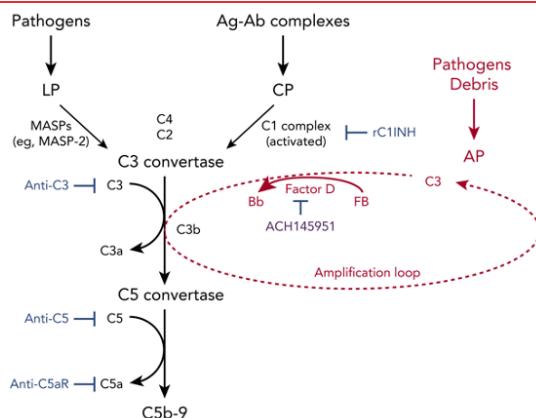


Figure 1: Schematic diagram summarizing clinical trials targeting different aspects of the complement system, registered on www.clinicaltrials.gov as of 3 September 2020. C3 with a cleaved thioester bond (ie, C3b or C3(H₂O)) binds factor B. Factor B is then cleaved by factor D to form C3bBb. Properdin (not shown) stabilizes this C3 convertase, which can cleave many molecules of C3 to C3b and thereby amplifies the AP. The factor D inhibitor tested in the paper by Yuan et al (ACH145951) is in purple and is not currently registered. Ag-Ab, antigen-antibody; C5aR, C5a receptor; CP, classical pathway; LP, lectin pathway; MASP, mannan binding lectin-associated serine proteases; rC1INH, recombinant C1-esterase inhibitor.

Created with www.biorender.com. For additional information, see Figure 6 in the article by Yu et al that begins on page 2080.

MENTAL HEALTH & RESILIENCE NEEDS

IMPACT ON PUBLIC MENTAL HEALTH

SCIENCE DENIAL AND COVID CONSPIRACY THEORIES: POTENTIAL NEUROLOGICAL MECHANISMS AND POSSIBLE RESPONSES

Miller BL.. JAMA. 2020 Nov 2. doi: 10.1001/jama.2020.21332. Online ahead of print.

Level of Evidence: 5 - Expert Opinion

BLUF

A Behavioral Neurologist from University of California, San Francisco describes that the neural mechanism behind false beliefs in COVID-19 conspiracy theories and science denial in healthy individuals is similar to those that have Lewy body dementia or Fronto-temporal dementia. He concludes that "developing frontal circuitry to support the process of reasoning is part of education and science literacy and stands at the core of a healthy democracy" and states that establishing this is the responsibility of the medical and scientific community through changes in the education system and working with political officials.

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