The Daily COVID-19 Literature Surveillance Summary

August 18, 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

Climate

- A journalist reports on efforts to include minority patients in COVID-19 vaccine trials given the pandemic's disproportionate impact on Black and Hispanic communities. The author suggests barriers to inclusive vaccine trials include failure to effectively connect with Black and Hispanic communities for recruitment, trepidation due to abusive research practices targeting these groups, fear of deportation, and lack of guidelines for measuring sufficient diversity in enrollment.

Epidemiology

- A multidisciplinary team from Johns Hopkins University conducted an observational study of a SARS-CoV-2 outbreak at a skilled nursing facility in Maryland and found residents undergoing dialysis were significantly more likely to contract COVID-19 compared to residents not receiving dialysis (47% SARS-CoV-2 positive by RT-PCR vs. 16%, $p<0.001$). While there were also differences by floor of residence (41% of nursing home patients on the second floor vs 4.5% on the first floor, $p<0.001$), authors suggest that dialysis may be a significant risk factor for COVID-19 due to associated behaviors (mask wearing, exposure to other patients and staff) and more serious underlying medical conditions and advocate for improved communication between dialysis centers and nursing homes as well as improved safety measures to promote mask wearing and physical distancing.

Understanding the Pathology

- Clinicians from Mount Sinai Hospital in New York present a case report of a COVID-19 positive 25-year-old multigravida patient with known red blood cell isoimmunization, undergoing percutaneous umbilical blood sampling (PUBS) and intrauterine transfusions due to evidence of fetal anemia. There was no evidence of transfer of passive immunity in the fetus either in utero or immediately after birth (via 2 intrauterine and neonatal cord blood samples) despite persistent maternal antibodies, implicating the need for further research in understanding of COVID-19 passive immunity to aid in vaccine development and fetal protection.

- Researchers in Beijing, China conducted a challenge-rechallenge study of SARS-CoV-2 infection in rhesus macaques with a 28 day interval period and found that rechallenged monkeys had a transient fever but no other clinical symptoms, negative viral load, and significantly increased serum IgG compared to initial challenge. Such findings suggest that rhesus macaques develop protection after primary exposure to SARS-CoV-2; however the exact protective mechanism and length of protection remain unclear, warranting further study with a longer interval period.

- An interdisciplinary group of researchers across the United States conducted a rhesus macaque infection model by inoculating 9 rhesus macaques with SARS-CoV-2 to determine if animal models could form immunity against re-infection. After inoculation and viral load assessments, all 9 macaques were re-infected on day 35 to assess the immunity response and the researchers found that:
  - Bronchoalveolar lavage viral loads were >5.1 log10 lower during the re-infection (re-challenge) assessment compared to initial infection ($p<0.001$)
  - Re-challenge group showed increased virus-specific ELISA titers ($P=0.0034$)
  - No recoverable virus was found in bronchoalveolar lavage and nasal swab plaque assay in the re-challenge group ($P = 0.009$)

  This study supports that animal models can mount an immunity to re-infection with SARS-CoV-2 and could be promising for its immunological prevention.

- A group of researchers from the United States and the Netherlands conducted a rhesus macaque infection model by developing six prototype DNA vaccines expressing different SARS-CoV-2 spike (S) protein variants and inoculating rhesus macaques (n=35). The authors found vaccine-elicited neutralizing antibodies and observed significantly low levels of RNA in the bronchoalveolar lavage and nasal mucosa samples from the vaccine groups compared to the control. This study shows a substantial viral load reduction using vaccines with S immunogens, suggesting for further studies with animal models and SARS-CoV-2 vaccine development for the prevention of SARS-CoV-2.

Transmission & Prevention

- A cross sectional study of emergency department patients (n=2022) conducted at Merano General Hospital in Italy found implementing a pre-triage protocol and dividing the emergency department (ED) into "clean" (patients presumed not to be infected; n=1840) and "infected" (patients with suspected infection; n=182) areas resulted in proper triage of 91.1% of COVID-19 positive patients and no healthcare worker infections, suggesting restructuring emergency departments to

include a pre-triage system may effectively optimize resources and limit COVID-19 transmission in the ED while protecting healthcare workers.

- A review of methanol toxicity reports and World Health Organization (WHO) hand sanitizer formulation standards were summarized by authors from Australia to warn against the potential dangers of distilleries producing alcohol-based hand rubs (ABHR) that use methylated spirits (denatured alcohol), which can contain methanol as a substitute for ethanol or isopropyl alcohol. These findings suggest that the general public should not be producing homemade ABHRs and that businesses such as pharmacies and distilleries should follow WHO guidelines in ABHR formulation to avoid potential methanol toxicity via inhalation/ingestion/transdermal absorption.

R&D: Diagnosis & Treatments

- Greek radiologists discuss the use of lung ultrasound (LUS) during the COVID-19 pandemic by proposing an 18-point lateral decubitus LUS with advantages including extensive lung surface inspection, elimination of gravity-related B-line changes (number and morphology), rapid single-operator performance, and minimized contamination risk by reducing patient repositioning and contact. Authors recommend using LUS as a safe, quick, and noninvasive alternative to computed tomography within the emergency department or intensive care unit for assessing lung involvement in COVID-19 pneumonia patients.

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CLIMATE

DISPARITIES

RESEARCHERS STRIVE TO RECRUIT HARD-HIT MINORITIES INTO COVID-19 VACCINE TRIALS

Jaklevic MC.. JAMA. 2020 Aug 13. doi: 10.1001/jama.2020.11244. Online ahead of print.
Level of Evidence: Other - Opinion

BLUF

A journalist reports on efforts to include minority patients in COVID-19 vaccine trials given the pandemic's disproportionate impact on Black and Hispanic communities. The author suggests barriers to inclusive vaccine trials include failure to effectively connect with Black and Hispanic communities for recruitment, trepidation due to abusive research practices targeting these groups, fear of deportation, and lack of guidelines for measuring sufficient diversity in enrollment.

NATIONAL PREFERRED INTERPERSONAL DISTANCE CURBS THE SPREAD OF COVID-19: A CROSS-COUNTRY ANALYSIS

Gokmen Y, Turen U, Erdem H, Tokmak İ.. Disaster Med Public Health Prep. 2020 Aug 12:1-15. doi: 10.1017/dmp.2020.295. Online ahead of print.
Level of Evidence: Other - Modeling

BLUF

An epidemiological modeling study by authors in Turkey found that national interpersonal distance preferences (using data from 40 countries, Sorokowska et. al. 2017) along three dimensions of distance (social, personal, and intimate) are correlated with observed COVID-19 growth rate (Our World in Data, OWD 2020 data) based on simple regression analysis (Table 2). These findings may inform public policy on social distancing as well as suggesting that countries with larger interpersonal distances may be less vulnerable to COVID-19 transmission.

ABSTRACT

OBJECTIVE: National Interpersonal distance preference is considered a cultural characteristic. Interpersonal distance is critical for the spread dynamics of COVID-19. COVID-19's spread trend shows various characteristics in different countries. We think that one of the factors influencing this variation could be national interpersonal distance preference. METHODS: We employed regression analysis based on data of national interpersonal distance preferences (social, personal, and intimate) presented by Sorokowska et al. (2017) and COVID-19 growth rate data for 40 different countries which are calculated using OWD's (2020) data. RESULTS: National interpersonal distance preferences with its three dimensions significantly decrease the growth rate of COVID-19 in countries. CONCLUSION: Understanding the relation between national interpersonal distance preference and contagion growth of COVID-19 might be very useful information to be utilized in decision-making processes of individuals, societies and governments to develop culturally well-suited counter-pandemic politics, strategies, and procedures during COVID-19 pandemic or any upcoming epidemic or pandemic threats in the future, instead of standard fit-to-all strategies.

FIGURES

ID	Country	Dependent Variable**	Independent Variables (cm)**			
		Growth Rate of Total Cases (GRTC)	Geometric Mean of Interpersonal Distance (GMID)	Social Distance (SD)	Personal Distance (PD)	Intimate Distance (ID)
1	Argentina	0.1338	57.45	77.33	59.33	41.33
2	Austria	0.1597	67.47	88.00	68.00	51.33
3	Brazil	0.1917	75.38	101.33	77.33	54.67
4	Bulgaria	0.0871	62.25	82.67	65.33	44.67
5	Canada	0.1884	85.80	102.67	84.67	72.67
6	China	0.0743	82.14	114.67	83.33	58.00
7	Colombia	0.1370	84.37	116.00	85.33	60.67
8	Croatia	0.1297	90.36	108.67	89.33	76.00
9	Czech Republic	0.1434	79.83	110.00	80.67	57.33
10	Estonia	0.0944	91.23	117.33	93.33	69.33
11	Germany	0.1788	65.94	96.00	70.00	42.67
12	Ghana	0.0647	78.51	106.67	82.00	55.33
13	Greece	0.0992	66.77	92.00	69.33	46.67
14	Hungary	0.1151	104.69	129.33	107.33	82.67
15	India	0.1621	82.39	110.00	86.67	58.67
16	Indonesia	0.1330	84.96	110.00	85.33	65.33
17	Iran	0.1482	82.12	112.00	83.33	59.33
18	Italy	0.1571	64.70	93.33	68.00	42.67
19	Kazakhstan	0.1433	67.69	94.67	67.33	48.67
20	Kenya	0.0724	82.18	110.00	88.00	57.33
21	Malaysia	0.1200	73.28	110.00	76.67	46.67
22	Mexico	0.1514	81.26	99.33	82.67	65.33
23	Nigeria	0.0746	80.36	102.67	80.67	62.67
24	Norway	0.1228	65.39	104.00	72.00	37.33
25	Pakistan	0.1377	84.43	118.00	90.00	56.67
26	Peru	0.1470	61.63	80.67	64.00	45.33
27	Poland	0.1562	68.25	96.67	66.67	49.33
28	Portugal	0.1861	73.63	110.00	76.67	47.33
29	Romania	0.1492	84.09	134.67	92.00	48.00
30	Russia	0.1914	67.57	89.33	74.00	46.67
31	Saudi Arabia	0.1332	107.76	125.33	104.00	96.00
32	Serbia	0.1505	65.32	92.67	67.33	44.67
33	Slovakia	0.0804	63.72	88.67	67.33	43.33
34	South Korea	0.0894	83.30	105.33	84.00	65.33
35	Spain	0.1966	72.55	90.00	74.00	57.33
36	Switzerland	0.1449	91.03	110.00	92.67	74.00
37	The United Kingdom	0.1850	76.86	99.33	80.67	56.67
38	The United States	0.2273	68.30	95.33	68.67	48.67
39	Turkey	0.2532	87.37	122.67	92.67	58.67
40	Ukraine	0.1890	61.14	86.00	65.33	40.67

(*) Hong Kong and Uganda are excluded from analysis, due to lack of COVID-19 total cases data. The decimal parts of independent variables are rounded to two digits.
(**) In order to ensure normality and homoscedasticity assumptions, transformation methods (logarithm and simple smoothing) are conducted before regression analysis.

Table 2: The data set of dependent and independent variables.

SYMPTOMS AND CLINICAL PRESENTATION

TRANSMISSION OF SARS-COV-2 INVOLVING RESIDENTS RECEIVING DIALYSIS IN A NURSING HOME - MARYLAND, APRIL 2020

Bigelow BF, Tang O, Toci GR, Stracker N, Sheikh F, Jacobs Slifka KM, Novosad SA, Jernigan JA, Reddy SC, Katz MJ.. MMWR Morb Mortal Wkly Rep. 2020 Aug 14;69(32):1089-1094. doi: 10.15585/mmwr.mm6932e4.
Level of Evidence: 3 - Local non-random sample

BLUF

A multidisciplinary team from Johns Hopkins University conducted an observational study of a SARS-CoV-2 outbreak at a skilled nursing facility in Maryland, USA in April 2020 (Figure 1) and found residents undergoing dialysis were significantly more likely to contract COVID-19 compared to residents not receiving dialysis (47% SARS-CoV-2 positive by RT-PCR vs. 16%, $p<0.001$) (Table). While there were also differences by floor of residence (41% of nursing home patients on the second floor vs 4.5% on the first floor, $p<0.001$)(Figure 2), authors suggest that dialysis may be a significant risk factor for COVID-19 due to associated behaviors (mask wearing, exposure to other patients and staff) and more serious underlying medical conditions. They advocate for improved communication between dialysis centers and nursing homes as well as improved safety measures to promote mask wearing and physical distancing.

ABSTRACT

SARS-CoV-2, the virus that causes coronavirus disease 2019 (COVID-19), can spread rapidly in nursing homes once it is introduced (1,2). To prevent outbreaks, more data are needed to identify sources of introduction and means of transmission within nursing homes. Nursing home residents who receive hemodialysis (dialysis) might be at higher risk for SARS-CoV-2 infections because of their frequent exposures outside the nursing home to both community dialysis patients and staff members at dialysis centers (3). Investigation of a COVID-19 outbreak in a Maryland nursing home (facility A) identified a higher prevalence of infection among residents undergoing dialysis (47%; 15 of 32) than among those not receiving dialysis (16%; 22 of 138) (p<0.001). Among residents with COVID-19, the 30-day hospitalization rate among those receiving dialysis (53%) was higher than that among residents not receiving dialysis (18%) (p = 0.03); the proportion of dialysis patients who died was 40% compared with those who did not receive dialysis (27%) (p = 0.42).Careful consideration of infection control practices throughout the dialysis process (e.g., transportation, time spent in waiting areas, spacing of machines, and cohorting), clear communication between nursing homes and dialysis centers, and coordination of testing practices between these sites are critical to preventing COVID-19 outbreaks in this medically vulnerable population.

FIGURES

FIGURE 1. SARS-CoV-2 testing results among residents of a nursing home receiving or not receiving dialysis — Maryland, April 2020

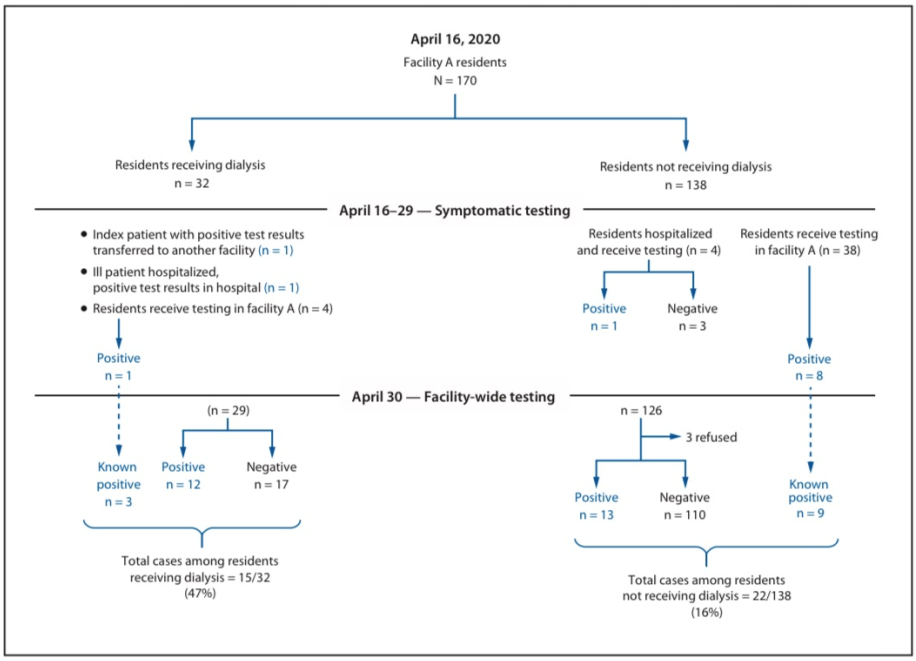
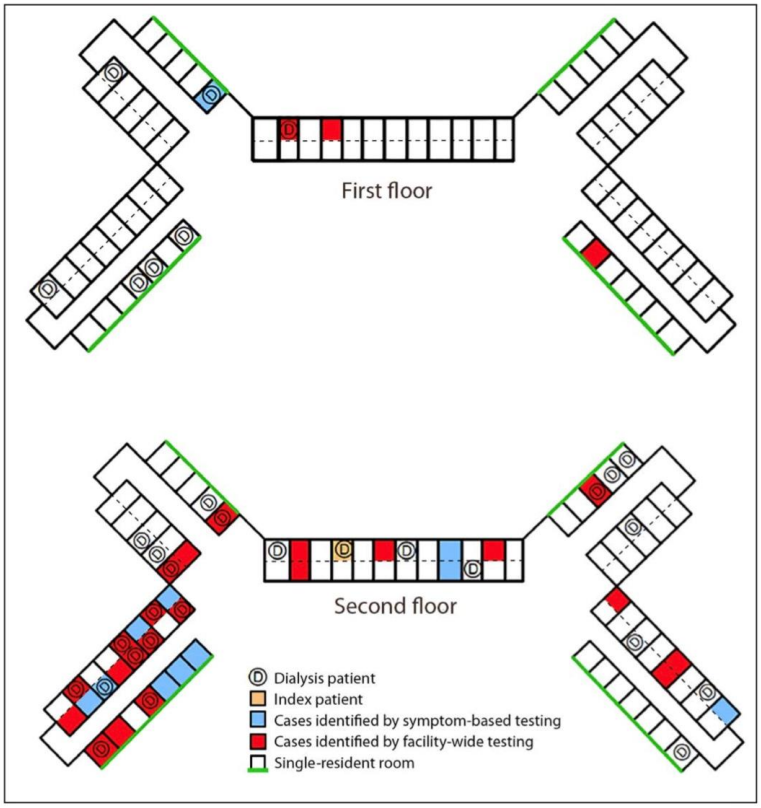


FIGURE 2. Distribution of COVID-19 cases among facility A residents receiving or not receiving dialysis, by floor* — Maryland, April 2020



Abbreviations: COVID-19 = coronavirus disease 2019; D = room of resident receiving dialysis.
* All dialysis treatments were completed in the dialysis center, which was co-located on site. Symptom-based testing referred to targeted testing of residents who were experiencing at least one of the following symptoms: fever >99°F (37.2°C), cough, malaise, headache, or upper respiratory symptoms. Facility-wide testing refers to the testing of all facility A residents who had not previously had test results positive for SARS-CoV-2, regardless of symptoms.

TABLE. Number of residents who had positive test results for SARS-CoV-2 RNA among facility A residents (N = 170), overall and by residence floor and dialysis schedule — Maryland, April 16–30, 2020

Characteristic	No. of residents	No. (%) of cases
Dialysis status, all residents		
Not receiving dialysis	138	22 (16)
Receiving dialysis	32	15 (47)
Facility residence (residents receiving dialysis only)		
First floor	7	2 (29)
Second floor	25	13 (52)
Dialysis schedule		
Monday/Wednesday/Friday	19	9 (47)
Shift 1	4	0 (0)
Shift 2	3	1 (33)
Shift 3	12	8 (67)
Tuesday/Thursday/Saturday	13	6 (46)
Shift 1	6	3 (50)
Shift 2	6	2 (33)
Shift 3	1	1 (100)

VASCULAR ENDOTHELIAL INJURY EXACERBATES CORONAVIRUS DISEASE 2019: THE ROLE OF ENDOTHELIAL GLYCOCALYX PROTECTION

Okada H, Yoshida S, Hara A, Ogura S, Tomita H.. Microcirculation. 2020 Aug 13:e12654. doi: 10.1111/micc.12654. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

A review of various COVID-19 pathophysiology studies by authors in Japan hypothesizes that disruption of the endothelial glycocalyx may play a role in the onset/exacerbation of severe COVID-19 complications. COVID-19 acute respiratory distress syndrome (ARDS) has been described to induce a multisystemic inflammatory thrombotic response in addition to disruption of the endothelial glycocalyx (Figure 1). Therapies that have been shown to protect the glycocalyx in vitro include: recombinant human thrombomodulin (rhTM), corticosteroids, sivelestat, antioxidants, and antithrombin. These findings suggest that endothelial glycocalyx restoration may be a potential therapeutic strategy for COVID-19 ARDS, and monitoring endothelial glycocalyx integrity (via hyaluronic acid) may be useful for tracking lung damage.

ABSTRACT

The potential for a rapid increase in severity is among the most frightening aspects of severe acute respiratory syndrome coronavirus 2 infection. Evidence increasingly suggests that the symptoms of coronavirus disease-2019 (COVID-19)-related acute respiratory distress syndrome (ARDS) differ from those of classic ARDS. Recently, the severity of COVID-19 has been attributed to a systemic, thrombotic, and inflammatory disease that damages not only the lungs but multiple organs, including the heart, brain, toes, and liver. This systemic form of COVID-19 may be due to inflammation and vascular endothelial cell injury. The vascular endothelial glycocalyx comprises glycoproteins, and plays an important role in systemic capillary homeostasis maintenance. The glycocalyx covers the entire vascular endothelium, and its thickness varies among organs. The endothelial glycocalyx is very thin in the pulmonary capillaries, where it is affected by gaseous exchange with the alveoli and the low intravascular pressure in the pulmonary circulation. Despite the clearly important roles of the glycocalyx in vascular endothelial injury, thrombosis, vasculitis, and inflammation, the link between this structure and vascular endothelial cell dysfunction in COVID-19 remains unclear. In this prospective review, we summarize the importance of the glycocalyx and its potential as a therapeutic target in cases of systemic COVID-19.

FIGURES

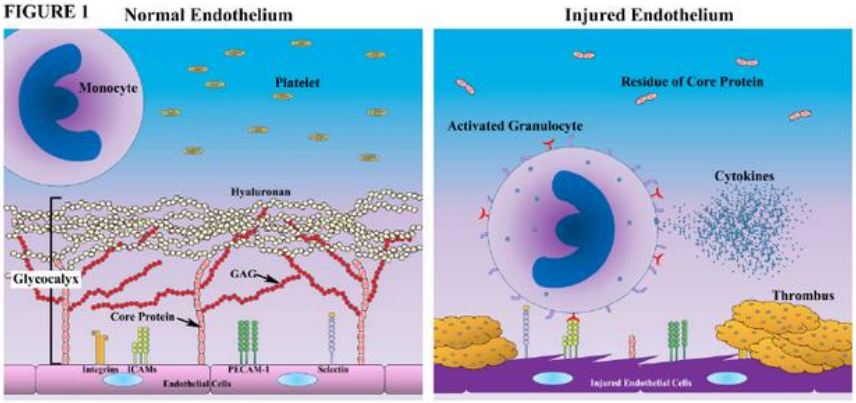


Figure 1. Schema of the endothelium. The surface and surface receptors of the normal endothelium are covered by the endothelial glycocalyx, which is composed of the core protein, GAG, and hyaluronan. Only the core protein binds to the endothelial cells, whereas GAG and hyaluronan do not directly interact with these cells (Left Panel). However, the endothelial glycocalyx is degraded under conditions of injury, such as the cytokine storm. Here, both the surfaces and surface receptors of endothelial cells are exposed to the vascular lumen. Granulocytes and platelets adhere to the endothelial cells, causing injury and thrombi, which block the blood flow (Right Panel). GAG: Glycosaminoglycan.

A CASE REPORT TO ASSESS PASSIVE IMMUNITY IN A COVID POSITIVE PREGNANT PATIENT

Toner LE, Gelber SE, Pena JA, Fox NS, Rebarber A.. Am J Perinatol. 2020 Aug 13. doi: 10.1055/s-0040-1715643. Online ahead of print.
Level of Evidence: Other - Case Report

BLUF

Clinicians from Mount Sinai Hospital in New York present a case report of a COVID-19 positive 25-year-old multigravida patient* with known red blood cell isoimmunization, undergoing percutaneous umbilical blood sampling (PUBS) and intrauterine transfusions due to evidence of fetal anemia. There was no evidence of transfer of passive immunity in the fetus either in utero or immediately after birth (via 2 intrauterine and neonatal cord blood samples) despite persistent maternal antibodies (Table 1), implicating the need for further research in understanding of COVID-19 passive immunity to aid in vaccine development and fetal protection.

SUMMARY

* A 25-year-old multigravida female (G4P4) with history of isoimmunization to D, C, and Le RBC antigens showed indications of fetal anemia at 18 weeks 2 days pregnancy. She subsequently underwent 5 percutaneous umbilical blood samplings (PUBS) and intrauterine transfusions throughout her pregnancy. At gestational week 26, she tested positive for COVID-19 by PCR due to mild symptoms (anosmia), with no evidence of fever or respiratory distress. At 27 weeks, she was positive for SARS-CoV-2 IgG at a dilution of 1:160, but fetal blood remained IgG negative. After 1 month, fetal blood still remained IgG negative, and the mother tested negative for COVID-19 via PCR. Following preterm labor and delivery at 33 weeks, umbillical cord antibody testing revealed the fetus was still IgG negative, despite the mother being IgG positive at a dilution of 1:320.

ABSTRACT

INTRODUCTION: Data regarding transplacental passage of maternal coronavirus disease 2019 (COVID-19) antibodies and potential immunity in the newborn is limited. CASE REPORT: We present a 25-year-old multigravida with known red blood cell isoimmunization, who was found to be COVID-19 positive at 27 weeks of gestation while undergoing serial periumbilical blood sampling and intrauterine transfusions. Maternal COVID-19 antibody was detected 2 weeks after positive molecular testing. Antibodies were never detected on cord blood samples from two intrauterine fetal cord blood samples as well as neonatal cord blood at the time of delivery. CONCLUSION: This case demonstrates a lack of passive immunity of COVID-19 antibodies from a positive pregnant woman to her fetus, neither in utero nor at the time of birth. Further studies are needed to understand if passage of antibodies can occur and if that can confer passive immunity in the newborn. KEY POINTS: Passive immunity should not be assumed in COVID-19 infection in pregnancy.. Isoimmunization may impair passive immunity of certain antibodies.. Vaccination to or maternal infection of COVID-19 may not be protective for the fetus..

FIGURES

Date	Test	Maternal result	Fetal result
March 30, 2020	Nasopharyngeal (PCR)	Positive	
April 6, 2020	Serum COVID-19 antibody	Positive (titer 160)	
April 6, 2020	In utero umbilical cord blood COVID-19 antibody		Negative
May 4, 2020	Nasopharyngeal (PCR)	Negative	
May 4, 2020	In utero umbilical cord blood COVID-19 antibody		Negative
May 16, 2020	Neonatal umbilical cord blood COVID-19 antibody		Negative
May 16, 2020	Neonatal umbilical cord blood rubeola antibody		Positive
May 16, 2020	Neonatal umbilical cord blood varicella antibody		Positive
May 18, 2020	Serum COVID-19 antibody	Positive (titer 320)	
January 1, 2020	Prenatal labs: maternal rubeola maternal varicella	Igg 125 AU/mL (Pos > 16.4) Igg 1889 (index) (Pos > 165)	

Table 1: Severe acute respiratory syndrome COVID 2 testing.

POTENTIAL EFFECTS OF SARS-COV-2 INFECTION DURING PREGNANCY ON FETUSES AND NEWBORNS ARE WORTHY OF ATTENTION

Dang D, Wang L, Zhang C, Li Z, Wu H.. J Obstet Gynaecol Res. 2020 Aug 10. doi: 10.1111/jog.14406. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

Neonatologists from Jilian University in China reviewed pathophysiological mechanisms of adverse pregnancy outcomes and poor outcomes in newborns born to mothers with SARS-CoV-2 infection and found multiple possible contributory changes, including hypoxia, angiotensin converting enzyme 2 deficiency, and loss of maternal-fetal immune tolerance (Figure 1). Due to apparent effects on fetal development, authors suggest vigilant management of pregnant women with SARS-CoV-2 and their fetuses, recommending further investigation into effects of SARS-CoV-2 on this important population.

ABSTRACT

The outbreak of the 2019 novel coronavirus disease (SARS-CoV-2) has resulted in a major epidemic threat worldwide. However, the effects of neoviruses on infected pregnant women and especially on their fetuses and newborns are not well understood. Most up-to-date evidences about how SARS-CoV-2 affected patients especially in pregnancy were collected by conducting a comprehensive search of medical literature electronic databases. Immune-related data of pregnant women, fetuses and newborns were further analysis. According to the limited literature, SARS-CoV-2 utilizes angiotensin converting enzyme 2 as its receptor and causes severe hypoxemia. Insufficiency of angiotensin converting enzyme 2 in pregnant women and the effects of hypoxia on the placental oxygen supply will cause severe perinatal complications. In addition, SARS-CoV-2 infection may disrupt maternal-fetal immune tolerance and cause immunological damage to embryos. Because of these reasons, pregnancy complications such as fetal demise or premature birth, preeclampsia, intrauterine growth restriction, respiratory dyspnea, nervous system dysplasia and immune system defects are likely to occur in pregnant women with COVID-19 or their newborns. Pregnant women infected with SARS-CoV-2 should be treated as a special group and given special attention. Fetuses and newborns of SARS-CoV-2-infected pregnant women should be given more protection to reduce the occurrence of adverse events. In this review, we intend to provide an overview of the physiological and immunological changes that induce the pregnancy complications. This article will benefit the treatment and prognosis of fetuses and newborns of SARS-CoV-2-infected pregnant women.

FIGURES

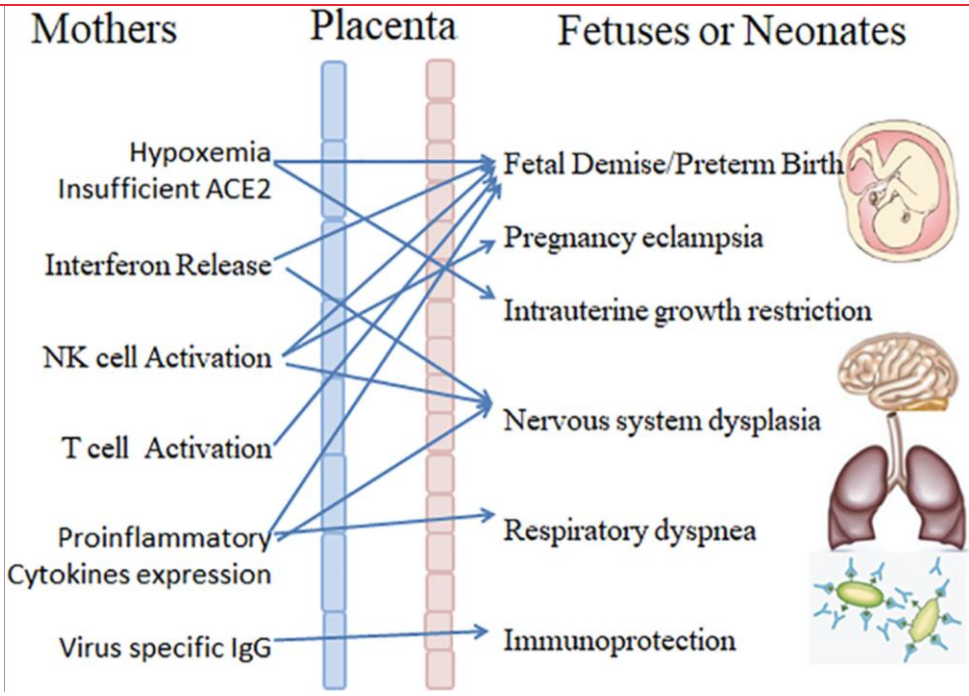


Figure 1: Graphical representation of possible underlying mechanisms contributing to poor prognosis in newborns born to mothers with SARS-CoV-2.

PRIMARY EXPOSURE TO SARS-COV-2 PROTECTS AGAINST REINFECTION IN RHESUS MACAQUES

Deng W, Bao L, Liu J, Xiao C, Liu J, Xue J, Lv Q, Qi F, Gao H, Yu P, Xu Y, Qu Y, Li F, Xiang Z, Yu H, Gong S, Liu M, Wang G, Wang S, Song Z, Liu Y, Zhao W, Han Y, Zhao L, Liu X, Wei Q, Qin C.. Science. 2020 Aug 14;369(6505):818-823. doi: 10.1126/science.abc5343. Epub 2020 Jul 2.
Level of Evidence: Other - Mechanism-based reasoning

BLUF

Researchers in Beijing, China conducted a challenge-rechallenge study of SARS-CoV-2 infection in rhesus macaques with a 28 day interval period and found that rechallenged monkeys had a transient fever but no other clinical symptoms, negative viral load, and significantly increased serum IgG compared to initial challenge. Such findings suggest that rhesus macaques develop protection after primary exposure to SARS-CoV-2; however the exact protective mechanism and length of protection remain unclear, warranting further study with a longer interval period.

ABSTRACT

Coronavirus disease 2019 (COVID-19), which is caused by infection with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has become a global pandemic. It currently remains unclear whether convalescing patients have a risk of reinfection. We generated a rhesus macaque model of SARS-CoV-2 infection that was characterized by interstitial pneumonia and systemic viral dissemination mainly in the respiratory and gastrointestinal tracts. Rhesus macaques reinfected with the identical SARS-CoV-2 strain during the early recovery phase of the initial SARS-CoV-2 infection did not show detectable viral dissemination, clinical manifestations of viral disease, or histopathological changes. Comparing the humoral and cellular immunity between primary infection and rechallenge revealed notably enhanced neutralizing antibody and immune responses. Our results suggest that primary SARS-CoV-2 exposure protects against subsequent reinfection in rhesus macaques.

SARS-COV-2 INFECTION PROTECTS AGAINST RECHALLENGE IN RHESUS MACAQUES

Chandrashekar A, Liu J, Martinot AJ, McMahan K, Mercado NB, Peter L, Tostanoski LH, Yu J, Maliga Z, Nekorchuk M, Busman-Sahay K, Terry M, Wrijil LM, Ducat S, Martinez DR, Atyeo C, Fischinger S, Burke JS, Slein MD, Pessaint L, Van Ry A, Greenhouse J, Taylor T, Blade K, Cook A, Finneyfrock B, Brown R, Teow E, Velasco J, Zahn R, Wegmann F, Abbink P, Bondzie EA, Dagotto G, Gebre MS, He X, Jacob-Dolan C, Kordana N, Li Z, Lifton MA, Mahrokhian SH, Maxfield LF, Nityanandam R, Nkolola JP, Schmidt AG, Miller AD, Baric RS, Alter G, Sorger PK, Estes JD, Andersen H, Lewis MG, Barouch DH.. Science. 2020 Aug 14;369(6505):812-817. doi: 10.1126/science.abc4776. Epub 2020 May 20.
Level of Evidence: Other - Mechanism-based reasoning

BLUF

An interdisciplinary group of researchers across the United States conducted a rhesus macaque infection model by inoculating 9 rhesus macaques with SARS-CoV-2 to determine if animal models could form immunity against re-infection. After inoculation and viral load assessments, all 9 macaques were re-infected on day 35 to assess the immunity response and the researchers found that:

- Bronchoalveolar lavage viral loads were >5.1 log10 lower during the re-infection (re-challenge) assessment compared to initial infection ($p<0.001$) (Fig. 5)
- Re-challenge group showed increased virus-specific ELISA titers ($P=0.0034$) (Fig. 6)
- No recoverable virus was found in bronchoalveolar lavage and nasal swab plaque assay in the re-challenge group ($P = 0.009$) (Fig. S9)

  This study supports that animal models can mount an immunity to re-infection with SARS-CoV-2 and could be promising for its immunological prevention.

ABSTRACT

An understanding of protective immunity to SARS-CoV-2 is critical for vaccine and public health strategies aimed at ending the global COVID-19 pandemic. A key unanswered question is whether infection with SARS-CoV-2 results in protective immunity

against re-exposure. We developed a rhesus macaque model of SARS-CoV-2 infection and observed that macaques had high viral loads in the upper and lower respiratory tract, humoral and cellular immune responses, and pathologic evidence of viral pneumonia. Following initial viral clearance, animals were rechallenged with SARS-CoV-2 and showed 5 log10 reductions in median viral loads in bronchoalveolar lavage and nasal mucosa compared with primary infection. Anamnestic immune responses following rechallenge suggested that protection was mediated by immunologic control. These data show that SARS-CoV-2 infection induced protective immunity against re-exposure in nonhuman primates.

FIGURES

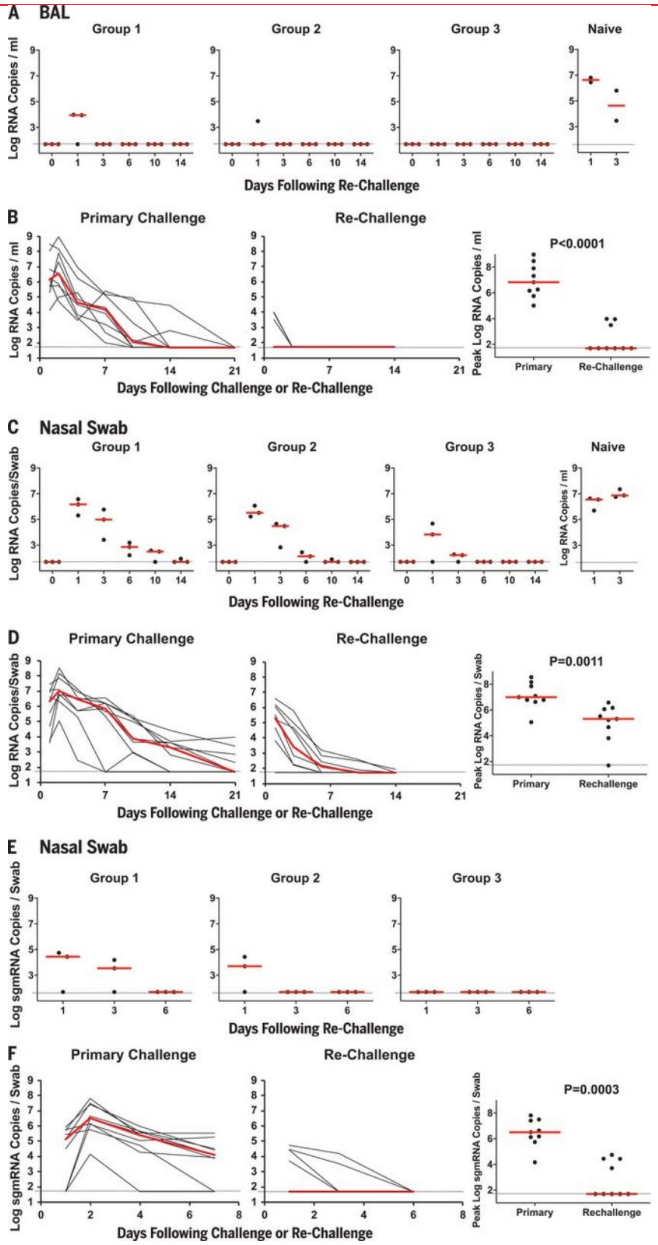


Figure 5: Viral loads after SARS-CoV-2 rechallenge in rhesus macaques. On day 35 after the initial infection (Fig. 1), rhesus macaques were rechallenged by the IN and IT routes with 1.1 × 106 PFU (Group 1; N = 3), 1.1 × 105 PFU (Group 2; N = 3), or 1.1 × 104 PFU (Group 3; N = 3) of SARS-CoV-2. Three naïve animals were included as a positive control in the rechallenge experiment. (A) Log10 viral RNA copies/ml (limit 50 copies/ml) were assessed in BAL at multiple time points after rechallenge. One of the naïve animals could not be lavaged. (B) Comparison of viral RNA in BAL after primary challenge and rechallenge. (C and E) Log10 viral RNA copies/ml (C) and log10 sgmRNA copies/swab (limit 50 copies/ml) (E) were assessed in NS at multiple time points after rechallenge. (D and F) Comparison of viral RNA (D) and sgmRNA (F) in NS after primary challenge and rechallenge. Red horizontal bars reflect median viral loads. P values reflect two-sided Mann-Whitney tests

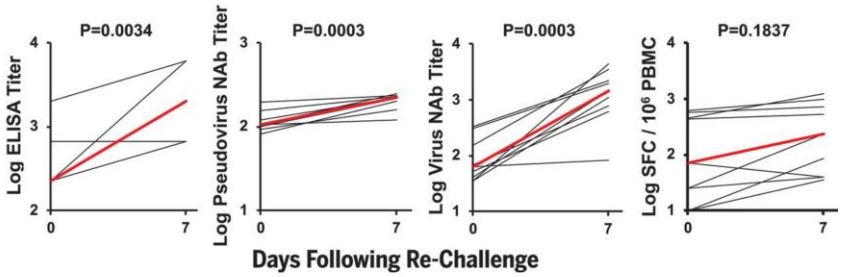


Figure 6: Anamnestic immune responses after SARS-CoV-2 rechallenge in rhesus macaques. Results of binding antibody ELISAs, pseudovirus neutralization assays, live virus neutralization assays, and IFNγ ELISPOT assays are depicted before and 7 days after SARS-CoV-2 rechallenge. Red lines reflect mean responses. P values reflect two-sided Mann-Whitney tests.

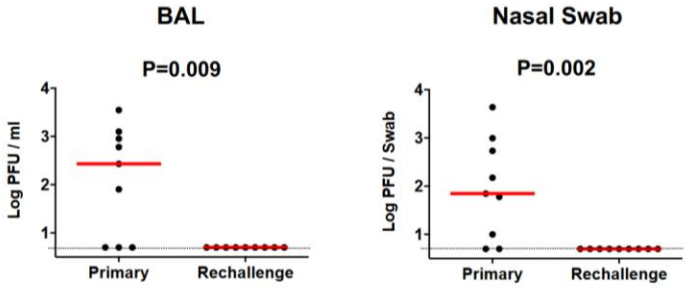


Figure S9: Plaque assays of BAL and nasal swabs following SARS-CoV-2 primary challenge and re-challenge. Peak plaque-forming units (PFU) per ml for BAL or per swab for nasal swabs from days 1-7 following primary challenge or re-challenge are shown. Red horizontal bars reflect median PFU titers.

DNA VACCINE PROTECTION AGAINST SARS-COV-2 IN RHESUS MACAQUES

Yu J, Tostanoski LH, Peter L, Mercado NB, McMahan K, Mahrokhian SH, Nkolola JP, Liu J, Li Z, Chandrashekar A, Martinez DR, Loos C, Atyeo C, Fischinger S, Burke JS, Slein MD, Chen Y, Zuiani A, Lelis FJN, Travers M, Habibi S, Pessaint L, Van Ry A, Blade K, Brown R, Cook A, Finneyfrock B, Dodson A, Teow E, Velasco J, Zahn R, Wegmann F, Bondzie EA, Dagotto G, Gebre MS, He X, Jacob-Dolan C, Kirilova M, Kordana N, Lin Z, Maxfield LF, Nampanya F, Nityanandam R, Ventura JD, Wan H, Cai Y, Chen B, Schmidt AG, Wesemann DR, Baric RS, Alter G, Andersen H, Lewis MG, Barouch DH.. Science. 2020 Aug 14;369(6505):806-811. doi: 10.1126/science.abc6284. Epub 2020 May 20.
Level of Evidence: Other - Mechanism-based reasoning

BLUF

A group of researchers from the United States and the Netherlands conducted a rhesus macaque infection model by developing six prototype DNA vaccines expressing different SARS-CoV-2 spike (S) protein variants (Figure 1) and inoculating rhesus macaques (n=35). The vaccinated macaques exhibited cellular immune responses via enzyme-linked immunosorbent spot assay and were subsequently challenged with SARS-CoV-2 (Figure 3). The authors found vaccine-elicited neutralizing antibodies and observed significantly low levels of RNA in the bronchoalveolar lavage and nasal mucosa samples from the vaccine groups compared to the control (Figure 4). This study shows a substantial viral load reduction using vaccines with S immunogens, suggesting for further studies with animal models and SARS-CoV-2 vaccine development for the prevention of SARS-CoV-2.

ABSTRACT

The global COVID-19 pandemic caused by the SARS-CoV-2 virus has made the development of a vaccine a top biomedical priority. In this study, we developed a series of DNA vaccine candidates expressing different forms of the SARS-CoV-2 Spike (S) protein and evaluated them in 35 rhesus macaques. Vaccinated animals developed humoral and cellular immune responses, including neutralizing antibody titers comparable to those found in convalescent humans and macaques infected with SARS-CoV-2. Following vaccination, all animals were challenged with SARS-CoV-2, and the vaccine encoding the full-length S protein resulted in >3.1 and >3.7 log10 reductions in median viral loads in bronchoalveolar lavage and nasal mucosa, respectively, as compared with sham controls. Vaccine-elicited neutralizing antibody titers correlated with protective efficacy, suggesting an immune correlate of protection. These data demonstrate vaccine protection against SARS-CoV-2 in nonhuman primates.

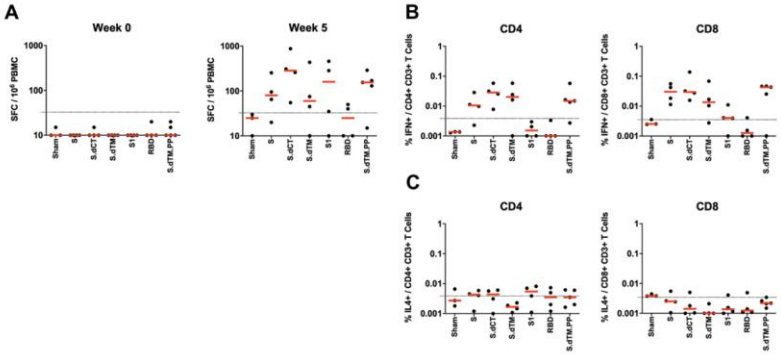
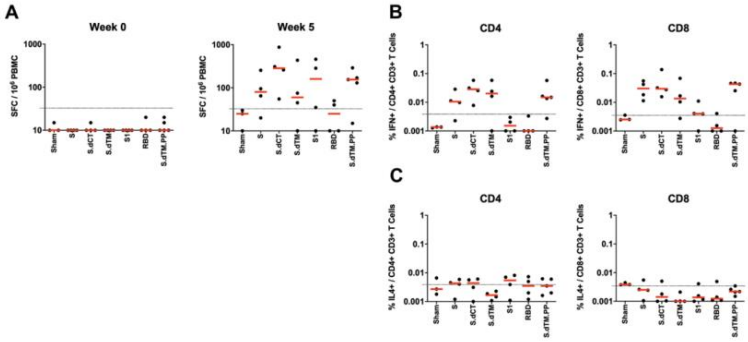


Fig. 3. Cellular immune responses in vaccinated rhesus macaques. Cellular immune responses were assessed at week 5 following immunization by (**A**) IFN-γ ELISPOT assays and (**B**) IFN-γ+ and (**C**) IL-4+ intracellular cytokine staining assays for CD4+ and CD8+ T cells in response to pooled S peptides. Red bars reflect median responses.



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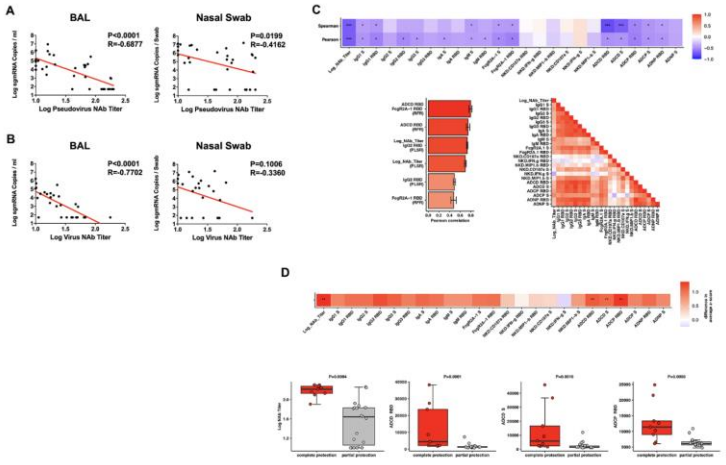

Fig. 5. Immune correlates of protection. Correlations of (**A**) pseudovirus NAb titers and (**B**) live NAb titers prior to challenge with log peak sgmRNA copies/ml in BAL or log peak sgmRNA copies/swab in nasal swabs following challenge. Red lines reflect the best-fit relationship between these variables. P and R values reflect two-sided Spearman rank-correlation tests. (**C**) The heat map (top panel) shows the Spearman and Pearson correlations between antibody features and $\log_{10}$ peak sgmRNA copies/ml in BAL (*q < 0.05, **q < 0.01, ***q < 0.001 with Benjamini-Hochberg correction for multiple testing). The bar graph (bottom left panel) shows the rank of the Pearson correlation between cross-validated model predictions and data using the most predictive combination or individual antibody features for partial least square regression (PLSR) and random forest regression (RFR). The correlation heatmap (bottom right panel) represents pairwise Pearson correlations between features across all animals. (**D**) The heat map (top panel) shows the difference in the means of the z-scored features between the completely protected and partially protected animals (**q < 0.01 with Benjamini-Hochberg correction for multiple testing). The dot plots show differences in $\log_{10}$ NAb titers, RBD-specific ADCD responses, S-specific ADCD responses, and RBD-specific ADCP responses between the completely protected and partially protected animals. P-values indicate two-sided Mann-Whitney tests.

THE COVID-19 EPIDEMIC AND REORGANISATION OF TRIAGE, AN OBSERVATIONAL STUDY

Turcato G, Zaboli A, Pfeifer N.. Intern Emerg Med. 2020 Aug 9. doi: 10.1007/s11739-020-02465-2. Online ahead of print.
Level of Evidence: Other - Guidelines and Recommendations

BLUF

A cross sectional study of emergency department patients (n=2022, Table 2) conducted at Merano General Hospital in Italy from March 4-31, 2020 found implementing a pre-triage protocol (Figure 2) and dividing the emergency department (ED) into "clean" (patients presumed not to be infected; n=1840) and "infected" (patients with suspected infection; n=182) areas resulted in proper triage of 91.1% of COVID-19 positive patients (Table 3) and no healthcare worker infections. In light of these results, restructuring emergency departments to include a pre-triage system may effectively optimize resources and limit COVID-19 transmission in the ED while protecting healthcare workers.

ABSTRACT

Recent studies have suggested different organisational strategies, modifying Emergency Departments (EDs) during the COVID-19 epidemic. However, real data on the practical application of these strategies are not yet available. The objective of this study is to evaluate the inclusion of pre-triage during the COVID-19 outbreak. In March 2020, the structure of the ED at Merano General Hospital (Italy) was modified, with the introduction of a pre-triage protocol to divide patients according to the risk of infection. The performance of pre-triage was evaluated for sensitivity, specificity and negative predictive value (NPV). From 4th to 31st March, 2,279 patients were successively evaluated at the pre-triage stage. Of these, 257 were discharged directly from pre-triage by triage out or home quarantine and none has subsequently been hospitalised. Of the 2022 patients admitted to ED, 182 were allocated to an infected area and 1840 to a clean area. The proportion of patients who tested COVID-19 positive was 5% and, of these, 91.1% were allocated to the infected area. The pre-triage protocol demonstrated sensitivity of 91.1%, specificity of 95.3% and NPV of 99.5%. In addition, none of the healthcare workers was infected during the study period. Pre-triage can be a useful tool that, if standardised and associated with a change in the structure of the ED, can limit the spread of infection within the ED, optimise ED resources and protect healthcare workers.

FIGURES

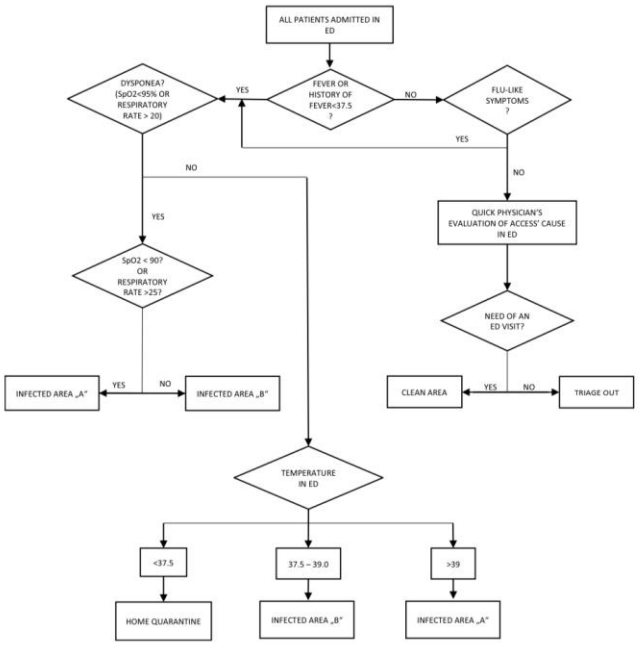

Fig. 2 Operative flow chart applied in pre-triage

Table 3 2×2 contingency table comparing the two areas (infected and clean) of ED with patients affected by COVID-19

	Infected by COVID-19	Non-infected by COVID-19
Infected area	92	90
Clean area	9	1831
Sensitivity	91.1% (88.3–93.3)	
Specificity	95.3% (94.8–95.7)	
NPV	99.5% (99.3–99.6)	
PPV	50.5% (43.2–57.7)	
Accuracy	90.5% (89.8–91.1)	

NPV Negative Predictive Value; *PPV* Positive Predictive Value

Table 2 Characteristics of patients divided between the two areas located inside the ED: the clean area and the infected area

Variables	Infected area	Clean area	*p*
Patients, *n* (%)	182 (9.0)	1840 (91.0)	
Age, years, median (IQR)	63 (44–78)	48 (28–69)	<0.001
Gender, *n* (%)			<0.001
Male	112 (61.5)	931 (50.6)	
Female	70 (38.5)	909 (49.4)	
Triage priority code, *n* (%)			<0.001
Blue and Green	84 (46.2)	1201 (65.3)	
Yellow	57 (31.3)	552 (30.0)	
Orange and Red	41 (22.5)	87 (4.7)	
Parameters, (IQR)			
Temperature (°C)	37.1 (36.5–38.1)	36.2 (36.0–36.6)	<0.001
RR (breaths per minute)	20 (16–28)	16 (14–18)	<0.001
Oxygen saturation (%)	93 (89–97)	98 (96–99)	<0.001
Systolic BP (mmHg)	150 (105–170)	140 (125–160)	0.093
HR (bpm)	90 (78–107)	82 (75–92)	<0.001
Symptoms (%)			
Abdominal pain	4 (2.2)	114 (6.2)	0.029
Trauma	1 (0.5)	443 (24.1)	<0.001
Flu-like symptoms	17 (9.3)	35 (1.9)	<0.001
Dyspnoea	67 (36.8)	45 (2.4)	<0.001
Vomiting or diarrhoea	5 (2.7)	69 (3.8)	0.677
Chest pain	2 (1.1)	86 (4.7)	0.020
Fever	119 (65.4)	33 (1.8)	<0.001
Gynaecological symptoms	0 (0.0)	96 (5.2)	<0.001
Cough	62 (34.1)	40 (2.2)	<0.001
Maxillofacial symptoms	0 (0.0)	345 (18.8)	<0.001
Nose and throat swab executed, *n* (%)	175 (96.2)	421 (22.9)	<0.001
Thorax CT executed, *n* (%)	87 (48.1)	85 (4.6)	<0.001

RAPID DEPLOYMENT OF A FREE, PRIVACY-ASSURED COVID-19 SYMPTOM TRACKER FOR PUBLIC SAFETY DURING REOPENING: SYSTEM DEVELOPMENT AND FEASIBILITY STUDY

Kassaye SG, Spence AB, Lau E, Bridgeland DM, Cederholm J, Dimolitsas S, Smart JC.. JMIR Public Health Surveill. 2020 Aug 13;6(3):e19399. doi: 10.2196/19399.
Level of Evidence: 1 - Mechanism-based reasoning

BLUF

An article from the Georgetown University School of Medicine discusses the creation of an efficient rapid response COVID-19 symptom tracker. The tool is geared toward providing institutions and agencies the ability to assess public safety and infection transmission (Figure 1) while producing convenient summary reports and, contrary to existing forms of contact tracing, protecting personal identifiers, suggesting the opportunity for increased compliance from users and respondents, ideally improving accuracy of COVID-19 tracking. Of note, the publication discusses limited results of a 6-day beta test they conducted, during which they had 48 participants and 1 individual reporting active COVID-19 infection (Table 1).

ABSTRACT

BACKGROUND: Since the emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the number of cases of coronavirus disease (COVID-19) in the United States has exponentially increased. Identifying and monitoring individuals with COVID-19 and individuals who have been exposed to the disease is critical to prevent transmission. Traditional contact tracing mechanisms are not structured on the scale needed to address this pandemic. As businesses reopen, institutions and agencies not traditionally engaged in disease prevention are being tasked with ensuring public safety. Systems to support organizations facing these new challenges are critically needed. Most currently available symptom trackers use a direct-to-consumer approach and use personal identifiers, which raises privacy concerns. OBJECTIVE: Our aim was to develop a monitoring and reporting system for COVID-19 to support institutions conducting monitoring activities without compromising privacy. METHODS: Our multidisciplinary team designed a symptom tracking system after consultation with experts. The system was designed in the Georgetown University AvesTerra knowledge management environment, which supports data integration and synthesis to identify actionable events and maintain privacy. We conducted a beta test for functionality among consenting Georgetown University medical students. RESULTS: The symptom tracker system was designed based on guiding principles developed during peer consultations. Institutions are provided access to the system through an efficient onboarding process that uses clickwrap technology to document agreement to limited terms of use to rapidly enable free access. Institutions provide their constituents with a unique identifier to enter data through a web-based user interface to collect vetted symptoms as well as clinical and epidemiologic data. The website also provides individuals with educational information through links to the COVID-19 prevention recommendations from the US Centers for Disease Control and Prevention. Safety features include instructions for people with new or worsening symptoms to seek care. No personal identifiers are collected in the system. The reporter mechanism safeguards data access so that institutions can only access their own data, and it provides institutions with on-demand access to the data entered by their constituents, organized in summary reports that highlight actionable data. Development of the system began on March 15, 2020, and it was launched on March 20, 2020. In the beta test, 48 Georgetown University School of Medicine students or their social contacts entered data into the system from March 31 to April 5, 2020. One of the 48 users (2%) reported active COVID-19 infection and had no symptoms by the end of the monitoring period. No other participants reported symptoms. Only data with the unique entity identifier for our beta test were generated in our summary reports. CONCLUSIONS: This system harnesses insights into privacy and data sharing to avoid regulatory and legal hurdles to rapid adaption by entities tasked with maintaining public safety. Our pilot study demonstrated feasibility and ease of use. Refinements based on feedback from early adapters included release of a Spanish language version. These systems provide technological advances to complement the traditional contact tracing and digital tracing applications being implemented to limit SARS-CoV-2 transmission during reopening.

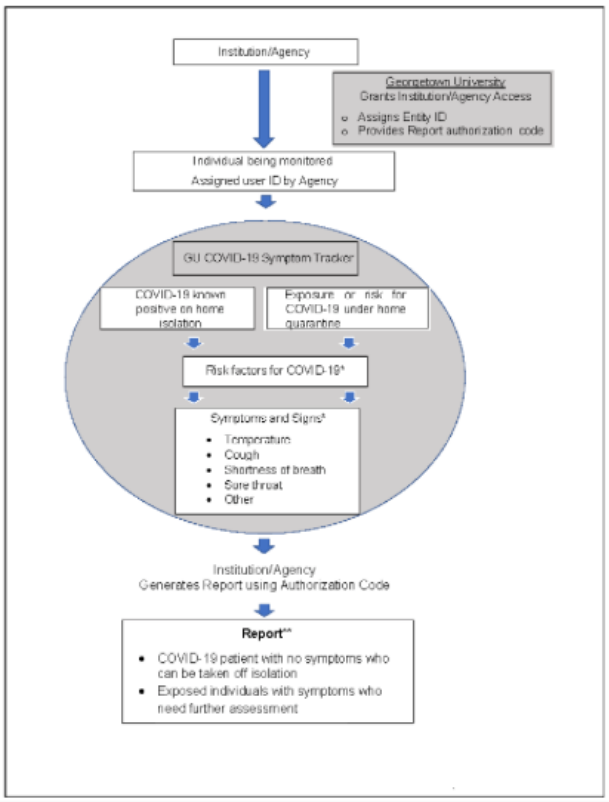

Figure 1. Schema of enrollment in and use of the COVID-19 Symptom Tracker system. COVID-19: coronavirus disease. GU: Georgetown University. *Individuals enter data without personal identifiers based on instructions from the institution or agency. The instructions provided on the website direct individuals with new or worsening symptoms to contact their health care providers. **Institutions and agencies can determine the frequency at which they generate reports.

Report from the beta test from March 31 to April 5, 2020 obtained at 5:49 PM on April 5 (N=48).

Characteristic	Value (%)
COVID-19[a] infection, n (%)	
Infected	1 (2)
Infected with temperature lower than 99.3 °F[b]	1 (2)
Infected with no cough	1 (2)
Infected with no shortness of breath	1 (2)
Infected without data in last 24 hours	0 (0)
Exposure, n (%)	
Exposed but not known to be infected	47 (98)
Exposed with temperature greater than 99.5 °F	0 (0)
Exposed with temperature greater than 100.0 °F	0 (0)
Exposed with cough	0 (0)
Exposed with shortness of breath	0 (0)
Exposed without data in the last 24 hours	38 (79)
Infection source, n (%)	
Infected, exposed by close contact	0 (0)
Infected, exposed by health care worker	1 (2)
Health care workers infected	1 (2)
Infected users, ID number[c]	
Infected with temperature lower than 99.3 °F	GUTST_001111
Infected with no cough	GUTST_001111
Infected with no shortness of breath	GUTST_001111

[a]COVID-19: coronavirus disease.

[b]F: degrees Fahrenheit.

[c]ID numbers have been altered for publication purposes.

Table 1. Report from the beta test from March 31 to April 5, 2020 obtained at 5:49 PM on April 5 (N=48)

POTENTIAL METHANOL TOXICITY AND THE IMPORTANCE OF USING A STANDARDISED ALCOHOL-BASED HAND RUB FORMULATION IN THE ERA OF COVID-19

Dear K, Grayson L, Nixon R.. Antimicrob Resist Infect Control. 2020 Aug 8;9(1):129. doi: 10.1186/s13756-020-00788-5.
Level of Evidence: Other - Review / Literature Review

BLUF

A review of methanol toxicity reports and World Health Organization (WHO) hand sanitizer formulation standards were summarized by authors from Australia to warn against the potential dangers of distilleries producing alcohol-based hand rubs (ABHR) that use methylated spirits (denatured alcohol), which can contain methanol as a substitute for ethanol or isopropyl alcohol. These findings suggest that the general public should not be producing homemade ABHRs and that businesses such as pharmacies and distilleries should follow WHO guidelines in ABHR formulation to avoid potential methanol toxicity via inhalation/ingestion/transdermal absorption.

ABSTRACT

OBJECTIVES: Hand sanitisers are urgently needed in the time of COVID-19, and as a result of shortages, some people have resorted to making their own formulations, including the repurposing of distilleries. We wish to highlight the importance of those producing hand sanitisers to avoid methylated spirits containing methanol and to follow WHO recommended formulations. METHODS: We explore and discuss reports of methanol toxicity through ingestion and transdermal absorption. We discuss the WHO formulations and explain the rationale behind the chosen ingredients. SHORT CONCLUSION: We advise those producing hand sanitisers to follow WHO recommended formulations, and advise those producing hand sanitisers using methylated spirits, to avoid formulations which contain methanol.

DIAGNOSTIC RADIOLOGY

A LOW-DOSE CHEST CT PROTOCOL FOR THE DIAGNOSIS OF COVID-19 PNEUMONIA: A PROSPECTIVE STUDY

Tabatabaei SMH, Talari H, Gholamrezanezhad A, Farhood B, Rahimi H, Razzaghi R, Mehri N, Rajebi H.. Emerg Radiol. 2020 Aug 13. doi: 10.1007/s10140-020-01838-6. Online ahead of print.
Level of Evidence: 4 - Case-control studies, or "poor or non-independent reference standard

BLUF

Radiologists from Kashan University of Medical Sciences in Iran conducted a prospective cohort study comparing radiology detection of COVID-19 pneumonia in low-dose (30 mAs) and standard-dose (150 mAs) chest CT in 20 COVID-19 patients over age 50 with normal chest x-ray between March 15-31, 2020. When compared to standard dose CT they found low dose chest CT also reliably detects COVID-19 pneumonia (intraclass correlation coefficient: 0.98-0.99, p-values<0.001, all readers) (Figure 1) suggesting low-dose CT is a feasible alternative for COVID-19 pneumonia detection with reduced radiation and cancer risk.

ABSTRACT

PURPOSE: The increasing trend of chest CT utilization during the COVID-19 pandemic necessitates novel protocols with reduced dose and maintained diagnostic accuracy. We aimed to investigate the diagnostic accuracy of 30-mAs chest CT protocol in comparison with a 150-mAs standard-dose routine protocol for imaging of COVID-19 pneumonia. METHODS: Upon IRB approval, consecutive laboratory-confirmed positive COVID-19 patients aged 50 years or older who were referred for chest CT scan and had same-day normal CXR were invited to participate in this prospective study. First, a standard-dose chest CT scan (150 mAs) was performed. Only if typical COVID-19 pneumonia features were identified, then a low-dose CT (30 mAs) was done immediately. Diagnostic accuracy of low-dose and standard-dose CT in the detection of typical COVID-19 pneumonia features were compared. RESULTS: Twenty patients with a mean age of 64.20 +- 13.8 were enrolled in the study. There was excellent intrareader agreement in detecting typical findings of COVID-19 pneumonia between low-dose and standard-dose (intraclass correlation coefficient [ICC] = 0.98-0.99, P values < 0.001 all readers). The mean effective dose values in standard- and low-dose groups were 6.60 +- 1.47 and 1.80 +- 0.42 mSv, respectively. Also, absolute cancer risk per mean cumulative effective dose values obtained from the standard- and low-dose CT examinations were 2.71 x 10-4 and 0.74 x 10-4, respectively. CONCLUSIONS: According to our study, it was found that proposed low-dose CT chest protocol is reliable in detecting COVID-19 pneumonia in daily practice with significant reduction in radiation dose and estimated cancer risk.

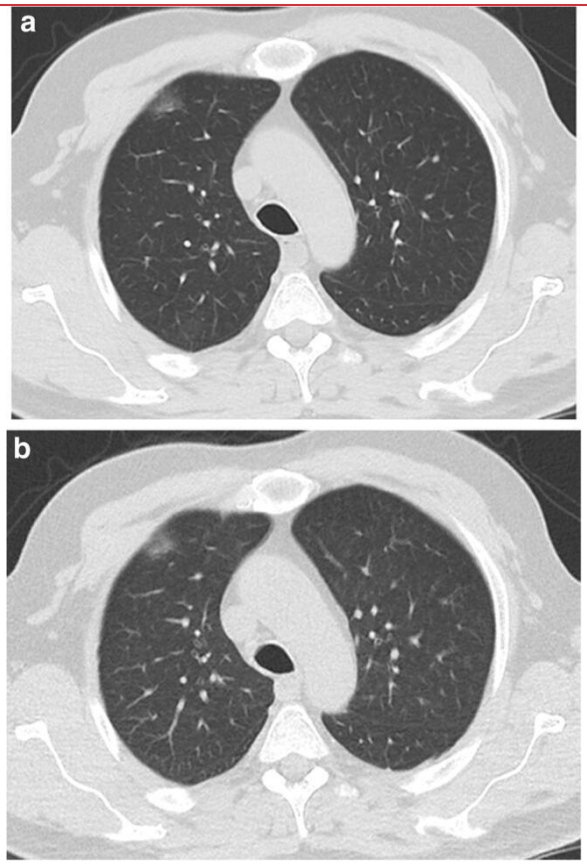

Figure 1a,b: Example chest CT scan of a 66-year-old man with COVID-19 pneumonia. a Standard-dose image; a peripheral patch of ground glass opacity is seen in the anterior segment of the right upper lobe. b Low-dose image at the same level; the lesion is clearly visible. The lesion was scored 2 (definitely present) by all the readers, both on standard- and low-dose CT scans.

COVID-19-ASSOCIATED DELAYED POSTHYPOXIC NECROTIZING LEUKOENCEPHALOPATHY

Radmanesh A, Derman A, Ishida K.. J Neurol Sci. 2020 Aug 15;415:116945. doi: 10.1016/j.jns.2020.116945. Epub 2020 May 27.

Level of Evidence: Other - Case Report

BLUF

A case report conducted at New York University describes a 50-year old male with reverse transcriptase polymerase chain reaction (RT-PCR)-confirmed COVID-19, controlled hypertension, and type 2 diabetes who required intubation on day 2 of care due to a 70% blood oxygen saturation. Although respiratory symptoms improved, depressed mental status persisted. A work-up with brain CT scan (Figure 1) and MRI (Figure 2) revealed hypodensities involving supratentorial white matter and T2 hyperintensities of the periventricular, deep, and subcortical white matter, respectively. This led to the diagnosis of delayed post-hypoxic leukoencephalopathy (white matter degradation) that likely resulted from COVID-19-related hypoxia, suggesting that clinicians who see COVID-19 patients with persistently depressed mental status seek brain imaging.

SUMMARY

A case study conducted at New York University describes a patient that developed delayed post-hypoxic leukoencephalopathy (white matter degradation) as a likely result of COVID-19 related hypoxia. The 50-year old male patient with controlled hypertension and type 2 diabetes presented after 1 week of dyspnea and cough with a 90% blood oxygen saturation that progressed to 70% and required intubation on the second day in care. The patient also received a 5-day course of hydroxychloroquine-azithromycin to treat COVID-19 (present based on a nasopharyngeal swab RT-PCR test), hemodilysis to treat acute tubular necrosis, and piperacillin/tazobactam to treat a Klebsiella becteremia. Over the course of two weeks, respiratory symptoms improved although depressed mental status persisted. A brain CT scan on day 17 of care and an MRI on day 21 of care revealed symmetric confluent hypodensities involving supratentorial white matter and symmetric confluent T2 hyperintensities involving the periventricular, deep, and subcortical white matter, respectively. This led to the diagnosis of delayed post-hypoxic leukoencephalopathy (white matter degradation) that likely resulted from COVID-19-related hypoxia, suggesting that clinicians who see COVID-19 patients with persistently depressed mental status seek brain imaging.

FIGURES

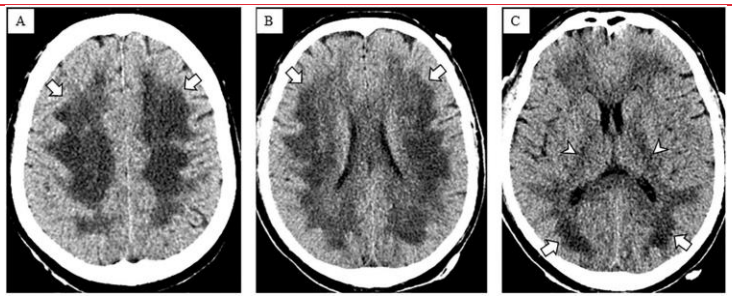

Figure 1: Non-contrast head CT. Axial CT images of the head at the level of the centrum semiovale (A), corona radiata (B), and basal ganglia (C) demonstrate diffuse confluent hypodensities in the supratentorial periventricular, deep and subcortical white matter (arrows) extending into the internal capsules (arrowheads).

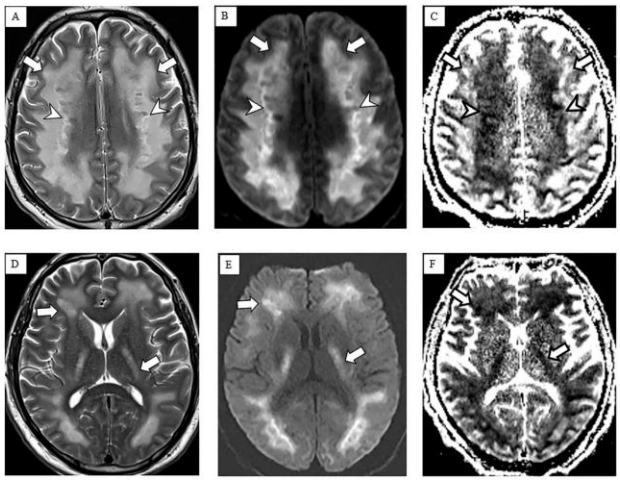

Figure 2: Non-contrast brain MRI. Multiple axial images including T2-weighted (A and D), diffusion-weighted (B and E) and apparent diffusion coefficient (C and F) images demonstrate symmetric confluent supratentorial white matter T2 hyperintensities extending into the internal capsules (arrows in A, D) sparing the subcortical U fibers and deep gray nuclei. Notably, there is reduced diffusion in the more central white matter (arrowheads in B, C) with geographic margins and corresponding internal T2 heterogeneity (arrowheads in A), suggesting areas of active demyelination and necrosis. Susceptibility-weighted images (not shown) did not show any appreciable blood products.

SURGICAL SUBSPECIALTIES

THORACIC SURGERY

THE IMPACT OF COVID-19 PANDEMIC ON CONGENITAL HEART SURGERY PRACTICE: AN ALARMING CHANGE IN DEMOGRAPHICS

Korun O, Yurdakök O, Arslan A, Çiçek M, Selçuk A, Kılıç Y, Altın F, Şaşmazel A, Aydemir NA.. J Card Surg. 2020 Aug 13. doi: 10.1111/jocs.14914. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A retrospective two-cohort study conducted by pediatric cardiac surgeons from Turkey compared data on patients that underwent congenital heart surgery prior to the COVID-19 pandemic (March 11th, 2019 to March 10th, 2020) and during the pandemic (March 11th to May 11th, 2020) at a single center. They found that the monthly average of patients operated on decreased (from 52 to 35, p<0.01), the median pre-operative hospital stay was shorter (3 days to 1 day, p<0.01), and there was no change in postoperative results, highlighting the safety of continuing cardiac surgery as long as appropriate measures such as social distancing are employed. They also found that the percent of patients operated on who were foreign nationals decreased from 7% to 1% (p=0.04), bringing to light the fact that children from deprived areas like Syria have reduced access to cardiac surgery care due to border closures during the pandemic.

ABSTRACT

BACKGROUND: The aim of this study is to investigate the effect of COVID-19 outbreak on congenital cardiac surgery practice in a single center. METHODS: The first case of COVID-19 in our country was seen on March 11th, 2020. The patients operated between March 11th, 2019-and March 10th, 2020 were taken as the pre-COVID group, and those operated between March 11th and May 11th, 2020 were taken as the COVID group. The data was retrospectively collected, and the two periods were compared. RESULTS: Monthly average number of cases which was 52 patients/month (626 patients in 12 months) before COVID decreased to 35 patients/month (70 patients in 2 months) during COVID periods (P < .01). During the pre-COVID period the median postoperative length of hospital stay was 3 (IQR: 1-5) days. During the COVID period, this decreased to 1 (IQR: 1-3) day (P < .01). During the pre-COVID period, the hospital expenses of 17% (8/47) of the foreign nationals were covered by their homeland. The remaining 83% (39/47) were paid from the asylum seekers' fund. The proportion of foreign nationals operated significantly decreased during the COVID period ([7%; 47/632 vs 1%; 1/70]; P = .04). No significant difference was observed in terms of STAT mortality scores and categories and postoperative results of the operations

performed between the two periods. CONCLUSIONS: Congenital cardiac surgery practice can be safely maintained with restricted case volume during the pandemic period. It is alarming that patients in the deprived areas cannot access pediatric cardiac surgery and possibly other health services because of closure of the borders between countries.

OUTCOMES OF PATIENTS DIAGNOSED WITH COVID-19 IN THE EARLY POSTOPERATIVE PERIOD FOLLOWING CARDIAC SURGERY

Yates MT, Balmforth D, Lopez-Marco A, Uppal R, Oo AY.. Interact Cardiovasc Thorac Surg. 2020 Aug 13:ivaa143. doi: 10.1093/icvts/ivaa143. Online ahead of print.
Level of Evidence: 4 - Case-series

BLUF

Cardiothoracic surgeons from St. Bartholomew's Hospital in London analyzed the length of hospital stay and mortality rate for nine patients who underwent cardiac surgery from March 1st, 2020 to March 27th, 2020 and were diagnosed with COVID-19 via positive throat swab (Table 2) in the early postoperative period. The length of hospital stay among patients diagnosed with COVID-19 postoperatively extended past the anticipated time period for elective cardiac surgery and the mortality rate was 44% compared to 5.5% in postoperative patients not diagnosed with COVID-19 (Table 1). The authors argue that additional precautions and protocols need to be implemented to ensure safety and minimize risk of infection with COVID-19 in patients undergoing elective and emergency surgeries.

ABSTRACT

The coronavirus 2019 (COVID-19) pandemic has disrupted patient care across the NHS. Following the suspension of elective surgery, priority was placed in providing urgent and emergency surgery for patients with no alternative treatment. We aim to assess the outcomes of patients undergoing cardiac surgery who have COVID-19 infection diagnosed in the early postoperative period. We identified 9 patients who developed COVID-19 infection following cardiac surgery. These patients had a significant length of hospital stay and extremely poor outcomes with mortality of 44%. In conclusion, the outcome of cardiac surgical patients who contracted COVID-19 infection perioperatively is extremely poor. In order to offer cardiac surgery, units must implement rigorous protocols aimed at maintaining a COVID-19 protective environment to minimize additional life-threatening complications related to this virus infection.

FIGURES

Patient	Male/ female	Age	Preoperative length of stay	Euro SCORE II	Elective/urgent	Operation	Bypass/ cross-clamp	Day of COVID diagnosis	Outcome	Time to outcome
1	Male	62	18	2.5	Urgent	CABG	75/96	3	Died	4
2	Male	56	1	1.03	Elective	CABG	77/86	8	Home	14
3	Male	21	4	0.77	Urgent	AVR	70/92	9	Home	12
4	Male	73	6	7.43	Urgent	MVR + CABG	144/173	8	Died	16
5	Male	72	22	2.97	Urgent	AVR + CABG	133/152	3	Died	11
6	Male	57	5	0.88	Urgent	CABG	84/104	4	Home	6
7	Male	71	16	1.26	Urgent	CABG	37/77	1	Home	16
8	Male	59	23	2.29	Urgent	MVR	84/101	23	Home	7
9	Female	79	1	4.91	Elective	MVR + TVR	73/123	37	Died	2

AVR: aortic valve replacement; CABG: coronary artery bypass grafts; COVID-19: coronavirus 2019; MVR: mitral valve replacement; TVR: tricuspid valve repair.

Table 1. Demographics and outcomes of patients diagnosed with COVID-19 in the postoperative period.

Patient	Day of COVID diagnosis	Outcome	Pyrexia	Raised WCC	Lymphopenia	Raised CRP	CXR changes
1	3	Died	38.4	No	Yes	Yes	Yes
2	8	Home	38	Yes	No	Yes	No
3	9	Home	38.5	No	No	Yes	No
4	8	Died	36.9	No	Yes	Yes	No
5	3	Died	36.7	No	Yes	Yes	Yes
6	4	Home	38.1	No	No	Yes	Yes
7	1	Home	36.5	No	No	No	Yes
8	23	Home	38.6	No	Yes	No	No
9	37	Died	?	Yes	No	Yes	Yes

COVID-19: coronavirus 2019; CRP: c-reactive protein; CXR: chest x-ray; WCC: white cell count.

Table 2. Clinical features on the day of COVID-19 diagnosis.

R&D: DIAGNOSIS & TREATMENTS

PROPOSED LUNG ULTRASOUND PROTOCOL DURING THE COVID-19 OUTBREAK

Vassalou EE, Karantanas AH, Antoniou KM.. J Ultrasound Med. 2020 Aug 6. doi: 10.1002/jum.15402. Online ahead of print.
Level of Evidence: 5 - Guidelines and Recommendations

BLUF

Greek radiologists discuss the use of lung ultrasound (LUS) during the COVID-19 pandemic by proposing an 18-point lateral decubitus LUS protocol (Table 1; modified from Vassalou et al, 2018) with advantages including extensive lung surface inspection, elimination of gravity-related B-line changes (number and morphology), rapid single-operator performance, and minimized contamination risk by reducing patient repositioning and contact. Authors recommend using LUS as a safe, quick, and noninvasive alternative to computed tomography within the emergency department or intensive care unit for assessing lung involvement in COVID-19 pneumonia patients.

FIGURES

Table 1. Recommended Anatomic Sites Assessed by the 18-Point LUS Protocol

	Intercostal Space	
Anatomic Line	**Right Lung**	**Left Lung**
Anterior chest		
Parasternal	–	–
Midclavicular	3rd	3rd
Anterior axillary	–	–
Midaxillary	3rd	3rd
Posterior chest		
Posterior axillary	7th, 8th	7th, 8th
Subscapular	7th, 8th	7th, 8th
Paravertebral	8th–10th	8th–10th

Modified from Vassalou et al.[4]

DEVELOPMENTS IN TREATMENTS

POSSIBLE ROLE OF ABCB1 IN LYSOSOMAL ACCUMULATION OF AZITHROMYCIN IN COVID-19 THERAPY

Scherrmann JM.. Clin Pharmacol Ther. 2020 Aug 17. doi: 10.1002/cpt.2020. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

In response to a review published in April 2020 by Damle et al on the use of azithromycin with hydroxychloroquine to treat COVID-19, an author on the Faculty of Pharmacy, University of Paris, France hypothesizes that the ATP-binding cassette ABCB1 (P-glycoprotein) could enhance their synergistic function by increasing transport and bioavailability. To better understand the mechanism of action of azithromycin as an adjuvant antiviral therapy, the author recommends further study into endolysosomal ABCB1.

ABSTRACT

The antiviral use of azithromycin in COVID-19 was recently reported by Damle et al. Its combination with hydroxychloroquine did not aim at preventing bacterial super-infection as often believed, but at benefiting from their common lysosomotropic properties which buffer the acidic conditions (pH 4-5) of the endolysosomal lumen where SARS-CoV-2 transits following its ACE-2 receptor-mediated endocytosis. These two powerful cationic and amphiphilic drugs increase up to neutrality the intravesicular pH causing disorders in lysosomal functions such as enzyme inhibitions involved in the virus replication cycle. We recently hypothesized that the ATP-binding cassette ABCB1 (P-glycoprotein) could be involved in this reported synergistic effect.

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