

# The Daily COVID-19 Literature Surveillance Summary

**June 5, 2020**



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# COVID-19 Daily Literature Surveillance

COVID19LST



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# 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)
<b>How common is the problem?</b>	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
<b>Is this diagnostic or monitoring test accurate? (Diagnosis)</b>	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
<b>What will happen if we do not add a therapy? (Prognosis)</b>	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
<b>Does this intervention help? (Treatment Benefits)</b>	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
<b>What are the COMMON harms? (Treatment Harms)</b>	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
<b>What are the RARE harms? (Treatment Harms)</b>	Systematic review of randomized trials or n-of-1 trial	Randomized trial or (exceptionally) observational study with dramatic effect	Non-randomized controlled cohort/follow-up study**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning
<b>Is this (early detection) test worthwhile? (Screening)</b>	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:

- High rates of [moral injury and loss of social identity among healthcare workers](#) has authors from the University of Hildesheim advocating for improved stress management techniques to promote positive coping skills. Reported stressors include separation from family, inability to speak out about unsafe working conditions, inadequate resources, and high death rate despite appropriate patient care.
- The COVID-19 pandemic continues to exacerbate health disparities, especially in these vulnerable populations:
  - [Elderly](#) (>85 years of age),
  - [racial and ethnic minorities](#)
  - [Sex workers](#)
  - [Nursing home residents](#), especially those with high minority populations

## Epidemiology:

- A multicenter, retrospective, cross-sectional study conducted in Zhejiang Province, China, from January 17 to February 12, 2020, found that 28.2% of 788 COVID-19-positive patients had elevated liver enzyme levels (ALT >35 for men, >25 for women) on admission, which were independently associated with male sex, being overweight, history of smoking, and symptom presentation of diarrhea (Table 4). No differences were found in disease severity or clinical outcomes between the groups with and without elevated liver enzymes (Figure 1), and the authors admit that the pathogenesis of the elevation remains unknown.
- Iranian researchers review [neurologic manifestations of COVID-19](#):
  - Over 1/3 of patients experienced neurologic symptoms, commonly as the initial or only chief complaint.
  - CNS manifestations: Headache, dizziness, altered consciousness, and acute cerebrovascular disease.
  - PNS Manifestations: Anosmia, ageusia, muscle pain, and rarely [Guillain-Barre syndrome \(GBS\)](#)
- 2 surveillance studies from Seattle, WA found a relatively low prevalence of asymptomatic disease among [pregnant](#) (1.2%) and [pre-procedural patients](#) (<1%) screened with RT-PCR testing.

## Understanding the Pathology:

- A cross-sectional study of 34 adult male COVID-19 patients in Wuhan, China found [no evidence of SARS-CoV-2 in semen samples](#) within 31 days of their COVID-19 diagnosis. This contradicts a [previous study](#) that found RT-PCR positivity in 6 of 38 patients, prompting the need for further investigation.
- A colonoscopy performed on a 40-year-old COVID-19 patient with pneumonia and bloody diarrhea, revealed [SARS-CoV-2 infection of intestinal endothelial cells](#) via immunohistochemistry (IHC). Authors promote IHC as a useful diagnostic adjunct, and propose direct intestinal injury as a potential disease mechanism.

## Transmission and Prevention:

- Harvard physicians review the literature on [asymptomatic and presymptomatic transmission](#) of COVID-19.
- Washington State public health officials [conducted extensive contact tracing](#) on the first patient diagnosed with COVID-19 in the US. They found that [none](#) of the 78% of identified contacts who agreed to testing were positive by either RT-PCR or follow-up serology, despite 29% reporting prolonged and unprotected exposure. This lack of secondary transmission may be explained by multiple factors including exposure type, duration, and frequency, as well as the patient's viral load, disease severity, and timing of exposure during the course of disease.

## Management:

- Guidelines for management of COVID-19 patients from today includes imaging guidance for [pediatric pulmonologists](#)
- Investigators detail treatment of a COVID-19 patient with significant cardiac comorbidities with [mechanical circulatory support and implantable ventricular assist devices](#).
- Cardiologists continue to warn of the dangers of [QT-prolonging medications](#) such as hydroxychloroquine and suggest that critically-ill COVID-19 patients be screened for cardiac abnormalities prior to treatment with these drugs.

## Adjusting Practice:

- Authors from Kaohsiung Medical University Hospital in Taiwan describe an algorithm for the [remote management of chronic wound care](#) and follow up care to during the pandemic.
- A group of US neuromuscular specialists call for equitable triage decision-making during the COVID-19 crisis and propose guidelines to ensure [triage algorithms take children into consideration](#).

## R&D Diagnosis and Treatment:

- A group of Harvard investigators detail the [current diagnostic methods for COVID-19](#) including the current status of nucleic antigen and serologic tests.

- A group of pathologists in Brazil [correlated specific ultrasound findings to histological patterns](#) through post-mortem analysis of COVID-19 lung tissue adding to the utility of ultrasound in characterization of the disease.
- Investigators compared the Roche [SARS-CoV-2 serologic antibody assay](#) to the Abbot and EUROIMMUN assays and found a specificity of 98.69% and sensitivity of 89.36%--results similar to the other two assays.

#### **Mental Health and Resilience:**

- German researchers studying [psychosocial responses and coping strategies from past pandemics](#) found that psychological reactions are often complex, contradictory, and a multi-step process.
- [Lessons from Lombardy](#): Italian authors outline the psychological support systems that were implemented for healthcare workers, patients, and their families during the peak of the COVID-19 pandemic.

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## CLIMATE

### AFFECTING THE HEALTHCARE WORKFORCE

#### SHATTERED SOCIAL IDENTITY AND MORAL INJURIES: WORK-RELATED CONDITIONS IN HEALTH CARE PROFESSIONALS DURING THE COVID-19 PANDEMIC

Kröger C.. Psychol Trauma. 2020 May 28. doi: 10.1037/tra0000715. Online ahead of print.

Level of Evidence: Other

#### BLUF

A review conducted at the University of Hildesheim found that many healthcare workers are experiencing loss of their social identities and increased moral injuries due to the stresses caused by the COVID-19 pandemic, suggesting a need to teach stress management techniques to healthcare providers. Examples of these stressors include separation from family, inability to speak out about unsafe working conditions, lack of access to adequate resources, loss of resilience, and high death rate despite appropriate patient care. Specific examples are provided in Table 1.

#### ABSTRACT

The present article assesses the effects of shattered social identity and moral injuries experienced by health care professionals (HCPs) due to the COVID-19 pandemic. Professional expertise and emotional-cognitive demands as key aspects of HCPs' social identity are introduced, and the effects of moral injuries-in terms of violation of medical-ethical and social-ethical norms-on the mental health of HCPs are discussed. (PsycInfo Database Record (c) 2020 APA, all rights reserved).

#### FIGURES

Table 1

*Experiences That Shattered Social Identity and Caused Moral Injuries*

Challanged beliefs	Experiences
Social identity	A chief physician recognized that he was not familiar with the respiratory procedure for patients with COVID-19; hence, he acknowledged that patients who died might be still alive.
Professional expertise	It is only now known that if the HCP's protective mask does not seal the mouth and nose area airtight, he or she is exposed to a high density of the COVID-19 virus while performing life-saving measures.
Emotional-cognitive demands	Two young physicians got into a dispute as to which kind of masks should be used inside a room full of patients with COVID-19. One physician pushed his colleague, whereupon the other reacted by delivering a heavy punch to his coworker's nose.
Moral injuries	After unsuccessful intensive medical care on the part of a colleague, a nurse realized how the usually strict separation of the roles between the health care professional and the patient (i.e., translated from Latin: "the sufferer") became artificial and vanished. She had to take a break for the rest of day because she was emotionally exhausted.
Medical-ethical norms	A chief physician decided against life-saving measures that may keep one patient alive but led to the death of others. The physician told a managing director about the stressful situation, hoping that he might provide more appropriate respirators. The manager interrupted him and said with a short laugh: "That's your job!"
Social-ethical norms	A nurse is encouraged to shut off the respirator and remove the tubes, knowing that she will cause the death of a patient. Due to fear of infection, HCPs are prohibited from entering certain shops and pharmacies, or from bringing their children to kindergarten. Although the right of parenting is coded into the law, HCPs are not allowed to see their children and must even live separated from their families following 12-hour deployments.

Note. HCP = health care professional.

## DISPARITIES

#### CHARACTERISTICS OF U.S. NURSING HOMES WITH COVID-19 CASES

Abrams HR, Loomer L, Gandhi A, Grabowski DC.. J Am Geriatr Soc. 2020 Jun 2. doi: 10.1111/jgs.16661. Online ahead of print.

Level of Evidence: 3

## BLUF

Authors from Boston Massachusetts discuss data from "a database [they created] of nursing homes with verified COVID-19 cases as of May 11, 2020". They found that traditional metrics (details below) for assessing nursing home quality do not reflect actual COVID-19 incidence rates. Rather, location, facility size, percentage of African-American residents, and non-chain status were correlated with higher probability of having a COVID-19 patient ( $p<0.05$ ), suggesting the need for new approaches to infection control.

## SUMMARY

The authors found that traditional metrics for assessing nursing home quality including: five-star rating, prior infection violation, Medicaid dependency, and ownership were not significantly related to the likelihood of a facility having COVID-19 patients. Rather, urban locations, larger facilities, facilities with a higher percentage of African-American residents, and non-chain nursing homes were more likely to have COVID-19 patients. However, state by state differences in reporting and lack of COVID-19 mortality data for May 2020 in some facilities may affect the results.

## ABSTRACT

**BACKGROUND:** COVID-19 has been documented in a large share of nursing homes throughout the United States. This has led to high rates of mortality for residents. In order to understand how to prevent and mitigate future outbreaks, it is imperative that we understand which nursing homes are more likely to experience COVID-19 cases.

**OBJECTIVE:** To examine the characteristics of nursing homes with documented COVID-19 cases in 30 states reporting individual facilities affected.

**DESIGN AND SETTING:** We constructed a database of nursing homes with verified COVID-19 cases as of May 11, 2020 via correspondence with and publicly available reports from state departments of health. We linked this information to nursing home characteristics and used regression analysis to examine association between these characteristics and the likelihood of having a documented COVID-19 case.

**RESULTS:** Of 9,395 nursing homes in our sample, 2,949 (31.4%) had a documented COVID-19 case. Larger facility size, urban location, greater percentage of African American residents, non-chain status, and state were significantly ( $p<0.05$ ) related to increased probability of having a COVID-19 case. Five-star rating, prior infection violation, Medicaid dependency, and ownership were not significantly related.

**CONCLUSIONS:** COVID-19 cases in nursing homes are related to facility location and size and not traditional quality metrics such as star rating and prior infection control citations. This article is protected by copyright. All rights reserved.

## FIGURES

Nursing Home Characteristics	Nursing Homes		Probability of any case n=9,395	Outbreak size n=2,575 Percentage Point Change
	Without COVID-19 n=6,446 (68.6%)	With COVID-19 n=2,949 (31.4%)		
	No. (%)	No. (%)		
Size				
Small (<50 Beds)	869 (86.9%)	131 (13.1%)	Reference	Reference
Medium (50-150 Beds)	4777 (70.9%)	1960 (29.1%)	2.63***	-10.80***
Large (>150 Beds)	800 (48.3%)	858 (51.7%)	6.52**	-15.88*
Ownership				
For-Profit	4651 (67.6%)	2227 (32.4%)	1.07	1.88*
Non-profit	1534 (70.4%)	644 (29.6%)	Reference	Reference
Government	261 (77.0%)	78 (23.0%)	0.84	-2.58
Non-Chain	2779 (67.9%)	1312 (32.1%)	Reference	Reference
Chain	3667 (69.1%)	1637 (30.9%)	0.89*	1.39
Resident characteristics				
Low Medicaid share	5827 (69.0%)	2623 (31.0%)	Reference	Reference
High Medicaid share	619 (65.5%)	326 (34.5%)	0.97	-0.79
Low Black resident share	5570 (71.7%)	2201 (28.3%)	Reference	Reference
High Black resident share	876 (53.9%)	748 (46.1%)	2.05***	1.44
Rural	2001 (89.7%)	229 (10.3%)	Reference	Reference
Urban	4445 (62.0%)	2720 (37.9%)	3.22***	1.28
Overall Five-Star Rating				
1	1109 (69.5%)	486 (30.5%)	Reference	Reference
2	1259 (66.9%)	622 (33.1%)	1.07	0.20
3	1162 (67.6%)	557 (32.4%)	1.23*	0.34
4	1394 (69.8%)	602 (30.2%)	1.07	-0.09
5	1522 (69.1%)	682 (30.9%)	1.18	1.07
No Infection Violation	3614 (69.5%)	1584 (30.5%)	Reference	Reference
Prior Infection Violation	2832 (67.5%)	1365 (32.5%)	0.99	-0.58
State				
CA	802 (69.3%)	356 (30.7%)	0.51***	Reference
CO	133 (66.5%)	67 (33.5%)	0.81	19.65***
CT	68 (31.9%)	145 (68.1%)	2.62***	13.54***
DE	29 (65.9%)	15 (34.1%)	0.54	N/A
FL	385 (58.3%)	275 (41.7%)	0.73	-4.51***
GA	132 (38.9%)	207 (61.1%)	1.98***	3.53
IA	383 (93.4%)	27 (6.6%)	0.19***	24.61***
IL	446 (64.2%)	249 (35.8%)	0.67*	4.86***
KY	258 (96.3%)	10 (3.7%)	0.07***	N/A
LA	240 (89.5%)	28 (10.5%)	0.10***	N/A
MA	81 (22.0%)	288 (78.0%)	4.36***	9.06***
MD	79 (36.1%)	140 (63.9%)	1.57*	10.28***
ME	89 (96.7%)	3 (3.3%)	0.08***	N/A
MI	270 (66.3%)	137 (33.7%)	0.69	4.80***
MN	278 (79.7%)	71 (20.3%)	0.54**	N/A
NC	355 (88.5%)	46 (11.5%)	0.14***	14.06***
ND	57 (73.1%)	21 (26.9%)	1.32	-7.31***
NJ	39 (11.4%)	303 (88.6%)	7.16***	28.37***
NM	50 (79.4%)	13 (20.6%)	0.55	N/A
NV	26 (53.1%)	23 (46.9%)	1.30	8.80
NY	512 (85.6%)	86 (14.4%)	0.10***	N/A

Table 1a. Characteristics of Nursing Homes with reported cases of COVID-19

OH	712 (80.9%)	168 (19.1%)	0.33***	3.59
OK	233 (84.1%)	44 (15.9%)	0.37***	7.25
OR	112 (91.1%)	11 (8.9%)	0.15***	N/A
RI	37 (50.0%)	37 (50.0%)	1.13	15.01 ***
SC	129 (72.9%)	48 (27.1%)	0.40***	-1.77
TN	265 (91.1%)	26 (8.9%)	0.12***	3.00
VT	29 (87.7%)	4 (12.1%)	0.43	18.88
WA	119 (60.1%)	79 (39.9%)	Reference	N/A
WV	98 (81.7%)	22 (18.3%)	0.46**	2.10

Notes: \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$ ; N/A: State does not report case counts. Outbreak size is the number of reported cases divided by the number of beds, multiplied by 100. Data were collected through May 11, 2020.

Table 1b. Characteristics of Nursing Homes with reported cases of COVID-19

## COVID-19 AND SEX WORKERS: HUMAN RIGHTS, THE STRUGGLE FOR SAFETY AND MINIMUM INCOME

Jozaghi E, Bird L.. Can J Public Health. 2020 Jun 2. doi: 10.17269/s41997-020-00350-1. Online ahead of print.

Level of Evidence: Other

### BLUF

This letter summarizes the impact COVID-19 has had on sex workers in Canada as the pandemic has exacerbated restrictions put in place by existing prostitution laws, resulting in financial hardship and increased “risky situations” for sex workers because they do not qualify for government aid during this pandemic. This has important implications from a public health standpoint as this is a vulnerable population and the authors speculate that current circumstances may predispose sex workers to COVID-19 infection. Additional harm may come to these workers from a COVID-19 infection due to a lack of health insurance.

## STAYING ISOLATED IN ORDER TO STAY SAFE: EXPLORING EXPERIENCES OF THE MIT AGELAB 85+ LIFESTYLE LEADERS DURING THE COVID-19 PANDEMIC

Miller JB, Patskanick TR, D'Ambrosio LA, Coughlin JF.. J Gerontol Soc Work. 2020 Jun 2:1-2. doi:

10.1080/01634372.2020.1772437. Online ahead of print.

Level of Evidence: Other

### BLUF

An ongoing study of persons 85 years of age and older during the COVID-19 pandemic found that this population experienced uncertainties over how to seek help should they require it, food scarcity, and their susceptibility to the disease. The authors suggest these areas be addressed through familiarizing leaders with technological tools to stay connected, providing volunteer opportunities to keep individual engaged in their community, and helping with food delivery.

### SUMMARY

In March 2020 the authors, utilizing the MIT AgeLab's 85+ Lifestyle Leaders panel, engaged in a mixed methods research study to learn about the struggles of persons 85 years of age and older during the COVID-19 pandemic. Through the use of an online survey, weekly phone interviews, and a longitudinal diary study, data was collected and continues to be gathered. The authors' early observations included that for those who already had physical mobility issues, the demands of social and physical isolation were “largely business as usual.” Additionally, many experienced uncertainty about who they could turn to for help should they require it, the scarcity of food, and, given the diseases predilection for older population, their own susceptibility to and mortality from the disease. The authors recommend recruiting social workers to address these concerns by increasing the 85+ Lifestyle Leaders' familiarity with technological tools that would help them stay connected, decrease their sense of helplessness by presenting practical volunteer opportunities, and help them get their basic necessities, such as food delivery, met. As the study continues, the authors anticipate making more discoveries on how to better serve this group.

## COVID-19 PANDEMIC: EXACERBATING RACIAL/ETHNIC DISPARITIES IN LONG-TERM SERVICES AND SUPPORTS

Shippee TP, Akosionu O, Ng W, Woodhouse M, Duan Y, Thao MS, Bowblis JR.. J Aging Soc Policy. 2020 May 31:1-11. doi: 10.1080/08959420.2020.1772004. Online ahead of print.

Level of Evidence: Other

### BLUF

The authors illustrate the increasing disadvantages in long-term services and supports (LTSS) faced by racial and ethnic minorities during the COVID-19 pandemic (see below). To reduce a disproportionate effect of the COVID-19 pandemic on

minority populations they recommend reporting COVID-19 LTSS data by race/ethnicity, increasing support for minorities, and addressing existing racial disparities.

## **SUMMARY**

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Issues faced by racial and ethnic minorities in accessing long-term services and supports (LTSS).

- Less access to health insurance and health care contribute to the cumulative health disparities.
- Worsening clinical and quality of care among non-white nursing home patients.
- Reduced level of care for patients with low English proficiency due to lower access to medical interpreters.
- Lack of resources to support and protect minority LTSS staff members.
- Substantially lower quality home and community-based LTSS for minorities compared to white counterparts.

## **ABSTRACT**

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What services are available and where racial and ethnic minorities receive long-term services and supports (LTSS) have resulted in a lower quality of care and life for racial/ethnic minority users. These disparities are only likely to worsen during the COVID-19 pandemic, as the pandemic has disproportionately affected racial and ethnic minority communities both in the rate of infection and virus-related mortality. By examining these disparities in the context of the pandemic, we bring to light the challenges and issues faced in LTSS by minority communities with regard to this virus as well as the disparities in LTSS that have always existed.

## EPIDEMIOLOGY

### SYMPTOMS AND CLINICAL PRESENTATION

#### ADULTS

#### PRE-PROCEDURAL SURVEILLANCE TESTING FOR SARS-COV-2 IN AN ASYMPTOMATIC POPULATION IN THE SEATTLE REGION SHOWS LOW RATES OF POSITIVITY

Mays JA, Greninger AL, Jerome KR, Lynch JB, Mathias PC.. J Clin Microbiol. 2020 Jun 3:JCM.01193-20. doi: 10.1128/JCM.01193-20. Online ahead of print.

Level of Evidence: 3

#### BLUF

A letter to the editor details an analysis from the University of Washington School of Medicine hospital system in Seattle, WA which used nasopharyngeal swab screening of patients prior to admission since April 13, 2020. They found <1% of asymptomatic patients without known exposure risk tested positive for COVID-19 (n not given for asymptomatic cohort) while 137 of 1336 (10.3%) symptomatic patients tested positive. Per the authors, this suggests a lower rate of asymptomatic carriage of COVID-19 than some reports have shown. It should be noted their letter does not detail participant characteristics except race and age and may not be generalizable to other populations.

#### LIVER ENZYME ELEVATION IN CORONAVIRUS DISEASE 2019: A MULTICENTER, RETROSPECTIVE, CROSS-SECTIONAL STUDY

Hao SR, Zhang SY, Lian JS, Jin X, Ye CY, Cai H, Zhang XL, Hu JH, Zheng L, Zhang YM, Jia HY, Yu GD, Wang XY, Gu JQ, Lu YF, Yu XP, Yu L, Xiang DR, Ye CY, Jin CL, Qiu YQ, Li LJ, Sheng JF, Liang TB, Yang YD.. Am J Gastroenterol. 2020 Jun 1. doi: 10.14309/ajg.0000000000000717. Online ahead of print.

Level of Evidence: 3

#### BLUF

A multicenter, retrospective, cross-sectional study conducted in Zhejiang Province, China, from January 17 to February 12, 2020, found that 28.2% of 788 COVID-19-positive patients had elevated liver enzyme levels (ALT >35 for men, >25 for women) on admission, which were independently associated with male sex, being overweight, history of smoking, and symptom presentation of diarrhea (Table 4). No differences were found in disease severity or clinical outcomes between the groups with and without elevated liver enzymes (Figure 1), and the authors admit that the pathogenesis of the elevation remains unknown.

#### ABSTRACT

**INTRODUCTION:** Elevated liver enzyme levels are observed in patients with coronavirus disease 2019 (COVID-19); however, these features have not been characterized. **METHODS:** Hospitalized patients with COVID-19 in Zhejiang Province, China, from January 17 to February 12, 2020, were enrolled. Liver enzyme level elevation was defined as alanine aminotransferase level >35 U/L for men and 25 U/L for women at admission. Patients with normal alanine aminotransferase levels were included in the control group. Reverse transcription polymerase chain reaction was used to confirm severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, and patients symptomatic with SARS-CoV-2 infection were defined as patients with COVID-19. Epidemiological, demographic, clinical, laboratory, treatment, and outcome data were collected and compared. **RESULTS:** Of 788 patients with COVID-19, 222 (28.2%) patients had elevated liver enzyme levels (median [interquartile range {IQR}] age, 47.0 [35.0-55.0] years; 40.5% women). Being male, overweight, and smoking increased the risk of liver enzyme level elevation. The liver enzyme level elevation group had lesser pharyngalgia and more diarrhea than the control group. The median time from illness onset to admission was 3 days for liver enzyme level elevation groups (IQR, 2-6), whereas the median hospitalization time for 86 (38.7%) discharged patients was 13 days (IQR, 11-16). No differences in disease severity and clinical outcomes were noted between the groups. **DISCUSSION:** We found that 28.2% of patients with COVID-19 presented with elevated liver enzyme levels on admission, which could partially be related to SARS-CoV-2 infection. Male patients had a higher risk of liver enzyme level elevation. With early medical intervention, liver enzyme level elevation did not worsen the outcomes of patients with COVID-19.

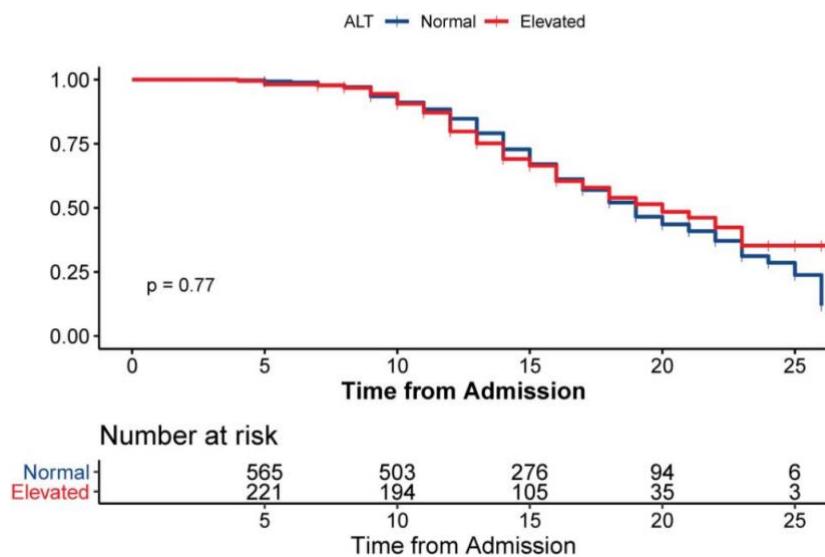
## FIGURES

**Table 4.** Univariable analysis of factors significantly associated with liver enzyme elevation

Risk factor	Odds ratio (95% CI)	P value
Male sex	1.552 (1.133–2.126)	0.006
Overweight	2.143 (1.417–3.240)	<0.001
Smoker	1.836 (1.042–3.235)	0.036
Traveled to Wuhan	0.708 (0.518–0.967)	0.030
Contact with confirmed patients	1.410 (1.032–1.927)	0.031
Pharyngalgia	0.449 (0.264–0.763)	0.003
Diarrhea	1.814 (1.065–3.092)	0.029
Hemoglobin	1.021 (1.011–1.031)	<0.001
Procalcitonin	10.811 (1.151–101.505)	0.037

Overweight was defined as BMI  $\geq 24.0 \text{ kg/m}^2$ .  
BMI, body mass index; CI, confidence interval.

Kaplan–Meier Curve for COVID–19 hospitalization time



## PREVALENCE, RISK FACTORS AND CLINICAL OUTCOMES OF COVID-19 IN PATIENTS WITH A HISTORY OF PANCREATITIS IN NORTHERN CALIFORNIA

Gubatan J, Levitte S, Patel A, Balabanis T, Sharma A, Jones E, Lee B, Manohar M, Swaminathan G, Park W, Habtezion A.. Gut. 2020 Jun 3:gutjnl-2020-321772. doi: 10.1136/gutjnl-2020-321772. Online ahead of print.  
Level of Evidence: 4

### BLUF

This retrospective study analyzed 14,235 patients who tested positive for SARS-CoV-2 RNA at Stanford Hospital from 4 March to 14 April 2020 in order to estimate the prevalence of COVID-19 patients with concomitant pancreatitis (Table 1). The results

concluded 102 of the patients that tested positive for SARS-CoV-2 also had either acute (85.3%) or chronic (14.7%) pancreatitis, and the prevalence of COVID-19 among patients with prior pancreatitis was 7.8%. Compared to the general population prevalence of COVID-19 (2.8%), these results suggest a higher susceptibility to COVID-19 in patients with history of pancreatitis.

## FIGURES

**Table 1** Baseline clinical characteristics of patients with prior pancreatitis tested for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)

Clinical variables	All prior pancreatitis	SARS-CoV-2 RNA	SARS-CoV-2-RNA	P value
	Patients (n=102)	Negative (n=94)	Positive (n=8)	
<b>Demographics</b>				
Age, years (SD)	55.3 ( $\pm 18.7$ )	54.2 ( $\pm 18.5$ )	69.3 ( $\pm 16.4$ )	0.039
Male gender, n (%)	41 (40.2)	35 (37.2)	6 (75.0)	0.036
Asian ethnicity, n (%)	11 (10.8)	8 (8.5)	3 (37.5)	0.011
<b>History of pancreatitis</b>				
Acute, total, n (%)	87 (85.3)	81 (86.2)	6 (75.0)	0.392
Chronic, total, n (%)	15 (14.7)	13 (13.8)	2 (25.0)	0.334
<b>Aetiology of pancreatitis</b>				
Idiopathic, n (%)	43 (42.2)	36 (38.3)	7 (87.5)	0.007
Gallstone, n (%)	30 (29.4)	29 (30.9)	1 (12.5)	0.274
Alcohol, n (%)	13 (12.7)	13 (13.8)	0 (0.0)	0.260
Drug induced, n (%)	7 (6.9)	7 (7.4)	0 (0.0)	0.424
Autoimmune, n (%)	4 (3.9)	4 (4.3)	0 (0.0)	0.552
Hypertriglyceridaemia, n (%)	1 (1.0)	1 (1.1)	0 (0.0)	0.768
Post-ERCP, n (%)	3 (2.9)	3 (3.2)	0 (0.0)	0.608
Cystic fibrosis, n (%)	2 (2.0)	2 (2.1)	0 (0.0)	0.769

ERCP, endoscopic retrograde cholangiopancreatography.

## THE NEUROLOGICAL MANIFESTATIONS OF COVID-19: A REVIEW ARTICLE

Niazkar HR, Zibaei B, Nasimi A, Bahri N.. Neurol Sci. 2020 Jun 1. doi: 10.1007/s10072-020-04486-3. Online ahead of print.

Level of Evidence: Other

### BLUF

Two Iranian researchers review neurologic manifestations of COVID-19 finding that headache, dizziness, impaired consciousness, and acute cerebrovascular disease are some of the most commonly reported central nervous system (CNS) symptoms. Hyposmia/anosmia, hypogeusia/ageusia, muscle pain, and rarely Guillain-Barre syndrome (GBS) are some of the most commonly reported peripheral nervous system (PNS) manifestations. Over 1/3 of patients with COVID-19 experienced neurologic symptoms during their illness and, for some of these patients, these symptoms were the initial or only presentation. These findings suggest that patients presenting with isolated neurologic symptoms warrant early testing and isolation.

### ABSTRACT

**RESULTS:** Various neurological manifestations have been reported in the literature associated with COVID-19, which in the current study are classified into Central Nervous System (CNS) related manifestations including headache, dizziness, impaired consciousness, acute cerebrovascular disease, epilepsy, and Peripheral Nervous System (PNS) related manifestations such as hyposmia/anosmia, hypogeusia/ageusia, muscle pain, and Guillain-Barre syndrome.

**CONCLUSION:** During the current context of COVID-19 pandemic, physicians should be aware of wide spectrum of neurological COVID-19 sign and symptoms for early diagnosis and isolation of patients. In this regard, COVID-19 has been associated with many neurological manifestations such as confusion, anosmia, and ageusia. Also, various evidences support the possible CNS roles in the COVID-19 pathophysiology. In this regard, further investigation of CNS involvement of SARS-CoV-2 is suggested.

## PREGNANT PERSONS

### LOW PREVALENCE OF SARS-COV-2 AMONG PREGNANT AND POSTPARTUM PATIENTS WITH UNIVERSAL SCREENING IN SEATTLE, WASHINGTON

LaCourse SM, Kachikis A, Blain M, Simmons LE, Mays JA, Pattison AD, Salerno CC, McCartney SA, Kretzer NM, Resnick R, Shay RL, Savitsky LM, Curtin AC, Huebner EM, Ma KK, Delaney S, Delgado C, Schippers A, Munson J, Pottinger PS, Cohen S,

## BLUF

A retrospective cohort study conducted in the Labor and Delivery Unit at the University of Washington early April found that approximately 20% (19.1-22.2%) of symptomatic women and 1.2% of asymptomatic women tested positive for COVID-19, suggesting a low prevalence of SARS-CoV-2 among pregnant and postpartum patients in Washington State. See figure for additional details on study findings.

## ABSTRACT

We found a low prevalence of SARS-CoV-2 (2.7% [5/188]) among pregnant and postpartum patients after initiating universal testing. Prevalence among symptomatic patients (22.2% [4/18]) was similar to initial targeted screening approaches (19.1% [8/42]). Among 170 asymptomatic patients, two were positive or inconclusive, respectively; repeat testing at 24 hours was negative.

## FIGURES

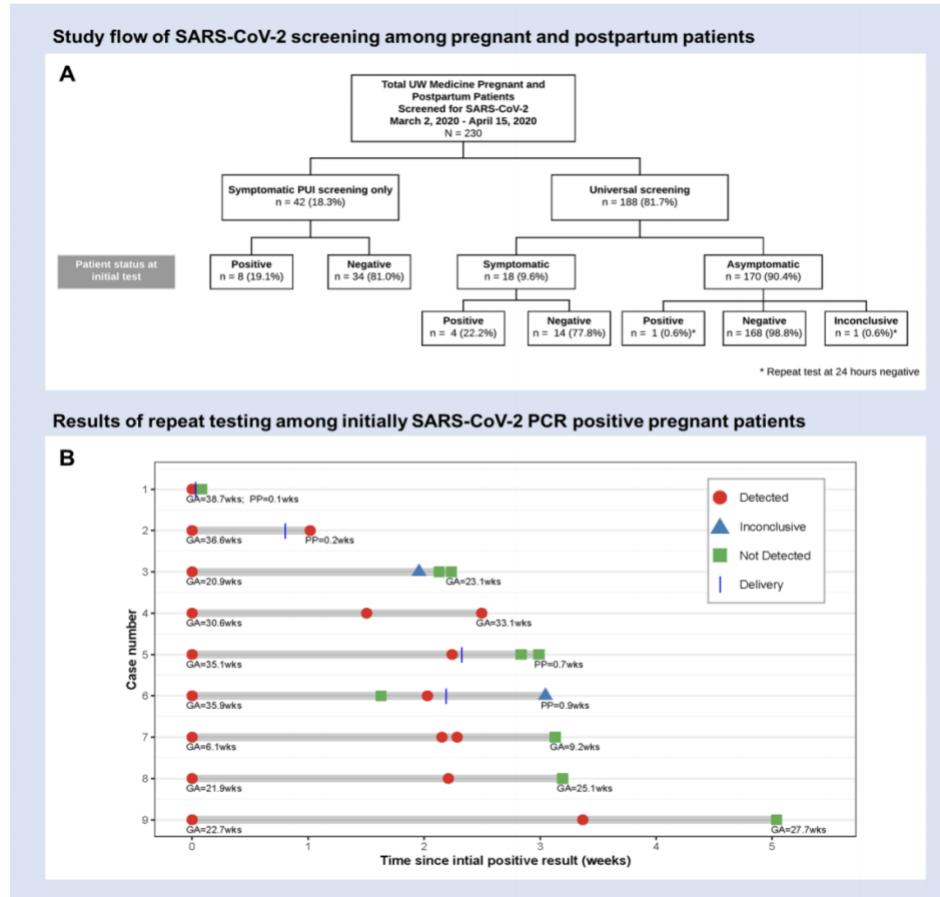


Figure 1: SARS-CoV-2 screening among pregnant and postpartum patients in the UW Medicine system, Seattle, Washington. Panel A: Study flow of pregnant and postpartum patients screened for SARS-CoV-2 prior to and after initiation of universal screening in Seattle, Washington. Figure includes results of initial testing only.

## PEDIATRICS

### COVID-19 PRESENTING WITH AUTOIMMUNE HEMOLYTIC ANEMIA IN THE SETTING OF UNDERLYING IMMUNE DYSREGULATION

Wahlster L, Weichert-Leahy N, Trissal M, Grace RF, Sankaran VG.. Pediatr Blood Cancer. 2020 Jun 3:e28382. doi: 10.1002/pbc.28382. Online ahead of print.

Level of Evidence: Other

## BLUF

A case report conducted in Boston, Massachusetts during April of 2020 by Boston Children's Hospital presents a case of a 17 y.o. male with a history of autoimmune thrombocytopenia developing concurrent hemolytic anemia while infected with SARS-CoV-2. Based on this case report, the authors suggest that patients with autoimmune disease who contract COVID-19 may present atypically.

## SUMMARY

The authors present the case of a 17 y.o. male with a history of refractory chronic immune thrombocytopenia (cITP) and pancytopenia with persistently elevated double negative T cells. The patient presented with jaundice and 4 day history of emesis, diarrhea, and fever and tested positive via PCR nasopharyngeal swab for SARS-CoV-2. Direct agglutination test (DAT) was positive and other laboratory studies suggested new development of autoimmune hemolysis (hemoglobin 2.5 g/dL, absolute reticulocyte count 0.011 cells/ $\mu$ L, LDH 1280 units/L, and total bilirubin of 8.9 mg/dL; history revealed previous DAT tests were negative) (Figure 1). Treatment included oxygen, blood transfusion, and IV corticosteroids. Oxygen status normalized following blood transfusion and within 48 hours the hemolysis improved with "stabilized hemoglobin and significant decrease in bilirubin and LDH" (post-treatment values not given). The steroids were tapered and the patient was restarted on eltrombopag and mycophenolate, which had previously afforded good control of the patient's cITP. Though the authors acknowledge no direct causal relationship between the development of hemolytic anemia and SARS-CoV-2 infection they suggest COVID-19 may contribute to the development of new autoantibodies.

## FIGURES

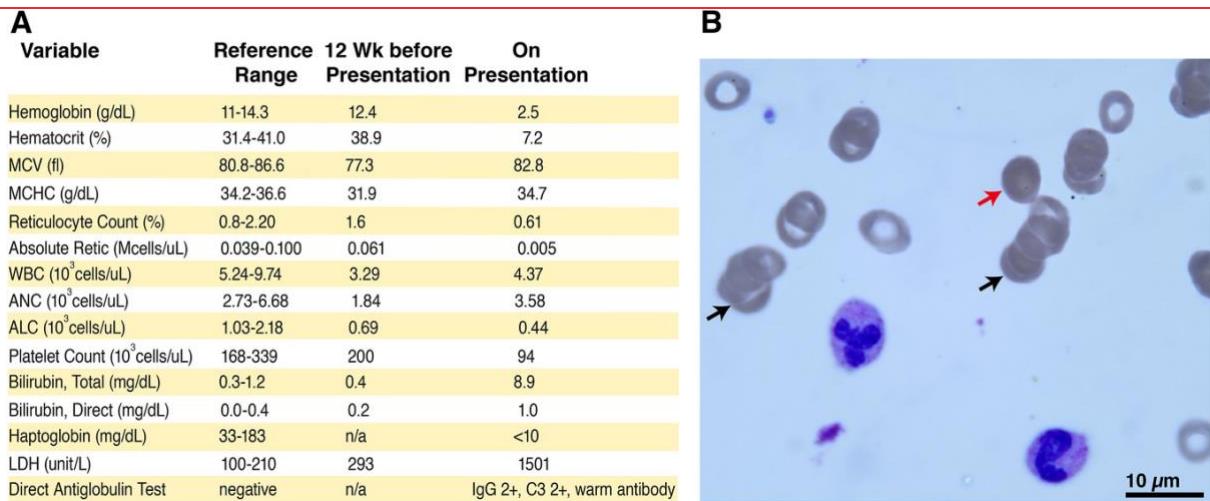


Figure 1. Laboratory evidence of autoimmune hemolytic anemia. A, Hematological parameters are shown prior to presentation and upon admission. B, A representative image of the peripheral blood smear is displayed, demonstrating rouleaux formation (black arrows), presence of microspherocytes (red arrow), hypochromic microcytic red blood cells, as well as large platelets.

## UNDERSTANDING THE PATHOLOGY

### NO EVIDENCE OF SEVERE ACUTE RESPIRATORY SYNDROME-CORONAVIRUS 2 IN SEMEN OF MALES RECOVERING FROM CORONAVIRUS DISEASE 2019

Pan F, Xiao X, Guo J, Song Y, Li H, Patel DP, Spivak AM, Alukal JP, Zhang X, Xiong C, Li PS, Hotaling JM.. Fertil Steril. 2020 Jun;113(6):1135-1139. doi: 10.1016/j.fertnstert.2020.04.024. Epub 2020 Apr 17.

Level of Evidence: 3

#### BLUF

This cross-sectional study conducted at a tertiary referral center in Wuhan, China collected data from 34 Chinese adult male COVID-19 patients and found that SARS-CoV-2 was not detected in any of the patients' semen samples within 31 days of their COVID-19 diagnosis. The authors indicate that more research is needed to determine if SARS-CoV-2 infection has long-term implications for male reproductive health.

#### ABSTRACT

**OBJECTIVE:** To describe detection of severe acute respiratory syndrome (SARS)-coronavirus 2 (CoV-2) in seminal fluid of patients recovering from coronavirus disease 2019 (COVID-19) and to describe the expression profile of angiotensin-converting enzyme 2 (ACE2) and Transmembrane Serine Protease 2 (TMPRSS2) within the testicle. **DESIGN:** Observational, cross-sectional study.

**SETTING:** Tertiary referral center.

**PATIENT(S):** Thirty-four adult Chinese males diagnosed with COVID-19 through confirmatory quantitative reverse transcriptase-polymerase chain reaction (qRT-PCR) from pharyngeal swab samples.

**INTERVENTION(S):** None.

**MAIN OUTCOME MEASURE(S):** Identification of SARS-CoV-2 on qRT-PCR of single ejaculated semen samples. Semen quality was not assessed. Expression patterns of ACE2 and TMPRSS2 in the human testis are explored through previously published single-cell transcriptome datasets.

**RESULT(S):** Six patients (19%) demonstrated scrotal discomfort suggestive of viral orchitis around the time of COVID-19 confirmation. Severe acute respiratory syndrome-CoV-2 was not detected in semen after a median of 31 days (interquartile range, 29-36 days) from COVID-19 diagnosis. Single-cell transcriptome analysis demonstrates sparse expression of ACE2 and TMPRSS2, with almost no overlapping gene expression.

**CONCLUSION(S):** Severe acute respiratory syndrome-CoV-2 was not detected in the semen of patients recovering from COVID-19 1 month after COVID-19 diagnosis. Angiotensin-converting enzyme 2-mediated viral entry of SARS-CoV-2 into target host cells is unlikely to occur within the human testicle based on ACE2 and TMPRSS2 expression. The long-term effects of SARS-CoV-2 on male reproductive function remain unknown.

### SARS-COV-2 AND GUILAIN-BARRÉ SYNDROME: AIDP VARIANT WITH FAVORABLE OUTCOME

Lascano AM, Epiney JB, Coen M, Serratrice J, Bernard-Valnet R, Lalive PH, Kuntzer T, Hübers A.. Eur J Neurol. 2020 Jun 1. doi: 10.1111/ene.14368. Online ahead of print.

Level of Evidence: 4

#### BLUF

Case series conducted in Switzerland during March and April 2020 by the Geneva and Lausanne University Hospitals reporting three patients who developed Guillain-Barré syndrome 7-22 days after developing symptoms of COVID-19. The clinical observations are reported in Table 1. The patients were treated with intravenous immunoglobins and had partial to full recovery, leading authors to surmise that SARS-CoV-2 may trigger Guillain-Barré syndrome by secondary immune-mediated mechanisms.

#### ABSTRACT

The entire world has been experiencing the outbreak of a novel infectious agent known as severe acute respiratory syndrome corona virus 2 (SARS-CoV-2), which is responsible for the coronavirus disease 19 (COVID-19). Life-threatening complications described in SARS-CoV-2 infected patients include acute respiratory distress syndrome, acute kidney failure and cardiac injury. Nonetheless, only few neurological complications have been described so far.

## FIGURES

	<b>Case 1</b>	<b>Case 2</b>	<b>Case 3</b>
Age/Gender	52/Female	63/Female	61/Female
Comorbidities	None	Type 2 diabetes	None
Symptoms of COVID-19	Dry cough, fever, odynophagia, arthralgia, diarrhoea	Dry cough, shivering, odynophagia, breathing difficulties, chest pain	Productive cough, fever, myalgia, vasovagal syncope, diarrhoea, nausea and vomiting
Method for COVID-19 diagnosis	Antibodies for SARS-CoV-2 IgM/IgG, followed by RT-PCR positive in nasopharyngeal swab (4 <sup>th</sup> test)	RT-PCR in nasopharyngeal swab (2 <sup>nd</sup> test)	RT-PCR in nasopharyngeal swab
Neurological signs and symptoms	Back pain, limb weakness, ataxia, distal paresthesia, dysgeusia, cacosmia. Developed respiratory failure, dysautonomia and tetraplegia with areflexia (day 4)	Lower limb pain, mild weakness and normal deep tendon reflexes. Developed tetraparesis, distal paresthesia and areflexia (day 5)	Lower limb weakness and distal paresthesia, dizziness, dysphagia, dysautonomia, areflexia. Presented worsening of bulbar symptoms and bilateral facial palsy (day 4)
Time of neurological symptom onset (days)	15	7	22
Cerebrospinal fluid findings	White cell count 3 cell/ $\mu$ L; Protein level 60 mg/dl; Negative PCR assay for SARS-CoV-2 (day 2)	White cell count 2 cell/ $\mu$ L; Protein level 40 mg/dl; PCR assay for SARS-CoV-2 was not performed (day 6)	White cell count 4 cell/ $\mu$ L; Protein level 140 mg/dl; Negative PCR assay for SARS-CoV-2 (day 1)
Serum studies	WBC 8900 cells/mm <sup>3</sup> ; Lymphocytes 1200 cells/mm <sup>3</sup> ; Platelets 45500 cells/mm <sup>3</sup> . Normal kidney and liver function. Antibodies to	WBC 3300 cells/mm <sup>3</sup> ; Lymphocytes 800 cells/mm <sup>3</sup> ; Platelets 119000 cells/mm <sup>3</sup> . Normal kidney function. Elevated transaminase levels	WBC 4000 cells/mm <sup>3</sup> ; Lymphocytes 600 cells/mm <sup>3</sup> ; Platelets 322000 cells/mm <sup>3</sup> . Normal kidney and liver function. Hyponatremia (127 mmol/l). Antibodies to ganglioside panel* was not performed
MRI results	Spinal cord: no nerve root gadolinium enhancement	Not performed	Spinal cord: lumbosacral nerve root enhancement. Normal brain imaging
Treatment	1 cycle of IVIg (day 2)	1 cycle of IVIg (day 10)	1 cycle of IVIg (day 2)
Clinical outcome at 5 weeks	Improvement of tetraparesis. Able to stand up with assistance. GBS disability clinical score 4/6	Dismissal with full motor recovery. Persistence of lower limb areflexia and distal paresthesia. GBS disability clinical score 1/6	Improvement of tetraparesis and ability to walk with assistance. Persistence of neuropathic pain and distal paresthesia. GBS disability clinical score 3/6

COVID-19 = coronavirus disease 2019; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; RT-PCR = reverse transcription polymerase chain reaction; WBC = white blood cell count; MRI = magnetic resonance imaging; IVIg = intravenous immunoglobulins

\*Anti-ganglioside antibodies panel includes anti-GM1, GD1a and GQ1b

Table 1. Clinical characteristics and laboratory findings of three patients with Guillain-Barré syndrome after COVID-19

## DIRECT ENDOTHELIAL DAMAGE AND VASCULITIS DUE TO SARS-COV-2 IN SMALL BOWEL SUBMUCOSA OF COVID-19 PATIENT WITH DIARRHEA

Carnevale S, Beretta P, Morbini P.. J Med Virol. 2020 Jun 3. doi: 10.1002/jmv.26119. Online ahead of print.

Level of Evidence: 5

### BLUF

A 40 year old woman who was diagnosed with interstitial pneumonia in the setting of a positive SARS-CoV-2 RT-PCR test also had positive fecal occult blood testing (FOBT), prompting performance of a colonoscopy (histology results shown in Figure 1). Immunohistochemical (IHC) staining showed SARS-CoV-2 particles in the cytoplasm of the intestinal endothelial cells, leading the authors to:

1. Conclude that direct infection of the intestinal epithelium may occur in some COVID-19 patients and
2. Suggest IHC as a modality for pathologists to use to support COVID-19 diagnosis.

## FIGURES

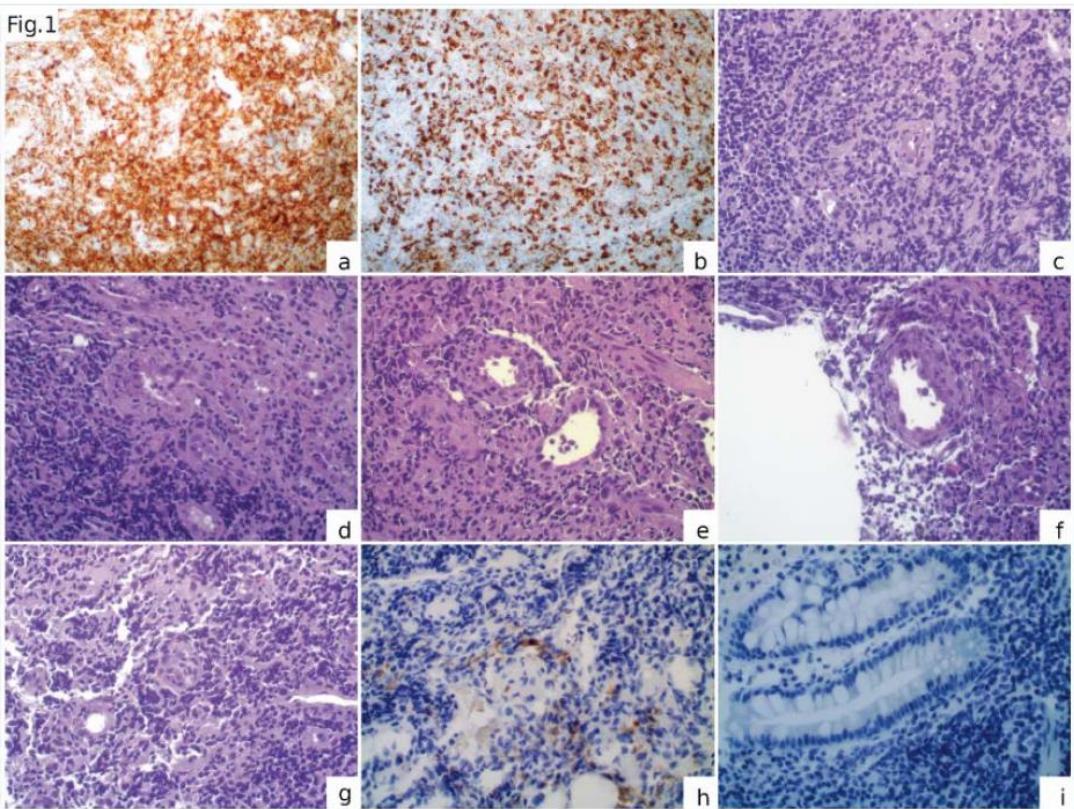


Figure 1. CD3 immunohistochemistry demonstrates the prevalent T-cell share of the inflammatory infiltrate: CD4+ T-cell share (a) is more consistent than CD8+ (b). (c-d): vasculitis of small diameter vessels, with bizarre nuclei and hobnail modifications (e-f), and aspects of obliteration (h). SARS-CoV-2 IHC demonstrates the direct presence of the virus within these endothelial cells. (i) No staining for SARS-CoV-2 is detectable in other cells. [a, b, h, i: IHC, 40x; c-g: HE, 40x]

## POTENTIAL NEUROINVASIVE PATHWAYS OF SARS-COV-2: DECIPHERING THE SPECTRUM OF NEUROLOGICAL DEFICIT SEEN IN CORONAVIRUS DISEASE 2019 (COVID-19)

Baig AM, Sanders EC.. J Med Virol. 2020 Jun 3. doi: 10.1002/jmv.26105. Online ahead of print.

Level of Evidence: Other

### BLUF

This review article summarizes what is currently understood about the neurotropic properties of SARS-CoV-2, and the authors hypothesize that the virus possibly accesses the human central nervous system (CNS) via 1. a hematogenous route, 2. a neuronal retrograde dissemination route, and/or 3. a transcribellar route (Figure 1). They call for more research to assess the neuroinvasive potential of SARS-CoV-2, which could have significant implications for the morbidity and mortality associated with COVID-19.

## FIGURES

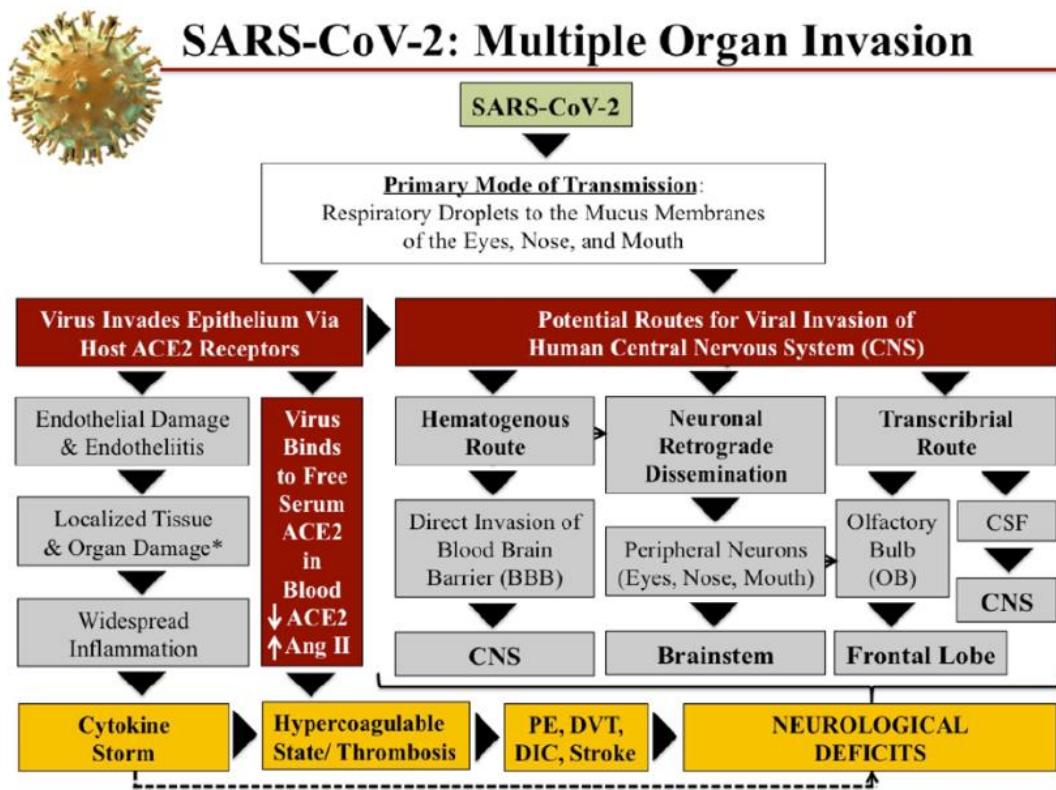


Figure 1. Proposed Pathogenesis of SARS-CoV-2 to Invade the Human CNS.

IN SILICO

## COMPARATIVE ANALYSIS OF CORONAVIRIDAE NUCLEOCAPSID AND SURFACE GLYCOPROTEIN SEQUENCES

Basu BV, Brown OR.. Front Biosci (Landmark Ed). 2020 Jun 1;25:1894-1900.

#### Level of Evidence: Other

BLUF

A genomic analysis conducted on several Coronaviridae identified a 111 amino acid motif that is highly conserved in human and bat coronaviruses, suggesting a close relationship between these strains and a potential interest for vaccine development. Findings also show protein sequence homologies with 58.9% surface glycoproteins and 82.5% nucleocapsids between the current 2019 coronavirus with the 2018 human SARS virus, suggesting existing anti-SARS vaccines may provide some protection against SARS-CoV-2 (Table 1).

## ABSTRACT

We analyzed the nucleocapsid and surface proteins from several Coronaviridae viruses using an alignment-free computer program. Three isolates of novel, human coronavirus (SARS-CoV-2) (2019) that are responsible for the current pandemic and older SARS strains of human and animal coronaviruses were examined. The nucleocapsid and glycoprotein sequences are identical for the three novel 2019 human isolates and they are closely related to these sequences in six bat and human SARS coronaviruses. This strongly supports the bat origin of the pandemic, novel coronavirus. One surface glycoprotein fragment of 111 amino acids is the largest, conserved, common permutation in the examined bat SARS-like and human SARS viruses, including the Covid-19 virus. BLAST analysis confirmed that this fragment is conserved only in the human and bat SARS strains. This fragment likely is involved in infectivity and is of interest for vaccine development. Surface glycoprotein and nucleocapsid protein sequence homologies of 58.9% and 82.5%, respectively, between the novel SARS-CoV-2 strains and the human SARS (2018) virus suggest that existing anti-SARS vaccines may provide some protection against the novel coronavirus.

## FIGURES

**Table 1.** Nucleocapsid and surface glycoprotein sequence relationships among various strains of coronaviruses

Coronavirus	SARS-CoV-2 AC: MT072688				
	Nucleocapsid protein		Surface glycoprotein		Accession
	%Homology	Largest Common Permutation	%Homology	Largest Common Permutation	
SARS-CoV-2(1) Feb 2020	100	419	100	1273	MN988668
SARS-CoV-2(2) Mar 2020	100	419	100	1273	NC_045512
Bat.RaTG13 Mar 2020	99	177	99	440	MN996532
Rhinophol. affins-2014	85.4	99	59.2	111	KF569996
SARS.BAT-July2017	83.7	66	57.9	111	JX993988
SARS.Human Aug 2018	82.5	43	58.9	111	NC_004718
SARS.Bat Dec 2017	82.5	43	59.4	111	KY417152
Kenyan Bats Feb 2020	73.3	44	50.9	97	KY352407
M.East.Res.Syndrome May 2016	16.6	8	5.4	14	KX034100
Avian Aug 2018	8.2	6	3.1	8	NC_001451
Human. Dec.2018	6.5	12	4.8	7	NC_003045
Bat.Corona.HKUB Apr 2008	1	4	2.1	8	EU420139

Actual fragments are shown in Figures 1-3. Viruses are arranged in decreasing order of homology with the novel coronavirus

## IN VITRO

### PHYSICOCHEMICAL PROPERTIES OF SARS-COV-2 FOR DRUG TARGETING, VIRUS INACTIVATION AND ATTENUATION, VACCINE FORMULATION AND QUALITY CONTROL

Scheller C, Krebs F, Minkner R, Astner I, Gil-Moles M, Wätzig H.. Electrophoresis. 2020 May 29. doi: 10.1002/elps.202000121. Online ahead of print.

Level of Evidence: Other

#### BLUF

A review conducted at Braunschweig, Germany by researchers from the Institute of Medicinal and Pharmaceutical Chemistry discusses physicochemical properties of SARS-CoV-2 including structure as well as buoyant density, isoelectric point (pI), pH stability, lipophilicity, susceptibility to disinfectants, and possible vaccine formulations. Please see the summary for structural details, additional physicochemical properties detailed in Table 1. The authors compare the similarities between SARS-CoV-2 and SARS-CoV-1 and believe past research data can be evaluated and applied to the new virus.

#### SUMMARY

Structural properties of SARS-CoV-2:

- Diameter of 60-140nm.
- Contains an envelope (E) protein, spike (S) protein, membrane (M) protein, and nucleocapsid (N) protein.
- Binds to hACE2 (human angiotensin-converting enzyme 2) as an entry receptor.
- Stable over a pH range of 3-10.
- Lipid envelope should make the virus susceptible to lipophilic disinfectants.
- Relatively stable in heat and radiation.

Other physicochemical properties detailed in Table 1.

#### ABSTRACT

The material properties of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and its proteins are discussed. We review the viral structure, size, rigidity, lipophilicity, isoelectric point, buoyant density and centrifugation conditions, stability against pH, temperature, UV light, gamma radiation and susceptibility to various chemical agents, including solvents and detergents. Possible inactivation, downstream and formulation conditions are given, including suitable buffers and some first ideas for quality-control methods. This information supports vaccine development and discussion with competent

authorities during vaccine approval and is certainly related to drug-targeting strategies and hygienics. Several instructive tables are given, including the pI and grand average of hydropathicity (GRAVY) of SARS-CoV-1 and -2 proteins in comparison. SARS-CoV-1 and SARS-CoV-2 are similar in many regards, so information can often be derived. Both are unusually stable, but sensitive at their lipophilic membranes. However, since seemingly small differences can have strong effects, e.g., on immunologically relevant epitope settings, unevaluated knowledge transfer from SARS-CoV-1 to SARS-CoV-2 cannot be advised. Published knowledge regarding downstream processes, formulations and quality assuring methods is, as yet, limited. However, standard approaches employed for other viruses and vaccines seem to be feasible, including virus inactivation, centrifugation conditions and the use of adjuvants. This article is protected by copyright. All rights reserved.

## FIGURES

Virus	Protein	UniProt-ID	MW [kDa]	pI	GRAVY
SARS-CoV-1	Replicase polyprotein 1a	P0C6U8 · R1A_CVHSA	486.373	5.91	-0.020
	Replicase polyprotein 1ab	P0C6X7 · R1AB_CVHSA	790.248	6.19	-0.071
	Spike glycoprotein	P59594 · SPIKE_CVHSA	139.125	5.56	-0.045
	Nucleoprotein	P59595 · NCAP_CVHSA	46.025	10.11	-1.027
	Protein 3a	P59632 · AP3A_CVHSA	30.903	5.75	0.239
	Protein 7a	P59635 · NS7A_CVHSA	13.941	8.24	0.218
	Envelope small membrane protein	P59637 · VEMP_CVHSA	8.361	6.01	1.141
	Membrane protein	P59596 · VME1_CVHSA	25.061	9.63	0.417
	Nonstructural protein 3b	P59633 · NS3B_CVHSA	17.750	10.82	0.099
	Nonstructural protein 6	P59634 · NS6_CVHSA	7.527	4.64	0.297
	Protein 9b	P59636 · ORF9B_CVHSA	10.802	4.90	-0.122
	Protein nonstructural 7b	Q7TFA1 · NS7B_CVHSA	5.302	3.77	1.414
	Nonstructural protein 8b	Q80H93 · NS8B_CVHSA	9.560	9.45	-0.029
	Nonstructural protein 8a	Q7TFA0 · NS8A_CVHSA	4.327	8.30	0.644
	Uncharacterized protein 14	Q7TLC7 · Y14_CVHSA	7.852	6.25	0.310
SARS-CoV-2	Replicase polyprotein 1a	P0DTC1 · R1A_SARS2	489.989	6.04	-0.023
	Spike glycoprotein	P0DTC2 · SPIKE_SARS2	141.178	6.24	-0.079
	Replicase polyprotein 1ab	P0DTD1 · R1AB_SARS2	794.058	6.32	-0.070
	Protein 3a	P0DTC3 · AP3A_SARS2	31.123	5.55	0.275
	Membrane protein	P0DTC5 · VME1_SARS2	25.147	9.51	0.446
	Protein 7a	P0DTC7 · NS7A_SARS2	13.744	8.23	0.318
	Nucleoprotein	P0DTC9 · NCAP_SARS2	45.626	10.07	-0.971
	Envelope small membrane protein	P0DTC4 · VEMP_SARS2	8.365	8.57	1.128
	Nonstructural protein 6	P0DTC6 · NS6_SARS2	7.273	4.60	0.233

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Protein 9b	P0DTD2 · ORF9B_SARS2	10.797	6.56	-0.085
Nonstructural protein 8	P0DTC8 · NS8_SARS2	13.831	5.42	0.219
Uncharacterized protein 14	P0DTD3 · Y14_SARS2	8.050	5.79	0.603
Protein nonstructural 7b	P0DTD8 · NS7B_SARS2	5.180	4.17	1.449
A0A663DJA2	A0A663DJA2_SARS2	4.449	7.93	0.637

Table 1. Molecular Weight (MW), isoelectric Point (pI) and grand average of hydropathicity (GRAVY) of the SARS-CoV-1 and SARS-CoV-2 proteins predicted by ProtParam [54], including the corresponding sequence identifier.

## TRANSMISSION & PREVENTION

### ASYMPTOMATIC TRANSMISSION DURING THE COVID-19 PANDEMIC AND IMPLICATIONS FOR PUBLIC HEALTH STRATEGIES

Huff HV, Singh A.. Clin Infect Dis. 2020 May 28:ciaa654. doi: 10.1093/cid/ciaa654. Online ahead of print.

Level of Evidence: 1

#### BLUF

In this review, Huff and Singh collect the current data on asymptomatic, pre-symptomatic, and symptomatic transmission of SARS-CoV-2 in order provide recommendations for public health strategies. Given increasing evidence that asymptomatic individuals can widely spread the virus, and that healthcare workers are not excluded from the possibility of being asymptomatic spreaders, the authors recommend increasing testing to exposed individuals, healthcare workers, caretakers, and emergency responders regardless of symptoms.

#### ABSTRACT

SARS-CoV-2 spread rapidly within months despite global public health strategies to curb transmission by testing symptomatic patients and encouraging social distancing. Here, we summarize rapidly emerging evidence highlighting transmission by asymptomatic and pre-symptomatic individuals. Viral load of asymptomatic carriers is comparable to symptomatic patients, viral shedding is highest before symptom onset suggesting high transmissibility before symptoms. Within universally tested subgroups, surprisingly high percentages of COVID-19 positive asymptomatic individuals were found. Asymptomatic transmission was reported in several clusters. A Wuhan study showed an alarming rate of intrahospital transmission, and several countries reported higher prevalence among healthcare workers than the general population. This raises concern that health workers could act as silent disease vectors. Therefore, current public health strategies relying solely on 'symptom onset' for infection identification need urgent reassessment. Extensive universal testing irrespective of symptoms may be considered with priority placed on groups with high frequency exposure to positive patients.

### SARS-COV-2 AND HUMAN MILK: WHAT IS THE EVIDENCE?

Lackey KA, Pace RM, Williams JE, Bode L, Donovan SM, Järvinen KM, Seppo AE, Raiten DJ, Meehan CL, McGuire MA, McGuire MK.. Matern Child Nutr. 2020 May 30:e13032. doi: 10.1111/mcn.13032. Online ahead of print.

Level of Evidence: 2

#### BLUF

A systematic review of case studies and case series, found that only 1 of 48 human breast milk samples from women infected with SARS-CoV-2 collected across 13 studies in China, Singapore, and Italy tested positive via reverse transcriptase (RT)-PCR for SARS-CoV-2 (Table 2), suggesting vertical transmission via breast milk may be unlikely. However, validation of previous studies' results, further rigorous studies (Box 2), and proper milk testing (Box 1) are required to more definitively determine the role of human breast milk in the transmission of SARS-CoV-2.

#### ABSTRACT

The novel coronavirus SARS-CoV-2 has emerged as one of the most compelling and concerning public health challenges of our time. To address the myriad issues generated by this pandemic, an interdisciplinary breadth of research, clinical and public health communities has rapidly engaged to collectively find answers and solutions. One area of active inquiry is understanding the mode(s) of SARS-CoV-2 transmission. Although respiratory droplets are a known mechanism of transmission, other mechanisms are likely. Of particular importance to global health is the possibility of vertical transmission from infected mothers to infants through breastfeeding or consumption of human milk. However, there is limited published literature related to vertical transmission of any human coronaviruses (including SARS-CoV-2) via human milk and/or breastfeeding. Results of the literature search reported here (finalized on 17 April 2020) revealed a single study providing some evidence of vertical transmission of human coronavirus 229E; a single study evaluating presence of SARS-CoV in human milk (it was negative); and no published data on MERS-CoV and human milk. We identified 13 studies reporting human milk tested for SARS-CoV-2; one study (a non-peer-reviewed preprint) detected the virus in one milk sample, and another study detected SARS-CoV-2 specific IgG in milk. Importantly, none of the studies on coronaviruses and human milk report validation of their collection and analytical methods for use in human milk. These reports are evaluated here, and their implications related to the possibility of vertical transmission of coronaviruses (in particular, SARS-CoV-2) during breastfeeding are discussed.

## FIGURES

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### Box 1. Key points of assay validation

Some factors to consider when validating methods for human milk testing of coronaviruses.

- Method of milk collection: use of manual milk expression versus electric pump, cleaning procedures of breast and pump, partial versus full breast expression and foremilk versus hindmilk.
- Sample handling and storage: container material, temperature and duration of refrigeration/freezing.
- Assay validation: nucleic acid extraction protocols, amplification protocols, reagent selection, proper positive and negative controls and fresh versus frozen milk.
- Viral quantification and viability: infectious dose and biologically relevant concentrations.

### Box 2. Future needs

To understand the role of human milk and SARS-CoV-2 infection, the following points must be rapidly addressed.

- Optimization of human milk collection and storage protocols for SARS-CoV-2 research.
- Validation of assays for identification of SARS-CoV-2 RNA and SARS-CoV-2-specific immune components in human milk.
- Multinational population studies documenting presence or absence of SARS-CoV-2 virus and immune factors (including antibodies) in milk produced by infected women, women with infected infants and women who have been exposed to SARS-CoV-2; if the virus is identified in milk, its viability must be verified.
- Multinational population studies documenting (or not documenting) risk of COVID-19 infections in breastfed versus nonbreastfed infants whose mothers are COVID-19 positive.
- Research delineating implications of skin-to-skin breastfeeding versus consumption of pumped human milk.

**TABLE 2** Characteristics of women and infants for whom human milk has been sampled and tested for SARS-CoV-2 using RT-PCR and for SARS-CoV-2 specific antibodies

Publication	Peer reviewed	Subjects (n)	Location	Repeated samples	Time of milk collection	Maternal age (year)	Gestational age at time of maternal infection	RT-PCR results	Milk antibody results	Infant age at the time of infant infection	Infant sex	Delivery mode	Infant breastfed
Chen et al. (2020)	Yes	6 <sup>a</sup>	China	No	Day 1	27	38 weeks, 2 days <sup>b</sup>	–	NA	NA	NS	Caesarean	NS
						26	36 weeks, 2 days <sup>b</sup>	–	NA	NA	NS	Caesarean	NS
						26	38 weeks, 1 day <sup>b</sup>	–	NA	NA	NS	Caesarean	NS
						26	36 weeks, 3 days <sup>b</sup>	–	NA	NA	NS	Caesarean	NS
						28	38 weeks <sup>b</sup>	–	NA	NA	NS	Caesarean	NS
						34	39 weeks, 4 days <sup>b</sup>	–	NA	NA	NS	Caesarean	NS
Cui et al. (2020)	Yes	1	China	Yes	55–57 days	NS	NA	–	NA	50 days	Female	NS	Yes
Dong et al. (2020)	Yes	1	China	No	6 days	29	34 weeks, 2 days	–	NA	NA	Female	Caesarean	No
Fan et al. (2020)	Yes	2	China	Yes	Days 1 and 17	34	37 weeks	–	NA	NA	Female	Caesarean	No
Kam et al. (2020)	Yes	1	Singapore	No	Day 1	29	36 weeks	–	NA	NA	Female	Caesarean	No
Li et al. (2020)	Yes	1	China	Yes	Days 1, 2 and 3	30	35 weeks	–	NA	NA	Male	Caesarean	NS
Salvatori et al. (2020)	No	2	Italy	No	Day 18	36	NA	–	NA	<18 days	Male	NS	Yes
Liu, Wang, Zhang et al. (2020)	No	2 <sup>d</sup>	China	Yes	Day 10	26	NA	–	NA	<10 days	Female	NS	Yes
					Days 2, 3 and 12	34	40 weeks	–	NA	NA	Male	Caesarean	No
Liu, Wang, Li et al. (2020)	Yes	10 <sup>e</sup>	China	No	Day 2	30	37 weeks	–	NA	NA	Unclear	Vaginal	NS
Wang et al. (2020)	Yes	1	China	No	36 h	34	40 weeks	–	NA	NA	Male	Caesarean	No
Wu et al. (2020)	No	3 <sup>f</sup>	China	Yes	Days 1, 6 and 27	29	35 weeks, 4 days	–	NA	NA	NS	Caesarean	NS
					Days 1, 6 and 27	28	35 weeks, 5 days	–	NA	NA	NS	Caesarean	NS
					Days 1, 3, 6 and 27	27	38 weeks, 2 days	+	NA	NA	NS	Vaginal	NS
Yu, Xu, Li, Hu, and Li (2020)	No	1	China	Yes	Days 1, 8, 15, 18 and 24 <sup>g</sup>	32	NA	– <sup>h</sup>	IgG+, IgM– <sup>i</sup>	13 months	Male	NS	Yes

(Continues)

**TABLE 2** (Continued)

Publication	Peer reviewed	Subjects (n)	Location	Repeated samples	Time of milk collection	Maternal age (year)	Gestational age at time of maternal infection	RT-PCR results	Milk antibody results	Infant age at the time of infant infection	Infant sex	Delivery mode	Infant breastfed
Yuehua et al. (2020)	Yes	1	China	No	3 months	NS	NA	–	NA	3.5 months	Female	NS	Yes

Abbreviations: NS, not specified; NA, not applicable; –, negative result; +, positive result.

<sup>a</sup>Study presented data from nine women but only presented data related to milk produced by six women.<sup>b</sup>Gestational age upon admission.<sup>c</sup>The infant's breastfeeding status was not specified in the report, but it is presumed that he was at least partially breastfed as the mother was producing milk at 6-month post-partum.<sup>d</sup>Study presented data from three women but only presented data on the milk produced by two women.<sup>e</sup>Study presented data from 19 women but only presented data on the milk produced by 10 women.<sup>f</sup>Study presented data from 13 women but only presented data on the milk produced by three women.<sup>g</sup>Days are reported from time of admission, not from time of birth as the other days in this column.<sup>h</sup>Milk was analysed on Days 1, 8, 15 and 18 of hospital admission.<sup>i</sup>Milk antibodies were tested on Days 8 and 24 of hospital admission.

## RETROAURICULAR DERMATITIS WITH VEHEMENT USE OF EAR LOOP FACE MASKS DURING COVID19 PANDEMIC

Bothra A, Das S, Singh M, Pawar M, Maheswari A.. J Eur Acad Dermatol Venereol. 2020 Jun 3. doi: 10.1111/jdv.16692. Online ahead of print.

Level of Evidence: 4

### BLUF

In this letter to the editor, a group of dermatologists in India describe 14 patients who experienced retroauricular dermatitis due to face mask ear loops, as shown in Image 1. They suggest that healthcare professionals use face masks kept in place with headbands and that the general population avoid application of disinfectants when cleaning cloth masks for reuse.

### ABSTRACT

The COVID-19 pandemic forged the exponential use of masks of various kinds, not just by health workers but also by general population as a personal protective equipment (PPE). Although contact dermatitis due to PPE is well reported, mask induced dermatitis is a relatively unexplored phenomenon. In this article, we report a preliminary data of patients experiencing retroauricular dermatitis due to ear loop face masks.

## FIGURES



Image 1. Erythema and scaling involving the retroauricular [sic] area following ear loop mask use

## INVESTIGATION AND SEROLOGIC FOLLOW-UP OF CONTACTS OF EARLY CONFIRMED CASE-PATIENT WITH COVID-19, UNITED STATES

Chu VT, Freeman-Ponder B, Lindquist S, Spitters C, Kawakami V, Dyal JW, Clark S, Bruce H, Duchin JS, DeBolt C, Podczervinski S, D'Angeli M, Pettrone K, Zacks R, Vahey G, Holshue ML, Lang M, Burke RM, Rolfs MA, Marlow M, Midgley CM, Lu X, Lindstrom S, Hall AJ, Fry AM, Thornburg NJ, Gerber SI, Pillai SK, Biggs HM.. *Emerg Infect Dis.* 2020 May 29;26(8). doi: 10.3201/eid2608.201423. Online ahead of print.

Level of Evidence: 5

### BLUF

The authors describe a contact investigation where they identified 50 contacts (Table 1), including healthcare workers (all with partial PPE including facemask/respirator) and civilians (11 without PPE), that had interaction with a man who was confirmed to be positive for COVID-19 on 20 January 2020 after returning to Washington State from Wuhan, China (Figures 1, 2). 30 of these contacts were monitored for SARS-CoV-2 RNA via real-time reverse transcription PCR (rt-PCR) and for COVID-19 antibodies via ELISA, which were negative for every patient despite eight of these contacts developing symptoms consistent with COVID-19, suggesting that the timeline of serologic testing could have missed positive cases and that the facemasks and respirators worn by the case-patient and healthcare workers could have prevented nosocomial transmission.

### ABSTRACT

We describe the contact investigation for an early confirmed case of coronavirus disease (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), in the United States. Contacts of the case-patient were identified, actively monitored for symptoms, interviewed for a detailed exposure history, and tested for SARS-CoV-2 infection by real-time reverse transcription PCR (rRT-PCR) and ELISA. Fifty contacts were identified and 38 (76%) were interviewed, of whom 11 (29%) reported unprotected face-to-face interaction with the case-patient. Thirty-seven (74%) had respiratory specimens tested by rRT-PCR, and all tested negative. Twenty-three (46%) had ELISA performed on serum samples collected 6 weeks after exposure, and none had detectable antibodies to SARS-CoV-2. Among contacts who were tested, no secondary transmission was identified in this investigation, despite unprotected close interactions with the infectious case-patient.

## FIGURES

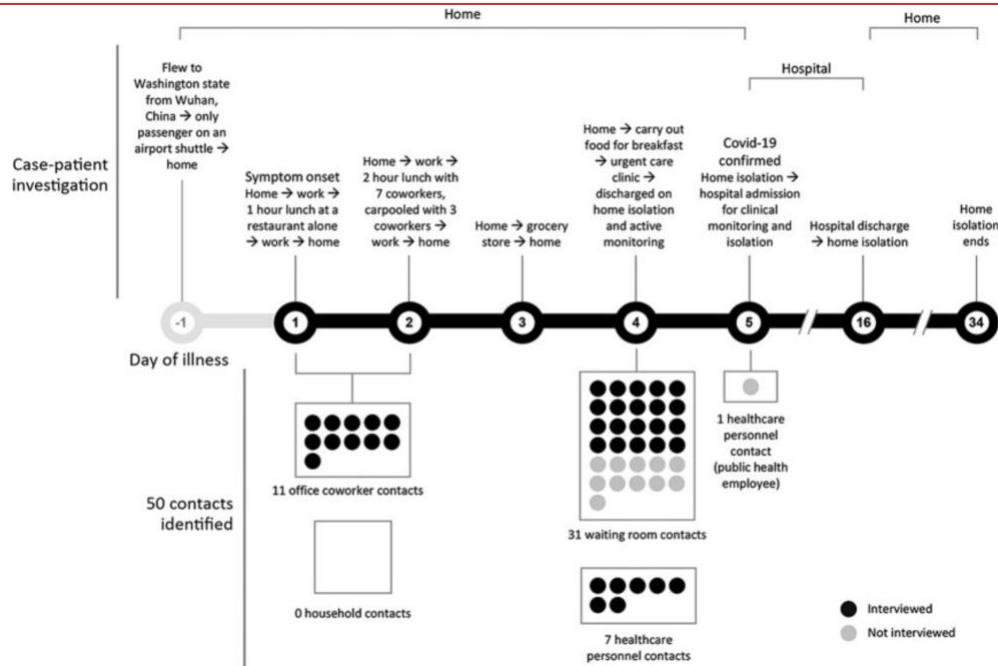


Figure 1. Case-patient investigation and contact identification during the investigation of an early confirmed US COVID-19 case, Washington, USA, 2020. The case-patient was asymptomatic when he arrived home from Wuhan, China. The next day, he developed a cough (day 1), followed by chills (day 2) and a subjective fever (day 3). When he arrived at the urgent care clinic (day 4), he was given a facemask and sat in the waiting room for ≈20 minutes. He was evaluated in a standard examination room, and received a chest radiograph in a radiology room down the hallway from the exam room. The case-patient was identified as meeting the Centers for Disease Control and Prevention (CDC) criteria at the time for a person under investigation for COVID-19, and specimens (nasopharyngeal and oropharyngeal swabs and serum samples) were collected for testing (6). He was clinically stable and discharged home pending SARS-CoV-2 test results. When COVID-19 was confirmed (day 5), the case-patient was admitted to a hospital for observation and isolation. After 11 days, he was discharged to home isolation until 2 negative sets of nasopharyngeal and oropharyngeal specimens were obtained >24 hours apart, in accordance with CDC guidance at the time (7). Persons exposed during transient interactions, such as restaurant waitstaff and persons encountered at the grocery store, were not considered community contacts. COVID-19, coronavirus disease;

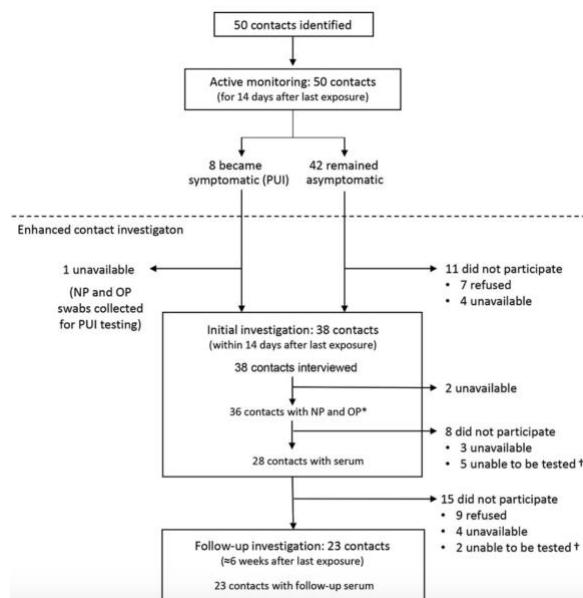


Figure 2. Contact investigation flowchart of identified contacts, active monitoring, and participation in the enhanced contact investigation of an early confirmed US coronavirus disease case, Washington, USA, 2020. NP, nasopharyngeal; OP, oropharyngeal; PUI, person under investigation. \*Includes contacts from whom specimens obtained for PUI testing. †Specimens were unable to be tested if blood could not be obtained ( $n = 5$ ) or if the standard specimen requirements for testing were not met ( $n = 2$ ).

Community contact	Any close contact (being within 6 feet of the case-patient) for a prolonged time (>10 min), other than office co-worker	0	None
Being an office co-worker of the case-patient with close contact of any duration	11 office co-workers	None	
Contact with infectious secretions from the case-patient	0	None	
Sharing a healthcare waiting room or area during the same time and up to 2 h after the case-patient was present	31 waiting room patients	7/31 of the waiting room contacts likely overlapped with the case-patient in the waiting room.	
Healthcare contact	Any face-to-face interactions between an HCP and the case-patient without the HCP wearing full PPE†	6 HCP	None
	Potential contact with the case-patient's infectious secretions by an HCP without wearing full PPE‡	2 HCP	2 HCP were EVS workers who did not have direct contact with the case-patient. They were included for potential exposure to infectious secretions from the case-patient while cleaning surfaces.

Figure 2. Contact investigation flowchart of identified contacts, active monitoring, and participation in the enhanced contact investigation of an early confirmed US coronavirus disease case, Washington, USA, 2020. NP, nasopharyngeal; OP, oropharyngeal; PUI, person under investigation. \*Includes contacts from whom specimens obtained for PUI testing.

†Specimens were unable to be tested if blood could not be obtained ( $n = 5$ ) or if the standard specimen requirements for testing were not met ( $n = 2$ ).

## PREVENTION IN THE HOSPITAL

### UNIVERSAL SCREENING FOR SARS-COV-2 IN ASYMPTOMATIC OBSTETRIC PATIENTS IN TOKYO, JAPAN

Ochiai D, Kasuga Y, Iida M, Ikenoue S, Tanaka M.. Int J Gynaecol Obstet. 2020 Jun 4. doi: 10.1002/ijgo.13252. Online ahead of print.

Level of Evidence: 4

#### BLUF

A retrospective study performed at Keio University Hospital in Tokyo, Japan analyzed the pre-admission SARS-CoV-2 screening results (by PCR per article) of 52 asymptomatic obstetric patients between April 6 - April 27, 2020, finding a 4% prevalence of COVID-19 in the sampled population. Results emphasize the importance of screening for asymptomatic SARS-CoV-2 to properly allocate staff/PPE and prevent transmission throughout labor and delivery wards.

# MANAGEMENT

## ACUTE CARE

### FIRST SUCCESSFUL TREATMENT OF CORONAVIRUS DISEASE 2019 INDUCED REFRactory CARDIOGENIC PLUS VASOPLEGIC SHOCK BY COMBINATION OF PERCUTANEOUS VENTRICULAR ASSIST DEVICE AND EXTRACORPOREAL MEMBRANE OXYGENATION: A CASE REPORT

Bemtgen X, Krüger K, Supady A, Duerschmied D, Schibilsky D, Bamberg F, Bode C, Wengenmayer T, Staudacher DL.. ASAIO J. 2020 Jun;66(6):607-609. doi: 10.1097/MAT.0000000000001178.

Level of Evidence: Other

#### BLUF

Herein, the case of a 52-year-old male with history of dilated cardiomyopathy, myocardial infarction, and heart failure (NYHA Class II) presenting with severe SARS-CoV-2 infection leading to moderate acute respiratory distress syndrome, refractory combined cardiogenic and vasoplegic shock, and acute kidney failure is detailed. Care for this patient is ongoing, but this case demonstrates how mechanical circulatory support and implantable ventricular assist devices can treat severely ill COVID-19 patients.

#### SUMMARY

Herein, the case of a 52-year-old male with history of dilated cardiomyopathy, myocardial infarction, and heart failure (NYHA Class II) presenting with severe SARS-CoV-2 infection leading to moderate acute respiratory distress syndrome, refractory combined cardiogenic and vasoplegic shock, and acute kidney failure is detailed. The patient received empiric SARS-CoV-2 therapy with combination of lopinavir/ritonavir and chloroquine. The cardiogenic shock was treated with an implantable peripheral ventricular assist device, and the patient underwent venoarterial extracorporeal membrane oxygenation for vasoplegic shock. Care for this patient is ongoing, but this case demonstrates how mechanical circulatory support and implantable ventricular assist devices can treat severely ill COVID-19 patients.

#### ABSTRACT

The novel coronavirus severe acute respiratory syndrome coronavirus 2 is infecting hundreds of thousands of humans around the globe. The coronavirus disease 2019 (COVID-19) is known to generate mild as well as critical courses. Complications on the intensive care units include acute respiratory distress syndrome, acute cardiac, and kidney injury as well as shock. Here, we present the first case report of a successful treatment of a COVID-19 patient presenting with adult respiratory distress syndrome plus refractory combined cardiogenic and vasoplegic shock, which could be successfully stabilized after implantation of a percutaneous ventricular assist device plus an extracorporeal membrane oxygenation. Although such intense treatment might not be feasible in case of a health care disaster as described for the hot spots of the COVID-19 pandemic, it might encourage treatment of younger patients on intensive care units not overcrowded by critically ill patients.

#### FIGURES

Day After Presentation	Baseline	0	1	3	4	14
Clinical parameters						
O <sub>2</sub> (L/min or Fio <sub>2</sub> %)	0 L/min	3 L/min	45%	50%	50%	40%
PEEP (mbar)	NA	5	10	9	13	
Temperature (°C)	36.7	38.3	39.6	39.5	39.5	37
Heart rate (beats/min)	111	105	141	123	95	114
ABP (mmHg) (systolic/diastolic mmHg)	119/80	104/66	84/67	82/54	78/50	110/74
CI (L/min/m <sup>2</sup> ) (PiCCO)	NA	NA	1.8	1.9	2.5	NA
SVRI (dyn × sec × cm <sup>-5</sup> )	NA	NA	1,160	1,230	1,976	NA
Norepinephrin (μg/kg/min)	0	0	0.084	0.8	0.8	0.1
Imipenem (mg/h)	NA	NA	3.4	3.4	3.4	3.3
Laboratory parameters						
Leukocytes (1,000/μl)	6,03	9.37	10.23	8.84	12.52	22.03
CRP (mg/dl)	6.4	37	37.2	113.1	113.8	366.8
Procalcitonin (ng/ml)	NA	0.22	0.57	26.8	41.4	12.5
proBNP (pg/ml)	2,274	9,995	14,270	25,580	30,031	NA

ABP, arterial blood pressure; CI, cardiac index; CRP, C-reactive protein; Fio<sub>2</sub>, fraction of inspired oxygen; NA, not available; PEEP, positive end-expiratory pressure; PiCCO, Pulse Contour Cardiac Output; proBNP, brain natriuretic peptide; SVRI, systemic vascular resistance index.

Table 1. Clinical and Laboratory Parameters

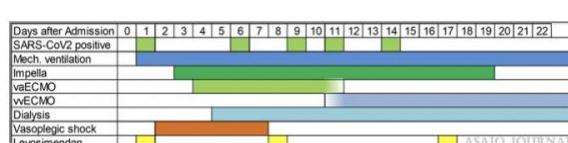


Figure 2. Time course of the coronavirus disease 2019 disease. SARS-CoV2, severe acute respiratory syndrome coronavirus 2; vaECMO, venoarterial extracorporeal membrane oxygenation; vvECMO, venovenous extracorporeal membrane oxygenation.

## CRITICAL CARE

### PULMONARY ARTERY THROMBECTOMY - A LIFE SAVING TREATMENT IN A PATIENT WITH PRESUMED COVID-19 COMPLICATED BY A MASSIVE PULMONARY EMBOLUS

Carlsson TL, Walton B, Collin G.. Br J Haematol. 2020 Jun 4. doi: 10.1111/bjh.16920. Online ahead of print.

Level of Evidence: 5

#### BLUF

A case report from physicians at Southmead Hospital in the UK describes the diagnosis and treatment of a large saddle pulmonary embolus through catheter directed thrombolysis and pulmonary artery thrombectomy in a patient presumed to have COVID-19. The patient had several negative COVID-19 tests, but displayed classic clinical and radiologic findings, leading the authors to worry about false negative swabs. The authors suggest that physical thrombolysis should be considered in hemodynamically unstable patients when necessary.

## NEONATAL/PEDIATRIC INTENSIVE CARE

### PRACTICAL GUIDE FOR PEDIATRIC PULMONOLOGISTS ON IMAGING MANAGEMENT OF PEDIATRIC PATIENTS WITH COVID-19

Foust AM, McAdam AJ, Chu WC, Garcia-Pena P, Phillips GS, Plut D, Lee EY.. Pediatr Pulmonol. 2020 May 28. doi: 10.1002/ppul.24870. Online ahead of print.

Level of Evidence: Other

#### BLUF

The authors reviewed current literature on imaging findings, guidance on requesting imaging studies, and diagnostic considerations for pediatric patients with COVID-19. The authors recommend following the algorithm for imaging studies included in Table 1 and encourage pediatricians to consider other infections, hypersensitivity pneumonitis, eosinophilic pneumonia, and electronic cigarette or vaping-associated lung injury in their differential diagnoses.

#### ABSTRACT

Understanding of coronavirus disease 2019 is rapidly evolving with new articles on the subject daily. This flood of articles can be overwhelming for busy practicing clinicians looking for key pieces of information that can be applied in daily practice. This review article synthesizes the reported imaging findings in pediatric COVID-19 across the literature, offers imaging differential diagnostic considerations and useful radiographic features to help differentiate these entities from COVID-19, and provides recommendations for ordering imaging studies to evaluate suspected cases of pediatric COVID-19. This article is protected by copyright. All rights reserved.

#### FIGURES

Table 1: Algorithm for Ordering Imaging Studies in Pediatric Patients with Suspected COVID-19 Infection

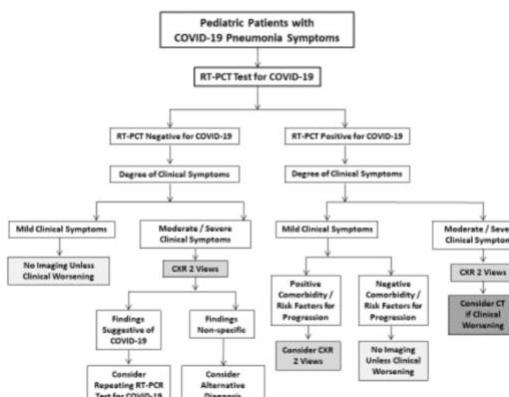


Table 1: Algorithm for Ordering Imaging Studies in Pediatric Patients with Suspected COVID-19 Infection

### CARDIOLOGY

#### CHLOROQUINE OR HYDROXYCHLOROQUINE FOR COVID-19: IS CARDIOTOXICITY A CONCERN?

Kamp TJ, Hamdan MH, January CT.. J Am Heart Assoc. 2020 May 28:e016887. doi: 10.1161/JAHA.120.016887. Online ahead of print.

Level of Evidence: Other

#### BLUF

Cardiologists at the University of Wisconsin-Madison describe the possible QT prolongation and arrhythmias associated with hydroxychloroquine. COVID-19 patients may be at especially high risk due to virus-induced cardiac irritation such as cytokine storm, possible hypoxia, and risk of myocarditis. Thus, the authors suggest that critically-ill COVID-19 patients should be pre-screened for any cardiac abnormalities and monitored by telemetry post-hydroxychloroquine delivery.

#### ABSTRACT

The SARS-CoV-2 viral pandemic causing COVID-19 disease begs for rapid and innovative treatments. In addition to flu-like respiratory symptoms, acute cardiac manifestations include cardiac injury, shock and arrhythmia. Several pharmacological therapies have been suggested including repurposing of existing drugs such as chloroquine and hydroxychloroquine, sometimes co-administered with azithromycin. Chloroquine and hydroxychloroquine were developed in the World War II era for treatment and prophylaxis of malaria, long before modern drug safety surveillance programs. Clinically they can prolong the QT interval to potentially initiate ventricular arrhythmias including torsades de pointes, and also cause QRS widening. Chloroquine interacts with multiple cardiac ion channels including the hERG potassium channel that is essential for normal electrical activity in the heart. A reduction in hERG channel potassium current is the principle cause of drug-induced long QT syndrome. Azithromycin also can cause modest QT interval prolongation, but not through potent hERG channel blockade, rather when used chronically through an increase in peak and late cardiac sodium current to cause potential loading of cardiomyocytes with sodium and calcium to produce calcium overload. How should we proceed with the use of chloroquine and hydroxychloroquine, potentially combined with azithromycin, for COVID-19 given that these agents bring some cardiac toxicity risk and their mechanisms for cardiac toxicity may not be the same? Is combining different and potentially additive mechanisms of cardiotoxicity wise? How great the risk is relative to the benefit in critically ill COVID-19 patients will need to await the outcome of ongoing, controlled clinical trials.

# ADJUSTING PRACTICE DURING COVID-19

## TELEMEDICINE ALGORITHM FOR CHRONIC WOUND CARE DURING COVID-19

Hsieh MW, Lee CC, Ou SF, Kuo YR.. Int Wound J. 2020 Jun 3. doi: 10.1111/iwj.13409. Online ahead of print.  
Level of Evidence: Other

### BLUF

Authors from Kaohsiung Medical University Hospital in Taiwan describe an algorithm for the remote management of chronic wound care and follow up care to during the pandemic, shown in Figure 1. The authors note that telemedicine can be an effective tool in managing chronic wound care while minimizing COVID-19 exposure.

### FIGURES

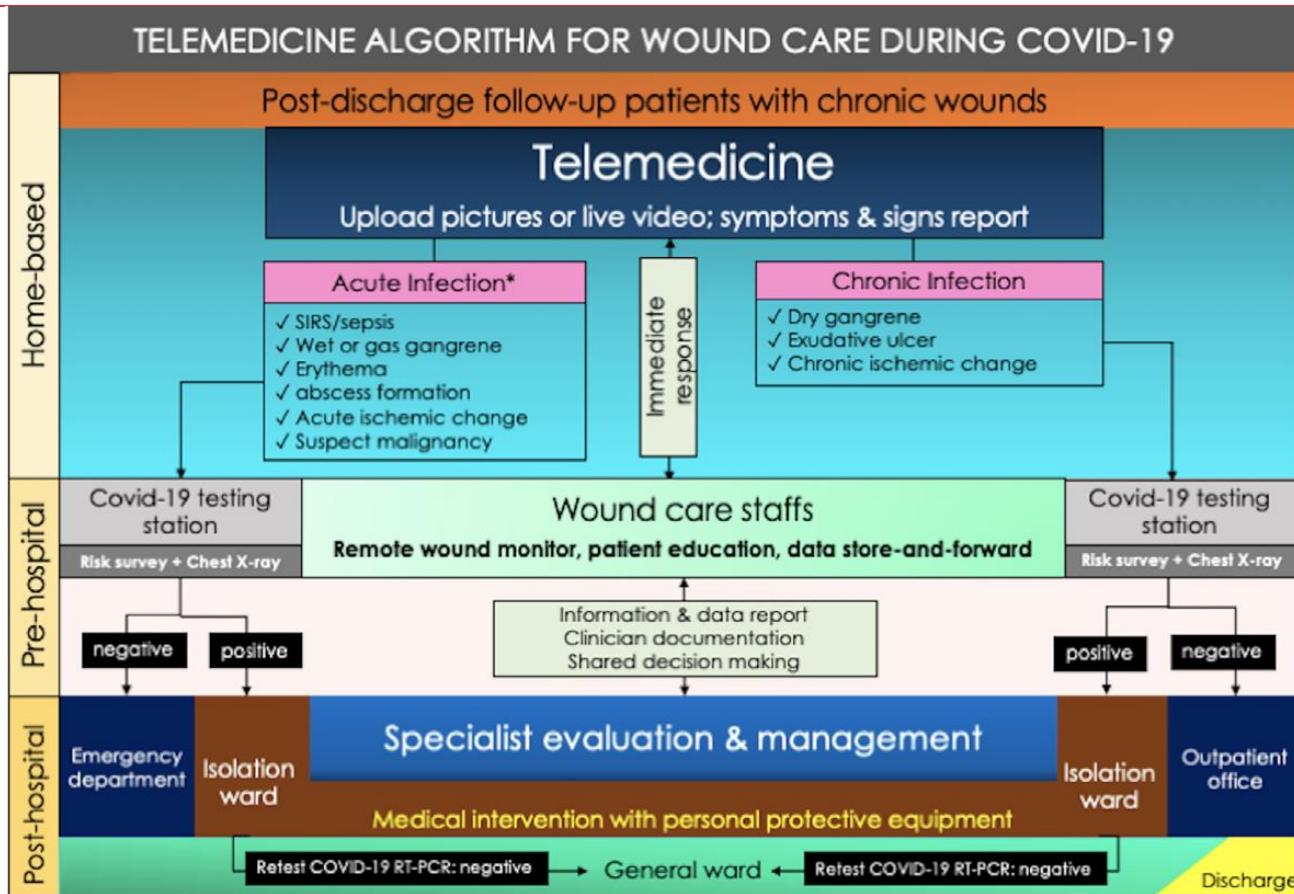


Figure 1. Algorithm for chronic wound care during COVID-19.

## PEDIATRICS

## ETHICAL DECISION-MAKING FOR CHILDREN WITH NEUROMUSCULAR DISORDERS IN THE COVID-19 CRISIS

Laventhal NT, Graham RJ, Rasmussen SA, Urion DK, Kang PB.. Neurology. 2020 Jun 1:10.1212/WNL.0000000000009936. doi: 10.1212/WNL.0000000000009936. Online ahead of print.  
Level of Evidence: Other

## **BLUF**

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A team of US specialists involved in pediatric neuromuscular care call for an equitable approach to triage decision-making and resource allocation during times of crisis, such as the COVID-19 pandemic. The authors propose guidelines to ensure triage algorithms are representative of children and adults living with chronic disabilities.

## **SUMMARY**

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The authors recommend the following guidelines to promote the use and creation of equitable triage algorithms:

- Triage algorithms should be transparent and accessible
- A plurality of perspectives and expertise should be represented in resource allocation policies and the priorities of diverse stakeholders should be considered
- Scarce treatments should be allocated based on contemporary and well-understood epidemiology of the individual patient's condition. Limitations should be acknowledged to avoid assumptions
- Existing or future disabilities should not be factors in scarce resource allocation due to an inherent potential for bias
- Those whose underlying conditions increase risk for more resource-intense treatment or slower recovery in acute care should not be disadvantaged if they have a similar chance of returning to functional baseline
- Ad hoc consultation with clinicians who are experts in the relevant condition, but not directly involved in responsibilities for the patient in question, should be considered

## **ABSTRACT**

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The sudden appearance and proliferation of COVID-19 has forced societies and governmental authorities across the world to confront the possibility of resource constraints when critical care facilities are overwhelmed by the sheer numbers of grievously ill patients. As governments and health care systems develop and update policies and guidelines regarding the allocation of resources, patients and families affected by chronic disabilities, including many neuromuscular disorders that affect children and young adults, have become alarmed at the possibility that they may be determined to have less favorable prognoses due to their underlying diagnoses and thus be assigned to lower priority groups. It is important for health care workers, policymakers, and government officials to be aware that the long term prognoses for children and young adults with neuromuscular disorders are often more promising than previously believed, due to a better understanding of the natural history of these diseases, benefits of multidisciplinary supportive care, and novel molecular therapies that can dramatically improve the disease course. Although the realities of a global pandemic have the potential to require a shift from our usual, highly individualistic standards of care to crisis standards of care, shifting priorities should nonetheless be informed by good facts. Resource allocation guidelines with the potential to affect children and young adults with neuromuscular disorders should take into account the known trajectory of acute respiratory illness in this population, and rely primarily on contemporary long-term outcome data.

# R&D: DIAGNOSIS & TREATMENTS

## CURRENT DIAGNOSTICS

### COVID-19 DIAGNOSTICS IN CONTEXT

Weissleder R, Lee H, Ko J, Pittet MJ.. Sci Transl Med. 2020 Jun 3;12(546):eabc1931. doi: 10.1126/scitranslmed.abc1931.

Level of Evidence: 5

#### BLUF

This expert opinion by American authors at Harvard describes current COVID-19 testing methods including details of Nucleic Antigen Tests (NATs) such as PCR and serologic tests such as ELISA (Table 2) and highlights the following:

- Test types and mechanisms of action.
- Cross-reactivity, turnaround time, and accuracy.
- Testing costs and prioritization.
- Patient viral load and potential for immunity.

The authors emphasize that long assay times, inaccuracies in specificity and sensitivity leading to false positives and/or negatives, and lack of testing availability are areas that require rapid improvement for better patient outcomes and containment of the COVID-19 pandemic.

#### FIGURES

Type	Target	Virus	Assay time	Process type	FDA-EUA	Examples
PCR	Viral RNA	SARS-CoV-2	2–8 hours; >12 hours	Plate	56	#Roche, #LabCorp, #BioMerieux, #Qiagen, #Perkin-Elmer, #Becton Dickinson, #Luminex, #Thermo Fisher, others
PCR-POC	Viral RNA	SARS-CoV-2	<1 hour	Cartridge	2	#Cepheid, #Mesa, Credo
ddPCR	Viral RNA	SARS-CoV-2	2–4 hours	Manual	1	#BioRAD
NEAR	Viral RNA	SARS-CoV-2	15 min	Cartridge	1	#Abbott
OMEGA	Viral RNA	SARS-CoV-2	1 hour	Plate	1	#Atila BioSystems
RCA	Viral RNA	SARS-CoV	2 hours		0	
SHERLOCK	Viral RNA	SARS-CoV-2	1.5 hours	Kit	1	#Sherlock Biosciences (CAS13a)
DETECTR	Viral RNA	SARS-CoV-2	1 hour	Kit	0	Mammoth Biosciences (CAS12a)
NGS	Viral RNA	SARS-CoV-2	Days		1	#IDbyDNA, Vision, Illumina
$\mu$ NMR	Viral RNA	SARS-CoV-2	2 hours	Cartridge	0	T2 Biosystems
LFA	IgG, IgM	SARS-CoV-2	15 min	Cartridge	3	#Cellex, #Sugentech, #ChemBio, Innovita
ELISA	IgG, IgM	SARS-CoV-2	2–4 hours	Plate	4	#Mount Sinai, #Ortho-Clinical (2), #EUROIMMUN US Inc., BioRAD, Sbiie, Zhejiang orient, Creative Di
CLIA	IgG, IgM	SARS-CoV-2	30 min	Cartridge	2	#Abbott, #DiaSorin
EIA	IgG, IgM	SARS-CoV-2	2 hours	Plate	1	#BioRAD
MIA	IgG, IgM	SARS-CoV-2		Plate	1	#Wadsworth Center
ECLIA	IgG, IgM	SARS-CoV-2	20 min	Plate	1	#Roche
ECS	IgG, cytokine	SARS-CoV-2	1 hour	Cartridge	0	Accure Health
VAT	Viral antigen	SARS-CoV-2	20 min	Cartridge	1	#Quidel, Sona NT, RayBiotech, SD Biosensors, Bioeasy
Microarrays	Ig epitopes	SARS-CoV-2	1.5 hours	Plate	0	RayBiotech, PEPperPRINT
IFM	Viral protein	SARS-CoV	3 hours	Manual	0	
WB	IgG, IgM; viral protein	SARS-CoV	4 hours	Manual	0	

Table 1. Performance comparison of different test types. Throughput is determined by process type and assay time. In general, automated plate-based assays have higher daily throughputs. Hashtag (#) indicates example systems that have received FDA emergency use authorization (FDA-EUA). See <https://cab.mgh.harvard.edu/civic> to access continuously updated information.

PCR, polymerase chain reaction; PCR-POC, PCR-point-of-care; ddPCR, digital droplet PCR; NEAR, nicking endonuclease amplification reaction; RCA, rolling circle amplification; SHERLOCK, specific high-sensitivity enzymatic reporter; DETECTR,

DNA endonuclease-targeted CRISPR trans reporter; NGS, next-generation sequencing; uNMR, micro-nuclear magnetic resonance; LFA, lateral flow assay; ELISA, enzyme-linked immunosorbent assay; CLIA, chemiluminescence immunoassay; EIA, enzyme immunoassay; ECLIA, electrochemiluminescence immunoassay; ECS, electrochemical sensing; VAT, viral antigen assay; IFM, immunofluorescence microscopy; WB, Western blot.

# HISTOLOGICAL-ULTRASONOGRAPHICAL CORRELATION OF PULMONARY INVOLVEMENT IN SEVERE COVID-19

Almeida Monteiro RA, de Oliveira EP, Nascimento Saldiva PH, Dolhnikoff M, Duarte-Neto AN; BIAS - Brazilian Image Autopsy Study Group.. Intensive Care Med. 2020 Jun 3. doi: 10.1007/s00134-020-06125-z. Online ahead of print.

Level of Evidence: Other

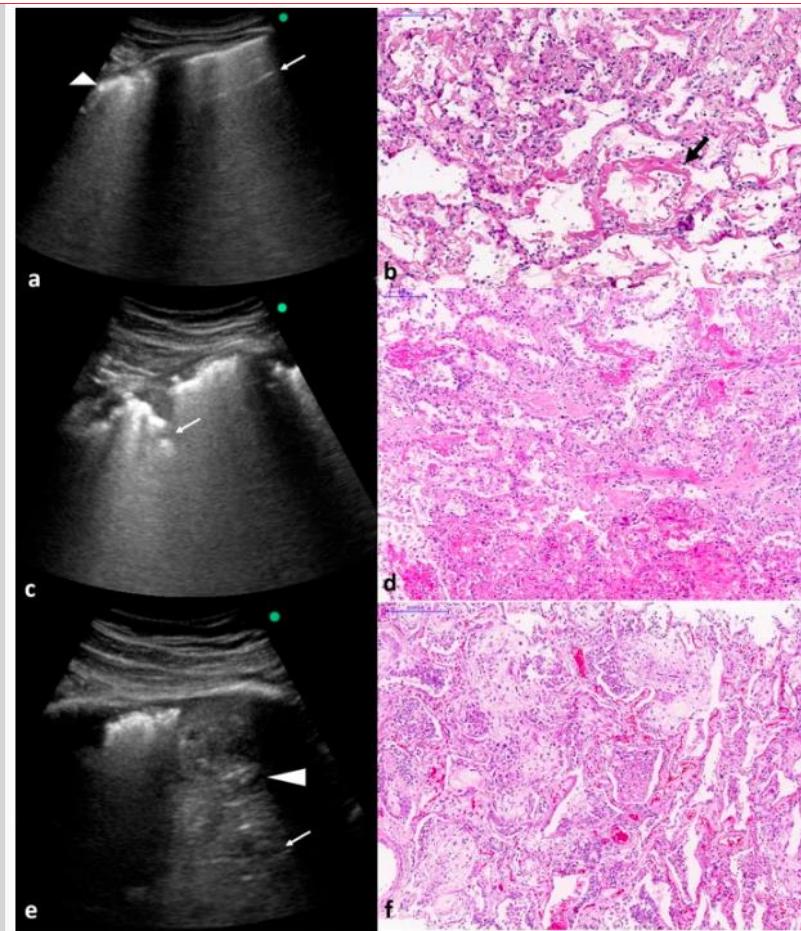
## BLUF

In this letter, Brazilian authors respond to a recent article by [Volpicelli et al (2020)] (<https://pubmed.ncbi.nlm.nih.gov/32367169/>) which recommends objective criteria for ultrasonographic evaluation of pulmonary manifestations in COVID-19. These authors blindly compared the diagnosis made by ultrasound versus histopathological analysis in 10 fatal COVID-19 cases. They found a full agreement between the two diagnostic modalities and determined that this fits with a high probability of COVID-19 based on lung ultrasound findings as recommended by Volpicelli et al. The authors suggest that ultrasound could be used to screen for suspected COVID-19 cases and monitor progression.

## SUMMARY

Summarizing excerpt: "We tested the agreement between US image patterns and histological alterations in 10 COVID-19 fatal cases by blindly comparing the diagnosis made by ultrasound and those obtained by histopathological analysis. A full agreement was obtained, fulfilling some criteria of category D of probability ("High probability") of COVID-19 based on patterns of lung ultrasound findings proposed by Volpicelli et al. (Figure 1)."

## FIGURES



"Correlation between lung ultrasound (LUS) postmortem images with histology findings in fatal cases of COVID-19. a, b COVID-19 pneumonia in the early phase with irregular and thickened pleural line (arrowhead) and spared areas with A line (arrow) at LUS examination. The histology shows acute pulmonary injury with hyaline membranes (arrow). c, d intermediary phase with pleural thickening and subpleural consolidations at LUS examination. The histology shows early fibroproliferative changes (in the center) associated with acute diffuse alveolar damage (DAD). e, f LUS examination shows thickened pleural line and consolidation (arrowhead) with air bronchograms (arrow) in the base of left lung. The histology shows fibroproliferative DAD."

## POTENTIAL PITFALLS OF ROUTINE SARS-COV-2 SEROLOGY FOR MASS SCREENING

Bélec L, Pétré H, Bouassa RM, Veyer D, Jenabian MA.. J Med Virol. 2020 Jun 2. doi: 10.1002/jmv.26034. Online ahead of print.

Level of Evidence: Other

### **BLUF**

Physicians and researchers in France highlight potential shortcomings for SARS-CoV-2 antibody serology testing. These shortcomings include an increased risk of false negative and false positive results and lack of detection for the unique neutralizing antibodies considered protective in convalescent COVID-19 individuals. They suggest that current SARS-CoV-2 serology may be inadequate for widespread screening.

### **ABSTRACT**

There are potential pitfalls of routine SARS-CoV-2 serology for mass screening.

## DEVELOPMENTS IN DIAGNOSTICS

### **CLINICAL PERFORMANCE OF THE ROCHE SARS-COV-2 SEROLOGIC ASSAY**

Tang MS, Hock KG, Logsdon NM, Hayes JE, Gronowski AM, Anderson NW, Farnsworth CW.. Clin Chem. 2020 Jun 2:hvaa132.

doi: 10.1093/clinchem/hvaa132. Online ahead of print.

Level of Evidence: 2

### **BLUF**

In this study the authors assess the Roche SARS-CoV-2 serologic assay which measures total immunoglobulin (IgG, IgA, and IgM) and compare it to the Abbott and EUROIMMUN (EI) assays they have previously examined. The specificity and sensitivity for the Roche assay, measured at least 14 days after the onset of symptoms, is 98.69% and 89.36% respectively (Fig. 1), which does not differ significantly from the Abbott or EI assays. The authors conclude that any of these three assays can detect antibodies to SARS-CoV-2 in the majority of people after 2 weeks of illness, but do not endorse their use prior to that time frame.

## FIGURES

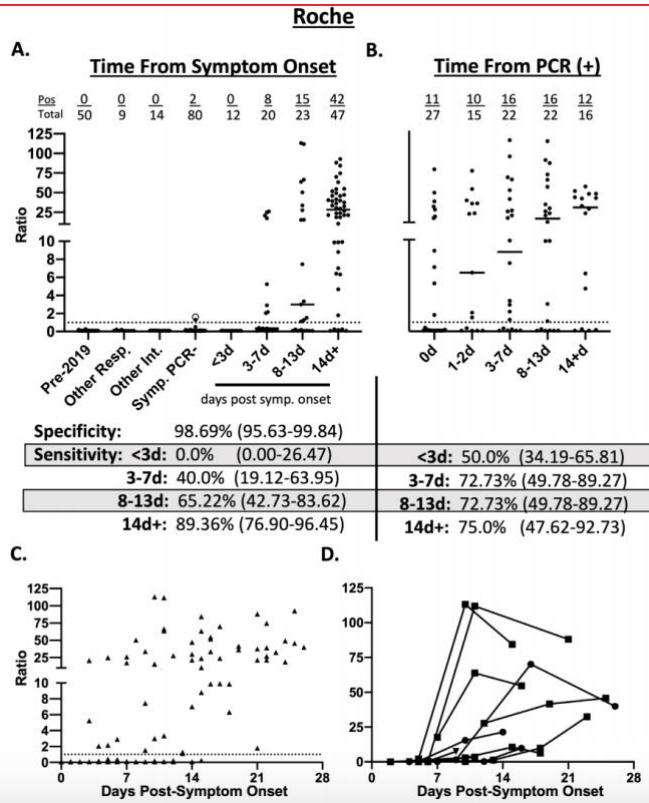


Figure 1. Clinical performance of Roche SARS-CoV-2 Immunoassay. (A) Seropositivity in 153 expected negative specimens and 102 specimens from 48 patients with PCR positive COVID-19 relative to days from onset of symptoms. (B) Seropositivity in 102 specimens from 48 patients with PCR-positive COVID-19 relative to days from testing positive by PCR. Pre-2019 -- 50 specimens collected in 2015 and stored at -80°C. Other. Resp. -- specimens from patients with PCR confirmed Influenza A (n=2), influenza B(n=2), other non-COVID-19 coronaviruses (n=5, including Coronaviruses HKU1, NL63, and 229E). Other Int. -- specimens from patients with positive CMV IgG (n=5), EBV VCA IgG (n=5), EBV VCA IgM (n=3), Rheumatoid factor (n=1). Symp. PCR- specimens from 80 patients presenting to the hospital with symptoms of respiratory infection and PCR negative for COVID-19. The large open circle represents a patient who was PCR negative but had symptoms consistent with COVID-19 and prolonged exposure to a family member with PCR confirmed COVID-19. Values in parentheses represent 95% confidence interval. (C) Seropositivity relative to days of symptom onset. Dotted line represents the cutoff off for positivity (Ratio  $\geq 1.0$ ). (D) Kinetics of the antibody response in 12 patients with serial samples.

## BIOSENSORS FOR MANAGING THE COVID-19 CYTOKINE STORM: CHALLENGES AHEAD

Russell SM, Alba-Patiño A, Baron E, Borges M, González-Freire M, de la Rica R.. ACS Sens. 2020 Jun 2. doi: 10.1021/acssensors.0c00979. Online ahead of print.

Level of Evidence: Other

### BLUF

This article proposes biosensor prototypes as instruments with promising potential for monitoring cytokine levels in COVID-19 patients and suggests their utility for minimizing side effects associated with anti-inflammatory therapeutics (Table 1). Biosensors have the capability to detect inflammatory markers, and this technological advancement may be harnessed to deliver versatility in monitoring many other biomarkers with future research. This technology has important implications for the future of precision medicine such as with real-time monitoring (Figure 3) of inflammatory syndromes caused by COVID-19.

### SUMMARY

Summarizing excerpt:

"All in all, we propose that the ideal device for managing the cytokine storm responsible for severe and critical COVID-19 cases

should encompass all the features of current biosensors, that is, they should monitor the levels of several cytokines simultaneously in raw blood samples, have a rapid turnaround time, be easy to dispose of and use portable readers. Paper biosensors can be destroyed by incineration which is important to meet biosafety regulations. Readers should also be easily disinfected, especially for decentralized testing. Wearable biosensors would enable the continuous monitoring of patients, a much-desired feature, however the technology still needs further development to be ready for clinical translation. The information provided by these devices should then be combined with patient data (age, comorbidities, treatments, microbiology results) in order to assess the risk of a bad prognosis. Using the information from these biosensors to train a neural network has the potential to achieve this goal."

## ABSTRACT

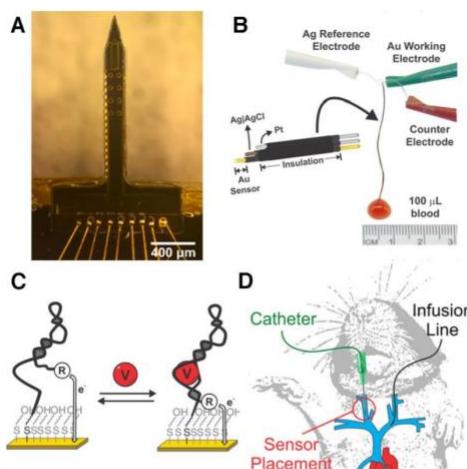
The global COVID-19 pandemic has oversaturated many intensive care units to the point of collapse, leading to enormous spikes in death counts. Before critical care becomes a necessity, identifying patients who are likely to become critically ill and providing prompt treatment is a strategy to avoid ICU oversaturation. There is a consensus that a hyperinflammatory syndrome or a "cytokine storm" is responsible for poor outcomes in COVID-19. Measuring cytokine levels at the point of care is required in order to better understand this process. In this Perspective paper we summarize the main events behind the cytokine storm in COVID-19 as well as current experimental treatments. We advocate for a new biosensor-enabled paradigm to personalize the management of COVID-19 and stratify patients. Biosensor-guided dosing and timing of immunomodulatory therapies could maximize the benefits of these anti-inflammatory treatments while minimizing deleterious effects. Biosensors will also be essential in order to detect complications such as co-infections and sepsis, which are common in immunosuppressed patients. Finally, we propose the ideal features of these biosensors using some prototypes from the recent literature as examples. Multisensors, lateral flow tests, mobile biosensors and wearable biosensors are seen as key players for precision medicine in COVID-19.

## FIGURES

Table 1. Main immunomodulators proposed so far for managing inflammation in COVID-19.

Immunomodulator	Target	Mechanism
Corticosteroids	Non-specific	Binding to receptor enhances or represses the transcription of inflammation genes
(hydroxy)chloroquine	Non-specific	Suppressing the activation of T cells
Convalescent plasma	Non-specific	Unknown
Immunoglobulins	Non-specific	Binding to Fc receptors
Azithromycin	Non-specific	Decreasing the pro-inflammatory response
Baricitinib	JAK	Inhibitor of Janus kinase (JAK)
Anakinra	IL-1	Antagonist of the IL-1 receptor
Tocilizumab/Sarilumab	IL-6	Binding to IL-6 receptor thus blocking the interaction with gp130

Table 1: Summarizes some anti-inflammatory treatments proposed so far for ameliorating the cytokine storm in COVID-19 patients. It should be noted that the evidence supporting these treatments is weak. In other words, randomized clinical trials for these drugs in the context of COVID-19 care have not yet been completed. Their use is not recommended in official protocols by WHO, only for clinical trials or compassionate motives. Many are repurposed drugs already in use for other diseases and syndromes, but not for infections.



**Figure 3.** Potential wearable biosensors for inflammation monitoring; (A) Needle shaped microelectrodes for IL-6 detection could be inserted into the blood stream for continuous cytokine monitoring. Reprinted with permission from reference 53. Copyright (2019) Elsevier (B) Electrode configuration, (C) aptamer conformational change and (D) *in vivo* implementation of electrochemical sensors. Reprinted with permission from reference 54. Copyright (2019) The American Chemical Society.

# DEVELOPMENTS IN TREATMENTS

## A LESSON FROM A SABOTEUR: HIGH MOLECULAR WEIGHT KININOGEN (HMWK) IMPACT IN COVID-19

Colarusso C, Terlizzi M, Pinto A, Sorrentino R.. Br J Pharmacol. 2020 Jun 4. doi: 10.1111/bph.15154. Online ahead of print.  
Level of Evidence: 5

### BLUF

A review written by researchers from the University of Salerno and ImmunePharma in Italy describe how the binding of the angiotensin converting enzyme 2 receptor by SARS-CoV-2 (Figure 1) leads to upregulation of bradykinin, the metabolites of which may be responsible for the manifestations of systemic inflammation commonly seen in COVID-19. As bradykinin upregulates the kallikrein-kinin system (Figure 2), the authors propose that pharmacologic blockade of high molecular weight kininogen metabolism by the drug lanadelumab (traditionally used for the treatment of hereditary angioedema) may be useful in the treatment of COVID-19.

### FIGURES

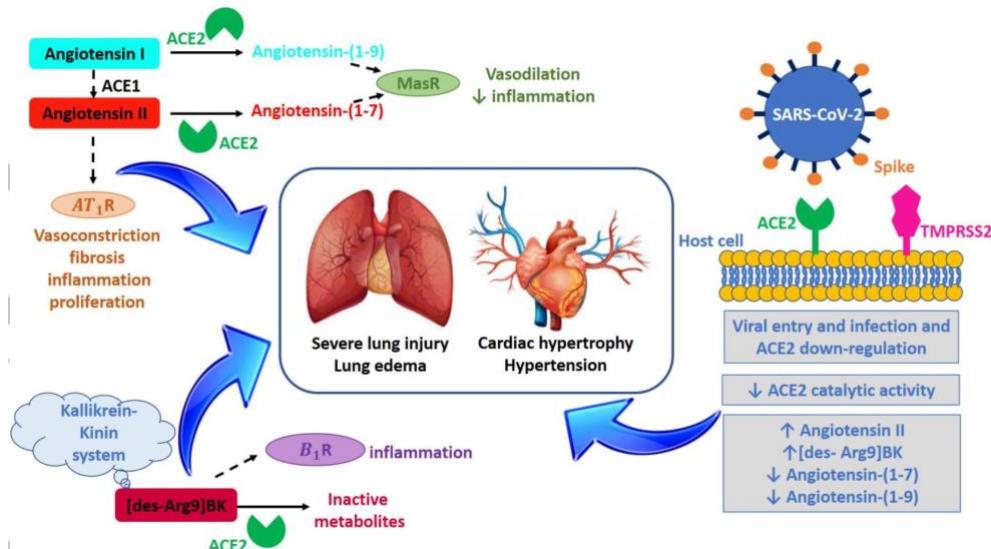


Figure 1: ACE2 function and its regulation in SARS-CoV-2 infection.

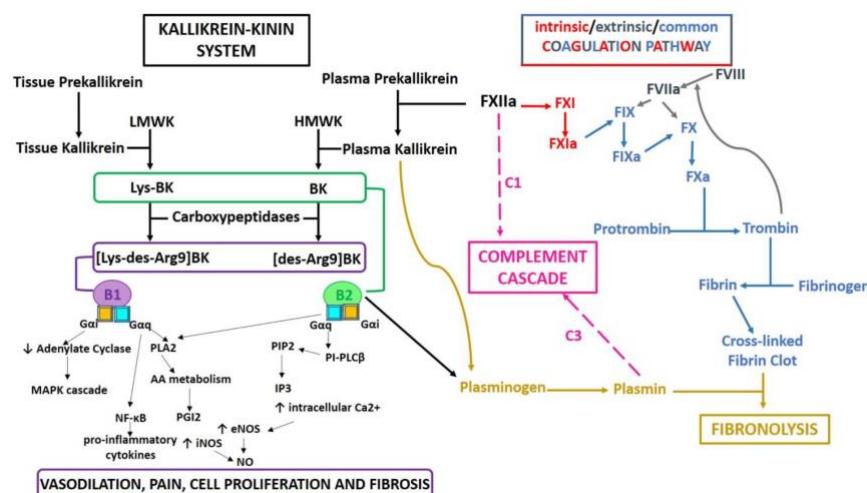


Figure 2: Crosstalk between Kallikrein-Kinin System (KKS), coagulation, fibrinolysis and complement cascade.

# SARS-COV-2 SPIKE PROTEIN: AN OPTIMAL IMMUNOLOGICAL TARGET FOR VACCINES

Salvatori G, Luberto L, Maffei M, Aurisicchio L, Roscilli G, Palombo F, Marra E.. J Transl Med. 2020 Jun 3;18(1):222. doi: 10.1186/s12967-020-02392-y.

Level of Evidence: 5

## BLUF

Authors from the Italian biotech industry describe current strategies and developmental vaccines to target the SARS-CoV-2 spike protein (Table 1), a strategy justified by preclinical studies on the homolog virus SARS-CoV. While there are concerns that antibody dependent enhancement of SARS-CoV-2 could be a barrier to vaccine development, animal models have not shown this effect. The authors' summary contributes to the body of knowledge necessary to develop an effective vaccine against SARS-CoV-2.

## FIGURES

Companies	Vaccination typology	Current development stage
Altimune	A replication-defective adenovirus vector incorporating the SARS-CoV-2 S protein administered by an intranasal single-dose	The vaccine design and synthesis steps are completed. Moving toward preclinical tests and manufacture, hoping to start phase 1 trial at mid-August
CanSino biologicals	Adenovirus type 5 vector that expresses S protein	Phase I (NCT04313127) completed Phase II started: It is China's first recombinant vaccine candidate for novel coronavirus entering Phase II of a human clinical trial, with 500 volunteer participants
(Sichuan) Clover Biopharmaceuticals (Chengdu, China) Partnered with GlaxoSmithKline	Recombinant SARS-CoV-2 S-protein trimer subunit produced by its patented Trimer-Tag® technology	Carrying out preclinical tests with GlaxoSmithKline's pandemic vaccine adjuvant technology and in collaboration with Dynavax, proprietary holder of toll-like receptor 9 agonist adjuvant, CpG 1018
Inovio Pharmaceuticals	Electroporation of DNA INO-4800 encoding SARS-CoV-2 S protein	Started trial in United States (Phase 1 NCT04336410). There are already 3000 doses available
LineaRx Takis Biotech (Rome) to clinical test candidates in Italy	Electroporation of linear DNA encoding S protein or its specific portions	Five candidates have been designed of linear DNA vaccine based on S protein and selected epitopes, ready for testing by the beginning of May or June
Moderna	The mRNA encoding SARS-CoV-2 S protein is encapsulated in ionizable lipid, stearoyl phosphatidylcholine, cholesterol and polyethylene glycol lipid	Phase 1 (NCT04283461) testing is underway
Novavax	Nanoparticle displaying SARS-CoV 2 S protein with saponin-based (Matrix-M) adjuvant	Currently assessing the candidates in animal models, expecting to start Phase 1 trial in June 2020
University of Queensland (Brisbane, Australia)	Recombinant subunit of SARS-CoV-2 S protein locked in prefusion conformation by polypeptide moiety (molecular clamp)	In preclinical testing, partnering with Dynavax Technologies Corp. in collaboration with GlaxoSmithKline plc and Seqirus GmbH

Table 1. Developmental vaccines targeting SARS-CoV-2 protein S

## MENTAL HEALTH & RESILIENCE NEEDS

### COVID-19 EMERGENCY IN THE HOSPITAL: HOW THE CLINICAL PSYCHOLOGY UNIT IS RESPONDING

Cao di San Marco E, Menichetti J, Vegni E.. Psychol Trauma. 2020 Jun 1. doi: 10.1037/tra0000684. Online ahead of print.  
Level of Evidence: Other

#### BLUF

The authors describe in a commentary the psychological services put into place in a large public hospital in Lombardy, Italy to serve healthcare workers, patients, and their families as they deal with the COVID-19 pandemic. The psychological services were set up with the express intention of addressing problems arising from the pressures and demands of the pandemic and are summarized below.

#### SUMMARY

Remedies put into place included the setup of a decompression room for healthcare workers, where they could find reprieve from the on-going demands of their duties, and small-group sessions where a psychologist would visit the workers at their worksite to allow them to mentally work through what they were experiencing while treating critically ill patients. For patients' families who could not visit the patients, phone calls were made by a psychologist to support the family not only during the courses of the illness, but also, if the patient died, 48 hours after their passing to help the family cope and find some degree of closure. Psychological services were also provided to the patient to help cope with feelings of isolation, anxiety, and depression. These various psychological procedures that were put into place by the hospital emphasized the need for services to maintain the mental well-being of the patient as well as the healthcare system.

#### ABSTRACT

The present commentary describes the main care services implemented by the clinical psychology unit of an Italian hospital to cope with the COVID-19 emergency outbreak. The unit's main goal has been to support and protect health care professionals, relatives of hospitalized patients, and patients themselves from further psychological distress. Details and insights are shared.

### DOMESTIC VIOLENCE AMID COVID-19

Anurudran A, Yared L, Comrie C, Harrison K, Burke T.. Int J Gynaecol Obstet. 2020 May 30. doi: 10.1002/ijgo.13247. Online ahead of print.  
Level of Evidence: Other

#### BLUF

Public health researchers affiliated with Harvard and Cambridge Universities discuss the risk of shelter-in-place orders for survivors of domestic violence and make a call-to-action to address this crisis. They note survivors are at risk for further violence and have limited access to support networks, following similar trends in domestic violence during times of natural disasters. The authors advocate that COVID-19 testing sites should incorporate domestic violence screenings, that grocery stores and other essential public places should establish discrete reporting platforms, and that domestic violence survivors and advocates must participate in the public health discussions regarding the COVID-19 response.

#### ABSTRACT

This manuscript highlights the risk that shelter-in-place instructions during COVID-19 places on victims of domestic violence and serves as a call-to-action to address this crisis. In the midst of the COVID-19 pandemic, "stay at home" has become the mantra of governments and public health organizations alike. But for victims of domestic violence, home is often not a place of safety. Staying at home not only places survivors of domestic violence at risk for further violence, but also isolates them from networks of support. Containment policies may lead to higher rates of domestic violence, substance abuse, anxiety, major depression, suicide, and other manifestations of unmet mental health needs. Job losses and financial insecurity may tip at-risk relationships into violence.

### PSYCHOSOCIAL REACTIONS TO PLAGUES IN THE CULTURAL HISTORY OF MEDICINE: A MEDICAL HUMANITIES APPROACH

Wigand ME, Becker T, Steger F.. J Nerv Ment Dis. 2020 Jun;208(6):443-444. doi: 10.1097/NMD.0000000000001200.  
Level of Evidence: Other

## **BLUF**

Researchers from Germany used previous historical narrations of plagues in Greece, Italy, and Algeria to provide psychiatrists with knowledge to better understand the psychosocial response and coping strategies of people during pandemics. They found that:

1. Psychological reactions are complex and often contradictory, consisting of multi-step phases
2. Volunteering can be used as a coping mechanism.

## **ABSTRACT**

The aim of this work is to elucidate psychosocial reactions to plagues by analyzing three landmark descriptions from different eras: Thucydides' description of the plague of Athens (430 BC) in *The History of the Peloponnesian War*, Giovanni Boccaccio's description of the plague in Florence (1348) in *The Decameron*, and Albert Camus' description in *The Plague* (1947). Using a narrative inquiry, we found psychosocial reactions to be complex and ambivalent and could discern several coping strategies. We propose that this knowledge can help psychiatrists and other healthcare professionals during the ongoing COVID-19 pandemic.

## **HEIGHTENED RISK OF CHILD MALTREATMENT AMID THE COVID-19 PANDEMIC CAN EXACERBATE MENTAL HEALTH PROBLEMS FOR THE NEXT GENERATION**

Cuartas J.. Psychol Trauma. 2020 May 28. doi: 10.1037/tra0000597. Online ahead of print.

Level of Evidence: Other

## **BLUF**

A commentary by a graduate student of social sciences at Harvard University demonstrates that during the COVID-19 pandemic and ensuing quarantine orders there has been an uptick of partner and child abuse. The author asserts that the children that are witnessing and subjected to this abuse will carry long term effects, like emotional dysregulation, including, but not limited to, depression and anxiety, necessitating that we take quick action to increase psychosocial and economic supports to decrease the stress loads on families.

## **ABSTRACT**

The spread of the COVID-19 disrupted ecological systems in which children develop, exacerbating threats to their safety and increasing their vulnerability to future psychopathology. Supports to reduce sources of stress for caregivers and protect children from threats to their safety are warranted.

## POSITIVE IMPACT OF MEASURES AGAINST COVID-19 ON REDUCING INFLUENZA IN THE NORTHERN HEMISPHERE

Chan CP, Wong NS, Leung CC, Lee SS.. J Travel Med. 2020 May 28:taaa087. doi: 10.1093/jtm/taaa087. Online ahead of print.  
Level of Evidence: Other

### BLUF

The authors analyzed weekly rates of laboratory-confirmed influenza cases between 2014-2015 and 2019-2020 and mobility trends in transit stations from the start of the COVID-19 epidemic in Hong Kong, South Korea, Taiwan, Europe, and the United States, as seen in Figure 1. It was determined that social distancing due to COVID-19 indirectly reduced and shortened the concurrent 2019-2020 winter influenza season in Northern Hemispheric countries with the onset of COVID-19 coinciding with declining weekly influenza rates and human mobility.

### FIGURES

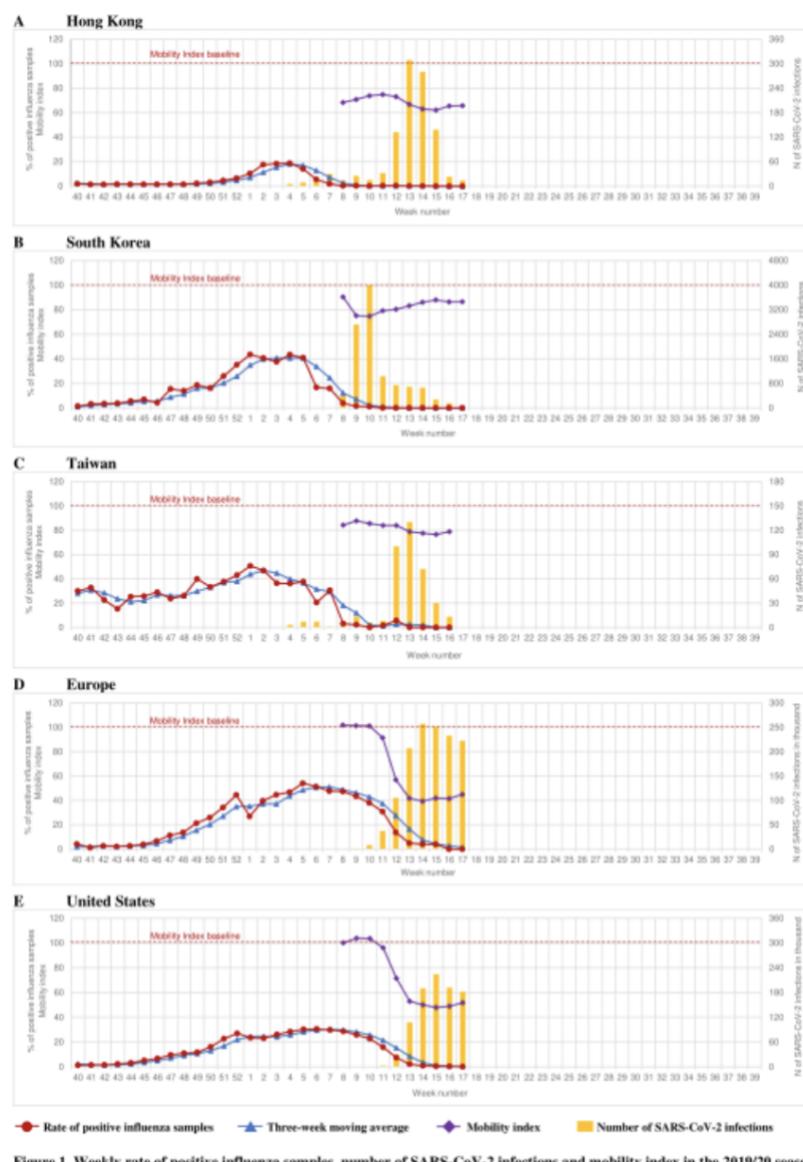


Figure 1. Weekly rate of positive influenza samples, number of SARS-CoV-2 infections and mobility index in the 2019/20 season

Figure 1. Weekly rate of positive influenza samples, number of SARS-CoV-2 infections and mobility index in the 2019/20 season in Hong Kong (A), South Korea (B), Taiwan (C), Europe (D) and the United States (E). The scales of number of SARS-CoV-2 infections in A-E were different. Mobility index reflected the visits and duration of stay at transit stations compared to the baseline period from 3rd January to 6th February 2020.

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