The Daily COVID-19 Literature Surveillance Summary

February 10, 2021

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

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

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

How to cite the Levels of Evidence Table

OCEBM Levels of Evidence Working Group*. "The Oxford 2011 Levels of Evidence".

Oxford Centre for Evidence-Based Medicine. http://www.cebm.net/index.aspx?o=5653

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

EXECUTIVE SUMMARY

Understanding the Pathology

- Immunologists, microbiologists, and other infectious disease experts from La Jolla Institute for Immunology and University of California, San Diego evaluated immunological memory in 188 patients who provided at least one post-SARS-CoV-2 infection blood sample, with 43 providing longitudinal samples. Spike protein IgG remained stable at 6 months. Compared to one month post-infection, at 6-8 months CD8+T cells declined (70% vs. 50%)(Figure 3) but CD4+T cell memory was maintained (93% vs 92%). Though more corroborating research is needed, authors suggest SARS-CoV-2 infection generates significant immune memory that may be protective against reinfection.

Management

- This study from Columbia University investigates the different phases of COVID-19 infectivity and relates them to targeted therapies in order to determine the most effective time periods in which clinicians ought to intervene. The authors divide infectivity into three periods and five distinct phases and urge scientists to use this framework when studying therapeutics in order to maximize efficacy, using the HIV/AIDS era as an example of how targeted intervention based off infectivity can lead to better outcomes.

Adjusting Practice During COVID-19

- This retrospective study from the Universidade da Coruña, Spain, investigates the impact of the COVID-19 pandemic and subsequent face mask use on the feasibility and results of exercise stress testing. While the patients using face masks during testing did have higher levels of dyspnea, there was no significant difference in baseline characteristics such as functional capacity. Thus the authors conclude that face mask usage does not change the clinical profile of patients undergoing cardiac exercise stress testing.

Mental Health & Resilience Needs

- Social epidemiologists and emergency physicians from Ontario, Canada compared the quantity of emergency department (ED) admissions to The Ottawa Hospital for sexual assault and domestic violence from a 2020 COVID-19 time period (March 4 2020 until May 5 2020) with a time matched control group from 2018. They found the number of ED admissions to the Sexual Assault and Domestic Violence Program decreased by 32.93% (56.52% for sexual assault, 48.48% for domestic violence cases). Psychological abuse and outdoor assault increased by 16.9% and 17.6%, respectively. Authors suggest pandemic conditions have decreased victims' access to services, and recommend the development of alternative resources as well as continued monitoring as countries change their lockdown policies.

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ADULTS

THE PROPORTION OF SARS-COV-2 INFECTIONS THAT ARE ASYMPTOMATIC : A SYSTEMATIC REVIEW

Oran DP, Topol EJ.. Ann Intern Med. 2021 Jan 22. doi: 10.7326/M20-6976. Online ahead of print.
Level of Evidence: 2 - Systematic review of surveys that allow matching to local circumstances

BLUF

A team from the Scripps Research Translational Institute in California conducted a systematic review of 61 studies assessing the frequency of asymptomatic SARS-CoV-2 infections published through November 17, 2020. A median of 65.9% of patients with a positive PCR (43 studies) and 41.2% with positive antibody test (18 studies) were asymptomatic at time of their positive test (Tables 1, 2). In 14 studies reporting longitudinal symptom evolution data, a median of 72.3% of those who tested positive were asymptomatic throughout each study's follow up period (Table 3) while nation-wide serosurveys from 6 countries indicated at least 33.3% of SARS-CoV-2 infections were asymptomatic. Authors suggest asymptomatic infection is common, and infection control measures should include measures to screen for asymptomatic infection.

ABSTRACT

BACKGROUND: Asymptomatic infection seems to be a notable feature of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the pathogen that causes coronavirus disease 2019 (COVID-19), but the prevalence is uncertain. PURPOSE: To estimate the proportion of persons infected with SARS-CoV-2 who never develop symptoms. DATA SOURCES: Searches of Google News, Google Scholar, medRxiv, and PubMed using the keywords antibodies, asymptomatic, coronavirus, COVID-19, PCR, seroprevalence, and SARS-CoV-2. STUDY SELECTION: Observational, descriptive studies and reports of mass screening for SARS-CoV-2 that were either cross-sectional or longitudinal in design; were published through 17 November 2020; and involved SARS-CoV-2 nucleic acid or antibody testing of a target population, regardless of current symptomatic status, over a defined period. DATA EXTRACTION: The authors collaboratively extracted data on the study design, type of testing performed, number of participants, criteria for determining symptomatic status, testing results, and setting. DATA SYNTHESIS: Sixty-one eligible studies and reports were identified, of which 43 used polymerase chain reaction (PCR) testing of nasopharyngeal swabs to detect current SARS-CoV-2 infection and 18 used antibody testing to detect current or prior infection. In the 14 studies with longitudinal data that reported information on the evolution of symptomatic status, nearly three quarters of persons who tested positive but had no symptoms at the time of testing remained asymptomatic. The highest-quality evidence comes from nationwide, representative serosurveys of England (n = 365 104) and Spain (n = 61 075), which suggest that at least one third of SARS-CoV-2 infections are asymptomatic. LIMITATION: For PCR-based studies, data are limited to distinguish presymptomatic from asymptomatic infection. Heterogeneity precluded formal quantitative syntheses. CONCLUSION: Available data suggest that at least one third of SARS-CoV-2 infections are asymptomatic. Longitudinal studies suggest that nearly three quarters of persons who receive a positive PCR test result but have no symptoms at the time of testing will remain asymptomatic. Control strategies for COVID-19 should be altered, taking into account the prevalence and transmission risk of asymptomatic SARS-CoV-2 infection. PRIMARY FUNDING SOURCE: National Institutes of Health.

Study or Report	Tested, *n**	Longitudinal Data*	Random Sampling*	SARS-CoV-2-Positive, *n* (%)	Positive, but No Symptoms, *n* (%)
England residents 1 (10-12)	**932 072**	No	**Yes**	3029 (0.3)	1425 (47.0)
Belgium long-term care facility residents and staff (13)	**280 427**	No	No	8343 (3.0)	6244 (74.8)
England residents 2 (14)	**36 061**	No	**Yes**	115 (0.3)	88 (76.5)
U.S. skilled-nursing facility residents (15)†	**22 368**	**Yes**	No	5403 (24.2)	2194 (40.6)
Iceland residents (16)	**13 080**	No	**Yes**	100 (0.8)	43 (43.0)
Vo', Italy, residents (17)	5155	**Yes**	No	102 (2.0)	34 (42.5)
U.S. Navy aircraft carrier crew (18)	4779	**Yes**	No	1271 (26.6)	572 (45.0)
Arkansas, North Carolina, Ohio, and Virginia inmates (19)	4693	No	No	3277 (69.8)	3146 (96.0)
San Francisco, California, residents (20)	3871	**Yes**	No	83 (2.1)	23 (27.7)
Arkansas poultry employees (21)	3748	No	No	481 (12.8)	455 (94.6)
Diamond Princess cruise ship passengers and crew (22)	3618	**Yes**	No	712 (19.7)	311 (43.7)
Indiana residents (23)†‡	3605	No	**Yes**	47 (1.7)	18 (44.2)
South London, England, nursing home residents and staff (24)	2455	No	No	160 (6.5)	115 (71.9)
U.S. Marine recruits (25)	1801	**Yes**	No	51 (2.8)	46 (90.2)
Charles de Gaulle aircraft carrier crew (26)	1568	**Yes**	No	1001 (63.8)	130 (13.0)
Marseille, France, long-term care facility residents (27)	1691	**Yes**	No	226 (13.4)	46 (23.0)
King County, Washington, homeless shelter residents and staff (28)	1434	No	No	29 (2.0)	21 (72.4)
Germany oncology clinic patients (29)	1286	No	No	40 (3.1)	37 (92.5)
Pasadena, California, long-term care facilities residents and staff (30)	938	No	No	631 (67.3)	257 (40.7)
Rutgers University students and employees (31)	829	No	No	41 (4.9)	27 (65.9)
Greek citizens evacuated from the United Kingdom, Spain, and Turkey (32)†	783	**Yes**	No	40 (5.1)	35 (87.5)
Boston, Massachusetts, obstetric patients (33)	757	No	No	20 (2.6)	9 (45.0)
Córdoba, Colombia, residents (34)	686	No	No	35 (5.1)	18 (51.4)
New York City obstetric patients 1 (35)	675	No	No	70 (10.4)	55 (78.6)
Santiago, Chile, obstetric patients (36)	586	No	No	37 (6.3)	16 (43.2)
Japanese citizens evacuated from Wuhan, China (37)	564	**Yes**	No	11 (2.0)	3 (27.3)
London nursing home residents and staff (38)	518	**Yes**	No	158 (30.5)	72 (45.6)
Indian citizens evacuated from Iran (39)	474	**Yes**	No	48 (10.1)	44 (91.7)
Maryland long-term care facility residents (40)	426	**Yes**	No	177 (41.5)	154 (87.0)
South India retinal surgery patients (41)	413	No	No	9 (2.2)	9 (100.0)
Boston homeless shelter occupants (42)	408	No	No	147 (36.0)	129 (87.8)
Seafood plant employees (43)§	376	No	No	124 (33.0)	118 (95.0)
Genoa, Italy, obstetric patients (44)	333	No	No	7 (2.1)	6 (85.7)
London maternity hospital staff (45)	266	**Yes**	No	47 (17.7)	16 (34.0)
Argentine cruise ship passengers and crew (46)	217	No	No	128 (59.0)	104 (81.3)
New York City obstetric patients 2 (47)	214	**Yes**	No	33 (15.4)	29 (87.9)
Bogotá, Colombia, airport employees (48)	212	**Yes**	No	35 (16.5)	24 (68.6)
Porto, Portugal, obstetric patients (49)	184	No	No	11 (6.0)	9 (81.8)
Los Angeles, California, homeless shelter occupants (50)	178	No	No	43 (24.2)	27 (62.8)
Illinois skilled-nursing facility residents (51)	126	**Yes**	No	33 (26.2)	13 (39.4)
Boston grocery store employees (52)	104	No	No	21 (20.2)	16 (76.2)
Los Angeles skilled-nursing facility residents (53)	99	**Yes**	No	19 (19.2)	6 (31.6)
King County nursing facility residents (54)	76	**Yes**	No	48 (63.2)	3 (6.3)

PCR = polymerase chain reaction; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
* Boldface indicates details that increase the likelihood of higher-quality evidence.
† Data clarified via personal communication with coauthor.
‡ Percentages reflect weighting by the study's authors to estimate statewide prevalence.
§ Estimated from incomplete source data.

Table 1: "Nucleic Acid PCR Testing".

Study or Report	Tested, *n**	Random Sampling*	SARS-CoV-2-Positive, *n* (%)	Asymptomatic, *n* (%)
England residents (55)	**365 104**	**Yes**	17 576 (4.8)	5694 (32.4)
Spain residents (56)	**61 075**	**Yes**	3053 (5.0)	1008 (33.0)
Detroit, Michigan, hospital staff (57)	**20 614**	No	1818 (8.8)	798 (43.9)
Wuhan, China, hospital staff (58)	8553	No	424 (5.0)	148 (34.9)
Bavaria, Germany, children aged 1–18 y (59)	4859	**Yes**	47 (1.0)	22 (46.8)
Louisiana residents (60)	4778	**Yes**	311 (6.5)	147 (47.3)
Munich, Germany, hospital staff (61)	4554	No	108 (2.4)	28 (25.9)
Cairo, Egypt, hospital staff (62)	4040	No	170 (4.2)	116 (68.2)
Health care personnel at 13 U.S. medical centers (63)	3248	No	194 (6.0)	56 (28.9)
Maranhão, Brazil, residents (64)	3156	**Yes**	1167 (37.0)	320 (27.4)
Ischgl, Austria, residents (65)	1473	No	622 (42.2)	529 (85.0)
Wuhan dialysis patients (66)	1027	No	99 (9.6)	50 (50.5)
Buenos Aires, Argentina, residents (67)	873	No	466 (53.4)	396 (85.0)
Connecticut residents (68)	567	**Yes**	23 (4.1)	5 (21.7)
Sweden nursing home staff (69)	459	No	86 (18.7)	40 (46.5)
London, England, dialysis patients (70)	356	No	129 (36.2)	52 (40.3)
Nashville, Tennessee, hospital staff (71)	249	No	19 (7.6)	8 (42.1)
London maternity unit staff (72)	200	No	29 (14.5)	10 (34.5)

SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
* Boldface indicates details that increase the likelihood of higher-quality evidence.

Table 2: "Antibody Testing".

Study	Initially Tested Positive Without Symptoms, *n*	Remained Asymptomatic, *n* (%)
U.S. skilled-nursing facility residents (15)	3227	2194 (68.0)
Vo', Italy, residents (17)	34	34 (100.0)
U.S. Navy aircraft carrier crew (18)	978	572 (58.5)
San Francisco, California, residents (20)	41	23 (56.1)
Diamond Princess cruise ship passengers and crew (22)	410	311 (75.9)
Greek citizens evacuated from the United Kingdom, Spain, and Turkey (32)*	39	35 (89.7)
Japanese citizens evacuated from Wuhan, China (37)	6	3 (50.0)
London, England, nursing home residents and staff (38)	67	46 (68.7)
Indian citizens evacuated from Iran (39)	44	44 (100.0)
Maryland long-term care facility residents (40)	177	154 (87.0)
New York City obstetric patients 2 (47)	29	26 (89.7)
Illinois skilled-nursing facility residents (51)	14	13 (92.9)
Los Angeles, California, skilled-nursing facility residents (53)	14	6 (42.9)
King County, Washington, nursing facility residents (54)	27	3 (11.1)

* Data clarified via personal communication with coauthor.

Table 3: "Evolution of Symptomatic Status".

THYROID DYSFUNCTION MAY BE ASSOCIATED WITH POOR OUTCOMES IN PATIENTS WITH COVID-19

Zhang Y, Lin F, Tu W, Zhang J, Choudhry AA, Ahmed O, Cheng J, Cui Y, Liu B, Dai M, Chen L, Han D, Fan Y, Zeng Y, Li W, Li S, Chen X, Shen M, Pan P; medical team from Xiangya Hospital to support Hubei, China.. Mol Cell Endocrinol. 2021 Feb 5;521:111097. doi: 10.1016/j.mce.2020.111097. Epub 2020 Dec 2.
Level of Evidence: 3 - Local non-random sample

BLUF

Physician and doctorate investigators from various medical institutions in China, Pakistan, and the US conducted a retrospective study of 71 COVID-19 patients admitted to West Court of Union Hospital in Wuhan, China, between January 29 through February 26, 2020, analyzing thyroid dysfunction (TD) in correlation with severity of COVID-19. The 25 patients with TD (elevated or decreased TSH, FT3, and/or FT4) had a statistically significant higher level of mortality (Figure 2), at 20% vs. 0% for non-TD patients (p = 0.002), as well as an increased hospital stay (defined as more than 28 days) of 80% vs. 56.52%, respectively (p = 0.048; Table 3). These results highlight that increased surveillance is needed for patients with TD, and suggest additional research and recognition be put into TD as a relevant comorbidity in the setting of COVID-19.

ABSTRACT

BACKGROUND: Coronavirus disease (COVID-19) has resulted in considerable morbidity and mortality worldwide. Thyroid hormones play a key role in modulating metabolism and the immune system. However, the prevalence of thyroid dysfunction (TD) and its association with the prognosis of COVID-19 have not yet been elucidated. In this study, we seek to address this gap and understand the link between TD and COVID-19. METHODS: Herein, we enrolled patients who were hospitalised with COVID-19 and had normal or abnormal thyroid function test results at the West Court of Union Hospital in Wuhan, China, between 29 January and 26 February 2020. We carried out follow up examinations until 26 April 2020. Data on clinical features, treatment strategies, and prognosis were collected and analysed. TD was defined as an abnormal thyroid function test result, including overt thyrotoxicosis, overt hypothyroidism, subclinical hypothyroidism, subclinical hyperthyroidism, and euthyroid sick syndrome. RESULTS: A total of 25 and 46 COVID-19 patients with and without TD, respectively, were included in the study. COVID-19 patients with TD had significantly higher neutrophil counts and higher levels of C-reactive protein, procalcitonin, lactate dehydrogenase, serum creatine kinase, aspartate transaminase, and high-sensitive troponin I and a longer activated partial thromboplastin time but lower lymphocyte, platelet, and eosinophil counts. A longitudinal analysis of serum biomarkers showed that patients with TD presented persistently high levels of biomarkers for inflammatory response and cardiac injury. COVID-19 patients with TD were more likely to develop a critical subtype of the disease. Patients with TD had a significantly higher fatality rate than did those without TD during hospitalisation (20% vs 0%, P<0.0001). Patients with TD were more likely to stay in the hospital for more than 28 days than were those without TD (80% vs 56.52%, P=0.048). CONCLUSIONS: Our preliminary findings suggest that TD is associated with poor outcomes in patients with COVID-19.

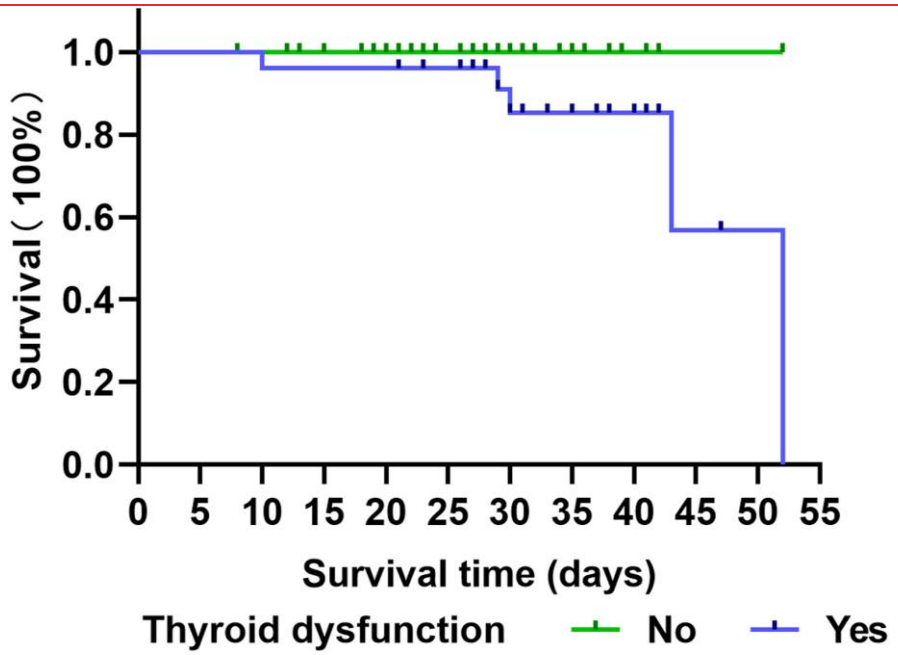

Figure 2. Kaplan-Meier Curve for mortality in COVID-19 patients with thyroid dysfunction (TD) or those without TD.

Table 3

Disease severity, treatment, and prognosis of COVID-19 patients.

Variable	Total (N = 71)	With TD (n = 25)	Without TD (n = 46)	*P*	COR (95%CI)	AOR (95%CI)
Severity, n (%)						
Mild to moderate	4 (5.6)	1 (4.0)	3 (6.5)	<0.001	0.597 (0.059, 6.063)	0.947 (0.064, 14.013)
Severe	50 (70.4)	10 (40.0)	40 (87.0)		0.100 (0.031, 0.323)	0.142 (0.040, 0.507)
Critical	17 (23.9)	14 (56.0)	3 (6.5)		18.242 (4.445, 74.862)	11.063 (2.478, 49.398)
Complications, n (%)						
Acute respiratory distress	14 (19.7)	11 (44.0)	3 (6.5)	<0.001	11.262 (2.744, 46.216)	8.494 (1.817, 39.717)
Acute cardiac injury	13 (18.3)	8 (32.0)	5 (10.9)	0.028	3.859 (1.103, 13.499)	1.707 (0.373, 7.804)
Acute kidney injury	7 (9.9)	5 (20.0)	2 (4.4)	0.035	4.190 (0.710, 24.730)	1.657 (0.213, 12.899)
Medication, n (%)						
Antiviral agent	66 (93.0)	24 (96.0)	42 (91.3)	0.460	2.286 (0.241, 21.642)	3.557 (0.251, 50.359)
Antibiotic	55 (77.5)	23 (92.0)	32 (69.6)	0.031	5.031 (1.041, 24.317)	4.459 (0.842, 23.598)
Corticosteroid	25 (35.2)	14 (56.0)	11 (23.9)	0.007	4.050 (1.431, 11.463)	3.270 (1.021, 10.475)
Oxygen support, n (%)						
Nasal cannula	57 (80.3)	22 (88.0)	35 (76.1)	0.228	2.305 (0.578, 9.193)	3.217 (0.652, 15.866)
High-flow oxygen	12 (16.9)	10 (40.0)	2 (4.4)	<0.001	14.667 (2.881, 74.659)	10.449 (1.787, 61.086)
Non-invasive ventilation	10 (14.1)	8 (32.0)	2 (4.4)	0.001	10.353 (1.993, 53.772)	10.639 (1.726, 65.567)
Invasive ventilation	5 (7.0)	7 (20.0)	0 (0)	0.002	N/A	N/A
Prognosis, n (%)						
Hospital stay≥28 days	46 (64.79)	20 (80.0)	26 (56.52)	0.048	3.077 (0.984, 9.623)	2.630 (0.713, 9.700)
Death	5 (7.0)	5 (20.0)	0 (0)	0.002	N/A	N/A
Discharged	66 (93.0)	20 (80.0)	46 (100)		N/A	N/A

TD, thyroid dysfunction. Data were presented as n (%).COR, crude odd ratios; AOR, Adjusted for age, sex and hypertension; CI, confidence interval. A P value < 0.05 was considered statistically significant.

LONG-TERM SERO-POSITIVITY FOR IGG, SEQUELAE OF RESPIRATORY SYMPTOMS, AND ABUNDANCE OF MALFORMED SPERMS IN A PATIENT RECOVERED FROM SEVERE COVID-19

Zhu M, Chen D, Zhu Y, Xiong X, Ding Y, Guo F, Zhu M, Zhou J.. Eur J Clin Microbiol Infect Dis. 2021 Feb 8. doi: 10.1007/s10096-021-04178-6. Online ahead of print.
Level of Evidence: 5 - Case Report

BLUF

Researchers from The First People's Hospital of Tianmen City and Hubei University of Medicine present a case of a 30-year-old male who battled severe COVID-19 from late January through early March 2020, detailing the sequelae of disease during his rehabilitation including development of sleep apnea, high rate of sperm deformity, and persistent IgG levels. This study highlights the importance of continued surveillance during the recovery period of COVID-19 in order to better understand and prevent long standing infection complications and treatment adverse effects.

SUMMARY

The patient, a 30-year-old previously healthy male with no past medical history, first presented to local center on January 19, 2020 with classic symptoms of COVID-19. He was instructed to recover in isolation, however returned on January 23 when symptoms increased and he was admitted to his local hospital. On January 30 he decompensated to ARDS, and transferred to Wuhan Jinyintan Hospital. Of note, throat swabs for SARS-CoV-2 were reported negative until January 30. He was treated with anti-fungal (itraconazole), antivirus (recombinant human interferon α2b spray), anti-infection (desloratadine citrate disodium) and glucocorticoid (methylprednisolone). His condition improved and he was discharged on March 1, 2020, however was readmitted from March 9 through 11 for dizziness, chest tightness, dry cough, and shortness of breath. He has been monitored through his recovery, with respiratory symptom sequelae persisting. Progression of lung manifestations can be seen in Figure 1 starting with original presentation on January 19, 2020 through May 25, 2020. Sleep study on May 31, 2020 revealed elevated apnea hypopnea index (AHI) at 8.53 (normal < 5.0), with oxygen saturation of 92% (normal 94– 98%), and he was diagnosed with obstructive sleep apnea hypopnea syndrome and nocturnal sleep hypoxemia. During rehabilitation period his sperm was also tested, revealing 219 out of 227 (96.48%) were abnormal (Figure 2), with head, middle, and tail deformities. Additionally, SARS-CoV-2 specific IgG antibodies continue to be elevated (Table 2), with most recent confirmation in December, 2020. This case highlights the enduring complications of COVID-19, with additional and unknown permanence of complications.

ABSTRACT

Patients with severe coronavirus disease in 2019 (COVID-19 pneumonia) may have many sequelae, which seriously affect their quality of life and work. Here, we report a case of infection in China, reviewed the course, treatment, and rehabilitation of a patient suffering from severe COVID-19 pneumonia, and collected his examination reports, including chest CT, laboratory examination results, lung function examination, sleep monitoring report, sex hormones, sperm morphology and activity. The patient's antiviral immunoglobulin G (IgG) continued to be positive for more than 11 months, and his small airway function was abnormal, and he suffered from respiratory problems (cough, chest pain, chest tightness, and shortness of breath), unstructured sleep apnea hypopnea syndrome, and nocturnal sleep hypoxemia. His abnormal sperm rate increased obviously, and sperm activity decreased obviously. Patients with severe COVID-19 pneumonia may have respiratory sequela, the abnormal sperm rate is obviously increased, and IgG positive can last for a long time.

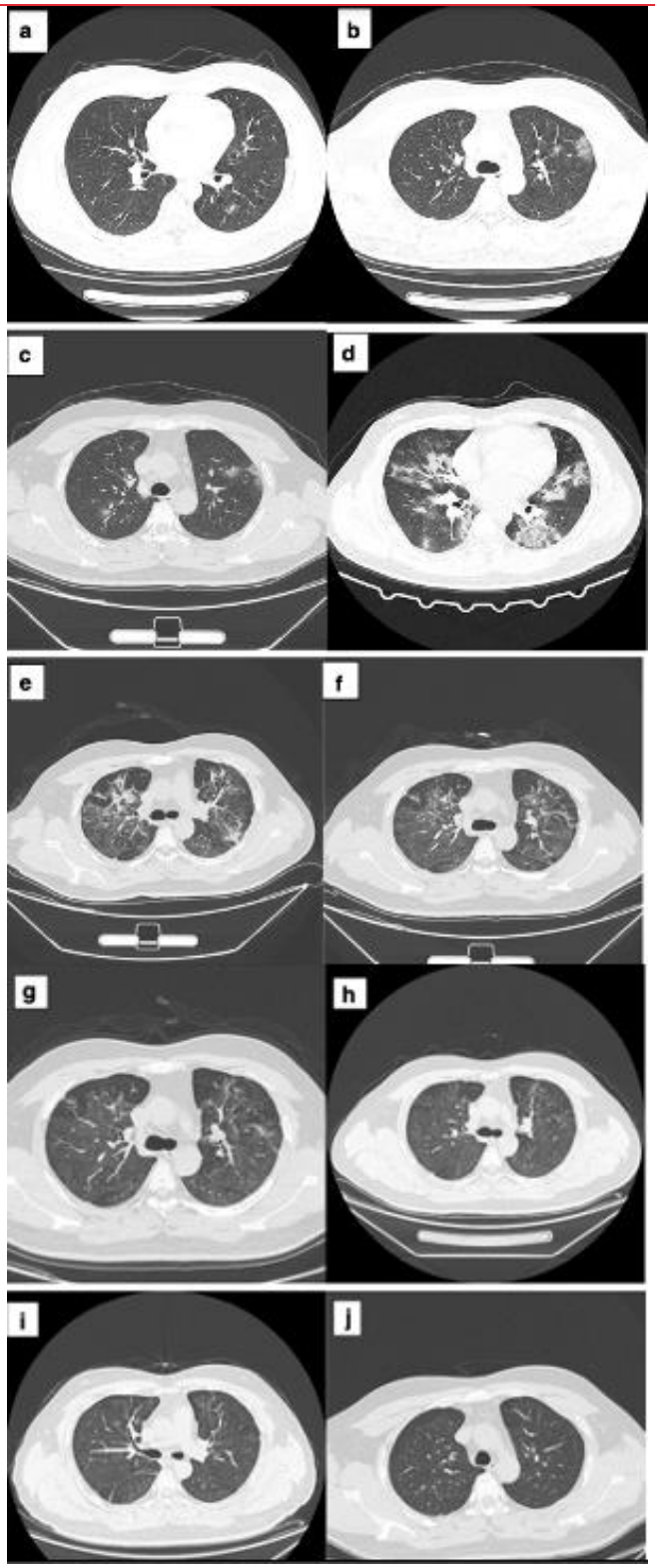

Figure 1. Chest CT of the patient. a Chest CT on January 19. b Chest CT on January 23. c Chest CT on January 25. d Chest CT on January 27. e Chest CT on February 22. f Chest CT on March 1. g Chest CT on March 9. h Chest CT on March 1. i Chest CT on April 17. j Chest CT on May 25.

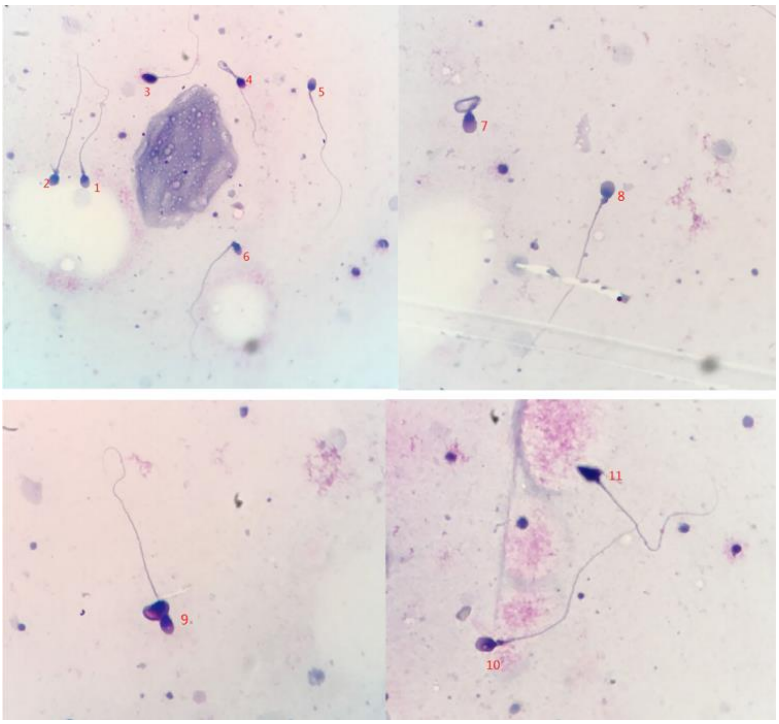

Figure 2. Sperm appeared various deformities. Sperm morphology detection conducted by Diff Quick staining. (1) Normal, (2) round, (3) thick, (4) Coiled, (5) normal, (6) bent neck, (7) coiled, (8) cytoplasm, (9) double, (10) PA vac, (11) tapered.

Table 2 Detection of SARS-CoV-2 nucleic acid, IgM, and IgG antibodies

	Jan-29	Jan-30	Feb-16	Mar-20	Apr-17	May-8	May-25	Jun-19	Jul-20	Reference range(COI)	Jul-20	Aug-27	Sep-29	Oct-30	Nov-30	Dec-30
SARS CoV-2 RNA(throat swab)	-	+	-	-	-	-	-	-	-							
2019-nCoV-IgG (CGM)	+	none	none	+	+	+	+	+	+							
2019-nCoV-IgM (CGM)	+	none	none	+	-	-	-	-	-							
2019-nCoV-IgG(CLIA)										<1.0	8.17	5.84	8.30	7.87	8.12	10.37
2019-nCoV-IgM(CLIA)										<1.0	0.15	0.05	0.06	0.04	0.03	0.01

Table 2. Detection of SARS-CoV-2 nucleic acid, IgM, and IgG antibodies.

MICROVASCULAR FLOW ALTERATIONS IN CRITICALLY ILL COVID-19 PATIENTS: A PROSPECTIVE STUDY

Abou-Arab O, Beyls C, Khalipha A, Guilbart M, Huette P, Malaquin S, Lecat B, Macq PY, Roger PA, Haye G, Bernasinski M, Besserve P, Soriot-Thomas S, Jounieaux V, Dupont H, Mahjoub Y.. PLoS One. 2021 Feb 8;16(2):e0246636. doi: 10.1371/journal.pone.0246636. eCollection 2021.
Level of Evidence: 3 - Local non-random sample

BLUF

Critical care physicians and pulmonologists from Amiens University Hospital in France assessed sublingual microvascular flow alterations in 43 COVID-19 patients (Table 1) within 48 hours of admission to the ICU between March 19 and April 7, 2020. They found microcirculatory flow index (MFI), perfused vessel density (PVD), and De Backer score (DBS) were significantly higher in ventilated patients versus the non-ventilated patients (Figure 1). PaCO2 levels correlated with MFI (Rho=0.428; p=0.005), PVD (Rho=0.363; p=0.023) and DBS (Rho=0.276; p=0.048) (Figure 2). Authors suggest mechanical ventilation influences microvascular velocities and recommend further investigation of hypocapnia on microvascular circulation.

ABSTRACT

BACKGROUND: Data on microcirculatory pattern of COVID-19 critically ill patients are scarce. The objective was to compare sublingual microcirculation parameters of critically ill patients according to the severity of the disease. METHODS: The study is a single-center prospective study with critically ill COVID-19 patients admitted in ICU. Sublingual microcirculation was assessed by IDF microscopy within 48 hours of ICU admission. Microcirculatory flow index (MFI), proportion of perfused vessel (PPV), total vessel density (TVD), De Backer score (DBS), perfused vessel density (PVD) and heterogeneity index (HI) were assessed. Patients were divided in 2 groups (severe and critical) according to the World health organization definition. FINDINGS: From 19th of March to 7th of April 2020, 43 patients were included. Fourteen patients (33%) were in the severe group and twenty-nine patients (67%) in the critical group. Patients in the critical group were all mechanically ventilated. The critical group had significantly higher values of MFI, DBS and PVD in comparison to severe group (respectively, PaCO2: 49 [44-45] vs 36 [33-37] mmHg; p<0,0001, MFI: 2.8 +- 0.2 vs 2.5 +- 0.3; p = 0.001, DBS: 12.7 +- 2.6 vs 10.8 +- 2.0 vessels mm-2; p = 0.033, PVD: 12.5 +- 3.0 vs 10.1 +- 2.4 mm.mm-2; p = 0.020). PPV, HI and TVD were similar between groups Correlation was found between microcirculatory parameters and PaCO2 levels. CONCLUSION: Critical COVID-19 patients under mechanical ventilation seem to have higher red blood cell velocity than severe non-ventilated patients.

Variables	Severe group (n = 14)	Critical group (n = 29)	P value
Age; *years*	62 [50–68]	63 [57–68]	0.343
Male gender; *n (%)*	12 (86)	26 (90)	1.000
BMI; $kg\ m^{-2}$	27.8 [24.3–34.7]	30.1 [29.2–33.2]	0.067
Medical history; *n (%)*			
Hypertension	6 (42)	17 (59)	0.442
Diabetes	4 (29)	4 (14)	0.404
Dyslipidemia	4 (29)	5 (17)	0.442
Severe obesity	1 (7)	5 (17)	0.645
COPD/Asthma	0	1 (3)	1.000
Days from symptom onset to ICU admission; *days*	8 [5–10]	5 [2–8]	**0.003**
Days from ward to ICU admission; *days*	4 [2–5]	2 [1–2]	**0.02**
Time from hospital admission to intubation; *hours*	-	2 [1–2]	-
Biological investigations			
WBC; mm^{-3}	6400 [5800–8400]	8300 [7250–1050]	0.053
Lymphocyte count; mm^{-3}	1000 [800–1300]	700 [600–1050]	**0.015**
Hemoglobin; $g\ l^{-1}$	11.9 [11.0–12.7]	11.3 [10.2–12.5]	0.211
C reactive protein; $mg\ l^{-1}$	152 [113–189]	217 [156–313]	**0.049**
Procalcitonin; $ng\ ml^{-1}$	0.39 [0.08–0.59]	1.47 [0.42–2.66]	**0.012**
Platelet count; $10^3\ mm^{-3}$	256 [235–313]	206 [150–321]	0.500
D-dimer; $\mu g\ l^{-1}$	2.5 [1.5–5.06]	4.7 [1.0–7.9]	0.901
Fibrinogen; $g\ l^{-1}$	6.2 [5.2–6.6]	6.9 [5.2–8.0]	0.124
Soluble fibrin complex; $\mu g\ ml^{-1}$	4.0 [3.6–4.3]	4.3 [3.7–6.0]	0.554
Respiratory support; n (%)			
Oxygen mask	11 (79)	-	
HFNC	3 (21)	-	
Mechanical ventilation	-	29 (100)	
CT scan at hospital admission			
Ground glass opacities; *n (%)*	12 (86)	26 (90)	0.628
Crazy paving; *n (%)*	4 (29)	8 (27)	0.836
Consolidation; *n (%)*	7 (50)	15 (52)	0.882
Pulmonary embolism; *n (%)*	0 (0)	1 (3)	0.934
SOFA score at inclusion	3 [1–4]	10 [7–13]	<0.0001
SAPS II score at inclusion	30 [23–32]	65 [55–71]	<0.0001

COPD: chronic obstructive pulmonary disease; **HFNC:** high flow nasal oxygen cannula, **SAPS II:** simplified acute physiology score II, **SOFA:** sequential organ failure assessment. Data were expressed as median [interquartile range] or as number (percentage). Data were compared using Mann-Whitney, Chi-2 or a Fischer exact test.

https://doi.org/10.1371/journal.pone.0246636.t001

Table 1. Demographics between severe and critical patients.

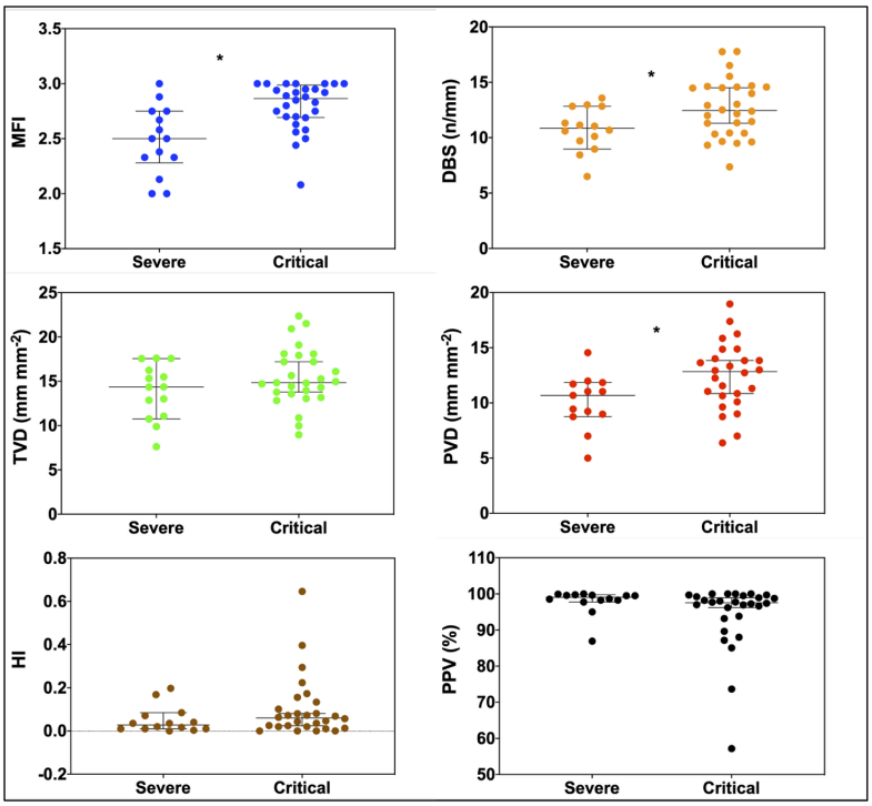

Fig 1. Comparisons of microcirculatory flow index (MFI), total vessel density (TVD), perfused vessel density (PVD), proportion of perfused vessel (PPV), De Backer score (DBS) and heterogeneity index (HI) in severe group and critical group.

*: P value <0.05 between groups comparisons using Mann-Whitney U test.

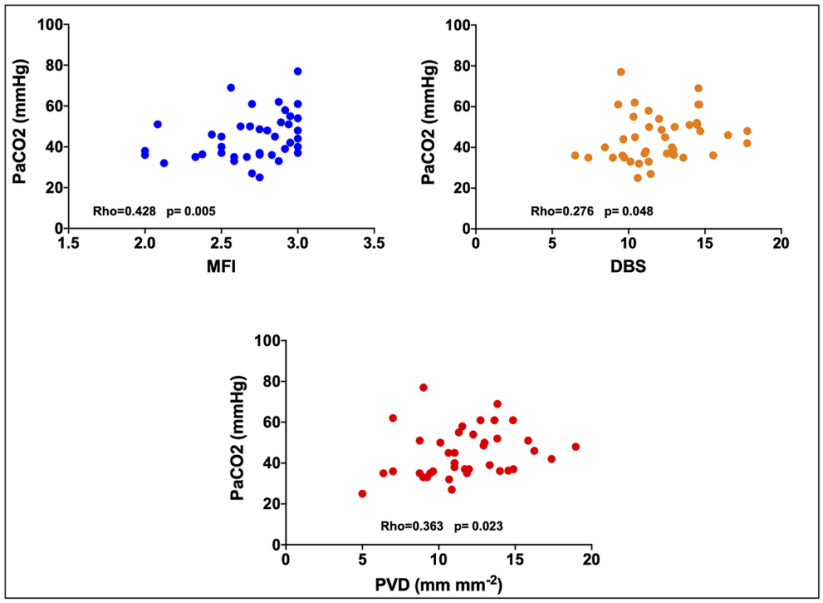

Fig 2. PaCO2 correlation with the microcirculatory flow index (MFI), the perfused vessel density (PVD) and the De Backer score (DBS).

IMMUNOLOGICAL MEMORY TO SARS-COV-2 ASSESSED FOR UP TO 8 MONTHS AFTER INFECTION

Dan JM, Mateus J, Kato Y, Hastie KM, Yu ED, Faliti CE, Grifoni A, Ramirez SI, Haupt S, Frazier A, Nakao C, Rayaprolu V, Rawlings SA, Peters B, Krammer F, Simon V, Saphire EO, Smith DM, Weiskopf D, Sette A, Crotty S.. Science. 2021 Feb 5;371(6529):eabf4063. doi: 10.1126/science.abf4063. Epub 2021 Jan 6.
Level of Evidence: 3 - Local non-random sample

BLUF

Immunologists, microbiologists, and other infectious disease experts from La Jolla Institute for Immunology and University of California, San Diego evaluated immunological memory in 188 patients who provided at least one post-SARS-CoV-2 infection blood sample, with 43 providing longitudinal samples (Table 1). Spike protein IgG remained stable at 6 months (Figure 1). Compared to one month post-infection, at 6-8 months CD8+T cells declined (70% vs. 50%)(Figure 3) but CD4+T cell memory was maintained (93% vs 92%). Though more corroborating research is needed, authors suggest SARS-CoV-2 infection generates significant immune memory that may be protective against reinfection.

ABSTRACT

Understanding immune memory to SARS-CoV-2 is critical for improving diagnostics and vaccines, and for assessing the likely future course of the COVID-19 pandemic. We analyzed multiple compartments of circulating immune memory to SARS-CoV-2 in 254 samples from 188 COVID-19 cases, including 43 samples at >= 6 months post-infection. IgG to the Spike protein was relatively stable over 6+ months. Spike-specific memory B cells were more abundant at 6 months than at 1 month post symptom onset. SARS-CoV-2-specific CD4+ T cells and CD8+ T cells declined with a half-life of 3-5 months. By studying antibody, memory B cell, CD4+ T cell, and CD8+ T cell memory to SARS-CoV-2 in an integrated manner, we observed that each component of SARS-CoV-2 immune memory exhibited distinct kinetics.

Table 1 Participant characteristics.

	COVID-19 (*n* = 188)
Age (years)	19 to 81 (median = 40, IQR* = 18.75)
Gender	
Male (%)	43% (80/188)
Female (%)	57% (108/188)
Race	
African American or Black (%)	3% (5/188)
Alaskan Native or American Indian (%)	1% (1/188)
Asian (%)	7% (14/188)
Native Hawaiian or Pacific Islander (%)	0% (0/188)
Multiracial (%)	1% (2/188)
Other (%)	1% (1/188)
Unknown (%)	10% (19/188)
White (%)	78% (146/188)
Ethnicity	
Hispanic or Latino (%)	15% (28/188)
Non-Hispanic (%)	80% (150/188)
Unknown (%)	5% (10/188)
Hospitalization status	
Never hospitalized (%)	93% (174/188)
Hospitalized (%)	7% (13/188)
Unknown if hospitalized (%)	1% (1/188)
Sample collection dates	March-October 2020
SARS-CoV-2 PCR positivity	
Positive	77% (145/188)
Negative	1% (2/188)
Not performed	20% (37/188)
Unknown	2% (4/188)
Peak disease severity (%) [Female (F), Male (M)]	
Asymptomatic (score 1)	2% (4/188) (2F, 2M)
Mild (nonhospitalized; score 2–3)	90% (170/188) (100F, 70M)
Moderate (hospitalized; score 4–5)	3% (6/188) (3F, 3M)
Severe (hospitalized; Score 6+)	4% (7/188) (3F, 4M)
Unknown	1% (1/188) (0F, 1M)
Days post–symptom onset at collection; *n* = 254	6–240 (median 88, IQR 97.75)
Blood collection frequency	
Multiple time point Donors (two to four times)	27% (51/188)
Single–time point donors	73% (137/188)

*IQR, interquartile range.

Table 1 Participant characteristics.

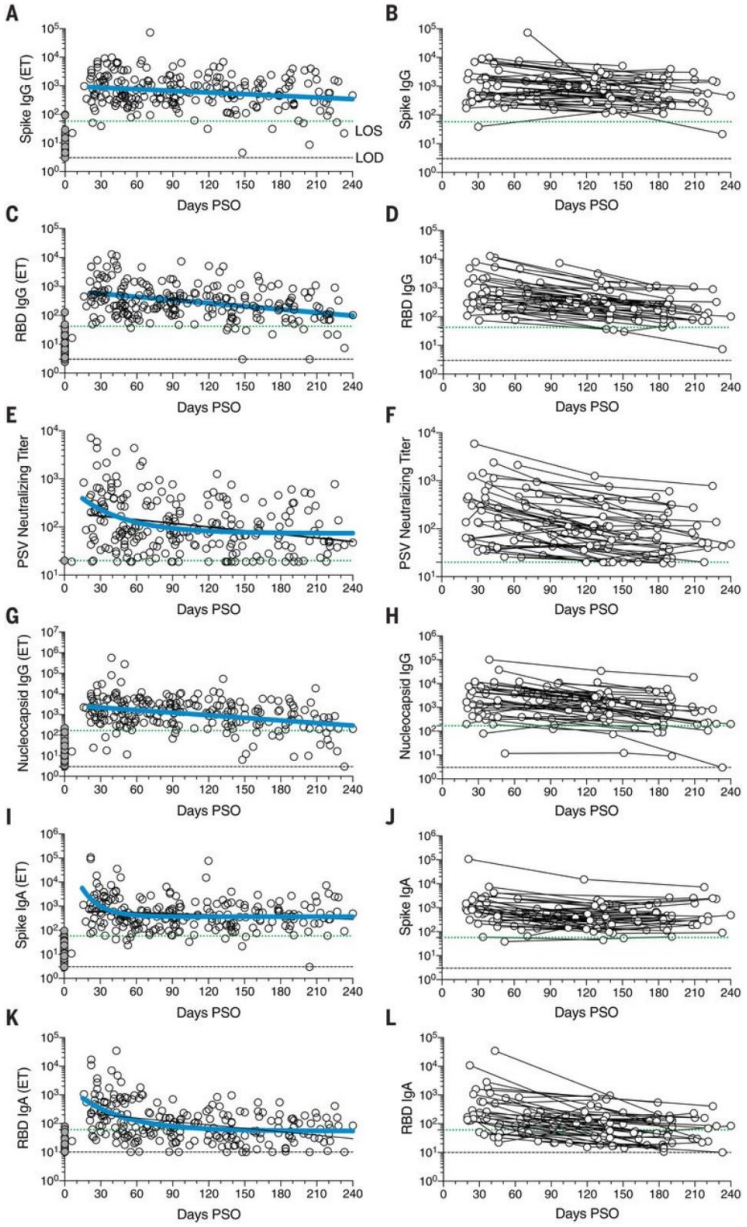

Fig. 1 Circulating antibodies to SARS-CoV-2 over time.

(A) Cross-sectional spike IgG from COVID-19 subject plasma samples (n = 228). Continuous decay preferred model for best fit curve, t1/2 = 140 days; 95% CI: 89 to 325 days. R = −0.23, p = 0.0006. (B) Longitudinal spike IgG (n = 51), average t1/2 = 103 days; 95% CI: 65 to 235 days. (C) Cross-sectional RBD IgG. Continuous decay preferred model for best fit curve, t1/2 = 83 days; 95% CI: 62 to 126 days. R = −0.36, p < 0.0001. (D) Longitudinal RBD IgG, average t1/2 = 69 days; 95% CI: 58 to 87 days. (E) Cross-sectional SARS-CoV-2 PSV-neutralizing titers. One-phase decay (blue line) preferred model for best fit curve, initial t1/2 = 27 days; 95% CI: 11 to 157 days. R = −0.32. Continuous decay fit line shown as black line. (F) Longitudinal PSV-neutralizing titers of SARS-CoV-2–infected subjects, average t1/2 = 90 days; 95% CI: 70 to 125 days. (G) Cross-sectional nucleocapsid IgG. Continuous decay preferred model for best fit curve, t1/2 = 68 days; 95% CI: 50 to 106 days. R = −0.34, p < 0.0001. (H) Longitudinal nucleocapsid IgG, average t1/2 = 68 days; 95% CI: 55 to 90 days. (I) Cross-sectional spike IgA titers. One-phase decay (blue line) preferred model for best fit curve, initial t1/2 = 11 days; 95% CI: 5 to 25 days. R = −0.30. Continuous decay fit shown as black line. (J) Longitudinal spike IgA, t1/2 = 210 days, 95% CI 126 to 627 days. (K) Cross-sectional RBD IgA. One-phase decay (blue line) preferred model for best fit curve, initial t1/2 = 27 days; 95% CI: 15 to 59 days. R = −0.45. Continuous decay line fit shown in black. (L) Longitudinal RBD IgA, average t1/2 = 74 days; 95% CI: 56 to 107 days. For cross-sectional analyses, SARS-CoV-2–infected subjects (white circles, n = 238) and unexposed subjects (gray circles, n = 51). For longitudinal samples, SARS-CoV-2 subjects (n = 51). The dotted black line indicates limit of detection (LOD). The dotted green line indicates limit of sensitivity (LOS) above uninfected controls. Unexposed subjects are depicted in gray, COVID subjects in white. Log data analyzed in all cases. Thick blue line represents best fit curve. When two fit curves are shown, the thin black line represents the alternative fit curve.

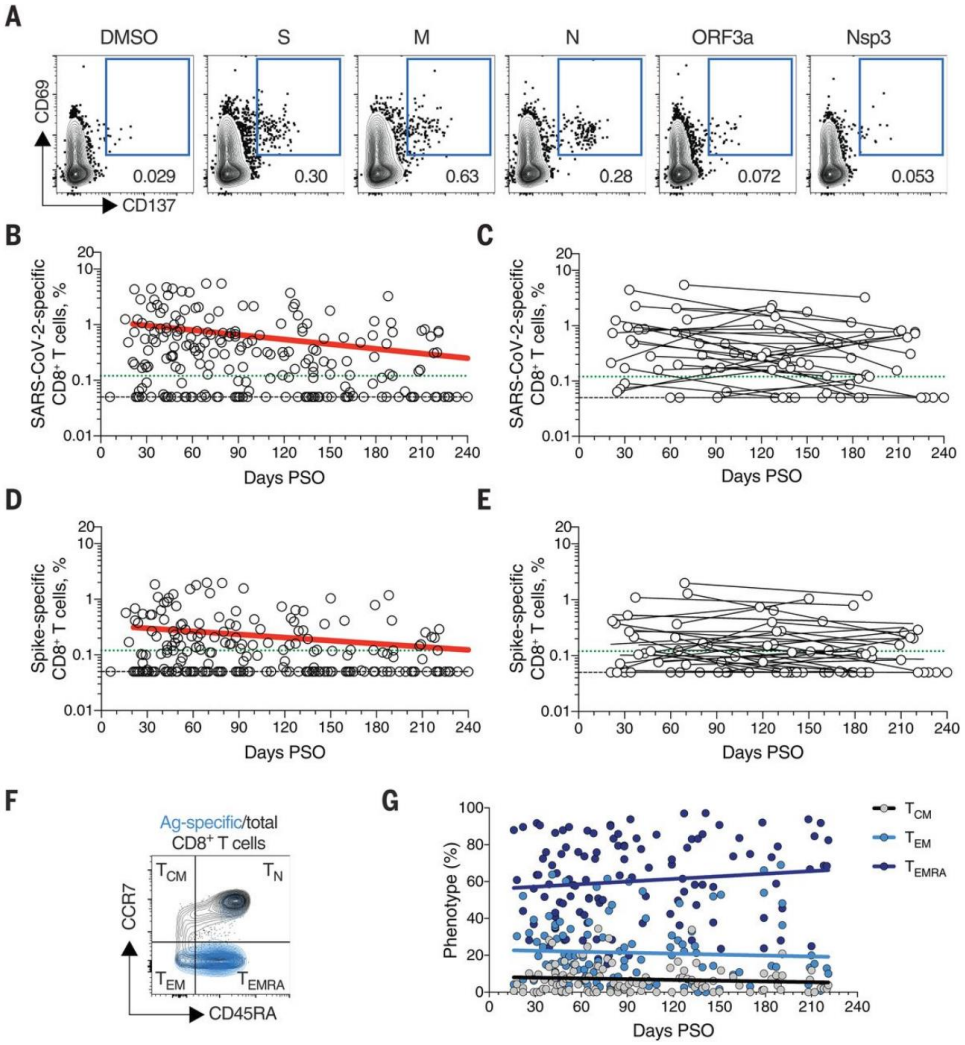

Fig. 3 SARS-CoV-2 circulating memory CD8+ T cells.

(A) Representative flow cytometry plots of SARS-CoV-2–specific CD8+ T cells (CD69+ CD137+; see fig. S3 for gating) after overnight stimulation with S, N, M, ORF3a, or nsp3 peptide pools, compared to negative control (DMSO). (B) Cross-sectional analysis of frequency (percentage of CD8+ T cells) of total SARS-CoV-2–specific CD8+ T cells. Continuous decay preferred fit model, t1/2 = 125 days. R = −0.24, p = 0.0003. (C) Longitudinal analysis of total SARS-CoV-2–specific CD8+ T cells in paired samples. (D) Cross-sectional analysis of spike-specific CD8+ T cells. Linear decay preferred model, t1/2 = 225 days. R = −0.18, p = 0.007. (E) Longitudinal analysis of spike-specific CD8+ T cells in paired samples. (F and G) Distribution of central memory (TCM), effector memory (TEM), and terminally differentiated effector memory cells (TEMRA) among total SARS-CoV-2–specific CD8+ T cells. n = 169 COVID-19 subjects (n = 215 data points, white circles) for cross-sectional analysis. n = 37 COVID-19 subjects (n = 83 data points, white circles) for longitudinal analysis. The dotted black line indicates LOD. The dotted green line indicates LOS.

DEVELOPMENTS IN TRANSMISSION & PREVENTION

ANAPHYLACTIC REACTIONS TO NOVEL MRNA SARS-COV-2/COVID-19 VACCINES

Kelso JM.. Vaccine. 2021 Feb 5;39(6):865-867. doi: 10.1016/j.vaccine.2020.12.084. Epub 2021 Jan 6.
Level of Evidence: 5 - Expert Opinion

BLUF

In this commentary, an allergist from Scripps Clinic in California discusses anaphylactic reactions to novel mRNA SARS-CoV-2/COVID-19 vaccines. He reviews the pathophysiology and treatment of anaphylaxis, and suggests some patients must have IgE antibodies to a vaccine component. Because reports indicate these mRNA vaccines may have higher anaphylactic rates, the author urges further investigation into apparent anaphylactic reactions to better identify those at risk.

THE IMPACT OF NON-PHARMACEUTICAL INTERVENTIONS ON SARS-COV-2 TRANSMISSION ACROSS 130 COUNTRIES AND TERRITORIES

Liu Y, Morgenstern C, Kelly J, Lowe R; CMMID COVID-19 Working Group, Jit M.. BMC Med. 2021 Feb 5;19(1):40. doi: 10.1186/s12916-020-01872-8.
Level of Evidence: 3 - Non-randomized controlled cohort/follow-up study

BLUF

Statisticians and scientists from London, UK compared the effectiveness of 13 non-pharmaceutical interventions (NPI) (Table 1) in reducing transmission of SARS-CoV-2 in 130 countries using longitudinal regression. They identified a strong association between reduced time-varying reproduction number and both school closures and internal movement restrictions (Figure 3,4). The authors suggest these two NPIs are particularly effective measures to curb SARS-CoV-2 spread, though they recommend using diverse NPI implementation profiles to address potential biases in their analysis and study design.

ABSTRACT

BACKGROUND: Non-pharmaceutical interventions (NPIs) are used to reduce transmission of SARS coronavirus 2 (SARS-CoV-2) that causes coronavirus disease 2019 (COVID-19). However, empirical evidence of the effectiveness of specific NPIs has been inconsistent. We assessed the effectiveness of NPIs around internal containment and closure, international travel restrictions, economic measures, and health system actions on SARS-CoV-2 transmission in 130 countries and territories. METHODS: We used panel (longitudinal) regression to estimate the effectiveness of 13 categories of NPIs in reducing SARS-CoV-2 transmission using data from January to June 2020. First, we examined the temporal association between NPIs using hierarchical cluster analyses. We then regressed the time-varying reproduction number (Rt) of COVID-19 against different NPIs. We examined different model specifications to account for the temporal lag between NPIs and changes in Rt, levels of NPI intensity, time-varying changes in NPI effect, and variable selection criteria. Results were interpreted taking into account both the range of model specifications and temporal clustering of NPIs. RESULTS: There was strong evidence for an association between two NPIs (school closure, internal movement restrictions) and reduced Rt. Another three NPIs (workplace closure, income support, and debt/contract relief) had strong evidence of effectiveness when ignoring their level of intensity, while two NPIs (public events cancellation, restriction on gatherings) had strong evidence of their effectiveness only when evaluating their implementation at maximum capacity (e.g. restrictions on 1000+ people gathering were not effective, restrictions on < 10 people gathering were). Evidence about the effectiveness of the remaining NPIs (stay-at-home requirements, public information campaigns, public transport closure, international travel controls, testing, contact tracing) was inconsistent and inconclusive. We found temporal clustering between many of the NPIs. Effect sizes varied depending on whether or not we included data after peak NPI intensity. CONCLUSION: Understanding the impact that specific NPIs have had on SARS-CoV-2 transmission is complicated by temporal clustering, time-dependent variation in effects, and differences in NPI intensity. However, the effectiveness of school closure and internal movement restrictions appears robust across different model specifications, with some evidence that other NPIs may also be effective under particular conditions. This provides empirical evidence for the potential effectiveness of many, although not all, actions policy-makers are taking to respond to the COVID-19 pandemic.

FIGURES

Table 1

Thirteen types of NPIs from OxCGRT, their general categorisations, and the coding schema used in our analysis to quantify their intensity

NPI groups	Specific NPIs	Coding schema
Internal containment and closure	School closure; workplace closure; cancellation of public events; limits on gathering sizes; closure of public transport; stay-at-home requirement; internal movement restriction	*Any effort scenario*:
International travel restrictions	International movement restriction	NPIs are binary variables, considered "present" as long as any (non-zero) effort is made.
Economic policies	Income support; debt/contract relief for households	*Maximum effort scenario*:
Health systems policies	Public information campaign; testing policy; contact tracing	NPIs are binary variables, considered "present" only if the maximum effort is made.
		For example, an intervention X has levels 0–3. A record at level 2 is converted to 1 under *any effort* and 0 under *maximum effort* scenarios.

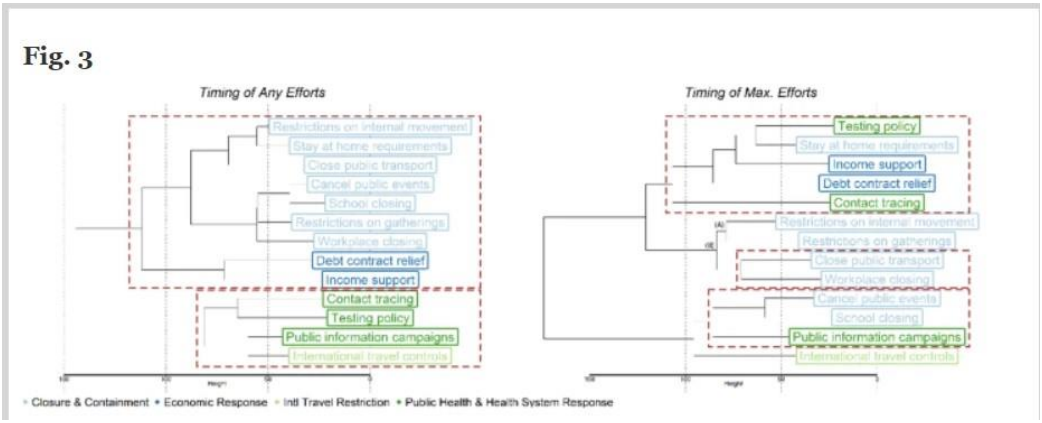

Figure 3. Dendrogram from the hierarchical cluster analysis of NPI time-series by scenario. The height of the node connecting two NPIs on the dendrogram represents the degree of similarity between their time-series. For example, under the Maximum Effort Scenario, the time-series of “restrictions on internal movement” is more similar to that of “restrictions on gatherings” (linked at point A), compared to that of “close public transport” (linked at point B). The hierarchical clustering analysis relies on Ward’s method and Euclidean distances. The color of the text boxes corresponds to the group each NPI is in; red dashed boxes indicate statistically significant temporal clusters identified through bootstrapping.

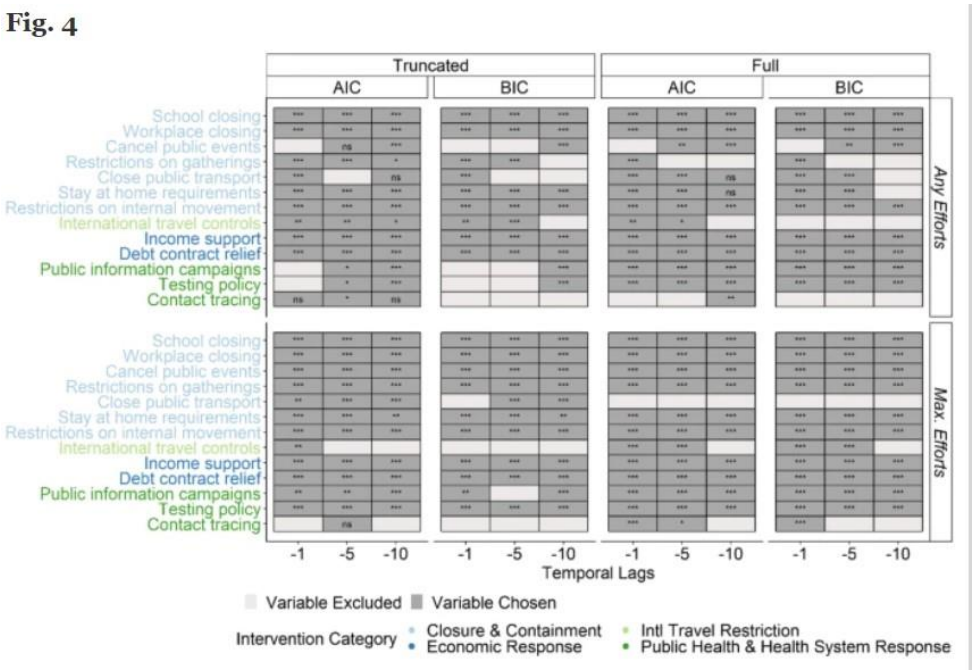

Figure 4. Variable selection results. Optimal models are based on a backward selection process using AIC/BIC. NPIs are color-coded based on their respective NPI categories. Cell-content represents corresponding p values: > 0.05—ns (i.e. non-significant); ≤ 0.05 and > 0.01—*; ≤ 0.01 and > 0.001—**; ≤ 0.001 —***

MANAGEMENT

THE IMPORTANCE OF UNDERSTANDING THE STAGES OF COVID-19 IN TREATMENT AND TRIALS

Griffin DO, Brennan-Rieder D, Ngo B, Kory P, Confalonieri M, Shapiro L, Iglesias J, Dube M, Nanda N, In GK, Arkfeld D, Chaudhary P, Campese VM, Hanna DL, Sawcer D, Ehresmann G, Peng D, Smorgorzewski M, Amstrong A, Vinjevoll EH, Dasgupta R, Sattler FR, Mussini C, Mitjà O, Soriano V, Peschanski N, Hayem G, Piccirillo MC, Lobo-Ferreira A, Rivero IB, Hung IFH, Rendell M, Ditmore S, Varon J, Marik P.. AIDS Rev. 2021 Feb 8. doi: 10.24875/AIDSRev.200001261. Online ahead of print.
Level of Evidence: 5 - Guidelines and Recommendations

BLUF

This study from Columbia University investigates the different phases of COVID-19 infectivity and relates them to targeted therapies in order to determine the most effective time periods in which clinicians ought to intervene. The authors divide infectivity into three periods and five distinct phases (Figure 3) and urge scientists to use this framework when studying therapeutics in order to maximize efficacy, using the HIV/AIDS era as an example of how targeted intervention based off infectivity can lead to better outcomes.

SUMMARY

This study from Columbia University aims to delineates specific periods and phases of COVID-19 infectivity in order to best determine when intervention should be pursued. The following is an overview of what each period or phase entails (Figure 3).

1. Pre-Exposure Period is when patients ought to be targeted to receive vaccination
2. Incubation Period carries the greatest risk of disease and thus should be the time where pharmacological viral disruption should be considered
3. Detectable Viral Replication Period is when pro-immune therapies are most likely to be effective. Viral load detection peaks at days 3-4 post-exposure
4. Viral Symptom Phase is when clinical attention is typically drawn given onset of symptoms
5. Early Inflammatory Phase is when patients are most likely to be hospitalized
6. Secondary infection Phase is when patients are most susceptible to secondary infections
7. Multisystem Inflammatory Phase is when patients are likely to suffer from autoimmune phenomenon
8. Tail Phase is the post-acute phase when patients can experience residual symptoms and is a growing area of interest

ABSTRACT

COVID-19, caused by SARS-CoV-2, continues to be a major health problem since its first description in Wuhan, China, in December 2019. Multiple drugs have been tried to date in the treatment of COVID-19. Critical to treatment of COVID-19 and advancing therapeutics is an appreciation of the multiple stages of this disease and the importance of timing for investigation and use of various agents. We considered articles related to COVID-19 indexed on PubMed published January 1, 2020-November 15, 2020, and considered papers on the medRxiv preprint server. We identified relevant stages of COVID-19 including three periods: pre-exposure; incubation, and detectable viral replication, and five phases: the viral symptom phase, the early inflammatory phase, the secondary infection phase, the multisystem inflammatory phase, and the tail phase. This common terminology should serve as a framework to guide when COVID-19 therapeutics being studied or currently in use is likely to provide benefit rather than harm.

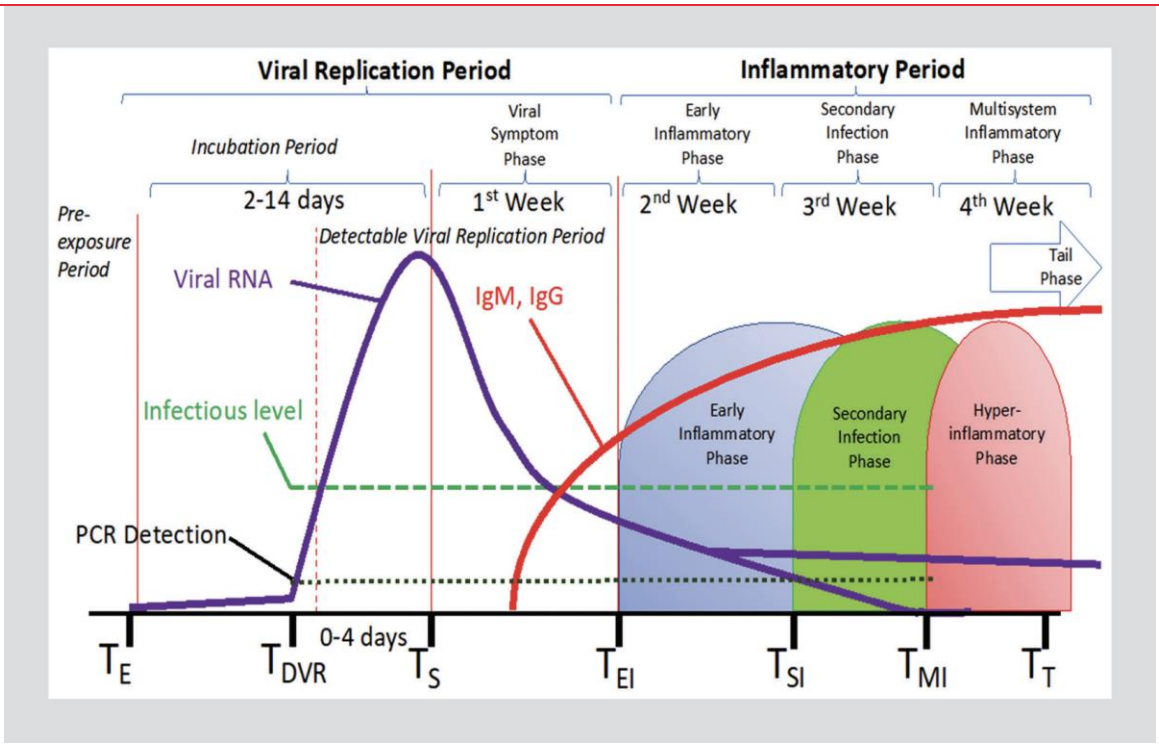

Figure 3. COVID-19 progresses through various stages with certain degree overlap but with distinct mechanisms targeting each stage. Dotted lines from left to right repent the Early Inflammatory Phase (blue), the Secondary Infection Stage (green), and the Hyperinflammatory Phase (red continuous line).

CARDIOLOGY

EXERCISE TESTING IN COVID-19 ERA: CLINICAL PROFILE, RESULTS AND FEASIBILITY WEARING A FACEMASK

Barbeito-Caamaño C, Bouzas-Mosquera A, Peteiro J, López-Vázquez D, Quintas-Guzmán M, Varela-Cancelo A, Martínez-Ruiz D, Yañez-Wonenburger JC, Piñeiro-Portela M, Vazquez-Rodriguez JM.. Eur J Clin Invest. 2021 Feb 6:e13509. doi: 10.1111/eci.13509. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

This retrospective study from the Universidade da Coruña, Spain, investigates the impact of the COVID-19 pandemic and subsequent face mask use on the feasibility and results of exercise stress testing. While the patients using face masks during testing did have higher levels of dyspnea, there was no significant difference in baseline characteristics such as functional capacity. Thus the authors conclude that face mask usage does not change the clinical profile of patients undergoing cardiac exercise stress testing.

ABSTRACT

BACKGROUND: No data are available about whether Coronavirus disease 2019 (COVID-19) pandemic have led to changes in clinical profiles or results of exercise testing once the usual activity was reassumed, as well as if wearing a facemask has any impact on the tests. The aim of this study is to evaluate differences in the patients referred to exercise stress testing in the context of COVID-19 pandemic and analyze the feasibility and results of these tests wearing a facemask. METHODS: We included all patients referred for an exercise test from 1st June to 30th September 2020 and compared them with the patients attended within the same period in 2019 before and after propensity score matching. All patients referred in 2020 wore a facemask. RESULTS: A total of 854 patients were included: 398 in the 2020 group and 456 in 2019. No significant differences in baseline characteristics of the patients were observed, with the exception of dyspnea, which was nearly twice as high in 2020 as compared with 2019. Regarding the results of the tests, no differences were observed, with almost 80% of maximal tests, similar functional capacity and over a 20% of positive exercise tests in both groups. These results remained after propensity score matching. CONCLUSION: COVID-19 pandemic has not changed the clinical profile of patients referred to exercise testing. In addition, performing exercise testing wearing a facemask is feasible, with no influence in functional capacity and clinical results.

SARS-COV-2 PERSISTENCE AT SUBZERO TEMPERATURES

Scarica C, Parmegiani L, Rienzi L, Anastasi A, Cimadomo D, Klinger FG, Licata E, Sosa Fernandez L, De Santis L.. J Assist Reprod Genet. 2021 Feb 5. doi: 10.1007/s10815-021-02094-4. Online ahead of print.
Level of Evidence: 5 - Opinion

BLUF

Reproductive health experts from the Italian Society of Embryology, Reproduction and Research discuss the risk of SARS-CoV-2 transmission from cryostored reproductive cells. The authors review data indicating that SARS-CoV-2 viral particles can remain biologically active on inanimate surfaces, especially at low temperatures and discuss the possible contamination risk posed by the liquid nitrogen (LN2) and nitrogen vapors (NV) used for cryopreservation. Though no cases of cross-contamination from cryostored gametes or embryos have been reported, authors suggest there is a risk of cross-contamination from LN2/NV that warrants attention.

COVID-19 PANDEMIC AND VIOLENCE: RISING RISKS AND DECREASING URGENT CARE-SEEKING FOR SEXUAL ASSAULT AND DOMESTIC VIOLENCE SURVIVORS

Muldoon KA, Denize KM, Talarico R, Fell DB, Sobiesiak A, Heimerl M, Sampsel K.. BMC Med. 2021 Feb 5;19(1):20. doi: 10.1186/s12916-020-01897-z.
Level of Evidence: 3 - Local non-random sample

BLUF

Social epidemiologists and emergency physicians from Ontario, Canada compared the quantity of emergency department (ED) admissions to The Ottawa Hospital for sexual assault and domestic violence from a 2020 COVID-19 time period (March 4 2020 until May 5 2020) with a time matched control group from 2018. They found the number of ED admissions to the Sexual Assault and Domestic Violence Program decreased by 32.93% (56.52% for sexual assault, 48.48% for domestic violence cases)(Table 1). Psychological abuse and outdoor assault increased by 16.9% and 17.6%, respectively (Table 3). Authors suggest pandemic conditions have decreased victims' access to services, and recommend the development of alternative resources as well as continued monitoring as countries change their lockdown policies.

ABSTRACT

BACKGROUND: There is little information on care-seeking patterns for sexual assault and domestic violence during the COVID-19 pandemic. The objective of this study was to examine the changes in emergency department (ED) admissions for sexual assault and domestic violence since the COVID-19 pandemic was declared. METHODS: Observational ED admissions data from The Ottawa Hospital were analyzed from March 4 to May 5 (62 days) in 2020 (COVID-19 period) and compared to the same period in 2018 (pre-COVID-19). Total and mean weekly admissions were calculated for all-cause ED admissions and for sexual and domestic violence cases. A Poisson regression (without offset term) was used to calculate the weekly case count ratio and 95% confidence intervals (CI) between the two time periods. Case characteristics were compared using chi-square tests, and percent differences were calculated. RESULTS: Compared to pre-COVID-19, total ED admissions dropped by 1111.22 cases per week (32.9% reduction), and the Sexual Assault and Domestic Violence Program cases dropped 4.66 cases per week. The weekly case count ratio for sexual assault cases was 0.47 (95% CI 0.79-0.27), equivalent of 53.49% reduction in cases, and 0.52 (95% CI 0.93-0.29), equivalent to a 48.45% reduction in physical assault cases. The characteristics of presenting cases were similar by age (median 25 years), sex (88.57% female), assault type (57.14% sexual assault, 48.57% physical assault), and location (31.43% patient's home, 40.00% assailant's home). There was a significant increase in psychological abuse (11.69% vs 28.57%) and assaults occurring outdoors (5.19% vs 22.86%). CONCLUSION: This study found a decrease in ED admissions for sexual assault and domestic violence during COVID-19, despite societal conditions that elevate risk of violence. Trends in care-seeking and assault patterns will require ongoing monitoring to inform the provision of optimal support for individuals experiencing violence, particularly as countries begin to re-open or lock-down again.

Table 1 Comparison of ED admissions for sexual assault and domestic violence between March 4 and May 5 ($n = 62$ days) in 2018 (pre-COVID-19 period) and 2020 (COVID-19 period)

	2018	2020	Absolute difference	Percent relative reduction (%)
ED admissions				
Total ED admissions	30,371	20,370	10,001	32.93
Mean weekly ED admissions	3374.56	2263.33	1111.22	32.93
Sexual Assault and Domestic Violence Program patients				
Total patients	77	34	43	55.84
Mean weekly patients	8.55	3.89	4.66	54.50
Case rate per 10,000 ED admissions	25.35	17.18	8.17	32.23
Sexual assault cases[1]				
Total cases	46	20	26	56.52
Mean weekly cases	5.11	2.22	2.89	56.56
Case rate per 10,000 ED admissions	15.15	9.82	5.33	35.18
Physical assault cases				
Total cases	33	17	16	48.48
Mean weekly cases	3.67	1.88	1.79	48.77
Case rate per 10,000 ED admissions	10.87	8.35	2.52	23.18

[1]The total sexual assault and physical assault do not sum to 100% as patients can experience both sexual and physical assaults

Table 3 Changes in Sexual Assault and Domestic Violence Program patient characteristics in March 4 to May 5, 2018 and 2020

Variables	2018, $N = 77$, n (%)	2020, $N = 35$, n (%)	Percent difference[1] (95% CI)	p value
Demographic characteristics				
Age (years, median, IQR)	27 (20–34)	25 (20–31)		0.913
Under 24 years	40 (51.95)	19 (54.29)	2.30 (– 17.30, 21.90)	0.818
Female vs male/trans[2]	67 (87.01)	31 (88.57)	1.50 (– 11.30, 14.30)	0.143
Arrived by ambulance (vs walk-in)	18 (23.38)	12 (34.29)	10.90 (– 7.10, 28.90)	0.227
Police involvement	32 (41.56)	17 (48.57)	7.00 (– 12.50, 26.50)	0.488
Current mental health conditions				
Depression	29 (37.66)	17 (48.57)	10.90 (– 8.50, 30.30)	0.277
Anxiety	26 (33.77)	11 (31.43)	– 2.30 (– 20.70, 16.10)	0.807
Substance use or dependency	9 (11.69)	8 (22.86)	11.20 (– 4.10, 26.50)	0.127
Assault characteristics				
Sexual assault	46 (59.74)	20 (57.14)	– 2.60 (– 22.00, 16.80)	0.796
Physical assault	33 (42.86)	17 (48.57)	5.70 (– 13.90, 25.30)	0.573
Psychological abuse	9 (11.69)	10 (28.57)	16.90 (8.00, 33.00)	0.027
Intimate partner assailant	33 (42.86)	18 (51.43)	8.60 (– 11.00, 28.20)	0.399
Unknown assailant	23 (29.87)	10 (28.57)	– 1.30 (– 19.10, 16.50)	0.889
Multiple assailants	5 (6.49)	< 5	–	–
Strangulation	7 (9.09)	7 (20.00)	10.90 (– 3.40, 25.20)	0.106
Assault with weapon	11 (14.29)	< 5	–	–
Visible injuries[3]	36 (46.75)	17 (48.57)	1.80 (– 17.80, 21.40)	0.858
Most common location of assault[4]				
Patient's home	26 (33.77)	11 (31.43)	– 2.30 (– 20.70, 16.10)	0.807
Assailant's home	25 (32.47)	14 (40.00)	7.60 (– 11.40, 26.60)	0.438
Outdoors	4 (5.19)	8 (22.86)	17.60 (3.30, 31.90)	0.005
Other[5]	26 (33.77)	10 (28.57)	– 5.20 (– 23.20, 12.80)	0.585
Health- and justice-related service provision				
Post-exposure prophylaxis				
Non-eligible	52 (67.53)	22 (62.86)	– 4.70 (– 23.50, 14.10)	0.640
Eligible, not started	12 (15.58)	8 (22.86)	7.30 (– 8.40, 23.00)	
Eligible, started	13 (16.88)	5 (14.29)	– 2.60 (– 16.70, 11.50)	
Sexual Assault Evidence Kit				
Non-eligible	28 (36.36)	18 (51.43)	15.10 (– 4.30, 34.50)	0.192
Eligible, not collected	28 (36.36)	7 (20.00)	– 16.30 (– 33.20, 0.60)	
Collected, released to police	8 (10.39)	6 (27.14)	16.80 (– 7.10, 20.70)	
Collected, not released to police	13 (16.88)	4 (11.43)	– 5.40 (– 18.70, 7.90)	
Forensic photography				
Non-eligible	41 (53.25)	17 (48.57)	– 4.70 (– 24.30, 14.90)	0.883
Eligible, not completed	19 (24.68)	10 (28.57)	3.90 (– 13.60, 21.40)	
Eligible, completed	17 (22.08)	8 (22.86)	0.80 (– 15.60, 17.20)	

[1]Percent differences only calculated for categorical variables. Continuous variables evaluated by Wilcoxon's rank sum test
[2]Due to small cell sizes, male and trans/non-binary people are combined
[3]Visible injuries can include lacerations, fractures, and contusions
[4]Most common location of assault—locations do not sum to 100% as assaults can occur in multiple places
[5]Other location includes dorm room, friends' home, shelter, do not know, and other

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